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POSTER PLUS VIDEO I – POSTER EXHIBITION – HALL XL

P0001 EUS GUIDED TRANSMURAL DRAINAGE OF WOPN; COMPARISON BETWEEN A NEW FULLY COVERED LARGE BORE WIDE FLARE METAL STENT (NAGI STENT) VS MULTIPLE PLASTIC STENTS: A SINGLE CENTRE RETROSPECTIVE STUDY

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INTRODUCTION: WOPN is a frequent sequel of acute necrotizing pancreatitis. The best approach for drainage of these collections is still controversial. We present our retrospective data comparing the two endoscopic methods for drainage of WOPN.
AIMS & METHODS: Outcomes of patients undergoing EUS guided transmural drainage (EUTMD) using a newly designed fully covered large-bore wide-flare metal stent (Nagi stent) (Gr I) were compared to the outcomes of patients who underwent placement of multiple plastic stents (Gr II). The pre-op CECT confirmed suitability of endoscopic drainage based on location, wall thickness & contents. Visual quantification of necrosis (>50% solid debris) by EUS excluded 8 patients (3 in Gr I and 5 in Gr. II). The procedure in both groups is done by standard technique by a single endoscopist. The difference between the two groups was tract dilatation (6 mm in Gr I vs. 18 mm in Gr II). Placement of NCT and subsequent necrosectomy was done whenever necessary. Follow-up imaging was done at 72 hrs and thereafter at 2, 4, & 6 weeks. The outcomes were compared in terms of clinical success, need for surgery, complications, hospital stay and mortality.
RESULTS: N: 21(Gr. I), 61(Gr. II). The two groups were comparable in terms of demographics, etiology of pancreatitis, cyst location, size and amount of debris. Placement of NCT, need of necrosectomy and no of sessions required were also not different between the two groups. Clinical success defined as resolution of symptoms was seen in 100% of Gr. I patients vs. 73% in Gr. II ($p=0.048$). None of the patients in Gr I required subsequent surgery vs 20/61 (32.7%) in Gr. II ($p=0.025$). Complications: 15% in Gr. I vs 37% in Gr. II ($p=0.016$)
Mean hospital stay was 4 days (1-33) in Gr. I vs 8 (4-65) in Gr II ($p=0.012$). Mortality was none in Gr. I vs. 6.5% (4/61) in Gr. II ($p=0.22$)
CONCLUSION: The Nagi stent™ is effective and safe for EUTMD of WOPN. It permits rapid clinical resolution with 100% technical and clinical success rates. It offers distinct advantage over plastic stents although further prospective studies are warranted.
Disclosure of Interest: None declared

P0002 ENDOSCOPIC ESOPHAGEAL RECONSTRUCTION FOR THE TREATMENT OF A TOTAL AND EXTENSIVE DISRUPTION OF THE ESOPHAGUS USING A "RENDEZ-VOUS" TECHNIQUE

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INTRODUCTION: Complete esophageal obstruction leads to definitive fasting. The rendez-vous endoscopic approach had already been described for complex stenoses as an alternative to surgery that has high morbid-mortality.
AIMS & METHODS: This is a case series report about six patients referred for complete esophageal disruption classified in two groups: 1/ Long disruption (> 5cm), one after caustic ingestion and two due to an esophageal stripping during SEMS removal. Two had an associated loss of the SES; 2/ Short disruption (< 5cm), consecutive to radiation therapy for a neck neoplasia. They had been fasting for 3 to 18 months. All the procedures were performed according the anterograde retrograde approach, under anesthesia and with CO2 insufflation and X-rays guidance.
RESULTS: There were 3 men and women between 25 and 71 years old. All the reconstructions have been successful in one to three endoscopic sessions, using the non hydrophilic tip of a guide wire passed through a straight catheter in 5 cases and a EUS needle in only one case. In 2 cases, a neo-SES had to be created, by transillumination ($n=1$) or head and neck surgery ($n=1$). In order to guide the reconstruction, SEMS was used in one case, NGT in one case, and both were used in one patient. The first dilation was performed with a CRE balloon (12-15mm). All the patients could eat mixed after 2 POD. There was no intra-operative or post-operative complication. Then, the patients underwent 3 to 18 dilations sessions during 1.5 to 15 months; two are still undergoing dilations and all eat normally.
CONCLUSION: Endoscopic rendez-vous for esophageal reconstruction is safe and effective in case of esophageal disruption even with loss of SES, avoiding surgery.
Disclosure of Interest: None declared

P0003 ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCERS USING THE CLUTCH CUTTER

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INTRODUCTION: To reduce the risk of complications related to ESD using conventional knives, we developed the Clutch Cutter (CC), which can grasp and incise the targeted tissue using electrosurgical current.
AIMS & METHODS: From June 2007 to March 2014, 325 consecutive patients (228 men, 97 women; mean age 74 years, range 35-95) with a diagnosis of intramucosal or superficial submucosal gastric cancer without lymph node involvement, that had been confirmed by preliminary endoscopy, EUS, and endoscopic biopsies, were enrolled into this prospective study. The CC was used for all steps of ESD (marking, circumferential marginal incision, submucosal dissection, and hemostatic treatment). The therapeutic efficacy and safety were assessed.
RESULTS: The mean size of the early gastric cancers and resected specimens was 17.3 mm and 46.7 mm, respectively. The mean operating time was 97.2 minutes. The rate of en-bloc resection was 99.7% (324/325), and en-bloc resection with tumor-free lateral/basal margins (R0 resection) was 95.1% (309/325), respectively. The R0 resection rates according to tumor size and location were 97.4% (229/235) in less than 20 mm, 88.9% (80/90) in larger than 20 mm; 96.9% (127/131) in lower portion, 91.9% (91/99) in middle portion, and 94.7% (91/95) in upper portion. The mean operating time according to tumor size and location was 93.4 min in less than 20 mm, 140 min in larger than 20 mm; 73.9 min in lower portion, 108.8 min in middle portion, and 117.2 min in upper portion. Perforation during ESD occurred in one case (0.3%), which was managed with conservative medical treatment after endoscopic closure of the perforation. Post ESD bleeding occurred in 11 cases (3.4%), which were successfully treated by endoscopic hemostatic treatment.
CONCLUSION: ESD using CC is a safe and technically efficient method for resecting early gastric cancers.
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Disclosure of Interest: K. Akahoshi Other: Kazuya Akahoshi and FUJIFILM have applied for the patent in Japan, Europe, and USA for the Clutch Cutter described in this article. China has already granted the patent., Y. Motomura: None declared, M. Kubokawa: None declared, J. Gibo: None declared, N. Kinoshita: None declared, S. Osada: None declared, Y. Shimokawa: None declared, K. Tokumaru: None declared, Y. Otsuka: None declared, T. Hosokawa: None declared, N. Tomoeda: None declared, R. Utsunomiya: None declared, T. Miyazaki: None declared, K. Miyamoto: None declared, M. Oya: None declared

P0004 ENDOSCOPIC MYOTOMY FOR ACHALASIA USING A COMBINATION OF NESTIS WATER JET SYSTEM AND HOOK KNIFE: EVALUATION OF THE SAFETY AND THE EFFECTIVENESS

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INTRODUCTION: The peroral endoscopic myotomy (POEM) is a promising method for the treatment of the esophageal achalasia. But the precise technique can be refined. We developed a combined technique of water jet system for tunnelling and hook knife section for myotomy and we evaluated its results in a prospective study.
AIMS & METHODS: The patients presented with an achalasia without any prior instrumental treatment. The submucosal tunnel was created 12 cm over the cardia and 3 cm below, and then the endoscopic myotomy was performed using the Olympus Hook Knife by a single operator with CO2 insufflation, beginning 8 cms over the cardia and finishing 2 cms below. The clinical evaluation was realized before and then after the procedure at 1, 3, 6 and 12 months (score of Eckardt, score of quality of life GIQLI). A high-resolution manometry was realized before POEM and 3 months later to classify the achalasia (classification of Chicago) and to measure basal pressure and pressure of relaxation integrated (PRI) of the lower esophageal sphincter. Then an esophageal pHmetry of 24 hours was performed at 3 months to diagnose GERD. The

data are expressed in median (extremes) and compared before and later myotomie by paired t-test.
RESULTS: 21 patients (13 men, average age 61 years) were included. 18 procedures were complete, 1 was not realized because of a large esophageal diverticulum, 2 were interrupted (1 sub-mucosal fibrosis preventing the realization of the tunnel and 1 mucosal injury of the tunnel in the cardia). 2 other mucosal injuries occurred but did not prevent to continue the procedure after mucosal closure by clips. Dual Knife ® (n = 7) or the water jet Nestis Enki 2 ® (n = 11) were used for the tunnel. No mucosal injuries were observed with the water-jet system. Hook Knife ® was used for all myotomies. The average time of procedure was 94.2 min with a clear learning curve (135-35 min). A pneumoperitoneum was exsufflated with a needle during the procedure in 13 cases without any visible perforation. CT scan at day 1 showed a pneumomediastinum (n = 14/18), a pneumoperitoneum (n = 14/18) and/or a peumothorax (n = 3/18). No sepsis was observed. Feeding was always possible with liquids at day 1. All patients noted a clinical improvement. At 3 months, the basal pressure of the SIO was decreased for all patients (8 mmHg (0-15) against 23 mmHg (7-48) initially, $p < 0.01$) as well as the PRI (8 mmHg (0-16) against 23 mmHg (9-28), $p < 0.01$). pH metry showed a pathological GERD (esophageal pH 4 during more than 5% of time in 3 cases.

		Inclusion	1 month	3 months	6 months	1 year
n	21	17	14	10	3	
Eckardt	6 (3-11)	1 (0-3)*	1 (0-3)*	0 (1-4)*	0 (0-0)*	
GIQLI	82 (50-114)	115 (66-135)*	115 (82-140)*	131 (94-143)*	140 (130-142)¥	

CONCLUSION: Water-jet injection allows rapid and safe tunneling of the submucosa and myotomy with hook knife is very precise. Safety and effectiveness of mytomy is reinforced using these technical refinements.
Disclosure of Interest: None declared

P0005 COMPUTER-AIDED DECISION SUPPORT SYSTEM IN HIGH-MAGNIFICATION AND NARROW-BAND IMAGING ENDOSCOPY FOR DIFFERENTIATION OF GASTRIC LESIONS

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INTRODUCTION: High-magnification endoscopy with narrow-band imaging (HME-NBI) has been used for diagnosis of gastric pathology because of its high accuracy. Nevertheless, the application of these advanced techniques in clinical practice is difficult due to the presence of various histological changes of gastric mucosa with different modifications of microvascular and microsurface patterns. Newly developed computer-aided decision support systems are designed to detect and/or classify abnormalities and thus assist a medical expert in improving the accuracy of medical diagnosis. However, there is lack of data for computer-aided devices for classification of gastric lesions with HME-NBI.
AIMS & METHODS: The aim of this study was to evaluate the effectiveness of computer-aided classifier of endoscopic magnification images of gastric lesions. We analyzed our database contains 78 endoscopy NBI magnification images of gastric lesions (Olympus Exera GIF Q160Z, Lucera GIF Q260Z). All images were classified into three classes: oval (13 images), tubular (31 images), and destroyed with vessel network (34 images). Initially we divided images of every class into two sets — training set and test set. Then we selected uniformly distributed random points with fixed density (one random point for every 300 pixels) at every picture, which were analyzed by extracting topological features for building the classifier. Training set images were used for classifier training with Adaboost algorithm and testing set images of each group were utilized for testing with previously trained classifier. We repeated the procedure described above for the estimation of classifier quality.
RESULTS: From 78 database images there were 50 images (66.6%) with the success rate of correct classification exceeding 80%. In 14 images (17.9%) all points (100%) were recognized correctly. The mean percentage of points with the correct classification was 79%.
CONCLUSION: Topological features were successfully used for description of endoscopic magnification images. The combination of topological features analyzed with Adaboost algorithm allowed for creating and effective training of computer-aided classifier of endoscopic magnification images of gastric lesions.
Disclosure of Interest: None declared

P0006 NOVEL NARROW-BAND IMAGING SYSTEM WITH DUAL FOCUS MAGNIFICATION IN ENDOSCOPIC MAPPING OF THE GASTRIC MUCOSA IN PATIENTS WITH PRECANCEROUS CONDITIONS AND LESIONS OF THE STOMACH

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INTRODUCTION: Endoscopic mapping of the entire stomach with advanced techniques has been recommended as an important step of surveillance of premalignant gastric conditions/lesions [1]. Although current imaging technologies, such as narrow-band imaging (NBI) and high-magnification endoscopy, allow enhanced visualization of gastric mucosa, their application is still limited due to low contrast and brightness of endoscopic view and complexity of usage. Newly developed NBI system with dual focus (DF) magnification might be a promising tool to overcome this challenge.
AIMS & METHODS: The aim of this study was to evaluate diagnostic accuracy of new NBI-DF system in detection, characterization of gastric lesions in patients with extensive atrophy and/or intestinal metaplasia. A total of 43 patients (mean age 51.3 years, SD = 12.1) were initially examined by conventional white light endoscopy (WLE) followed by NBI overview. Afterwards chromoendoscopy (CE) with indigocarmine was performed as the ''gold standard'' for detection of lesions. Any suspicious areas detected by NBI or CE were subsequently further assessed with NBI with DF (Olympus Exera III GIF H190) and characterized accordingly. Biopsies were taken from all lesions for histological assessment.
RESULTS: From 93 detected gastric lesions there were 75 non-neoplastic (chronic gastritis, intestinal metaplasia), 3 low-grade dysplasia, and 15 high-grade dysplasia/early gastric cancer. All lesions (100%) detected by CE were found with NBI observation. Endoscopic histology prediction was successful in 88 cases (94.6%) Endoscopic misdiagnosis was found in 5 cases (5.4%): overestimation in 3 cases, underestimation in 2 cases; sensitivity, specificity, positive predictive value and negative predictive value were 80%, 97.4%, 85.7% and 96.2% respectively for early gastric cancer/high-grade dysplasia.
CONCLUSION: Observation of gastric mucosa with a novel NBI system was at least as effective as CE with indigocarmine in detection of suspicious gastric lesions in patients with precancerous conditions and lesions of the stomach. Dual focus magnification provides sufficient assessment of microvascular and microsurface patterns in order to differentiate gastric lesions. Further randomized controlled studies are needed to be performed for clarifying the role of novel endoscopic system in diagnosis of gastric pathology.
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Disclosure of Interest: None declared

P0007 DEVELOPMENT OF A PROTOTYPE OF VIDEO SYNCHRONISATION FOR RELOCALISATION OF BIOPSY SITES DURING ENDOSCOPIC EVALUATION OF BARRETT'S OESOPHAGUS: PRELIMINARY EXPERIMENTAL AND CLINICAL STUDY

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INTRODUCTION: The prevalence of Barrett's oesophagus (BE) is 5 to 6% in the general population, with a progression from dysplasia to adenocarcinoma 0.6 to 0.7 patient-years. Hence, endoscopic surveillance is justified to detect early lesions accessible to endoscopic treatment. However, the relocalisation of lesions detected by biopsies may be difficult during follow-up endoscopies. The purpose of this study was to evaluate the prototype of a magnetic probe for accurate location of the position of the endoscope, allowing the relocalisation of this position in a subsequent endoscopy. We report the results of a feasibility study in pigs and the use of this device in two patients with BE.
AIMS & METHODS: The system consists of an electromagnetic (EM) field transmitter and an EM probe constituting the electromagnetic tracking system (EMS) (NDI, Aurora). The EM probe is inserted through the operating channel of a double channel gastroscope. The EM field generator is positioned on the patient's chest wall. The system also includes new software developed at IHU/IRCAD, which performs simultaneous recording of the video from the endoscope alongwith its corresponding position, as measured by the EMS. During a second endoscopy, this software allows automatic synchronisation of the recorded video to provide relocalisation of the endoscope in front of previous biopsy sites in the oesophagus.
The system was tested in 5 anesthetised pigs. During the first endoscopy, ten markings were performed by argon plasma electrocoagulation (ERBE Tübingen, Germany) in the distal oesophagus. The position of each marking was recorded by the system. A second operator to then performed a blind endoscopy on the same pigs and was asked to follow the system implicitly as a guide to relocate the markings.
In 2 patients with BE, the system was then tested to facilitate relocalisation of the biopsy sites.
RESULTS: Ten markings were made in the distal oesophagus of 5. After withdrawal of the endoscope the second operator found 48 of the 50 markings (96%)

using the guidance provided by the system. The positioning of the endoscope provided by the EMS system was within a 2mm range from the initial positionning. In the evaluation of BE patients, the system relocalised the biospy sites within a range of 3mm.
CONCLUSION: This preliminary study shows the feasibility of the EMS prototype to relocalise the endoscope in the oesophagus within an acceptable range. The clinical usefulness of this system should be evaluated further during the follow-up of patients with BE.
Disclosure of Interest: None declared

P0008 THE UTILITY OF ROUTINE CHROMOENDOSCOPY FOR DETECTION OF DYSPLASTIC LESIONS DURING SURVEILLANCE COLONOSCOPY IN PATIENTS WITH COLONIC INFLAMMATORY BOWEL DISEASE. DOES RESEARCH TRANSLATE TO CLINICAL PRACTICE?

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INTRODUCTION: Dysplasia in colonic inflammatory bowel disease (IBD) is often multifocal and flat. Chromoendoscopy (CE) has been shown in prospective studies to improve dysplasia detection rates by improving the ability to detect subtle mucosal changes. (1) The utility of CE in dysplasia detection in patients with IBD during routine clinical practice has not been reported so far. We aimed to compare the yield of dysplastic lesions detected by CE with standard white light endoscopy (WLE).
AIMS & METHODS: Retrospective cohort study of patients with long standing (>7 years) colonic IBD undergoing surveillance colonoscopy at Leeds Teaching Hospital NHS Trust between January 2012 to December 2013. Details of diagnosis, duration of disease and outcomes of the colonoscopy were collected from the endoscopy database, electronic patient records and patient notes.
RESULTS: There were 120 colonoscopies in the CE group and 220 colonoscopies in the WLE group. The groups were well matched for all demographic variables. 27 dysplastic lesions were detected in 20 patients in the CE group and 9 dysplastic lesions were detected in 6 patients in the WLE group. All the lesions were detected on targeted biopsy and harboured low grade dysplasia. The adjusted prevalence ratio (on a per patient basis) for detecting any dysplastic lesion was 4.6 (95% CI 1.6-13.7) in favour of CE.
CONCLUSION: CE colonoscopy improves detection of dysplastic lesions during surveillance colonoscopy of patients with colonic IBD even in routine clinical practice, confirming data from prospective trials. CE should be the standard of care for all IBD surveillance procedures as advocated by both BSG and ECCO guidelines.
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Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
LIVER & BILIARY I – POSTER EXHIBITION – HALL XL

P0009 INVOLVEMENT OF B-CELLS IN HEPATIC INFLAMMATION DURING NONALCOHOLIC STEATO-HEPATITIS (NASH)

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INTRODUCTION: Growing evidence indicates that adaptive immunity contributes to the process leading to chronic hepatic inflammation in NASH. However, the mechanisms involved are still incompletely characterized. Recently, B-lymphocytes have emerged as players in orchestrating adipose tissue inflammation in obesity contributing to the development of insulin resistance.
AIMS & METHODS: We investigated the possible role of B-cell responses in the pathogenesis of NASH. NASH was induced by feeding four weeks C57BL/6 mice with a methionine-choline deficient (MCD) diet.
RESULTS: In mice receiving the MCD diet the development of steatohepatitis was associated with an increased hepatic infiltration by B220 (CD20) positive B-lymphocytes and by the detection of circulating IgG targeting oxidative stress-derived antigens such as malonildialdehyde- (MDA) and 4-hydroxynonenal-protein adducts. Moreover, immunohistochemistry showed the presence of IgG deposits within the hepatic inflammatory infiltrates that co-localized with MDA-derived antigens, indicating the formation of immunocomplexes. To substantiate the role of oxidative stress in triggering B-cell responses in NASH, mice were immunized with MDA-adducted bovine serum albumin (MDA-BSA) before feeding the MCD diet. In MCD-fed, but not in control mice, MDA-BSA immunization promoted liver B-cell expansion and enhanced transaminase release, lobular inflammation and the hepatic production of the pro-inflammatory cytokines TNF-α, IFN-γ, IL-12. Among immunized MCD-fed mice there were also positive correlations between the individual expression of the B-cell marker B220 and those of macrophage M1 activation markers IL-12p40 and iNOS ($r = 0.87$ and 0.71 respectively; $p < 0.02$).
This effect was likely mediated by B-cell interaction with CD4 T-cells as in the same animals B220 expression also positively correlated with that of IFN-γ ($r = 0.76$; $p < 0.03$) and of the co-stimulatory molecule CD40 ($r = 0.72$; $p < 0.05$). Furthermore, depleting $CD4^+$ T-cells in MCD-fed immunized mice by using an anti-CD4 monoclonal IgG did not affected B220 expression, but significantly lowered the hepatic mRNAs IFN-γ, iNOS and IL-12p40 and ameliorated lobular inflammation and focal necrosis.
CONCLUSION: These results indicate that B-cell responses triggered by oxidative stress can contribute to inflammation in NASH by stimulating T-cellular responses.
Disclosure of Interest: None declared

P0010 GENERATION OF A VECTOR CONTAINING AN SHRNA FOR THE RECEPTOR CB1 AS AN ANTIFIBROGENIC STRATEGY IN LIVER DISEASE

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INTRODUCTION: Blockade of cannabinoid type I receptor (CB1) by pharmacological antagonist has demonstrated antifibrogenic effects in models of cirrhosis. Gene therapy with a shRNA molecule for CB1 wthinin an adenovirus has the advantage of hepatic tropism, which will reduce side effects and increase the transduction efficiency.
AIMS & METHODS: Design a shRNA that efficiently inhibit the expression of CB1, evaluate its antifibrogenic effect in an experimental model of liver cirrhosis and generate an adenoviral vector coding for the shRNA-CB1.
shRNA sequences were designed to blockade mRNA of CB1 at positions 877, 1232, 1501 (pshCB1-A, B, D). The effectiveness of the shRNA was evaluated by inhibition of the mRNA-CB1 after transfection of the plasmids in primary culture rHSC. To determine the optimum dose for transfection in primary cultures, lipofectamine 2000 and Fugene ® HD were tested using a GFP expressing plasmid (pITR-GFP). Later, we evaluated shRNA mediated-CB1 inhibition in cirrhotic rats intoxicated with CCl_4. The plasmids were administrated by hydrodynamic injection in a volume of 4 mL. Then, in animals transfected with the most potent shRNA-CB1, mRNA levels of fibrogenic molecules (TGF-β1, Col 1 and α-SMA) and percentage of fibrotic liver tissue was measured. Finally, Ad5 backbone coding for shRNACB1-1232 or shRNA-Irrelevant was generated by homologous recombination between pshRNA and the pAd / BLOCK-iT ™ DEST.
RESULTS: In vitro shRNA designed to block position 877 and 1232 significantly inhibited mRNA ($p > 0.05$) CB1 gene expression in 77% and 91%, respectively using Fugene ® HD. The sequence of shRNA-Irrelevant did not affect mRNA expression of CB1. Hydrodynamics-based transfection of shRNA-CB1 via iliac vein in the rat allows efficient and repeatable delivery to the liver. A volume of 4 mL carrying 3 mg/kg was administered in 5-7 seconds. In CCl_4 model shCB1-1232 showed major decrease in CB1 mRNA and protein ($p < 0.05$), and in consequence fibrogenic molecules TGF-β1, Col I, α-SMA also reduced (60%, 47% and 77% ($p < 0.05$); respectively). Fibrosis diminished 49% ($p < 0.05$) compared to untreated controls. Thus pshRNACB1-1232 was selected for production of adenovector. Homologous recombination between attL and attR regions between pshRNA-1232-CB1 and pAd / BLOCK-iT ™ DEST allowed the generation of Ad-shRNA1232-CB1 backbone.
CONCLUSION: shCB1-1232 demonstrates CB1 gene and protein silencing in vitro and in vivo, decreasing mRNA levels of key fibrogenic molecules and fibrosis, showing potential to be used as therapeutic strategy for liver fibrosis. Recombinant adenovirus expressing this shRNA will have the advantage of high titers production conserving efficient liver transduction, which will facilitate its therapeutic application in experimental models of liver cirrhosis or even clinical scenarios.
Disclosure of Interest: None declared

P0011 CORRELATION BETWEEN INDIRECT SERUM MARKERS AND MORPHOMETRIC VALUES OF FIBROTIC TISSUE IN PBC

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INTRODUCTION: The accuracy of non-invasive methods for the quantification of liver fibrosis in patients with PBC is still debated. Moreover, the Ludwig's PBC stages do not represent a measurement of quantitative fibrosis.
AIMS & METHODS: We determined the histomorphometrical measurement of fibrotic tissue and analyzed the accuracy of a number of indirect markers of liver fibrosis for the detection of different histological stages of PBC and the association between indirect serum markers and morphometric values (MV) of fibrotic tissue.
Methods: Sections of liver tissue were stained with hematoxylin/eosin and Sirius red. Only samples with a > 25 mm length and including at least 11 complete portal tracts were considered adequate for the study. Histomorphometrical measurement of fibrotic tissue was performed on sirius red stained sections of liver biopsies. Area percentage measures of fibrotic tissue were ranked into 4 groups reflecting Ludwig's staging and compared with values of the following serum markers of liver fibrosis: APRI, LOK, FORNS, FIB-4. The percentage of fibrosis was calculated with ImageJ. All results were expressed as mean ± standard deviation. The numerical comparison of continuous data was performed using the Wilcoxon signed ranks test applied to two-samples. Linear regression analysis between two variables was performed by using Pearson correlation. Statistical significance was set at a value of $p < 0.05$.

RESULTS: We enrolled 50 patients with PBC (mean age, 57±12.30 years; 43 F and 7 M; 8 AMA negative, 42 AMA positive). There were 19 (38%) patients in Ludwig's PBC stage I, 14 (28%) in stage II, 12 (24%) in stage III and 5 (10%) in stage IV. The morphometric values (Table 1) of fibrotic tissue were significantly different in the various Ludwig's stages of PBC ($p<0.05$). Only LOK score was statistically different between stage II and III ($p=0.02$). No other significant differences were found in the various Ludwig's stages of PBC for APRI, FORNS, FIB-4 and LOK scores (Table 1). A statistically significant correlation was found between MV and Forns ($R^2=0.3643$, $p=0.0004$), MV and FIB-4 ($R^2=0.3945$, $p=0.0002$), MV and LOK ($R^2=0.3367$, $p=0.0010$), MV and APRI ($R^2=0.1476$, $p=0.0361$).
Table 1.

Ludwig's stages	Morphometric values	FORNS	FIB-4	LOK	APRI
Stage I	**0.74% ± 0.65**	**3.61 ± 1.62**	**0.24 ± 0.26**	**0.20 ± 0.16**	**0.61 ± 0.76**
Stage II	**3.87% ± 1.5**	**4.55 ± 1.8**	**0.35 ± 0.39**	**0.22 ± 0.18**	**0.49 ± 0.35**
Stage III	**6.15% ± 1.68**	**5.52 ± 2.06**	**0.35 ± 0.16**	**0.38 ± 0.19**	**0.67 ± 0.44**
Stage IV	**14.06% ± 8.45**	**8.05 ± 1.76**	**1.00 ± 0.76**	**0.69 ± 0.34**	**1.24 ± 0.79**

CONCLUSION: Histomorphometric values of fibrotic tissue increase progressively in Ludwig's stages of PBC, where non-invasive markers do not, and correlate positively with indirect serum markers of liver fibrosis.
Disclosure of Interest: None declared

P0012 THE NGF RECEPTOR P75NTR LEADS TO NEURAL HYPERTROPHY DURING THE DEVELOPMENT OF LIVER CIRRHOSIS AND MALIGNANT LIVER TUMORS

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INTRODUCTION: The autonomic nervous system is the involuntary part of the peripheral nervous system and regulates the intestinal motor activity, smooth muscles and exocrine glands. Autonomic nerves that innervate the liver reach the organ via the hepatic hilum and run together with the portal vein, the hepatic artery and the bile duct. In the full clinical picture of liver cirrhosis, no parenchymal innervation can be detected. In addition, malignant liver tumors, such as hepatocellular carcinoma (HCC) and cholangiocellular carcinoma (CCC), are not innervated.
AIMS & METHODS: The aim of this work is the characterization of a possible hepatic neuroplasticity, including responsible neurotrophic factors. In the present work, a collective consisting of 103 patients (22 patients with normal liver tissue, 23 patients with liver cirrhosis, 45 patients with HCC and 13 patients with CCC) was examined for variations in nerve number and nerve size. In addition, growth factors, such as Growth-Associated Protein (GAP-43) and Nerve Growth Factor (NGF), as well as their receptors TrkA and p75NTR were investigated by immunohistochemistry and qRT-PCR in terms of their involvement in a possible hepatic neuroplasticity.
RESULTS: The multiple comparison of median nerve sizes of the examined entities showed a clearly significant difference. The largest nerves were discovered in HCC samples. However, no difference in neural density was detected. Furthermore, significant differences were observed for the high affinity NGF-receptor TrkA and the low affinity NGF-receptor p75NTR with regards to immunoreactivity and relative expression. The highest p75NTR expression was found in normal liver tissue and both, relative expression as well as immunoreactivity, decrease with increasing nerve size.
CONCLUSION: The results of the present study suggest that the observed neural changes in the liver are related to active neural remodeling processes. The NGF receptor p75NTR seems to take on a key role in this context. Since p75NTR binds all neurotrophins with low affinity, further research is warranted concerning its involvement in the plasticity of hepatic nerves.
Disclosure of Interest: None declared

P0013 HIGH CONCENTRATION OF FIBROTIC AND INFLAMMATORY MARKERS AMONG PATIENTS WITH SCHISTOSOMAL LIVER DISEASES

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INTRODUCTION: Worldwide the commonest cause of portal hypertension is cirrhosis, but in tropics it is schistosomiasis. Some parts of Zambia are hyperendemic with prevalence of 77%. Hepatocellular function is preserved in hepatosplenic schistosomiasis hence prognosis is better than cirrhosis. Liver biopsy can confirm fibrosis but it is invasive.
AIMS & METHODS: This is an ongoing case control study involving 70 cases and 20 controls. All cases had varices and were negative for HIV, hepatitis B and C viruses. Hyaluran was used as a marker of liver fibrosis while TNF receptor 1, sCD14, IL1 beta, IL 6 and CRP were inflammatory markers.
We set out to investigate fibrotic and inflammatory makers in hepatosplenic schistosomiasis patients at the University Teaching Hospital, Lusaka, Zambia.
RESULTS: Eighty patients were evaluated and serology for schistosomiasis was positive in 74 (93%) and negative in 6 (7%). Hyaluran levels compared with controls were higher, $p<0.001$ (median 111.6ng/ml, IQR 39.1, 240.3). Inflammatory markers were elevated: TNF receptor 1 concentrations compared with controls were higher, $p<0.001$ (median 3150.1pg/ml (IQR 1703.2, 10460.0), sCD14 values were higher than in controls $p<0.001$, median 2365.0ng/ml (IQR1744.9, 3128.6). IL 1 beta values were higher than in controls $p=0.013$, median 4.3pg/ml (IQR 0.8, 13.2) and so were IL 6 values $p=0.001$ (median 15.26pg/ml, IQR 10.15, 38.13). Spearman's rank correlation of hyaluran and TNF receptor 1 was positive ($r=0.44$, $p=0.002$) and so was hyaluran and IL6 ($r=0.251$, $p=0.045$).
CONCLUSION: Schistosomiasis is a leading cause of portal hypertension in Zambia and induces a liver fibrotic marker which could be used to assess disease severity. It seems hepatosplenic schistosomiasis also induces high levels of TNF receptor 1, sCD14, IL1 beta and IL6. These elevated markers could be due to bacterial translocation which needs to be confirmed by markers of bacterial translocation such as LPS.
Disclosure of Interest: None declared

P0014 LIVER FIBROSIS PREVENTION AFTER INTRAMUSCULAR ADMINISTRATION OF MATRIX METALLOPROTEINASE-8 ADENOVIRAL VECTOR IN A MODEL OF HEPATIC FIBROSIS

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INTRODUCTION: MMP-8 degrades preferentially collagen type I (collagen of higher proportion of hepatic fibrosis). We delivered MMP-8 gene in to the muscle, using an Adenovirus vector, protein is released systemically and is activated in the liver.
AIMS & METHODS: Our aim was to evaluate profibrogenic gene expression pattern and liver fibrosis prevention.
We used four groups of rats ($n=15$): control; thioacetamide (TAA), induced-fibrosis; TAA+AdGFP; TAA+AdMMP8. At the beginning of the fifth week of TAA intoxication, administration of vectors in soleum muscle was accomplished. Sub-groups of rats ($n=5$) at the end of first, second and third week after vector administration were sacrificed. Percentage of fibrosis, liver function, gene expression of MMP8, proinflammatory genes (IL1-beta, TNF-alpha), profibrogenic genes (collagen α1(I), CTGF and TGF-beta) and antifibrogenic genes (MMP1 and MMP9), were determined.
RESULTS: After 3 weeks of treatment: In the liver and serum, amount of MMP8 protein was sustained, fibrosis decreased up to 48%, proinflammatory genes expression was modified only at the end of the third week, profibrogenic gene expression decreased (Col α1(I) 4 times, TGF-beta 3 times and CTGF 2 times), antifibrogenic genes expression increased (MMP9 2.8 times and MMP1 10 times). According to Knodell score, a clearly diminution of inflammatory cells infiltration in comparison with counterpart animals treated with AdGFP, could be appreciated.
CONCLUSION: A single dose of AdMMP8 in muscle is enough in order to obtain a stable liver MMP8 protein expression and activity during 21 days. Degradation of collagen in the liver modifies pro and anti-fibrogenic gene expression allowing a restoration of hepatic architecture.
Disclosure of Interest: None declared

P0015 WHOLE-PROTEIN MASS SPECTROMETRY TO IDENTIFY CONGENITAL DISEASE OF GLYCOSYLATION IN END-STAGE LIVER DISEASE

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INTRODUCTION: Congenital disorders of glycosylation (CDG) are a heterogeneous group of autosomal recessive metabolic diseases with a wide spectrum of clinical symptoms. Depending on localization of the defective protein, two types are distinguished (CDG-I; endoplasmatic reticulum and CDG-II; Golgi apparatus). Liver involvement is frequent in both groups and can even be predominant for some CDG-II variants. Abnormal glycosylation is seen in liver cirrhosis, probably resulting from affected liver synthesis. We hypothesized that mass spectrometry (MS) differentiates between secondary and bonafide genetic causes in end-stage liver disease.
AIMS & METHODS: To determine the effect of a diminished liver function on glycosylation we analyzed anonymous serum samples drawn from end-stage liver disease patients prior to their liver transplantation. As a first step we used transferrin isoelectric focusing (tIEF) to detect abnormal glycosylation. Selected samples were further analyzed with transferrin whole-protein MS to obtain a comprehensive readout of the glycosylation profile.
We also obtained serum from 100 patients with a presumed CDG. Patients with a predominant liver phenotype were selected for further analysis using exome sequencing for identification of the pathogenic mutation.
RESULTS: We collected 1065 serum samples and found an abnormal tIEF pattern in 30%. All abnormalities were mild and resembled a CDG-II pattern.

MS of abnormal tIEF samples had increased fucosylation of transferrin and loss of one sialic acid.
We identified 18 patients with a phenotype resembling Wilson disease with liver fibrosis, elevated transaminases, low ceruloplasmin and liver copper accumulation. DNA is currently prioritized for exome sequencing. MS comparison of the Wilson disease-like patients and liver transplant patients showed that desialization is more abundant in Wilson disease-like patients and transferrin fucosylation is seen more often in liver transplant patients.
CONCLUSION: Whole protein MS enables differentiation between abnormal glycosylation secondary to liver failure and bonafide CDG. This can aid in the detection of CDG as a cause for liver pathology.
Disclosure of Interest: None declared

P0016 MICRORNA EXPRESSION PROFILE IN SIMPLE STEATOSIS AND NON-ALCOHOLIC STEATOHEPATITIS

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INTRODUCTION: Simple steatosis (SS) and non-alcoholic steatohepatitis (NASH) are regarded as histological subtypes of non-alcoholic fatty liver disease (NAFLD). The distinctive pathological difference between SS and NASH is that NASH induces chronic liver inflammation and fibrogenesis, which can lead to liver cirrhosis. The difference in pathogenesis between SS and NASH is still not clear. MicroRNAs (miRNAs) are endogenous, non-coding short RNAs that regulate gene expression by repressing translation or degrading target mRNAs. Accumulating evidence indicates that miRNAs play important roles in various life functions including inflammation, metabolism, and fibrosis.
AIMS & METHODS: The purpose of this study was to examine the relationship of miRNA expression profiles with SS and NASH in animal models and humans. DD Shionogi (DS), Fatty Liver Shionogi (FLS), and FLS ob/ob mice were subjected as the normal control, SS model, and NASH model, respectively. Microarray analysis was used to assess 375 miRNA expression profiles in mouse liver tissue. Normalized miRNA expression ratios over ±2log2 between FLS and FLS ob/ob were identified as candidates. Real time PCR was used to check the reproducibility of the microarrays predicting miRNAs from 4 mice in each group. The putative miRNA target genes were predicted using the web-driven software DIANA microT-CDS. DAVID 6.7 was used to perform gene ontology annotation and KEGG pathway enrichment analysis. The putative miRNA expression profiles in human serum were also examined in every 10 patients with asymptomatic gallbladder stones, SS, and NASH.
RESULTS: In microarray analysis, 18 miRNAs were identified as candidates. Among the 18 miRNAs, 6 showed good expression ratio reproducibility in real time PCR and were confirmed to express commonly between mice and humans. The expression levels of miR-200a and miR-200b increased in the order of normal control, SS, and NASH. miR-1 was downregulated in NASH. miR-376c, miR-409, and miR-411 showed potent high expression in SS, over 30-fold of DS. KEGG pathway analysis indicated that the strongly expressed miRNAs in SS (miR-376c, miR-409, and miR-411) had multiple targets in the TGF-β signaling pathway including TGFR, smad 2, 3, and 4. The analysis suggests that miR-376c, miR-409, and miR-411 may protect liver fibrosis through silencing the TGF-β signaling pathway. In human serum, hierarchical clustering analysis of the putative miRNA expression also showed clearly different expression profiles between SS and NASH.
CONCLUSION: The expression profiles of 6 miRNAs were different between SS and NASH models. Some potential target genes of the putative miRNAs were found to be involved in the TGF-β signaling pathway. Furthermore, the putative miRNA expression profiles in human serum were also clearly different between SS and NASH patients. These miRNAs have high potential as biomarkers to distinguish the fate of NAFLD patients and contribute to further research in the pathogenesis and treatment of NASH.
Disclosure of Interest: None declared

P0017 PROTECTIVE EFFECTS OF MELATONIN ON THIOACETAMIDE-INDUCED LIVER FIBROSIS IN RATS

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INTRODUCTION: The aim of the present study was to determine the effect of melatonin on liver fibrosis induced with long-term administration of thioacetamide (TAA) in an animal model. The antifibrotic effects of melatonin were assessed by determining activity indirect markers of fibrosis, i.e. aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), and direct markers represented by proinflammatory cytokines such as interleukin 6 (IL-6), interleukin beta 1 (IL-beta1), tumour necrosis factor alpha (TNF-alpha, transforming growth factor beta 1 (TGF-beta1) and platelet-derived growth factor (PDGF- AB). Moreover, parameters of oxidative stress were determined, i.e. concentrations of oxidised glutathione (GSSG) and reduced glutathione (GSH), activity of paraoxonase 1 (PON-1), an enzyme of antioxidative properties. Inflammatory changes and extent of fibrosis were evaluated histologically.
AIMS & METHODS: Experiments were carried out in Wistar rats. Animals were divided into 4 groups, 8 individuals each: group I- controls receiving drinking water ad libitum for 12 weeks, group II – TAA, 300 mg/L ad libitum for 12 weeks, group III- melatonin, 10 mg/kg b.w. administered intraperitoneally (IP) daily for 4 weeks, group IV – TAA, 300 mg/L ad libitum for 12 weeks followed by melatonin, 10 mg/kg/b.w. administered IP daily for 4 weeks.
RESULTS: Results of serum determinations demonstrated significantly lower activity of AST, ALT and AP in the group receiving TAA followed by melatonin (IV) compared to the group receiving only TAA (II). Immunoenzymatic findings regarding the effect of melatonin on concentration of proinflammatory cytokines (Il-6, Il-beta1, TNF-alpha, TGF-beta 1, PDGF-AB) confirmed these data.
CONCLUSION: Biochemical examinations in liver homogenates revealed statistically significant improvement of oxidative stress parameters (concentration of GSH increases and concentration of GSSG decreases) in animals with TAA-induced liver damage receiving melatonin (IV). Moreover, the activity of PON-1 toward phenyl acetate and paraoxon was found to be increased in liver homogenates and serum in the group receiving TAA followed by melatonin (IV) compared to the TAA group (II). Microscopic evaluation disclosed inhibitory effects of melatonin on inflammatory changes and extent of liver fibrosis.
Disclosure of Interest: None declared

P0018 ROLE OF GAMMA-KETOALDEHYDES AS NOVEL MEDIATORS OF EXPERIMENTAL FIBROGENESIS AND STELLATE CELLS ACTIVATION

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INTRODUCTION: Reactive lipid aldehydes formed during lipid oxidation such as 4-hydroxynonenal (4-HNE), are key activators of hepatic stellate cells (HSCs) to a pro-fibrogenic phenotype. γ-Ketoaldehydes (γ-KAs) are highly reactive lipid aldehydes formed during oxidation of arachidonic acid or as a by-product of the cyclo-oxygenase pathway. γ-Ketoaldehydes are ~100x more reactive than HNE, and form protein adducts and cross-links. Increased circulating concentrations of proteins cross-linked to γ-ketoaldehydes are present in patients with alcoholic liver disease.
AIMS & METHODS: The aim of this study was to investigate whether one specific γ-ketoaldehyde, namely levuglandin E_2 (LGE_2), can induce activation of HSCs. Cultured activated, serum-starved primary mouse and human HSCs were exposed to various concentrations (0.5 pM-5 μM) of levuglandin E_2 (LGE_2) for up to 48 hours. Endpoints measured included proliferation (BrdU incorporation), cytotoxicity (lactate dehydrogenase (LDH) release and tetrazolium (MTS) reduction), RNA expression (qRT-PCR), protein expression (Western Blot), and collagen secretion in conditioned medium (SirCol assay).
RESULTS: HSCs exposed to LGE_2 exhibited profound cytotoxicity at 5 μM concentration, as indicated by LDH leakage and reduced MTS. This was mediated by an induction of apoptosis, indicated by an increase in PARP cleavage, occurring as early as 8 hours after LGE_2 exposure. However, at lower, non-cytotoxic doses (ranging from 50 pM-500 nM, with a maximum effect observed at 0.5 nM), LGE_2 promoted HSC activation as indicated by increased expression of α-smooth muscle actin and vimentin, as well as increased proliferation and collagen secretion. In addition, LGE_2 exposure promoted sustained activation of signalling pathways, as indicated by the increased phosphorylation of the kinases ERK1/2 and JNK, as well as an increase in mRNA levels of chemokines such as IL-8 and MCP-1. We are currently investigating the potential protective action of administration of a γ-ketoaldehyde scavenger in an animal model of hepatic fibrosis.
CONCLUSION: γ-Ketoaldehydes represent a newly identified class of activators of HSCs *in vitro*, which are biologically active at concentrations as low as 50 pM.
Disclosure of Interest: None declared

P0019 NONINVASIVE SERUM FIBROSIS MARKERS IN COMPARISON WITH GRADING AND STAGING IN CHRONIC HEPATITIS

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INTRODUCTION: Chronic hepatitis is defined as a necroinflammatory disease of the liver continuing for at least six months. The aim of this study was to evaluate the role of noninvasive fibrosis markers by assessing the association among grading and staging and these diagnostic parameters in patients with chronic hepatitis.
AIMS & METHODS: We retrospectively studied 221 patients with chronic hepatitis between 2011 and 2013. Routine biochemical indices and serum fibrosis indexes such as aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio (AAR), AST to platelet ratio index (APRI) and Fibrosis 4 score (FIB-4) were determined, and the histological grade and stage of the liver biopsy specimens were scored according to the Ishak scoring system. Receiver operating characteristic curve (ROC) analysis was conducted to compare diagnostic accuracies of these markers for prediction of significant fibrosis.
RESULTS: We identified 221 liver biopsies from chronic hepatitis patients with contemporaneous laboratory values for imputing AAR, APRI and FIB-4. From all, 135 males (61.1%) and 86 females (38.9%), with the mean age of 39.6±14.4 were studied. FIB-4, APRI and AAR were correlated significantly with the stage of fibrosis, with a higher correlation coefficient than other markers in the patients

with Hepatitis B ($r = 0.46$), C ($r = 0.58$) and autoimmune hepatitis ($r = 0.28$). FIB-4 (AUROC = 0.84) and APRI (AUROC = 0.78) was superior to AAR at distinguishing severe fibrosis from mild-to-moderate fibrosis and gave the highest diagnostic accuracy.
CONCLUSION: Application of these markers was good at distinguishing significant fibrosis and decreased the need for staging liver biopsy specimens among patients with chronic hepatitis.
Disclosure of Interest: None declared

P0020 REVEALING THE MOLECULAR MECHANISM OF RAT LIVER RESPONSE TO LONG-TERM OMEPRAZOLE TREATMENT WITH BIOINFORMATICS APPROACH

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INTRODUCTION: Omeprazole is a widely prescribed acid-suppressing drug available for clinical use for 25 years. Despite well-studied adverse effects of short-term omeprazole treatment, underlying mechanisms of some hepatotoxic effects of long-term injection of high omeprazole doses (e.g. development of oxidative stress and histopathologic changes [1]) are not understood. Transcriptome analysis is a powerful tool for elucidation of possible mechanisms of cellular response to different conditions on molecular level. Bioinformatics approach is suitable for processing of large datasets, prediction of possible regulatory circuits and generation of hypotheses on involved molecular mechanisms [2].
AIMS & METHODS: The purpose of the research was to find out possible molecular mechanisms of rat liver cells response to long-term injection of omeprazole.
GSE8858 dataset and GPL2454 platform description were downloaded from NCBI Genome Expression Omnibus database. Gene expression data from livers of rats treated with 30 mg/kg and 415 mg/kg for 1 and 25 days were compared in order to reveal differentially expressed genes (DEGs). DEGs were determined with GEO2R tool on the basis of t-criterion and adjusted p value. Gene ontology (GO), pathway enrichment analyses and building of protein-protein interactions (PPI) network were performed with STRING 9.1. Prediction of miRNAs and *cis*-elements for DEGs was carried out with WebGestalt toolkit. Clusters were identified by K-means analysis in ClusterONE. All networks were visualized using Cytoscape.
RESULTS: In total 79 DEGs (21 up- and 58 down-regulated) and 87 DEGs (41 up- and 46 down-regulated) were identified in samples of rat livers treated with 30 and 415 mg/kg during 25 days, respectively. At the same time 22 genes with similar pattern of expression (9 up- and 13 down-regulated) were found for both types of dosage. Among them are *Arntl*, *Cdk1a*, *Chka*, *Gpam*, *Litaf*, *Slc2a5*, *Usp2* etc. Enrichment in such GO terms was revealed: cell cycle, mitosis, nuclear division, lipid metabolism. Only genes involved in lipid metabolism were up-regulated, while others were suppressed. Genes involved in PPAR signalling pathway were found to be differentially regulated upon 25-day treatment with omeprazole. Most of DEGs (51 genes) were of cytoplasmic proteins (housekeeping genes). PPI networks were constructed for 98 proteins and 102 interactions revealed. The optimal amount of clusters was equal to 3. MiRNA-9, 17-5p, 20A, 20B, 106A, 106B, 200B, 200C, 429, 506 and 519D were found to be involved in regulation of revealed DEGs. 24 probable *cis*-elements were predicted for promotors of identified DEGs.
CONCLUSION: Thus, long-term treatment of rats with omeprazole is associated with changes in expression of housekeeping genes: down-regulation of genes involved in cell-cycle process and cellular division, up-regulation of genes involved in lipid metabolism, and changes in expression of PPAR signalling pathway genes.
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Disclosure of Interest: None declared

P0021 MORPHOLOGICAL AND FUNCTIONAL CHANGES OF LIVER MACROPHAGES DURING THE PROGRESSION OF NONALCOHOLIC STEATOHEPATITIS (NASH)

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INTRODUCTION: Recent reports indicate that both human and experimental NASH is characterized by an increase in hepatic monocyte infiltration and that macrophages have an important role in regulating the disease evolution. However, little is known about the functional changes occurring in liver macrophages during the progression of NASH.
AIMS & METHODS: NASH was induced in C57BL/6 mice by feeding a methionine-choline deficient (MCD) diet up to 8 weeks.
RESULTS: Mice receiving the MCD diet showed a progressive worsening of parenchymal damage and lobular inflammation, while liver fibrosis was evident only after 8 weeks of treatment. Hepatic F4/80-positive macrophages increased in parallel with the disease progression. In the early phases of NASH after 4 weeks on the MCD diet these cells prevalently expressed markers of inflammatory monocytes such as Ly6C and CD11b, but the prevalence of $Ly6C^+/CD11b^+$ cells decreased by extending the treatment up to 8 weeks. This paralleled with a lowering in the monocyte chemokines CCL1/CCL2 and their receptors CCR8/CCR2. We observed that the expression of the macrophage M1 activation markers iNOS and IL-12 also peaked at 4 weeks and declined thereafter. No appreciable changes were instead observed in the levels of M2 polarization markers arginase-1 and MGL-1. Histology revealed that the macrophages accumulating in advanced NASH (8 weeks MCD) were enlarged, vacuolized and formed small aggregates. Immunofluorencesce showed that these cells contained lipid vesicles positive for the apoptotic cell marker Annexin V suggesting that they have phagocytosed apoptotic bodies derived from dying fat-laden hepatocytes. At flow cytometry, enlarged macrophages were characterized by a weak Ly6C/CD11b expression and by a low IL-12 production. On the other hand, these cells showed an enhanced expression of the anti-inflammatory mediators IL-10 and annexin A1. The production of the pro-fibrogenic cytokine TGF-β was increased in the macrophages obtained from NASH livers, irrespective of the cell phenotype.
CONCLUSION: Altogether, these data indicate that during the progression of NASH liver macrophages down-modulate their pro-inflammatory phenotype in parallel with the phagocytosis of apoptotic hepatocytes and acquired anti-inflammatory properties.
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Disclosure of Interest: None declared

P0022 MICRORNA-27B DEVELOP THE FATTY LIVER FORMATION AND INSULIN RESISTANCE AT THE SAME ONSET

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INTRODUCTION: Nonalcoholic fatty liver disease (NAFL) morbidity rate in Asia Pacific region is close to 12–24%, while in Western countries is about 20–30%[1)]. And nonalcoholic fatty liver disease (NAFLD) can progress to nonalcoholic steatohepatitis (NASH), cirrhosis and hepatocellular carcinoma. In spite of its high prevalence, up till now there is no proven effective treatment for NAFLD[3)]. Along with the ''obesity epidemic,'' the worldwide prevalence of NAFLD is increasing rapidly and is generally assumed to be a consequence of obesity-induced insulin resistance [2)]. On the other hand, not all obese individuals are insulin resistant, nor are all insulin-resistant individuals obese [4)]. MicroRNAs (miRs) are a class of small non-coding RNAs that function to control gene expression by inducing the degradation or inhibiting the translation of mRNA through an association with its 3'-untranslated region (3'UTR). Although miRs play a key role in the pathogenesis of nonalcoholic fatty liver disease (NAFLD) and diabetes mellitus (DM), detailed mechanisms of this pathogenesis remain unclear.
AIMS & METHODS: We found that miR-27b increased in liver biopsy specimens of NAFLD patients with DM using microarray analysis, as compared with controls. The aim of this study was to investigate whether overexpression of miR-27b in liver could cause fatty liver formation and insulin resistance, and to examine the mechanism of NAFLD and DM onset in a murine model.
Five-week-old male C57BL/6J mice were randomized into 2 groups (n = 16 mice): basal diet (BD)-fed control mimic (BD-Con, n = 4), BD-fed miR-27b-mimic (BD-miR-27b, n = 4). In this study, miR-27b mimic is injected intravenously at 7mg/kg. We comfirmed the target genes of miR-27b using quantitative RT-PCR analysis. Insulin serum concentrations were measured by a local laboratory for clinical examinations. As an alternative method for assessing insulin resistance (IR), the homeostasis model assessment of IR (HOMA-IR) was calculated using the following formula: fasting insulin (mU/mL) plasma glucose (mg/dL) / 405.
RESULTS: BD-miR-27b significantly showed steatosis using oil red o staining and increased hepatic tryglyceride content, as compared with BD-Con. In the analysis of fat accumulation-related gene expression, hepatic Peroxisome proliferator-activated receptor α (PPARα) and Microsomal triglyceride transfer protein (MTTP) are significantly decreased. At the same time, BD-miR-27b showed hyperinsulinemia and insulin resistance. In the analysis of insulin resistance-related gene expression, hepatic Insulin receptor substrate 1 (IRS-1) is significantly decreased.
CONCLUSION: miR-27b controls multiple gene levels that are involved in fat accumulation and insulin resistance, resulting in the NAFL and DM pathology. These results propose a therapeutic approach for NAFL and DM by targeting miR-27b.
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P0023 EFFICACY OF ABSORBABLE EMBOLIZATION MATERIALS FOR PORTAL VEIN EMBOLIZATION TO INDUCE LIVER REGENERATION IN A RABBIT MODEL

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INTRODUCTION: Unilateral portal vein embolization (PVE) is used to increase future remnant liver volume in patients requiring extended resections. Reversible PVE is of interest when generating sufficient hypertrophy while preserving the embolized liver lobe. The concept of reversible PVE requires an absorbable embolization material.
AIMS & METHODS: The aim of this study is to modulate lysis time of a fibrin-glue based embolization material while using different concentrations of Aprotinin. Aprotinin inhibits fibrinolysis and thereby delays absorption of FG. PVE of the cranial liver lobe was performed in twenty-four rabbits, divided into 5 groups:
- Fibrin glue with Aprotinin (FG1000 KIU (Kallikrein Inactivotor Unit), n = 4)
- Fibrin glue with Aprotinin (FG700KIU, n = 5)
- Fibrin glue with Aprotinin (FG500KIU, n = 5)
- Fibrin glue with Aprotinin (FG300KIU, n = 5)
- Fibrin glue without Aprotinin (FG-Aprot, n = 5)

The rabbits were sacrificed after 7, 14 and 49 days, respectively. CT volumetry of non-embolized lobe (NELVol), liver damage parameters, liver-to-body weight ratio of NEL were evaluated.
RESULTS: Data were compared with a previous series using a permanent embolization material, i.e. polyvinyl alcohol + coils (PVAc), showing complete and permanent occlusion of the embolized portal vein branch in all rabbits after 7 days.
FG-Aprot was completely absorbed in 7 days and did not give any hypertrophy response of the NEL. At sacrifice on day 7, the embolized portal vein in all 4 of the FG+1000KIU Aprotinin group was still occluded and showed a hypertrophy response comparable to the PVAc group. The group of FG 700KIU Aprotinin survived 14 days and in two of the five rabbits, the embolized portal vein was recanalized at sacrifice. The hypertrophy response in these rabbits was not different from the PVAc group. The rabbits with FG 500KIU and 300KIU Aprotinin were sacrificed at day 49. In the group with FG 500KIU Aprotinin, 4 out of 5 showed recanalization of the cranial portal branches. In the group with FG 300KIU Aprotinin, 3 out of 5 rabbits showed recanalization. Both groups showed hypertrophy response rates not different compared to the PVAc group.
CONCLUSION: Fibrin glue with the concentrations 300KIU and 500KIU Aprotinin resulted in 70% reversible embolization with a hypertrophy response comparable to the PVAc group.
Disclosure of Interest: None declared

P0024 TRANSPLANTATION OF HUMAN AMNION-DERIVED MESENCHYMAL STEM CELLS AMELIORATES CARBON TETRACHLORIDE-INDUCED LIVER FIBROSIS IN RATS

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INTRODUCTION: Liver fibrosis is a progressed stage of chronic hepatic disease caused by a variety of factors, such as viral infections, alcohol, drugs and chemical toxicity. The only effective available treatment for end stage liver fibrosis is transplantation; however, due to the lack of donors, complications and transplant rejection, alternative treatment is needed. Mesenchymal stem cells (MSCs) have been reported to be a valuable cell source in cell therapy. Recently, bone marrow- or adipose tissue-derived MSCs have been reported to be effective in the treatment of liver fibrosis. In addition, several studies have shown that MSCs can be easily isolated from human amnion, and a large amount of cells can be obtained. Therefore, we examined the effects of transplantation of human amnion-derived MSCs (hAMSCs) in rats with liver fibrosis.
AIMS & METHODS: All pregnant women gave written informed consent, and amnion was obtained at Cesarean delivery. hAMSCs were isolated by collagenase treatment, and expanded with culture medium containing fetal bovine serum. Liver fibrosis was induced in 6-week-old male Sprague-Dawley rats by intraperitoneal injection of 2 ml/kg of 50% carbon tetrachloride (CCl_4) twice a week for 7 weeks. At 3 weeks, hAMSCs (1×10^6 cells) were transplanted intravenously. Rats were sacrificed at 7 weeks, and histological analyses and quantitative RT-PCR were performed.
RESULTS: Transplantation of hAMSCs significantly reduced the fibrotic area and deposition of type I collagen. In addition, hAMSC transplantation significantly decreased the number of α-SMA-positive hepatic stellite cells and and CD68-positive Kupffer cells in the liver of hAMSC-treated rats. mRNA expression of α-SMA was significantly decreased in the liver of hAMSC-treated rats, and mRNA expression of type I collagen, TGF-β and IL-1β tended to be decreased by hAMSC transplantation.
CONCLUSION: Transplantation of hAMSCs provided significant improvement in a rat model of liver fibrosis, possibly through inhibition of inflammatory reaction. hAMSC would be considered as a new cell source for the treatment of liver fibrosis.
Disclosure of Interest: None declared

P0025 VITAMIN D: HYPOTHESIS OF TROPHIC EFFECT ON LIVER CELLS IN AN ANIMAL MODEL OF NAFLD

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INTRODUCTION: Nonalcoholic fatty liver disease (NAFLD), the most common liver disease in Western countries, is pathogenetically related to a sedentary lifestyle as well as to poor quality diet characterized by an excessive energy intake including high fatty foods and high amounts of fructose, the so-called Western Diet (WD). The hallmark of NAFLD is hepatic accumulation of triglycerides. Vitamin D in addition to the effects on lipid metabolism, plays other biological functions, among which a trophic effect on human cultured cells.
AIMS & METHODS: To evaluate, in a rat model of NAFLD induced by Western Diet, the relationship between body weight, liver weight and grade of steatosis; and if these parameters are modified by vitamin D supplementation. Methods: Eighteen male Wistar rats were divided into 3 groups, each of 6 rats. The 3 groups were fed respectively with Standard Diet (SD); Western Diet (WD); WDVitD: WD supplemented with 23 IU/day/rat of vitamin D3. The experiment was conducted for 6 months. Weekly, the rats, body weight was recorded. At sacrifice, livers were excised and weighed and samples were stored at -80°C. Liver histology was examined by haematoxylin/eosin and Oil Red-O staining. Steatosis was numerically scored following semi-quantitative pathological standard.
RESULTS: During the experiment the increase of *body* weight was similar in the three groups. In the two groups fed with WD *liver* weight was significantly higher than SD group ($p<0.01$). A positive correlation between *body* weight and *liver* weight was observed in WD groups ($p<0.0001$). The *liver*/*body* weight ratio was significantly higher in WD and WDVitD groups than SD: 2.9±0.05, 2.8±0.07 and 2.0±0.04, respectively; $p<0.001$). Steatosis was present in 61% and 21% of hepatocytes in WD group and WDVitD group, respectively, and absent in SD group. No correlation was found between the grade of steatosis and liver or body weight nor between the grade of steatosis and liver/body weight ratio. Although vitamin D supplementation reduced the degree of steatosis, liver/body weight ratio in WDVitD group was similar to WD group.
CONCLUSION: In a rat model of NAFLD induced by WD the presence and extent of steatosis are independent from body weight. Interestingly and unexpectedly, in WD groups the supplementation with vitamin D reduces liver steatosis but not liver weight: this sustains the hypothesis of a trophic effect of vitamin D on liver cells.
Disclosure of Interest: None declared

P0026 VITAMIN D PREVENTS STEATOSIS AND DIABETES IN A RAT MODEL OF NAFL

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INTRODUCTION: The last decade has seen nonalcoholic fatty liver disease (NAFLD) rise to become the most common cause of chronic liver disease in Western countries. It is known that insulin resistance and type 2 diabetes mellitus (T2DM) have an important role in the pathogenesis of obesity and NAFLD. A growing body of evidence points to a linked and potentially causative relationship between serum 25-hidrossivitamin D3 [25-(OH)D] levels and NAFLD.
AIMS & METHODS: Aim of this study was to evaluate whether daily vitamin D3 supplementation is able to modulate the liver effects and glucose homeostasis of a westernized diet, high in fat and fructose, in an animal model of NAFL without vitamin D deficiency. Methods: Eighteen male Wistar rats were divided into 3 groups, each of 6 rats. Group 1: Standard Diet (SD); Group 2: Western Diet (WD) containing 13 IU/day/rat of vitamin D3; Group 3: WD containing 23 IU/day/rat of vitamin D3 (WDVitD). The experiment was conducted for 6 months. Liver histology was examined by haematoxylin/eosin and Oil Red-O staining. Insulin resistance was determined according to the Homeostasis Model of Assessment (HOMA-IR) method. Grade of liver steatosis was evaluated according to Brunt EM et al.
RESULTS: In SD group, livers were normal and no hepatocytes contained fat; in WD group the percentage of hepatocytes with steatotic vacuoles was 61%, while in WDVitD group only 27% of hepatocytes contained fat. In WD group HOMA-IR was significantly higher than in SD (41.9±8.9 *vs* 6.17±1.3, $p<0.01$) and it was reduced by vitamin D supplementation in WDVitD group (41.9±8.9 *vs* 19.4±5.2, $p<0.05$). Interestingly SD and WDVitD rats were not diabetic (98.7±8.0 and 103.2±6.1, respectively) while all rats in WD group were diabetic (139±9.6) with glycemic values significantly higher than SD ($p<0.01$) and WDVitD ($p<0.05$).
CONCLUSION: These results suggest that a daily supplementation of vitamin D3 is able to improve insulin sensitivity and to prevent the development of diabetes and hepatic steatosis in WD rats.
Disclosure of Interest: None declared

P0027 INVOLVEMENT OF SPHINGOMYELIN METABOLISM IN THE DEVELOPMENT OF NAFLD AND INSULIN RESISTANCE

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INTRODUCTION: Sphingomyelin (SM) is a major component in lipid microdomains, and SM is synthesized from ceramide by the action of SM synthase (SMS). We have recently reported that mice deficient for SMS2 are resistant to high fat diet-induced obesity, fatty liver and insulin resistance (J Biol Chem 2011:286;28544). In this study, we examined the relationship between SM and ceramide molecular species and the development of NAFLD and insulin resistance in human.
AIMS & METHODS: Non-alcoholic students of our university with body mass index (BMI) $\geq$ 35 kg/m^2 at the regular physical checkup in 2013 were enrolled, and volunteer students with BMI of 20-22 kg/m^2 were set as a control group. Serum levels of SM and ceramide containing saturated (C14:0, C16:0, C18:0, C20:0, C22:0 and C24:0) and unsaturated (C16:1, C18:1, C20:1, C22:1 and C24:1) fatty acids were measured using LC/MS/MS. Serum levels of liver enzymes, lipids and insulin resistance were measured by blood examination. Abdominal ultrasound was performed to confirm the existence of fatty liver, and body composition including percent body fat (PBF) was measured by bioimpedance analysis.
RESULTS: The levels of total SM and ceramide were not altered in obese group (19-28 y.o., n = 12), compared with control group (18-27 y.o., n = 11). The concentrations of SM C18:0 and C24:0 in the obesity group were significantly higher than in the control group. Moreover, in the obese group, SM C20:0 and C22:0 tended to be higher than in the control group. In the analysis of total 23 cases, the serum levels of SM containing saturated fatty acids positively correlated with PBF, ALT, ChE, LDL-C, TG and HOMA-R. However, SM species containing unsaturated acyl chain and almost all ceramide species did not correlate with those items.
CONCLUSION: The present study demonstrated that the serum levels of SM species containing saturated fatty acids (C18:0, C20:0, C22:0 and C24:0) are correlated with liver function and insulin resistance, suggesting that distinct SM species are involved in the development of NAFLD and insulin resistance.
Disclosure of Interest: None declared

P0028 GOOD CORRELATION BETWEEN PLASMA CYTOKERATIN-18 AND CONTROLLED ATTENUATION PARAMETER (CAP) IN HEALTHY POPULATION

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INTRODUCTION: Liver steatosis measurement by controlled attenuation parameter (CAP) is a non-invasive method for diagnosing steatosis, based on transient elastography. Plasma caspase-generated cytokeratin-18 fragments (CK-18) have been proposed as a non-invasive alternative for the diagnosis of NAFLD, especially NASH.
AIMS & METHODS: Aims: compare CK-18 serum levels in apparently healthy individuals with and without steatosis. **Methods:** Recruitment from a prospective epidemiological study of the general Portuguese adult population. Steatosis evaluated using CAP and ultrasound. Performance of CK-18 for diagnosing steatosis compared with US and CAP was assessed using AUROC.
RESULTS: 146 individuals studied (60% male), mean age and BMIs (body mass index) were 52.6±17.1 years and 28.2±4.9 kg/m2, respectively; 25% had a normal BMI, 46% were overweight and 29% were obese. Prevalence of steatosis on ultrasound was 52.1%.
The mean (SD), median (minimum-maximum), and 5th and 95th percentile values of CK-18 values were 73.4 (67.7), 57.6 (25-508), 25 and 220.1 U/L, respectively. Median CK-18 were elevated in patients with vs. without hepatic steatosis by ultrasound: 33.4 [IQR: 25–151] vs. 73.7 [IQR: 25–508] U/L, p < 0.0001.
CK-18 significantly correlated with steatosis (ρ = 0.40), ALT (ρ = 0.40), CAP (ρ = 0.38), triglyceride (ρ = 0.32), waist circumference (ρ = 0.30), HDL (ρ = -0.28), AST (ρ = 0.27), LDL (ρ = 0.26), total cholesterol (ρ = 0.21) and the number of metabolic syndrome criteria (ρ = 0.29), but not with LSM or BMI.
The CK-18 AUROC to predict steatosis using ultrasound and CAP (cut-offs of 243 dB/m) were 0.78 (95% CI = 0.71–0.86) and 0.74 (95% CI = 0.65–0.82), respectively.
CONCLUSION: In the absence of steatosis, CK-18 serum levels were below 151, with a very large range. It showed a good discriminating capacity for diagnosing steatosis.
Support: Cerega/SPG; Bolsa APEF, Roche Farmacêutica; Gilead Sciences
Disclosure of Interest: None declared

P0029 PREVALENCE OF HEPATIC STEATOSIS IN THE GENERAL PORTUGUESE POPULATION: USING FATTY LIVER INDEX (FLI) AND ULTRASOUND

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INTRODUCTION: The fatty liver index (FLI) derived from an Italian population includes serum triglycerides, serum gamma-glutamyltransferase, body mass index (BMI) and waist circumference. It has been used as a noninvasive measure of hepatic steatosis (HS), but has not been widely validated and not examined in the Portuguese population.
AIMS & METHODS: Estimate the prevalence of HS in the Portuguese adult population by fatty liver index (FLI) and correlate with the ultrasound findings; validate FLI for prediction of fatty liver in the Portuguese population.
Methods: Recruitment from a prospective epidemiological study of the general Portuguese adult population. Steatosis evaluated using ultrasound (US) and FLI. Performance of FLI for diagnosing steatosis compared with US was assessed using AUROC.
RESULTS: We studied 950 subjects, 50.5% men. The mean age, waist circumference and BMIs were 50.5±18.4 years, 94.4±12.7 cm and 26.9±4.7 kg/m2, respectively; 43% were overweight and 22% were obese. The median of FLI was 38.1. Ultrasound was performed in 411 subjects, showing fatty liver in 35%. Using the FLI, 27.6% of subjects had HS (FLI > 60), 41.8% had no HS (FLI < 30) and 30.6% were not classifiable (FLI 30-60). However, these cut-offs proposed by Bedogni appears to be inappropriate as 11.5% of subjects with FLI <30 exhibited HS on ultrasound and 13.4% of subjects with FLI > 60 showed no steatosis. For the FLI, the area under the ROC curve was 0.88 for the diagnosis of HS.
There was a significant correlation (p < 0.01) between the FLI and the following variables: weight (ρ = 0.80), waist circumference (ρ = 0.74), presence of steatosis (ρ = 0.65), triglycerides (ρ = 0.58), BMI (ρ = 0.51), ALT (ρ = 0.43), GGT (ρ = 0.39), HDL (ρ = -0.36), age (ρ = 0.33), female sex (ρ = -0.33), insulin (ρ = 0.29), AST (ρ = 0.28), LDL (ρ = 0.24) and total cholesterol (ρ = 0.22). No correlation was found with physical activity.
CONCLUSION: FLI could accurately identify hepatic steatosis in the general Portuguese population. The calculation of FLI may be useful to suggest the possibility of the presence of steatosis and indicate the need for an abdominal ultrasound.
Support: Cerega/SPG; Bolsa APEF, Roche Farmacêutica; Gilead Sciences
Disclosure of Interest: None declared

P0030 "NORMAL" CONTROLLED ATTENUATION PARAMETER (CAP) VALUES: A POPULATION-BASED STUDY OF HEALTHY SUBJECTS

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INTRODUCTION: Liver steatosis measurement by controlled attenuation parameter (CAP) is a non-invasive method for diagnosing steatosis, based on transient elastography. The normal range of controlled CAP values needs to be explored in clinical and anthropometrically diverse healthy subjects. A recent study has shown an association of CAP with BMI and the number of metabolic syndrome criteria.
AIMS & METHODS: Aim: define the normal range of CAP values in healthy subjects and evaluate the associated factors.
Methods: Recruitment from a prospective epidemiological study of the general Portuguese adult population. CAP was performed using Fibroscan in 134 healthy subjects, without fatty liver on ultrasonography or positivity serology for HBsAg, anti-HBc and anti-HCV, and normal aminotransferase levels.
RESULTS: From 134 consecutive individuals studied (66 males), 4 were excluded due to failure/unreliable liver stiffness measurements (LSM). The mean age and BMIs (body mass index) were 46.9±18.0 years and 24.9±3.5 kg/m2, respectively; 50% had a normal BMI, 43% were overweight and 7% were obese. The mean (SD), median (minimum-maximum), and 5th and 95th percentile values of CAP values were 202.29 (48.4), 205.5 (100.0-297.0), 108.2 and 276.3 dB/m, respectively. Men had a higher mean CAP value than women (mean±SD: 213.1±47.1 dB/m versus 191.8±47.8 dB/m, respectively; p = 0.012).
CAP significantly correlated with gender (ρ = 0.22), age (ρ = 0.22), waist circumference (ρ = 0.33), BMI (ρ = 0.22), alcohol consumption (ρ = 0.25), systolic blood pressure (ρ = 0.27), ALT (ρ = 0.27), fasting glucose (ρ = 0.24) and the number of metabolic syndrome criteria.
After allowance for potential confounders, CAP was not independently associated with BMI or other risk factors for nonalcoholic fatty liver disease.
CONCLUSION: CAP values vary between 108.2 and 276.3 dB/m in healthy subjects and is not associated with BMI or the number of metabolic syndrome criteria.
Support: Cerega/SPG; Bolsa APEF, Roche Farmacêutica; Gilead Sciences
Disclosure of Interest: None declared

P0031 EFFECT OF LANREOTIDE ON POLYCYSTIC LIVER AND KIDNEY GROWTH IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: AN OBSERVATIONAL TRIAL

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INTRODUCTION: Several trials have demonstrated that somatostatin analogues decrease liver volume in mixed populations of patients with autosomal dominant polycystic kidney disease (ADPKD) and isolated polycystic liver disease. Chronic renal dysfunction in ADPKD may affect treatment efficacy of lanreotide and possibly enhances risk for adverse events.
AIMS & METHODS: The aim of this open-label clinical trial (RESOLVE trial) was to assess efficacy of 6 months lanreotide treatment 120 mg subcutaneously every 4 weeks in ADPKD patients with symptomatic polycystic liver disease. We excluded patients with an estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73m^2. Primary outcome was change in liver volume, secondary outcomes were changes in kidney volume, eGFR, symptom relief and health-related quality of life (Euro-Qol5D). We used the Wilcoxon signed-rank test or paired two-sided t-test to analyze within-group differences.
RESULTS: We included 43 ADPKD patients with polycystic liver disease (84% female, median age 50 years, mean eGFR 63 ml/min/1.73m^2). Median liver volume decreased from 4,859 ml to 4.595 ml (-3.1%;$p<0.001$), and median kidney volume decreased from 1.023 ml to 1.012 ml (-1.7%;$p=0.006$). eGFR declined 3.5% after the first injection and remained stable up to study end. Lanreotide significantly relieved postprandial fullness, shortness of breath and abdominal distension, but had no effect on any of the EuroQol-5D dimensions. Three participants had a suspected episode of hepatic or renal cyst infection during the study.
CONCLUSION: Lanreotide reduced polycystic liver and kidney volumes and decreases symptoms in ADPKD patients. Moreover, eGFR decreased acutely after starting lanreotide, but stabilized thereafter.
Disclosure of Interest: None declared

P0032 THE EFFECTS OF POLY-UNSATURATED FATTY ACIDS (PUFAS) IN A RODENT NUTRITIONAL MODEL OF NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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INTRODUCTION: NAFLD and subsequent NASH are probably the most common chronic liver diseases in western countries and have a high risk of development of liver cirrhosis associated with high morbidity and mortality.
AIMS & METHODS: The aim of the study was to determine effects of administration of PUFAs in the MCD dietary model of NASH and to assess the potential anti-inflammatory role of PUFAs in the pathogenesis of NASH.
For 6 weeks were male mice fed either with MCD or with chow. There were 4 groups of animals. Both experimental and control groups received from the beginning either PUFAs or saline. Detailed liver histology, serum biochemistry, total lipid and fatty acids compound, adiponectin and leptin levels were determined. Expressions of mRNA of key pro- and anti-inflammatory cytokines were measured.
RESULTS: Feeding with MCD resulted in histopathological changes of NAFLD/NASH and these changes were ameliorated in PUFAs-group (MP). Administration of PUFAs led to significant decreases of total animal and liver weight in MP. PUFAs also decreased cholesterol levels ($P<0.001$), ALT ($P<0.01$) and AST levels ($P<0.01$). MP developed significantly less pro-inflammatory cytokine profile, had lower leptin ($P<0.01$) and higher adiponectin levels ($P<0.01$) than controls. Administration of PUFA led also to lower serum concentrations of saturated and monounsaturated FA and to higher serum concentrations of polyunsaturated FA in MP. Total lipid content of liver was significantly lower in MP.
CONCLUSION: We conclude that PUFAs may play a causal role in the pathophysiology of NASH. In summary, PUFAs have favorable effects on histopathological changes, serum markers of liver damage, fatty acid compound and show anti-inflammatory properties. We expect that PUFAs may represent a promising way in prevention and treatment of this increasingly common disorder.
Disclosure of Interest: None declared

P0033 DYSBIOSIS SIGNATURE OF FECAL MICROBIOTA IN HUMANS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD) is characterized by a broad spectrum of hepatic pathology that is closely linked to obesity and ranges from simple steatosis (SS), to non-alcoholic steatohepatitis (NASH) and even cirrhosis. NAFLD is recently believed to be under the influence of the gut microbiota, which may have toxic effects on the human host after intestinal absorption and delivery to the liver via the portal vein.
AIMS & METHODS: We explored the composition of gut bacterial communities of NAFLD and healthy subjects using 16S ribosomal RNA Illumina next-generation sequencing.
RESULTS: Partial least-squares discriminant analysis (PLS-DA) indicated that most of the microbiota samples were clustered by disease status. Differences were abundant at phylum, family, and genus levels between NAFLD and healthy subjects. *Lentisphaerae* at phylum level was significant higher in NAFLD microbiota. Among those taxa with greater than 0.1% average representation in all samples, five genera including *Alistipes* and *Prevotella* were the genus types exhibiting significant higher level in healthy microbiota, while genera *Escherichia*, *Anaerobacter, Lactobacillus* and *Streptococcus* were increased in NAFLD microbiota. In addition, lymphocyte profiles ($CD4^+$T cell and $CD8^+$T cell) and proinflammatory cytokines (TNF-α, IL-6 and IFN-γ) in gut biopsies of patients and healthy controls was analyzed to monitor the inflammation caused by dysbiosis microbiota. The levels of $CD4^+$ T cells and $CD8^+$ T cells were lower in NAFLD patients compared with healthy subjects, and the proinflammation cytokine TNF-α, IL-6 and IFN-γ showed high level in NAFLD patients. What was more, irregular arrangements of microvilli and widening of the tight junction were observed in gut mucosa of the NAFLD patients by transmission electron microscope.
CONCLUSION: The increased abundance of dysregulated bacteria in NAFLD microbiota, decreased numbers of $CD4^+$T cells and $CD8^+$T cells, and increased levels of TNF-α, IL-6 and IFN-γ in gut mucosa of NAFLD patients suggest a role for gut microbiota in the gut inflammation and the dysregulated gut immunity, which promote pathogenesis of NAFLD. We postulate that the distinct composition of the gut microbiome among NAFLD and healthy controls could offer a target for intervention or a marker for disease.
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Disclosure of Interest: None declared

P0034 ASCITIC FLUID LACTOFERRIN FOR DIAGNOSIS OF SPONTANEOUS BACTERIAL PERITONITIS

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INTRODUCTION: The diagnosis of spontaneous bacterial peritonitis (SBP) is based on a manual count of ascitic fluid polymorphonuclear cells (PMNs). This procedure is operator-dependent and lysis of PMNs during transport to the laboratory may lead to false-negative results. Furthermore, ascitic fluid culture is insensitive and leads to delays in diagnosis. The aim of this study was to assess the utility of ascitic fluid lactoferrin (AFLAC) for the diagnosis of SBP and to identify a cut-off level that can be used for future development of a rapid bedside test.
AIMS & METHODS: Sixty ascites samples from cirrhotic patients were examined for PMN count, bedside culture, and lactoferrin concentration. AFLAC concentrations were determined using a polyclonal antibody-based enzyme-linked immunosorbent assay. An ascitic fluid PMN count of 250 cells/mL or greater with or without a positive culture was used for diagnosis of SBP.
RESULTS: Fifteen (25%) samples fulfilled diagnostic criteria for SBP. Samples with SBP had a significantly higher lactoferrin concentration (median, 3200 ng/mL; compared with non-SBP samples (median, 39 ng/mL $P < .001$). The sensitivity and specificity of the assay for diagnosis of SBP were 95.5% and 97%, respectively. The area under the receiver operating characteristic curve was 0.98.
Conclusions: AFLAC can serve as a sensitive and specific test for diagnosis
CONCLUSION: AFLAC can serve as a sensitive and specific test for diagnosis of SBP. Qualitative bedside assays for the measurement of AFLAC can be developed easily and may serve as a rapid and reliable screening tool for SBP in patients with cirrhosis.
Disclosure of Interest: None declared

P0035 MODULAR COMPUTER-AIDED DIAGNOSIS AND PREDICTION SYSTEM FOR EARLY HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS

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INTRODUCTION: Hepatocellular carcinoma (HCC) is one of the most complex treatable malignancies as its management is dependent on the stage of the underlying condition – liver cirrhosis. An early diagnosis assures best curative chances, as liver resection or transplantation have good survival rates in the general population. Computer aided diagnostic and prognosis (CADP) models are currently being developed for a number of malignancies to help clinicians manage cases based on individual needs of the patients rather than general statistics.
AIMS & METHODS: Our aim was to develop a CADP based on our previous work involving artificial neural networks (ANN) [1] for successfully diagnosing early HCC cases and better prognosticate their evolution, based on a set of criteria in accordance with current guidelines.
Ethical clearance was obtained from the local board and 107 consecutive patients with previously diagnosed liver cirrhosis signed informed consents for entering the study, between January 2009 and February 2010. Clinical and demographic parameters (age, sex, body mass index, waist circumference, type of viral

infection, alcohol consumption, smoking, clinical ascites, jaundice), laboratory data (AST, ALT, GGT, alkaline phosphate, bilirubin, triglycerides, thrombocyte count, prothrombin time, alpha fetoprotein), ultrasound data (portal vein thrombosis, size and number of possible tumors), elastography data (strain ratio, complexity, kurtosis, skewness, contrast, entropy, inverse difference moment, angular second moment, correlation) and stiffness value (FibroScan) were collected and imputed in the CADP. For patients with clear liver tumors contrast-enhanced ultrasound was performed and time-intensity curve parameters were calculated and fed to the ANN system: peak enhancement, time to peak, rise time, fall time, mean transit time, area under the curve. We have followed the 4-year incidence of HCC patients in tumor-free cases and assessed the evolution when any formation, either regeneration nodule or early HCC was found.

RESULTS: We found liver tumors in 21 patients; 12 were regeneration nodules [median number of tumors per patient: 2 (min: 1, max: 5), median size 1.1 cm (min: 0.4, max: 1.6)] and 9 were early HCC [median number of tumors per patient: 1 (min: 1, max: 2), median size 1.8 cm (min: 0.7, max: 2.4)]. The CADP system correctly diagnosed HCC in all 9 cases and in 8/12 regeneration nodules based on clinical, laboratory and imaging data. A total of 28 patients also developed HCC in the four-year follow-up period; the system correctly predicted high possibility for HCC occurrence in 26 of these patients (92.85%), while giving high estimates for HCC in another 16 patients that remained cancer-free until now.

CONCLUSION: We could successfully predict the rate of malignancy in cirrhotic patients by using a novel CADP system. We believe that such tools may become worthy aids to clinical management of patients with various types of digestive pathologies.

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Disclosure of Interest: None declared

P0036 POSTOPERATIVE RESOURCE UTILIZATION AND SURVIVAL AMONG LIVER TRANSPLANT RECIPIENTS WITH A MELD SCORE GREATER THAN OR EQUAL TO 40: A RETROSPECTIVE COHORT STUDY

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INTRODUCTION: Cirrhotic patients with Model for End-stage Liver Disease (MELD) score ≥40 have high risk of death without liver transplant (LT). This study aimed to evaluate these patients' outcomes after transplant.

AIMS & METHODS: The retrospective cohort included 519 adult cirrhotic patients who underwent LT at one Canadian center between 2002 and 2012. Primary exposure was severity of end-stage liver disease measured by MELD score at transplant (≥40 vs. <40). Primary outcome was duration of first intensive care unit (ICU) stay after LT. Secondary outcomes were duration of first hospital stay after LT, rate of ICU readmission, re-transplant rate, and survival rates.

RESULTS: On the day of LT, 5% (28/519) of patients had a MELD score ≥40. These patients had longer first ICU stay after LT (14 vs. 2 days; $p < 0.001$). MELD score ≥40 at transplant was independently associated with first ICU stay after transplant ≥10 days (OR, 3.21). These patients had longer first hospital stay after LT (45 vs. 18 days; $p < 0.001$); however, there was no significant difference in the rate of ICU readmission (18% vs. 22%; $p = 0.58$) or re-transplant rate (4% vs. 4%; $p = 1.00$). Cumulative survival at 1 month, 3 months, 1 year, 3 years, and 5 years was 98%, 96%, 90%, 79%, and 72%, respectively. There was no significant difference in cumulative survival stratified by MELD score ≥40 vs. <40 at transplant ($p = 0.59$).

CONCLUSION: Cirrhotic patients with MELD score ≥40 at transplant utilize greater postoperative health resources; however, derive similar long-term survival benefit with LT.

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Disclosure of Interest: None declared

P0038 DISTINGUISHING NASH CIRRHOSIS FROM NON-CIRRHOTICS BY URINE VOLATILE ORGANIC COMPOUND ANALYSIS - A PILOT STUDY

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INTRODUCTION: There is a quest for biomarker discovery in liver disease especially to detect cirrhosis at an early stage. Current methods are invasive, more often requiring a liver biopsy to confirm the diagnosis. For patients with Non-alcohol related Steatohepatitis (NASH), the use of fibroscan whilst generally helpful, is unable to confirm the presence of fibrosis particularly in the presence of fat within the liver which is inevitable in most cases with NASH.

The gut microbiome is altered in several gastrointestinal disorders, resulting in altered gut fermentation patterns, which we (and others) have been able to recognise by analysis of volatile organic compounds (VOC) in urine, breath and faeces[1]. The altered structure of the small intestinal mucosa and increased gut permeability (noted in liver disease), we hypothesised, would also change the microbiome, hence recognisable by its unique "fermentome" pattern, making NASH distinguishable from controls.

AIMS & METHODS: To determine if NASH results in an altered VOC pattern in the urine, detectable by ion mobility spectrometry (FAIMS), and distinguishable from cirrhotics vs non-cirrhotics.

33 patients were recruited; 8 with NASH cirrhosis; (confirmed histologically), 8 with non-cirrhotic NASH; 5 with NAFLD (non-alcohol fatty liver disease) and 12 controls (normal synthetic liver function). Urine was collected and 10 ml aliquots were stored frozen in universal containers. For assay, the containers were first heated to 40 ± 0.1°C. The headspace (the air above the sample) was then pumped from the containers and analysed by Field Asymmetric Ion Mobility Spectrometry (FAIMS). Linear discriminant analysis (LDA) was used for initial statistical evaluation, with a re-classification using a "leave one out" for calculating sensitivity and specificity.

RESULTS: LDA showed that FAIMS is able to distinguish the VOC pattern in these different groups of liver disease. The control group was significantly different to all of the other groups with a sensitivity of 100%. Of the disease groups, NASH and NASH with cirrhosis had sensitivity of 83% and 77% respectively with specificity of 80%. NAFLD however had sensitivity of 50% but specificity of 80%.

CONCLUSION: This pilot study suggests the IMS (FAIMS – technology) offers a novel non-invasive approach to separate not only NASH from controls but also those with established cirrhosis using urine. It offers the potential for early non-invasive tracking of NASH and its complications.

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P0039 ELASTOGRAPHY PLUS PLATELET COUNT RATHER THAN ENDOSCOPY TO SCREEN FOR LARGE OESOPHAGEAL VARICES

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INTRODUCTION: Endoscopic screening for gastro-oesophageal varices (GOV) is currently recommended for all cirrhotic patients. Noninvasive methods for liver fibrosis assessment are identifying increasing numbers of patients with "cirrhosis-range" liver stiffness measurements (LSM), increasing the number of referrals for screening endoscopy. The identification of simple non-invasive markers for the presence/absence of large gastroesophageal varices (GOV) would be clinically useful. We evaluated the performance of liver stiffness measurement (LSM) ± platelet count to identify the presence of large GOV in patients with Child Pugh (CP) A cirrhosis.

AIMS & METHODS: Data were collected retrospectively. The presence of cirrhosis was defined by LSM > 13.6 kPa using elastography. We performed a database search for patients with LSM > 13.6 kPa who underwent screening gastroscopy (2010 – 2013). Only patients with compensated liver disease were included. Large GOV were defined by diameter > 5mm or the presence of high risk stigmata. We assessed the accuracy of LSM, platelet count (Pl) or the combination of these factors to identify patients with large GOV. A training set of 71 patients was used, and results were validated using a second cohort of 201 patients from two independent centres.

RESULTS: The combination of LSM and Pl was more accurate for identifying CSPH than either marker alone (training cohort AUROC: 0.87 [0.77-0.94] vs. 0.78 [0.66 – 0.87] and 0.77 [0.66-0.86] for LSM or Pl alone). The optimal risk score was 0.11 (Sens = 0.88, Spec = 0.77, PPV = 0.33, NPV = 0.98, accuracy = 78%). Results in the validation cohort confirmed the discriminatory power of this model (AUROC: 0.76 [0.68-0.83]). We then tested clinically relevant cut-offs to improve the negative predictive value (NPV) for large GOV. The NPV for the combination of LSM < 25 kPa and Pl ≥ 100 and was 100% in both the training cohort and validation cohort. 82 (42%) of patients overall met this criteria.

CONCLUSION: The combination of LSM < 25 kPa and Pl ≥ 100 can be used to identify patients with compensated cirrhosis who do not have large GOV. These patients do not benefit from endoscopic screening, but could be followed with annual LSM and full blood count.

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P0040 PATIENTS EXPERIENCING REPEATED EPISODES OF HEPATIC ENCEPHALOPATHY HAVE INCREASING RISK OF SUBSEQUENT EPISODES. A POST HOC ANALYSIS OF RIFAXIMIN-A OPEN LABEL STUDY DATA

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INTRODUCTION: Hepatic encephalopathy (HE) is a chronic complication of cirrhosis. In recurrent, overt, episodic HE, which is the most common subcategory, its seriousness is due to the chronic debilitating effects of the recurrent episodes.
AIMS & METHODS: The aim of this study was to characterise the impact of the number of prior HE episodes on the risk of future HE episodes. A post-hoc analysis was carried out using data from 322 patients with a history of HE from a phase 3, open-label study evaluating the long-term safety and tolerability of rifaximin-α 550mg BID. All eligible patients had a Conn score of 0–2 at enrolment, and had either successfully participated in a previous HE study with rifaximin-α (RFHE3001), or they were new patients enrolled with $\geq$1 verifiable episode of HE within the preceding 12 months.
RESULTS: 319 of 322 patients (647 observations) aged $\geq$18 years had all the information required for analysis. Median duration of follow-up was 17 months (IQR 8.9–25.4). Stratifying patient observations by number of prior HE episodes and using the Kaplan Meier method the probability of being event free at year one was 0.644 (95% CI; 0.543-0.763), 0.615 (0.541-0.700), 0.396 (0.303-0.518) and 0.302 (0.246-0.371) and the probability at year two was 0.579 (0.469-0.713), 0.539 (0.455-0.638), 0.292 (0.1999-0.428) and 0.218 (0.163-0.290) for 'one', 'two', 'three' and 'four or more' prior HE episodes, respectively. Plotting the Kaplan Meier curves of time to next HE episode, stratified by the number of prior HE episodes, a clear association between decreased time to next HE episode and increased number of prior episodes was seen. Using log-rank tests, there was no significant difference between the survival curves of one prior and two prior HE episodes ($\chi^2 = 0$ on 1 degree of freedom (d.f.), $p = 0.899$), however there were significant differences between survival curves of one prior or two prior episodes and greater numbers of prior episodes ($\chi^2 = 72$ on 3 d.f., $p < 0.001$).
CONCLUSION: This study supports the current understanding of the natural history of end-stage encephalopathy; as the number of prior HE episodes increased, the risk of subsequent HE episodes increased.
Disclosure of Interest: C. Bannister Consultancy for: Norgine, P. Conway Other: Employee of Norgine, A. Radwan Other: Employee of Norgine, K. Nanuwa Other: Employee of Norgine, C. Morgan Consultancy for: Norgine, E. Berni Consultancy for: Norgine, C. Currie Consultancy for: Norgine

P0041 NEW QUALITY CRITERIA FOR TRANSIENT ELASTROGRAPHY CAN INCREASE THE PROPORTION OF VALID MEASUREMENTS WITH HIGH ACCURACY FOR DETECTION OF LIVER CIRRHOSIS AND PORTAL HYPERTENSION

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INTRODUCTION: Transient elastography (TE) is a non-invasive, easily repeatable tool to assess liver fibrosis and portal hypertension (HVPG). Recently, new quality criteria for TE measurements have been proposed (Boursier et al. Hepatology 2013): very reliable: IQR/M $<$0.1; reliable: IQR 0.1–0.3, or IQR/M $>$0.3 if TE $<$7.1 kPa; poor reliable: IQR/M $>$0.3 if TE $>$7.1 kPa.
AIMS & METHODS: We evaluated the diagnostic power and accuracy of TE measurements according to these new quality criteria (accurate = very reliable + reliable) for non-invasive assessment of liver fibrosis (liver biopsy) and portal hypertension. Therefore we retrospectively identified patients undergoing TE, HVPG measurement and liver biopsy within 3 months at our tertiary care center.
RESULTS: Among 278 patients (48.7±13.1 years, 74.7% male, 75.7% viral etiology, 57% F3/F4), traditional TE quality criteria identified 71.6% reliable measurements, while new criteria yielded in 83.2% accurate LS measurements (23.1% very reliable, 60.1% reliable). Reliable TE values according to traditional or new criteria were all significantly and similarly strong correlated with fibrosis stage ($R = 0.648$ vs. $R = 0.636$) and HVPG ($R = 0.836$ vs. $R = 0.846$). The accuracy for diagnosing liver cirrhosis (F4, cut-off: 14.5 kPa) was 76.5% and 75.0% for traditional and new TE criteria, respectively. The positive (PPV) and negative (NPV) values for new criteria at the 14.5 kPa cut-off were 83% and 70%. For predicting HVPG $\geq$10mmHg (cut-off: 16.1 kPa), the accuracies were 88.9% and 89.8% using traditional or new criteria, respectively. Both criteria resulted in AUCs for diagnosis of HVPG $\geq$10mmHg of over 0.95 with a PPV and NPV of 76% and 97%, respectively.
CONCLUSION: Applying new quality criteria for TE measurements significantly increases the number of valid TE measurements without affecting accuracy of TE for diagnosis of liver cirrhosis and portal hypertension.
Disclosure of Interest: None declared

P0042 EVALUATION OF A NOVEL, PORTABLE, PROBE-BASED TRANSNASAL ENDOSCOPE: SUPERIOR PATIENT PREFERENCE AND ACCEPTABLE DIAGNOSTIC ACCURACY FOR OESOPHAGEAL VARICES COMPARED TO CONVENTIONAL ENDOSCOPY

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INTRODUCTION: Conventional oesophagogastroduodenoscopy (C-OGD) remains the gold standard test to screen for oesophageal varices (OV) in patients with liver cirrhosis. However, it has many limitations in terms of costs, accessibility and tolerability. Hence, there is a need for less invasive and simple techniques to replace C-OGD in this setting.
AIMS & METHODS: We aimed to compare the accuracy and acceptability of a portable, disposable, office-based, unsedated transnasal video endoscope (EG Scan™ II) with C-OGD for the detection of OV.
This was a prospective diagnostic study. Consecutive adult patients with confirmed liver cirrhosis, scheduled for screening or surveillance of OV, were invited to participate in this study. We excluded patients with recurrent epistaxis (more than once a week); nasal obstruction; disease of the nasal cavity; history of variceal bleeding or band ligation therapy in the past 12 weeks. All subjects underwent two procedures on the same day (EG Scan followed by C-OGD), performed by two different operators blinded to the findings of the other test. Patients completed validated tolerability (10-point visual analogue scale (VAS)) and adverse events questionnaires on day 0 and day 14.
The primary outcome measure was diagnostic accuracy of EG scan (performed by one operator) against C-OGD (reference standard). In addition, interobserver agreement of the EG scan was calculated using the kappa (k) statistic, by nine blinded endoscopists, evaluating video recordings of 47 EG Scan procedures.
RESULTS: 50 patients were recruited to the study (mean age 59 years +/-11, 70% males). The majority (78%) had compensated cirrhosis. 45 patients (90%) completed both procedures (3 failed EG Scan (6%) and 2 failed C-OGD (4%), $p = 0.882$). OV prevalence was 48.9%.
Sensitivity, specificity and area under the receiver operating characteristic curve (AUROC) of the EG Scan for the diagnosis of any varices were 0.82 (95% confidence interval (CI) 0.60-0.95), 0.78 (95%CI 0.56-0.93), and 0.80 (95%CI 0.68-0.92), respectively. Corresponding values for the diagnosis of medium/large varices were 0.92 (95%CI 0.62-1.0), 0.97 (95%CI 0.84-1.0), and 0.94 (95%CI 0.86-1.0), respectively. Interobserver agreement was modest for the diagnosis of any size OV ($K = 0.45$, 95%CI 0.40-0.49) and medium/large OV ($K = 0.47$, 95%CI 0.42-0.52).
Patients reported better experience (mean VAS+/-standard deviation (SD)) and higher preference (percentage) with EG Scan compared to C-OGD at day 0 (7.8+/-2.2 vs. 6.8+/-3.0, $p = 0.058$; 76.5% vs. 23.5%, $p < 0.001$, respectively) and day 14 (7.0+/-2.3 vs. 5.5+/-3.2, $p = 0.0013$; 77.8% vs. 22.2%, $p < 0.001$, respectively). There was no association between procedure preference and sedation use for C-OGD (day 0: odds ratio (OR) 0.16, 95%CI 0.02-1.49, $p = 0.106$; day 14: OR 0.24, 95%CI 0.02-2.56, $p = 0.238$). 4 patients (8.5%) experienced minor self-limiting epistaxis. No serious adverse events occurred.
CONCLUSION: EG Scan was accurate for the diagnosis of any varices and clinically significant OV. Interobserver agreement was modest. More importantly, patients' experience and preference remained significantly higher for EG Scan 14 days after procedures independent of sedation use.
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P0043 NONINVASIVE PREDICTIVE MODEL FOR DETECTION OF HIGH-RISK ESOPHAGEAL VARICES IN B-VIRAL LIVER CIRRHOSIS: THE PH RISK SCORE AND VARICES RISK SCORE

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INTRODUCTION: Periodic endoscopic screening for esophageal varices (EVs) and prophylactic treatment for high-risk EVs ((HEVs); (1) medium/large EVs and (2) small EVs with red sign or decompensated cirrhosis) are currently recommended for all cirrhotic patients. Recently, two new liver stiffness measurement (LSM)-based statistical equation models (PH risk score and Varices risk score) were introduced as a noninvasive, simple, accurate models for identifying presence of EVs and clinically significant portal hypertension [1].
AIMS & METHODS: We aimed to validate predictive value of the two models for detection of HEVs comparing with LSM alone or LSM-spleen diameter to platelet ratio score (LSPS) [2]. We tried to suggest a cutoff of the two models, as well.
Between November 2004 and October 2011, we recruited 675 B-viral cirrhosis patients. All underwent laboratory workups, endoscopy, LSM, and ultrasonography. LSM was measured by transient elastography; endoscopy was used as the standard for detection of EVs. PH risk score, Varices risk score and LSPS were calculated in all cases as follows: PH risk score = -5.953 + 0.188 x LSM + 1.583 x sex (1: male; 0: female) + 26.705 x spleen diameter/platelet count ratio,

Varices risk score = -4.364 + 0.538 x spleen diameter – 0.049 x platelet count – 0.044 x LSM + 0.001 x (LSM x platelet count).
RESULTS: Among all the patients, 239 (35.4%) patients had EVs and 172 (25.5%) had HEVs. The area under the receiver-operating characteristic curve (AUROC) of PH risk score was 0.951 (95% CI 0.934-0.968) and LSPS was 0.950 (95% CI 0.931-0.970), showing superiority of diagnostic accuracy over other factors: Varices risk score (0.907, 95% CI 0.876-0.939, $p<0.001$), LSM alone (0.873, 95% CI 0.842-0.904, $p<0.001$). At PH risk score < 4.0, 94.6% negative predictive value (NPV) was provided (481 patients), whereas 94.3% positive predictive value (PPV) was achieved (70 patients) at PH risk score > 10.0. In the same way, at Varices risk score < -2.5, 95.6% NPV was provided (413 patients), whereas 91.7% PPV was achieved (72 patients) at Varices risk score > 1.3. Overall, the likelihood of HEVs was correctly diagnosed in 551 patients (81.6%) and 485 patients (71.9%), respectively.
CONCLUSION: The PH risk score is a reliable, noninvasive predictive model for detection of HEVs. Furthermore, the LSPS is considered as more simply applicable model having similar predictive value. Patients with PH risk score < 4.0 may avoid endoscopy safely, whereas those with > 10.0 should be considered for appropriate prophylactic treatments.
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Disclosure of Interest: None declared

P0044 PLALA SCORE PREDICT CIRRHOSIS PATIENT IN NONALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Nonalcoholic fatty liver disease (NAFLD) is an important cause of chronic and progressive liver injury in many countries[1)]. NAFLD includes a wide spectrum of liver diseases that range from simple steatosis, which is generally a nonprogressive condition, to nonalcoholic steatohepatitis (NASH), which can progress to liver cirrhosis and hepatocellular carcinoma (HCC), despite the absence of significant alcohol consumption. If NAFLD patients have liver cirrhosis, they need to be kept under surveillance for early detection of hepatocellular carcinoma and gastroesophageal varices. Liver biopsy is the gold standard for diagnosis and staging of fibrosis in patients with NAFLD[2)]. However, ad the number of NAFLD patients has reached 80–100 million in the United States and about 10 million NAFLD patients are estimated in Japan, it is virtually impossible to enforce in all patients.
AIMS & METHODS: To develop a mass screening system for general physicians, which can be used for predicting liver cirrhosis in NAFLD patients, using routine laboratory parameters.
A total of 1048 patients with liver-biopsy-confirmed NAFLD were enrolled from nine hepatology centers in Japan (stage 0, 216; stage 1, 334; stage 2, 270; stage 3, 190; stage 4, 38). Statistical analysis was conducted using SPSS version 12.0. Continuous variables were expressed as mean ± SD.
RESULTS: Platelet counts, serum albumin levels, and aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio were selected as independent variables associated with cirrhosis in NAFLD patients by multiple logistic regression analysis. The optimal cutoff value of platelet count, serum albumin, and AST/ALT ratio was set at $<15.3\ 10^4/\mu l$ (sensitivity; 81.6% specificity; 88.6%), <4.0 g/dl (sensitivity; 84.2% specificity; 84.6%), and >0.9 (sensitivity; 78.9%, specificity; 82.0%), respectively, by the receiver operating characteristic curve. These three variables were combined in an unweighted sum (platelet count = 1 point, serum albumin = 1 point, AST/ALT ratio = 1 point) to form an easily calculated composite score for predicting cirrhosis in NAFLD patients, called the PLALA (platelet, albumin, AST/ALT ratio) score. The diagnosis of PLALA ≥2 had sufficient accuracy for detecting liver cirrhosis in NAFLD patients (86.8% sensitivity, 90.8% specificity, 99.4% negative predictive value, 26.1% positive predictive value).
CONCLUSION: The PLALA score may be an ideal scoring system for detecting cirrhosis in NAFLD patients with sufficient accuracy and simplicity to be considered for clinical use.
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Disclosure of Interest: None declared

P0045 CARVEDILOL VERSUS NON-SPECIFIC BETABLOCKERS AND MORTALITY IN ALCOHOLIC CIRRHOSIS. A NATIONWIDE RETROSPECTIVE STUDY

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INTRODUCTION: Carvedilol may have a greater effect on portal and systemic hypertension than propranolol although reports are conflicting [1, 2]. The impact of carvedilol versus non-specific betablockers (NSBB) on mortality on patients with cirrhosis remains to be evaluated.
AIMS & METHODS: We wanted to compare the impact on mortality of carvedilol versus NSBB in patients with cirrhosis. We identified patients with alcoholic cirrhosis from the Danish National Patient Register during the period 1995 through 2010. We used the anatomical therapeutic chemical (ATC) classification to identify the user of NSBB (C07AA) or carvedilol (C07AG02). We defined risk time as the time from the first prescription of either carvedilol or NSBB until death or end of follow-up (December 31, 2010). We adjusted for gender, age, heart disease, variceal bleeding, socioeconomic status, Charlson score, and use of diuretics. We used univariate and multivariate Cox proportional hazard models to assess the HR. Persons with missing data were excluded from the analyses (0.03%). All analyses were done using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).
RESULTS: We identified 83 and 2.060 patients, who were treated with carvedilol and NSBB, respectively. Three patients had received both carvedilol and NSBB and were excluded. Patients from the carvedilol group were mainly classified with uncomplicated cirrhosis without a history of laparocentesis (96%). Hence, we only included patients with uncomplicated cirrhosis in our mortality analysis (80 versus 1.857 patients). Significantly fewer patients in the carvedilol group died during follow-up compared with the NSBB group (20.5% vs. 46.5%, Chi-square $p<0.0001$). We found the un-adjusted HR for carvedilol vs. NSBB to be 0.45 (95% CI 0.3-0.7) and the HR adjusted for covariates was 0.46 (95% CI 0.3-0.7). The prevalences of variceal bleeding (11% vs. 40%) or heart disease (70% vs. 14%) prior to cohort entry were un-evenly distributed between users of carvedilol and NSBB. We did a sub-analysis where we matched patients on the presence of heart disease and variceal prior to cohort entry. In this sub-analysis we compared 80 patients using carvedilol with 240 patients (1:3 ratio) using NSBB and found an adjusted HR of 0.38 (95% CI 0.2-0.7).
CONCLUSION: The use of carvedilol compared with NSBB in patients with cirrhosis was associated with lower mortality in this retrospective study.
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Disclosure of Interest: None declared

P0046 RESULTS OF THE UK MULTI-REGIONAL AUDIT OF BLOOD COMPONENT USE IN CIRRHOSIS

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INTRODUCTION: Cirrhosis is a complex acquired disorder of coagulation with a recent paradigm shift in understanding to consider cirrhosis as a pro-thrombotic disorder. It is a frequent indication for transfusion of blood components, both for prophylaxis and for treatment of bleeding, although indications and patterns of blood use are poorly characterised.
AIMS & METHODS: All NHS trusts with representation on the British Society of Gastroenterology membership list were invited to take part in a national audit. Data were collected prospectively on consecutive admissions with a confirmed diagnosis of liver cirrhosis over a 4 week period, with follow up to discharge/death/day 28. Specific information was requested on use of blood components, including indication, type of component and laboratory indices prior to transfusion. Standards were defined against guidelines on the use of red blood cells (RBCs), fresh frozen plasma (FFP), platelets and cryoprecipitate.
RESULTS: Data on 1313 consecutive patients with cirrhosis (mean age 58 years, 65% male) were collected from 85 hospitals. The predominant aetiology was alcohol (70%; 921/1313); 74% of admissions were for features of decompensation; and 21% (275/1313) cases had a positive septic screen. 30% (391/1313) of all admissions were transfused a blood component; in 61% (238/391) this was for treatment of bleeding and in 39% (153/391) for prophylaxis. In patients transfused for bleeding (81%, 192/238 for gastrointestinal bleeding), 92% (220/238) received RBCs, 32% (77/238) FFP, 14% (34/238) platelets and 4% (10/238) cryoprecipitate; in patients with bleeding who received RBCs, the Hb threshold was >8g/dL prior to RBC transfusion in 31% (69/220) cases. For prophylaxis the majority (61%, 94/153) received transfusion in the absence of a planned procedure. In patients transfused for prophylaxis prior to a procedure (59/153): 19% (3/16) received FFP at an INR ≤1.5 for high risk procedures and 33% (6/18) received FFP at an INR≤2 for low risk procedures; 36% (9/25) received platelet transfusion at a platelet count>50 prior to a procedure. The most frequent procedures resulting in prophylactic transfusion were paracentesis (18/59), surgery (15/59) and endoscopy (10/59). In-hospital venous thromboembolism was documented in 2% (29/1313) cases. Case fatality during follow up was 10% overall (128/1313) with decompensated cirrhosis (41%; 52/128) as the most frequent cause of death.
CONCLUSION: Patients with cirrhosis are frequently transfused during hospitalisation. This audit highlights areas where greater scrutiny of blood component use is required, particularly in the group transfused for prophylaxis of bleeding. Further work is needed to improve patterns of blood use in cirrhosis to ensure patients are not exposed to unnecessary transfusion and its attendant harms.
Disclosure of Interest: None declared

P0047 SVR12 OF 99% ACHIEVED WITH A RIBAVIRIN-FREE REGIMEN OF ABT-450/R/OMBITASVIR AND DASABUVIR IN HCV GENOTYPE 1B-INFECTED PATIENTS

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INTRODUCTION: ABT-450 is an HCV NS3/4A protease inhibitor (identified by AbbVie and Enanta) dosed with ritonavir (r). Ombitasvir (formerly ABT-267) is an NS5A inhibitor, and dasabuvir (formerly ABT-333) is a non-nucleoside NS5B RNA polymerase inhibitor. We report the sustained virologic response 12 weeks post-treatment (SVR12) achieved in HCV genotype 1b-infected patients after treatment with these 3 direct-acting antivirals (3D regimen) with or without ribavirin (RBV).
AIMS & METHODS: Five hundred ninety-nine treatment-naïve and prior pegIFN/RBV-experienced HCV genotype 1b-infected patients without cirrhosis were enrolled and received study drugs in the PEARL-II and PEARL-III randomized phase 3 studies. Patients were randomized 1:1 to co-formulated ABT-450/r/ombitasvir (150 mg/100 mg/25 mg once daily) and dasabuvir (250 mg twice daily) with or without weight-based RBV (1000 – 1200 mg daily).
RESULTS: The combined SVR12 rate from PEARL-II and PEARL-III was 99.3% in 301 patients who received 3D regimen without RBV vs. 98.7% in 298 patients who received 3D + RBV. Two patients (0.7%) receiving 3D without RBV did not achieve SVR12, both due to missing week 12 post-treatment follow-up. Four 3D + RBV patients did not achieve SVR12: 1 (0.3%) due to virologic breakthrough, 1 (0.3%) due to missing SVR12 data, and 2 (0.7%) due to study drug discontinuation for adverse events. SVR12 rates did not differ between 3D and 3D + RBV by baseline factors including IL28B genotype, sex, age, race, ethnicity, BMI, fibrosis stage, and HCV RNA viral load. No patients receiving 3D and 0.7% of patients receiving 3D + RBV discontinued due to adverse events.

SVR12 by baseline factors, n/N (%)	3D	3D + RBV
Overall	299/301 (99.3)	294/298 (98.7)
Treatment-naïve	208/210 (99.0)	209/210 (99.5)
PegIFN/RBV Treatment-experienced	91/91 (100)	85/88 (96.6)
IL28B non-CC genotype	249/250 (99.6)	240/244 (98.4)
Female	160/160 (100)	147/149 (98.7)
Age ≥65	34/34 (100)	29/29 (100)
Black race	16/16 (100)	13/13 (100)
BMI ≥ 30 kg/m^2	62/64 (96.9)	44/45 (97.8)
Fibrosis stage, F3	31/33 (93.9)	33/34 (97.1)

CONCLUSION: Irrespective of previous pegIFN/RBV treatment response and other baseline factors, HCV genotype 1b-infected patients achieved high SVR rates after 12 weeks of 3D without RBV. Overall, only 1 (3D + RBV) of 599 (0.2%) patients experienced virologic breakthrough and none experienced relapse. Both regimens were well tolerated. ABT-450/r/ombitasvir and dasabuvir without RBV achieves optimal treatment efficacy in HCV genotype 1b-infected patients without cirrhosis.
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P0048 ADHERENCE TO PRESCRIBED DOSES OF ABT-450/R/OMBITASVIR, DASABUVIR, AND RIBAVIRIN IN THE PHASE 3 PEARL-II, PEARL-III, AND PEARL-IV TRIALS

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INTRODUCTION: ABT-450 is an HCV NS3/4A protease inhibitor identified by AbbVie and Enanta, dosed with ritonavir(r); ombitasvir(ABT-267) is an NS5A inhibitor; dasabuvir(ABT-333) is an NS5B RNA polymerase inhibitor. The phase 3 PEARL trials examined the efficacy and safety of all-oral, interferon-free, 12-week regimens of ABT-450/r/ombitasvir+dasabuvir(3D) with or without ribavirin(RBV) in HCV genotype(GT) 1a- and 1b-infected patients(pts). We report pt adherence to the regimens in these trials.
AIMS & METHODS: Pts were randomized to co-formulated ABT-450/r/ombitasvir(150mg/100mg/25mg QD)+dasabuvir(250mg BID) with either weight-based RBV or placebo (PBO)/no RBV. Adherence was calculated by pill counts as the percentage of capsules/tablets taken relative to the total capsules/tablets expected to be taken.
RESULTS: In each trial, mean pt adherence to every study drug was >98.5%(Table). Adherence was comparable in those who received 3D with RBV, 3D with PBO, or 3D alone. SVR12 rates were 96.6-100% in treatment-experienced and treatment-naïve HCV GT1b-infected pts receiving 3D+/-RBV. SVR12 rates were 97.0% and 90.2%, respectively, in treatment-naïve GT1a-infected pts receiving 3D+RBV or 3D+PBO. Only 1 GT1b-infected pt had virologic failure. Pts with virologic failure had adherence rates comparable to the overall rates, but the majority was GT1a-infected and did not receive RBV. Five pts had adherence rates <80% for one or more study drugs, none of whom had virologic failure. Among 401 pts receiving 3D with RBV and 509 pts receiving 3D without RBV, 2(0.5%) and 2(0.4%), respectively, discontinued study drug due to adverse events.

	PEARL-II Treatment-experienced* GT1b		PEARL-III Treatment-naïve GT1b		PEARL-IV Treatment-naïve GT1a	
	3D+RBV	3D	3D+RBV	3D+PBO	3D+RBV	3D+PBO
Adherence, Mean % (SD)						
ABT-450/r/ ombitasvir	99.7 (2.3) n = 87	100.0 (2.6) n = 92	99.8 (1.2) n = 205	100.0 (1.1) n = 205	99.7 (1.9) n = 98	99.7 (3.3) n = 190
dasabuvir	99.0(3.2) n = 90	99.2 (1.6) n = 94	99.8 (1.2) n = 205	99.9 (1.1) n = 205	99.2 (2.0) n = 98	99.1 (3.6) n = 190
RBV	99.1 (6.5) n = 87	NA	99.6 (2.1) n = 205	99.6 (2.6) n = 203	98.6 (3.2) n = 90	98.7 (3.6) n = 181
SVR12, % (n/N)	96.6 (85/88)	100 (91/91)	99.5 (209/210)	99.0 (207/209)	97.0 (97/100)	90.2 (185/205)

Adherence data for each capsule/tablet not available for all pts.
In PEARL-II, 7 randomized patients were excluded from the intent-to-treat efficacy population because they received non-coformulated ABT-450/r/ombitasvir (N = 6) or could not be genotyped (N = 1).
CONCLUSION: Participants in these phase 3 trials had excellent adherence (>98.5%) to doses of ABT-450/r/ombitasvir, dasabuvir, and RBV. Low adherence rates, while infrequent, were not associated with virologic failure.
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P0049 ASSOCIATION BETWEEN TLR-3 GENE POLYMORPHISM RS3775291 AND PROGRESSION OF HEPATITIS C VIRUS INFECTION

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INTRODUCTION: Hepatitis C virus (HCV) is a major global health problem with about 210 million people infected worldwide, and constitutes the most important cause of chronic liver disease. HCV is an enveloped positive-strand RNA virus belonging to the genus *Hepacivirus* of the family Flaviviridae. During the viral replication cycle, double-stranded RNA (dsRNA), produced as an intermediate, is sensed by several pattern recognition receptors (PRRs) of the innate immune system including Toll-like receptors (TLR). TLRs constitute a family of receptors playing a key role in innate and adaptive immune response, among them TLR3,-7 and -8, which are expressed on endosomal membrane, and have been suggested to play an important role in antiviral immune responses based on their recognition of dsRNA and single-stranded RNA (ssRNA). Single nucleotide polymorphisms (SNPs) may shift balance between pro- and anti-inflammatory cytokines, contributing to successful resistance to infection or leading to chronic inflammation and cancer. The aim of this study was to investigate the association between the TLR-3, -7 and -8 polymorphism and the outcome of HCV infection.
AIMS & METHODS: 517 patients were enrolled in the study and genotyped for the TLR3, -7 and -8 SNPs. Logistic regression was used to assess the association between the polymorphisms and the outcome of the infection.
RESULTS: A significant association between TLR-3 SNP at rs3775291 and risk of advanced liver disease was identified. The rs3775291-A/A genotype was more common in subjects with advanced liver disease than subjects with mild chronic

hepatitis C (OR = 3.81; 95% CI, 2.16-6.72; p = 0.000004) and this difference was higher with healthy controls (OR = 5.34; 95% CI, 2.70-10.58; p = 0.000002).
CONCLUSION: Our findings indicate that a TLR-3 SNP rs3775291 is associated with progression of HCV infection to cirrhosis and hepatocellular carcinoma.
Disclosure of Interest: None declared

P0050 LOW INCIDENCE OF HYPERBILIRUBINAEMIA EVENTS WITH ABT-450/R/OMBITASVIR AND DASABUVIR WITH OR WITHOUT RIBAVIRIN IN HCV GENOTYPE-1 INFECTED PATIENTS

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INTRODUCTION: Ribavirin (RBV) is known to cause haemolytic anaemia that can lead to hyperbilirubinaemia. In addition, the NS3/NS4A protease inhibitor ABT-450 can increase unconjugated bilirubin levels due to transporter inhibition. We report the rate of hyperbilirubinaemia in HCV genotype 1-infected patients treated with ABT-450/r/ombitasvir (formerly ABT-267) and dasabuvir (formerly ABT-333) (3D regimen) with or without RBV.
AIMS & METHODS: Data from 910 patients randomized in 3 phase 3 trials (PEARL-II, PEARL-III, and PEARL-IV), which examined the contribution of RBV to the safety and efficacy of the 3D regimen, were used to evaluate the incidence and severity of clinical events related to bilirubin (hyperbilirubinaemia, jaundice) during 12 weeks of treatment. Total, direct, and indirect bilirubin were assessed at baseline and every 1-2 weeks per protocol.
RESULTS: Total bilirubin elevations of >3X ULN occurred in 23/401 (5.7%) 3D+RBV patients and in 2/509 (0.4%) patients receiving the RBV-free 3D regimen. The majority of patients in each group (>90%) had normal total bilirubin levels at the end of treatment. Mean total bilirubin levels were significantly higher at each treatment visit in the RBV-containing treatment groups. Mean total bilirubin peaked at week 1 in both treatment groups (predominantly indirect), and declined to baseline by week 2 in the RBV-free group. Events of hyperbilirubinaemia and jaundice were mostly mild, occurred within the first 2 weeks of treatment and did not result in study drug discontinuation. One patient underwent RBV dose modification and one interrupted study drug due to hyperbilirubinaemia; both patients achieved sustained virologic response 12 weeks post-treatment. Two patients receiving 3D+RBV experienced ALT ≥3X ULN and total bilirubin ≥2X ULN, however, the timing and predominance of indirect bilirubin were not consistent with drug induced liver injury. No serious adverse events related to hyperbilirubinaemia were reported.

Bilirubin-related events, n (%)	3D+RBV (N = 401)	3D (N = 509)
Any bilirubin-related event	21 (5.2)	4 (0.8)
Hyperbilirubinaemia	13 (3.2)	3 (0.6)
Jaundice	11 (2.7)	1 (0.2)
Total bilirubin >3X ULN	23 (5.7)	2 (0.4)

CONCLUSION: Low rates of hyperbilirubinaemia were observed with both 3D regiments but was less frequent in the RBV-free 3D regimens, suggesting that increases in bilirubin associated with ABT-450-containing regimens are enhanced by RBV-induced haemolysis. Bilrubin-related adverse events were infrequent with both regimens and did not affect treatment response.
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P0051 SUSTAINED VIROLOGIC RESPONSE 12 WEEKS POST-TREATMENT WITH ABT-450/RITONAVIR/OMBITASVIR AND DASABUVIR WITH RIBAVIRIN (SAPPHIRE I AND II) IS INDEPENDENT OF PATIENT SUBGROUPS

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INTRODUCTION: ABT-450 is a potent hepatitis C virus (HCV) protease inhibitor (dosed with ritonavir 100mg, ABT-450/r) identified by AbbVie and Enanta; ombitasvir (ABT-267) is an NS5A inhibitor and dasabuvir (ABT-333) is a non-nucleoside polymerase inhibitor. In phase 3 trials of this 3 direct-acting antiviral (3D) regimen with ribavirin (RBV) in non-cirrhotic HCV genotype 1-infected patients, 96.3% of treatment-naïve patients (SAPPHIRE-I trial) and 96.2% of pegINF/RBV-experienced patients (SAPPHIRE-II trial) achieved SVR12 (HCV RNA <25 IU/mL at post-treatment week 12).
AIMS & METHODS: Patients in the SAPPHIRE-I and -II trials were randomized to receive the 3D regimen of co-formulated ABT-450/r/ombitasvir (150mg/100mg/25mg QD) and dasabuvir (250mg BID) with weight-based RBV (1000 or 1200 mg daily divided BID), or placebo, for 12 weeks. Data from the two trials were pooled, and SVR_{12} rates were calculated overall and according to race, ethnicity, and region.
RESULTS: 770 patients assigned to the 3D+RBV regimen received ≥1 dose of study drug. The overall SVR12 rate in the combined studies was 96.2%; high SVR rates were achieved regardless of race, ethnicity, or region (Table). Tolerability was similar across populations. Most adverse events were mild or moderate; the 3 most common adverse events were headache (34.3%), fatigue (34.2%) and nausea (22.3%). Few patients discontinued due to adverse events (6/770, 0.8%).

		3D+RBV % with SVR12 (n/N)
Overall	SAPPHIRE-I and SAPPHIRE-II	96.2 (741/770)
Race	Black	96.0 (48/50)
	Non-black	96.3 (693/720)
Ethnicity	Hispanic/Latino	93.9 (46/49)
	Non-Hispanic/Latino	96.4 (695/721)
Region	Australia/New Zealand	95.5 (42/44)
	Europe	95.8 (346/361)
	North America	96.7 (353/365)

CONCLUSION: High pooled SVR12 rates were achieved in non-cirrhotic HCV GT1 treatment-naïve and pegINF/RBV-experienced patients in the SAPPHIRE-I and SAPPHIRE-II trials, regardless of the baseline demographics assessed in this analysis.
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P0052 SAFETY OF ABT-450/R/OMBITASVIR + DASABUVIR WITH OR WITHOUT RIBAVIRIN IN HCV GENOTYPE 1-INFECTED PATIENTS: RESULTS FROM PEARL II, PEARL III, AND PEARL IV

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INTRODUCTION: ABT-450 is an HCV NS3/4A protease inhibitor dosed with ritonavir (r) 100mg, identified by AbbVie and Enanta. Ombitasvir (formerly ABT-267) is an NS5A inhibitor, and dasabuvir (formerly ABT-333) is an NS5B RNA polymerase inhibitor. The phase 3 trials PEARL II, PEARL III, and PEARL IV examined the efficacy and safety of 12 week regimens of ABT-450/r/ombitasvir + dasabuvir (3D) with or without ribavirin (RBV) in non-cirrhotic patients with HCV genotype (GT) 1a and 1b infection. Safety outcomes in patients receiving RBV-containing and RBV-free regimens in these trials are reported.
AIMS & METHODS: GT1b-infected treatment-experienced patients (PEARL II), GT1b-infected treatment-naive patients (PEARL III), and GT1a-infected treatment-naive patients (PEARL IV) were randomized to co-formulated ABT-450/r/ombitasvir (150mg/100mg/25mg QD) + dasabuvir (250mg BID) with weight-based RBV or placebo/no RBV. Adverse event (AE) assessment and clinical laboratory testing occurred at study visits during treatment and follow-up and included all randomized patients who received at least one dose of study drug.
RESULTS: In PEARL II, PEARL III, and PEARL IV, respectively, 186, 419, and 305 patients were randomized and received at least one dose of study drug. In total across the 3 trials, 401 patients received 3D+RBVand 509 received 3D. Treatment-emergent AEs and laboratory values of note are in the Table. In both the 3D+RBV and 3D groups, the majority of AEs were mild. AEs occurring in >20% of patients in both the 3D+RBV and 3D groups were fatigue (29.9% and 26.5%) and headache (24.4% and 25.3%). 8.5% of patients receiving 3D+RBV had an AE leading to RBV dose modification; all of these patients achieved SVR12. The rate of discontinuation due to AEs was 0.5% or less among patients treated with 3D+RBV or 3D.

	3D+RBV N = 401	3D N = 509
Any AE, n (%)	332 (82.8)	383 (75.2)
Any AE leading to study drug discontinuation, n (%)	2 (0.5)	2 (0.4)
Any serious AE, n (%)	9 (2.2)	7 (1.4)
Any AE leading to RBV/placebo dose modification, n (%)	34 (8.5)	1* (0.2)
RBV/placebo dose modification due to decrease in hemoglobin, n (%)	25 (6.2)	0
Hemoglobin (g/dL), n (%)	209 (52.1)/ 23 (5.7)/2 (0.5)	34 (6.7)/0/0
Total bilirubin >3X ULN, n (%)	23 (5.7)	2 (0.4)
ALT >5X ULN, n (%)	3 (0.7)	1 (0.2)

CONCLUSION: In the PEARL II, PEARL III, and PEARL IV trials, ABT-450/r/ombitasvir + dasabuvir was well tolerated either with or without RBV. Comparable low rates of discontinuation were observed in patients receiving the RBV-containing and RBV-free regimens. Clinically significant hemoglobin reductions and bilirubin elevations were infrequent and not treatment-limiting.
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P0053 ALBENDAZOLE CAN ENHANCE THE RESOLUTION OF EOSINOPHILIC LIVER ABSCESS ASSOCIATED WITH TOXOCARIASIS

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INTRODUCTION: Visceral larva migrans, which is caused by *Toxocara canis* and *Toxocara cati*, has emerged as a significant cause of eosinophilic liver abscess (ELA). It is sometimes difficult to differentiate ELA associated with toxocariasis (ELA-T) from metastasis or primary liver malignancy. However, the role of albendazole treatment remains uncertain in this condition. We aimed to evaluate whether albendazole can enhance the radiologic resolution of ELA-T.
AIMS & METHODS: We retrospectively reviewed the medical records of the patients diagnosed with ELA-T at our institution between January 2008 and December 2011. ELA-T was diagnosed based on the imaging findings on computed tomography or magnetic resonance imaging and the presence of positive serum IgG antibody for *Toxocara canis*. Among a total of 163 patients, 32 patients received albendazole (albendazole group) and 131 did not (control group). Baseline characteristics and fate of liver nodules were compared between the two groups.
RESULTS: Baseline characteristics (age, sex, number and maximal size of lesions, eosinophil count) were similar between the two groups. Median duration for achieving radiologic resolution in the albendazole group was significantly shorter than in control group (207 days [range 186-228] vs. 302 days [range 224-380], $p = 0.023$). Cox regression analysis of the cumulative rates of radiologic resolution showed that hazard ratio for albendazole treatment was 1.99 (95% confidence interval: 1.22-3.23).
CONCLUSION: Radiologic resolution of ELA-T can be accelerated with albendazole treatment. Hence, inconvenience associated with long-term follow-up and unnecessary worries among the patients can be eliminated with albendazole treatment.
Disclosure of Interest: None declared

P0054 ABERRANT EXPRESSION OF KERATIN 7 IN HEPATOCYTES AS A PREDICTIVE MARKER OF RAPID PROGRESSION TO HEPATIC FAILURE IN ASYMPTOMATIC PRIMARY BILIARY CIRRHOSIS

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INTRODUCTION: Routine testing for antimitochondrial antibodies has increased the identification of patients with asymptomatic primary biliary cirrhosis (PBC). A predictive marker of the rapid progression to hepatic failure is desired for patients with asymptomatic PBC.
AIMS & METHODS: We performed a systematic cohort analysis of 101 patients diagnosed as having asymptomatic PBC and the rapid progression to liver failure, by focusing on cholestasis. Cholestasis was assessed by aberrant keratin (CK) 7 expressions in the patients' hepatocytes.
RESULTS: Intralobular expressions of CK-7 were found in nine of the 101 patients (9%). The grades of CK-7 expression was significantly associated with the levels of alanine aminotransferase, alkaline phosphatase, and total bilirubin ($p = 0.0060$, 0.020, and 0.0015, respectively), but not with bile duct loss or cholestasis in orcein staining. The stepwise logistic regression analysis revealed that high grades of CK-7 expression in hepatocytes had positive correlations with high levels of total bilirubin ($p = 0.0020$). During the follow-up period, eight patients developed jaundice, and the mean period until the development of jaundice was 5.2 years. The proportional hazards models for the risk of developing jaundice identified only high grades of aberrant CK-7 expression in hepatocytes as significant risk factor (hazards ratio 8.7, $p = 0.019$).
CONCLUSION: Aberrant CK-7 expression in hepatocytes can be used as an additional marker to predict the rapid progression to liver failure in patients with asymptomatic PBC at the time of diagnosis.
Disclosure of Interest: None declared

P0055 THE VALUE OF 2D SHEAR WAVE ELASTOGRAPHY (2D-SWE) IN THE EVALUATION OF ESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS

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INTRODUCTION: 2D-SWE is a new elastographic technique for the evaluation of chronic liver disease.
AIMS & METHODS: To evaluate the feasibility of 2D-SWE in cirrhotic patients with esophageal varices and the performance of 2D-SWE for predicting the presence of esophageal varices.
The study group included 71 subjects diagnosed with cirrhosis by clinical, biological, ultrasound and/or endoscopic criteria. All subjects underwent 2D-SWE with an AixplorerTM ultrasound system (SuperSonic Imagine S. A., Aix-en-Provence, France). In each patient we aimed to perform three liver stiffness measurements, with the patient in supine position and then a mean value was calculated and expressed in kiloPascals (kPa).
RESULTS: The study included 71 subjects, 65.2% men and 34.8% women with a median age of 60.5 years (ranging between 22-82 years). The etiology of liver cirrhosis was: HCV-22.2%, HBV- 12.5%, HCV and HBV-2.7%, ethanol-13.8% and other etiologies-47.2%. Esophageal varices were present in 39.4% of cases and significant esophageal varices (grade II and III) in 22.5% of cases. 2D-SWE had similar feasibility in patients with and without esophageal varices: 85.7% vs. 88.3%, ($p = 0.90$). The mean 2D-SWE values (kPa) were not statistically different in patients with and without esophageal varices: 30±13.5 vs. 24.8±12.7, ($p = 0.1$). The mean 2D-SWE values (kPa) were also not statistically different in patients with significant esophageal varices (grade II and III) vs. those without or grade I esophageal varices: 32.4±13.4 vs. 25.3±14 kPa, ($p = 0.1$).

CONCLUSION: 2D-SWE is a feasible method in patients with cirrhosis and esophageal varices but seems unable to predict the presence of esophageal varices. Further studies, in a larger number of patients, are still needed.
Disclosure of Interest: None declared

P0056 IMPLEMENTING A VIRTUAL PALPATION MODEL COMBINING SPIRAL CT AND ELASTOGRAPHY DATA INTO MEDICAL TRAINING – A PILOT STUDY

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INTRODUCTION: There are inherent problems in providing training to novices in any safety critical task. In particular, teaching medical clinicians to perform procedures poses challenges and possible risk to patients. A palpation procedure involves the examination of a patient through direct contact. That means that palpation is traditionally restricted to organs in direct contact with the outer layers of the body.
AIMS & METHODS: Our aim was to implement a previously described virtual reality model for palpation of liver tumors based on combined spiral CT and real-time elastography (RT-E) data in a haptic simulator used by medical students in a pilot study. After clearing all ethical concerns with the local committees and obtaining written consent, we acquired spiral CT and full RT-E imaging data stored in DICOM format from 15 patients with primary liver cancers scheduled for surgery. By using previously described methods [1] we created a three-dimensional model of the liver and the tumor using the CT data and integrated elasticity information by superimposing the RT-E data on the stiffness of each tumor. We thus obtained 15 distinct virtual models containing segmented color-map data superimposed on a high-fidelity representation of the tumors. These computerized models were later integrated in a virtual reality system which projected a three-dimensional image of the tumor to the operator and allowed physical interaction through haptic devices attached to the students' body. We tested the system on a pilot group of 60 medical students in the fifth year of training. Students were presented with the experimental design and were asked to perform a series of tasks involving spatial manipulation and virtual palpation of the virtual model. They were also presented with data on the real tumor (size, shape, location). After completion, a standardized questionnaire was given to each student and results were quantified using descriptive statistics and inter-group analysis.
RESULTS: All students considered the model to be accurate in both size and shape with the actual image of the tumor (60/60, 100%). The general impression was that it increased knowledge on tumoral pathology of the liver and students agreed that it provided useful insights otherwise unobtainable through standard teaching techniques. The main issue with the physical haptic system were related with the optical system for virtual reality, which the students found hard to wear and interact. The tactile feedback device was however well accepted by the test group.
CONCLUSION: We successfully tested a haptic medical simulator in a pilot study involving medical students with already acquired clinical knowledge. The general consensus was that the haptic simulator is useful for increasing knowledge on liver tumors and provide additional data otherwise unobtainable through traditional methods.
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Disclosure of Interest: None declared

P0057 COMPARISON OF THE ACCURACY OF SHEAR WAVE ELASTOGRAPHY AND ACOUSTIC RADIATION FORCE IMPULSE IN DETERMINING LIVER FIBROSIS AMONG PATIENTS WITH CHRONIC LIVER DISEASE

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INTRODUCTION: The prognosis of chronic liver diseases (CLD) depends on the extent of liver fibrosis. Liver fibrosis is the excessive accumulation of extracellular matrix proteins including collagen that occurs in most types of chronic liver diseases.
AIMS & METHODS: The study aims to compare the accuracy of Shear Wave Elastography (SWE) and Acoustic Radiation Force Impulse (ARFI) in determining liver fibrosis among patients with chronic liver disease.
Cross-sectional study conducted between March-July 2012. SWE, ARFI and ultrasound-guided liver biopsy were performed on 120 patients. Liver fibrosis using Knodell's histologic activity index and AUROC were determined for F0-F1 vs. F2-F4, F0-F2 vs. F3-F4, and F0-F3 vs. F4. SPSS 16.0, OpenEpi 2.3.1, and Stata 11.0 software were utilized in the statistical analysis.
RESULTS: AUROCs were 0.858 (ARFI) and 0.893 (SWE), 0.944 (ARFI) and 0.95 (SWE), and 0.919 (ARFI) and 0.965 (SWE), between F0-F1 vs. F2-F4, F0-F2 vs. F3-F4, and F0-F3 vs. F4, respectively. ARFI has a sensitivity and specificity of 87.5% (64-96.5) and 84.6% (76.5-90.3), 95.8% (79.8-99.3) and 78.1% (68.9-85.2), 91.3% (79.7 – 96.6) and 43.2% (32.6-54.6) for F4 vs. F0-F3, F3-F4 vs. F0-F2, and F2-F4 vs. F0-F1. SWE has a sensitivity and specificity of 100% (80.6-100) and 83.7% (75.4-89.5), 95.8% (79.7-99.3) and 85.4% (77-91.1), and 78.3% (64.4-87.7) and 86.5% (76.9-92.5).
CONCLUSION: SWE is more accurate in assessing liver cirrhosis. Both sensitivity and specificity of ARFI and SWE increased with the severity of liver fibrosis. SWE is more sensitive between F4 vs. F0-F3 and more specific between F3-F4 vs. F0-F2 and F2-F4 vs. F0-F1. ARFI is more specific between F4 vs. F0-F3 and more sensitive between F2-F4 vs. F0-F1. Differences in estimates between SWE and ARFI were statistically significant between F0-F1 and F2-F4. Thus, both SWE and ARFI can be used as non-invasive tools in detecting liver fibrosis.
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P0058 NON-INVASIVE ASSESSMENT OF PORTAL HYPERTENSION USING ELASTOGRAPHY OF SPLEEN

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INTRODUCTION: The degree of portal hypertension is one of crucial prognostic factors in patients with liver cirrhosis. Standard method used for the assessment is measurement of hepatic venous pressure gradient (HVPG) during liver vein catheterisation. Being an invasive procedure this approach is not common, has complications and moreover it does not enable monitoring of changes in the long term. Recently non-invasive approaches have been increasingly employed in evaluation of liver fibrosis; one such method is elastography.
AIMS & METHODS: The aim of our study was to evaluate the possibility of assessment of portal hypertension with elastography of the spleen in patients with various etiology of liver cirrhosis. Elastography of liver and spleen was assessed using ARFI (Acoustic Radiation Force Impulse) measurement with ultrasound system Siemens Acuson S2000 and then HVPG was measured in all patients. A total of 20 patients was examined (13 men, 7 women), average age 59±10.9, with different etiology of liver cirrhosis (10 ethylic, 4 viral hepatitis, 6 other). Diagnosis of cirrhosis was confirmed by liver biopsy or with presence of portal hypertension. There was a control group of 20 healthy individuals without signs of liver disease.
RESULTS: Clinically significant portal hypertension was diagnosed in 15 from 20 examined patients. The HVPG values were (mmHg; median, IQ range) 15 (3-26), ARFI of liver (m/s; median, IQ range) 2.96 (1.31-3.54), ARFI of spleen 3.13 (1.99-3.74). The value of ARFI of spleen significantly correlated with the degree of portal hypertension ($p = 0.038$), the ARFI of liver did not ($p = 0.251$).
CONCLUSION: Spleen elastography which is simple, reproducible and easy to repeat, could enable assessing portal hypertension in cirrhotic patients noninvasively.
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Disclosure of Interest: None declared

P0059 OUR PRELIMINARY EXPERIENCE WITH ELASTOPQ® SHEAR WAVE ELASTOGRAPHY TECHNIQUE AND DOPPLER INDICES IN THE NON-INVASIVE ASSESSEMENT OF LIVER FIBROSIS

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INTRODUCTION: Real-time shear wave elastography (RTE) is a novel non-invasive technique that assesses liver fibrosis by measuring liver stiffness (in kPa). The purpose of this study was to determine the efficacy and the feasibility for the assessment of hepatic fibrosis as compared with the histological grade in patients undergoing liver biopsy (LB).
AIMS & METHODS: Consecutive patients scheduled for LB were studied by using the iU22 Philips ultrasound system with ElastPQ technique. In addition, Doppler indices at various sites, hepatic vein and portal venous blood velocity and flows were evaluated. The correlations between these quantitative parameters and the Metavir score were analyzed using Spearman correlation and ROC curve analyses were performed to calculate AUC for $F > 2$, $F > 3$, and $F = 4$.
RESULTS: We enrolled 60 patients (39/21 males/females) who underwent LB for viral or non-viral chronic hepatitis (HCV – 58%; NASH – 30%). Liver stiffness measurements performed on the right lobe were reliable in almost all cases, while 15% of left lobe measurements were not obtainable/unreliable. Median kPa values were 4.43(range 2.98–4.82) and 3.92(2.51-6.73) for F0-F1, 7.65(4.28-12.9) and 8.21(5.43-12.3) for F2-F3, 15.12(9.9-29.16) and 18.54(9.31-31.34) for F4 in the right and left lobe, respectively. AUCs calculated for the right lobe were 0.90(0.84–0.92;95%CI) for $F > 2$, 0.84(0.73–0.88;95%CI) for $F > 3$ and 0.92(0.90–0.96;95%CI) for $F = 4$. Adding Doppler indices to liver stiffness increased no further the diagnostic accuracy of RTE.

CONCLUSION: RTE with ElastPQ appears to be a useful tool for non-invasive evaluation of fibrosis in patients with viral and non-viral chronic hepatitis, although these findings need to be confirmed in larger studies.
Disclosure of Interest: None declared

P0060 LIVER FIBROSIS ASSESSED BY TRANSIENT ELASTOGRAPHY IN LONG-TERM METHOTREXATE-TREATED PATIENTS

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INTRODUCTION: Methotrexate (MTX) is among most commonly used immunosupressive agents but requires careful monitoring due to risks of hepatotoxicity. The amino-terminal of type III pro-collagen peptide (serum P3NP) is used as a surrogate of collagen turnover. Its measurement has been proposed as a marker for ongoing hepatic fibrogenesis. Liver stiffness measurement (LSM) is a simple non-invasive method for assessment of liver fibrosis (LF). Currently, only liver biopsy for assessment of liver fibrosis in long-term (>24weeks) MTX-treated patients is used. Our aim was to evaluate the presence of liver fibrosis by transient elastography (TE) in patients treated with MTX in a long-term clinical practice.
AIMS & METHODS: We consecutively enrolled 34 patients with rheumatoid arthritis or psoriasis taking MTX between 2011 and 2012. We only included patients with normal liver function and no history of underlying chronic liver disease. All patients had P3NP measurements close to TE. Liver stiffness was evaluated by TE (single operator). Cut-off of LSM to predict liver fibrosis was 7.1 KPa.
RESULTS: The study population consists of 34 patients (12 males, 35%) at mean age of 65.2 years (range 34-77, SD 11.04). Seven patients (20%) had psoriasis, 23 (68%) had RA and the remaining were with SLE. Mean MTX cumulative dose was 5320 (SD 3682) mg, and mean treatment duration was 427 weeks (range 104-670). Mean hepatic stiffness was 7.4 KPa (SD 4.46) and mean level of P3NP was 6.7 mcg/l (SD 2.25). In six patients abdominal ultrasound was suggestive of fatty liver disease and they were excluded from further analysis. The remaining 28 patients had mean LSM of 7.4 KPa (SD 4.74), which correlated significantly with serum P3NP (Pearson $r=0.46$, $p<0.02$). Ten patients had LSM > 7.2 KPa, suggestive of significant fibrosis. Patients' age, steroids, treatment duration or cumulative doses of MTX were not associated with LF.
CONCLUSION: In our series, 33% of long-term MTX treated patients developed liver fibrosis, as assessed by LSM. Transient elastography may be potentially useful in evaluation and follow-up of liver fibrosis in long-term MTX-treated patients. Further work is required to evaluate the diagnostic yield of TE as a predictor of liver fibrosis in these patients.
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Disclosure of Interest: None declared

P0061 XL VS. M PROBE FOR LIVER FIBROSIS ASSESSMENT BY TRANSIENT ELASTOGRAPHY

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INTRODUCTION: Liver stiffness measurement (LSM) using Transient Elastography (TE) for liver fibrosis assessment is difficult to perform in obese and overweight patients by standard M probe, thus the XL probe was developed.
AIMS & METHODS: The aim of our paper was to compare the LS values obtained by the XL probe vs. M probe in daily clinical practice.
Our study included 88 difficult to evaluate patients (mean BMI 29.6±3.4 kg/m^2) with chronic hepatopathies, in which paired measurements were made with the M (3.5MHz) and XL (2.5 MHz) probes in the same session. In each patient 10 valid LSM were acquired with each probe, a median was calculated, expressed in kiloPascals (kPa). Unreliable TE measurements were considered: fewer than 10 valid shots; with a success rate (SR)<60% and/or interquartile range interval (IQR)≥30%. We used published cut-offs for M probe (7.6kPa) to divide p with no significant fibrosis (F<2 Metavir) from those with significant fibrosis (F≥2), and those with no cirrhosis (F<4) vs. cirrhosis (F4) (15kPa)*.
RESULTS: XL LS values strongly and significantly correlated with those obtained by M probe (Spearman $r=0.782$, $p<0.0001$), but were significantly lower [median 6.3 kPa (range 3.1–52.3) vs. 7.2 kPa (range 3.7–57.3), Wilcoxon paired t test $p<0.001$)]. XL LS values were also lower in the F<2 group (47 patients): median 5.1 kPa (range 3.1–12.7) vs. 5.9 kPa (range 3.7–7.4), Wilcoxon paired t test $p=0.0006$); in the F2-F3 group (23 patients): median 7.3 kPa (range 5.1–16.3) vs.10.5 kPa (range 7.7–14.1), Wilcoxon paired t test $p=0.0154$); and in the cirrhotic group (18 patients): median 18.2 kPa (range 13.3–52.3) vs. 21.3 kPa (range 15.9–57.3), Wilcoxon paired t test $p<0.0001$.
CONCLUSION: LSM by XL probe are significantly correlated, but lower, than those obtained by M probe in patients with no significant fibrosis (F<2), in patients with moderate and severe fibrosis (F2,F3) and in patients with cirrhosis (F4).

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Disclosure of Interest: None declared

P0062 THE USEFULNESS OF SPLEEN STIFFNESS EVALUATED BY 2D-REAL TIME SHEAR WAVE ELASTOGRAPHY (2D-SWE) FOR PREDICTING THE PRESENCE OF LIVER CIRRHOSIS

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INTRODUCTION: Recently, spleen stiffness (SS) assessed by various elastographic methods was evaluated for predicting liver fibrosis. Recently (Leung-Radiology, 2013) good results were published for predicting liver cirrhosis byusing SS by 2D-SWE.
AIMS & METHODS: Our aim was to validate this cut-off in an independent cohort, considering liver stiffness (LS) by Transient Elastography (TE) as the reference method.
We analyzed 89 patients with chronic liver disease. In each of the patients, in the same session LS was evaluated by TE (FibroScan, Echosens, Paris, France) and SS by 2D-SWE (Aixplorer, SuperSonic Imagine S. A., Aix-en-Provence, France). TE reliability criteria defined as: median of 10 valid LS measurements with a SR≥60% and IQR<30%. 2D-SWE results were recorded as median value of 3 valid SS measurements. For predicting the presence if liver cirrhosis, we used the LS cut-off proposed in the most recently published meta-analysis (Tsochatzis-J Hepatol 2011): 14.5 kPa. For SS the following cut-off was analyzed (Leung-Radiology2013): 22 kPa.
RESULTS: Reliable LS measurements by TE were obtained in 71 (79.7%) patients and valid SS measurements by 2D-SWE in 63/71 (88.7%) patients, who were included in the final analysis. According to the pre-specified cut-off values for LS and SS, the performance of SS assessed by 2D-SWE for predicting the presence of liver cirrhosis was: 58.3% sensitivity, 82.3% specificity, 43.7% positive predictive value (PPV), 89.3% negative predictive value (NPV) and 77.7% accuracy.
CONCLUSION: In our patient cohort, SS by 2D-SWE was a good method for excluding liver cirrhosis, with a very good NPV (89.3%), but less useful for predicting cirrhosis, with a rather poor PPV(only 43.7%).
Disclosure of Interest: None declared

P0063 COMPARISON BETWEEN 2D-REAL TIME SHEAR WAVE-ELASTOGRAPHY (2D-SWE) AND SIMPLE SEROLOGICAL SCORES FOR LIVER FIBROSIS ASSESSMENT FOR CLINICAL ROUTINE, CONSIDERING TRANSIENT ELASTOGRAPHY (TE) AS REFERENCE METHOD

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INTRODUCTION: 2D-Shear Wave elastography (2D-SWE) is a new method for non-invasive assessment of liver fibrosis.
AIMS & METHODS: Our aim was to assess the performance of 2D-SWE and simple serological scores for liver fibrosis assessment, considering TE as reference method.
Our study included 127 consecutive patients with chronic liver disease undergoing both TE (FibroScan, Echosens, Paris, France) and 2D-SWE (Aixplorer, SuperSonic Imagine S. A., Aix-en-Provence, France). Biochemical parameters were recorded to calculate the noninvasive fibrosis scores. TE reliability criteria defined as: median of 10 valid LS measurements with a SR≥60% and IQR<30%. 2D-SWE results were recorded as median value of 3 valid LS measurements. TE cut-offs to stage liver fibrosis were used according to a recent meta-analysis (Tsochatzis-J Hepatol 2011): F1: 6kPa, F2: 7.2kPa, F3: 9.6kPa and F4: 14.5kPa.
RESULTS: Reliable LS measurements by TE and 2D-SWE were obtained in 74.8% and 98.4% of patients ($p<0.0001$), respectively. The following noninvasive fibrosis scores were correlated in univariate analysis with fibrosis estimated by TE: 2D-SWE ($r=0.699$; $p<0.0001$), Forns ($r=0.534$; $p<0.0001$), King's ($r=0.512$; $p<0.0001$), APRI ($r=0.373$, $p=0.001$) Fibrosis Index score ($r=0.363$; $p=0.0008$) and Lok score ($r=0.316$, $p=0.006$), while FIB-4 ($r=0.195$; $p=0.09$) was not correlated. In multivariate analysis only LS by SWE was significantly correlated with fibrosis estimated by means of TE ($p<0.0001$).
The best LS cut-off by 2D-SWE for predicting different stages of liver fibrosis, considering TE as the ''reference method'', are presented in the table.
Table to abstract P0063

Fibrosis	SWE Cut-off (kPa)	AUC	Se (%)	Sp (%)	PPV (%)	NPV (%)	Accuracy (%)
F≥2	> 8.03	0.832	77.1	76.1	77.1	76.1	76.5
F≥3	> 9.2	0.919	88.2	85	76.9	92.7	86.1
F=4	> 13.1	0.915	76.2	94.5	80	93.2	90.4

CONCLUSION: 2D-SWE results in a higher rate of successful liver stiffness measurements than TE and is superior to simple serological scores for non-invasive liver fibrosis assessment.
Disclosure of Interest: None declared

P0064 THE CONTROLLED ATTENUATION PARAMETER (CAP) EVALUATED WITH TRANSIENT ELASTOGRAPHY ACCURATELY ESTIMATES THE SEVERITY OF STEATOSIS INDEPENDENT OF FIBROSIS AND DISEASE ETIOLOGY IN PATIENTS WITH CHRONIC LIVER DISEASE

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INTRODUCTION: Currently only liver biopsy can accurately establish the diagnosis and severity of hepatic steatosis. Few studies to date have addressed the feasibility of the Controlled Attenuation Parameter (CAP) measured by transient elastography for measuring hepatic fat content. However, the effects of hepatic fibrosis and disease etiology on the accuracy of CAP values for grading the severity of liver steatosis are still unclear.
AIMS & METHODS: The aims of this study were (1) to determine whether CAP values can discriminate grades of steatosis in a sample of consecutive patients with a spectrum of liver disease etiology and steatosis severity, and (2) to evaluate the effect of hepatic fibrosis and disease etiology on the quantification of steatosis by CAP measurements. The study involved 50 sequential patients (64% males; mean age, 47.4 years; range, 19-70 years) who had undergone a percutaneous liver biopsy and CAP measurements. The causes of liver disease were nonalcoholic fatty liver disease (n = 20), chronic viral hepatitis (n = 23), autoimmune hepatitis (n = 3), and others (n = 4). A pathologist scored the specimens in a four-graded scale as follows: $<5\%$ steatosis = S0, 5-33% = S1, 33-66% = S2, and $>66\%$ = S3. All liver biopsy specimens were at least 20 mm long and/or contained more than 11 complete portal tracts.
RESULTS: The pathology results showed that 16 (32%) patients had S0, 12 (24%) had S1, 9 (18%) had S2, and 13 (26%) had S3. Overall a close relationship was observed between the CAP values and histology steatosis scores ($r = 0.709$, $P < 0.001$). There was a stepwise increase in CAP with increasing stages of hepatic steatosis: S0, 222 dB/m; S1, 250 dB/m; S2, 270 dB/m; and S3, 318 dB/m. Regression analysis, that included a number of potential confounders, was performed to determine the influence of hepatic fibrosis and disease etiology on the relationship between CAP values and the histological assessment of steatosis. However, neither liver fibrosis ($p = 0.58$) nor disease etiology ($p = 0.96$) were found to have an interaction between CAP and the stage of steatosis.
CONCLUSION: Liver fibrosis or disease etiology does not impact on the accuracy of CAP for the assessment of steatosis. The results of this study strengthen the role of CAP measured by transient elastography as a non-invasive alternative to liver biopsy for the evaluation of liver fat content in subjects with liver disease. Given its accuracy and lack of confounding by fibrosis and disease etiology, CAP assessment is an attractive method to evaluate the presence and severity of steatosis in clinical practice and may also be a useful tool to monitor change in steatosis in subjects undergoing an intervention.
Disclosure of Interest: None declared

P0065 FOCAL LIVER LESIONS CLASSIFICATION BY ARTIFICIAL NEURAL NETWORKS AND SUPPORT VECTOR MACHINES EMPLOYING DYNAMIC IMAGING DATA

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INTRODUCTION: Early diagnostic of liver malignancies is essential for therapy efficiency; differentiating hepatocellular carcinoma (HCC) from intrahepatic cholangyocarcinoma, liver metastases or benign lesions is therefore essential even in early phases. Successful classification of liver lesions by computerized methods is currently possible and artificial neural networks emerged as optimal tools for independent diagnostic.
AIMS & METHODS: Our aim was to test the validity of two separate decision making systems – an artificial neural network (ANN) and a support vector machine (SVM) in classifying focal liver lesions (FLLs) by using dynamic imaging data.
Expanding on our previous work involving ANN use in interpreting imaging data for HCC [1], we now proposed a comparative approach between two different machine learning systems, one based on ANNs and contrast-enhanced ultrasound (CEUS) quantitative data and one employing a SVM and spiral computed tomography (CT). After obtaining ethical clearance and signing individual consent forms, we prospectively included 191 patients who underwent both spiral CT and CEUS as part of their clinical work-up at the University County Hospital of Craiova between January 2009 – September 2013. Final diagnosis was based on post-treatment evaluation, follow-up and pathology, when available. Imaging data from CEUS was obtained through time-intensity curve (TIC) analysis and the main parameters (time to peak, rise time, fall time, mean transit time, area under the curve) were fed to an ANN. Spiral CT data was obtained through manually segmenting the tumor and a tumor-free parenchyma portion in distinctive images and obtaining Gray Level Co-occurrence Matrix – GLCM parameters (entropy, correlation and contrast) by using the free ImageJ software and a dedicated plug-in. These parameters were then fed to a SVM.
RESULTS: We included 54 cases of HCC, 9 intrahepatic cholangiocarcinomas, 71 liver metastases (41 hypervascular), 38 liver hemangiomas and 19 focal fatty changes. The SVM classified lesions into malignant or benign, obtaining 141 correct classifications (malignant: 113/134, benign: 28/57). Overall, the ANN in correlation with TIC-derived parameters proved to be a superior combination to SVM and GLCM.
CONCLUSION: ANNs are superior to SVMs when employed in medical classification problems. Established quantitative parameters improve the diagnostic accuracy. The differences shown here were not given by the quality of the two investigations, showing rather the adequacy of the chosen parameters and the diagnostic yields of the computer methods employed.
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Disclosure of Interest: None declared

P0066 LONG-TERM OUTCOMES AFTER TREATMENT OF SINGLE SMALL HEPATOCELLULAR CARCINOMA IN ELDERLY PATIENTS WITH WELL-PRESERVED LIVER FUNCTION AND GOOD PERFORMANCE STATUS

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INTRODUCTION: Aging of general population and advances in diagnostic imaging have led to more frequent detection of small hepatocellular carcinoma (HCC) in elderly adults. However, long-term outcome and its predictive factors after treatment of small HCC in these patients have not been established.
AIMS & METHODS: Between 2006 and 2009, 897 patients who had Eastern Cooperative Oncology Group (ECOG) score 0-1 and Child-Pugh class A liver function were diagnosed with single small HCC (size≤3 cm) at Samsung Medical Center. They were divided into elderly group (age≥65 years, n = 186) and young group (age<65 years, n = 711). We compared baseline characteristics, initial treatment modality, and treatment outcomes between the two groups.
RESULTS: At baseline, male patients were less common, and HCV infections and alcoholic liver disease were more common in elderly group. Elderly group underwent surgical resections less frequently but TACE more frequently compared to young group (21.5% vs. 38.8% for surgery and 26.9% vs. 12.9% for TACE, $p<0.001$). One-, 3-, and 5-year overall survival (OS) rates (OSR) of elderly group were lower than those of young group (96.7%, 81.4%, and 60.5% vs. 97.3%, 87.9%, and 82.4%, respectively, $p<0.001$).
One-, 3-, and 5-year OS rates were after surgery, RFA, and TACE were 94.9%, 89.7%, and 86.6% vs. 97.9%, 79.6%, and 56.7% vs. 96.0%, 80.0%, and 50.6%, respectively in elderly group ($p = 0.014$); 98.2%, 91.8%, and 89.5% vs. 98.2%, 87.6%, and 80.3% vs. 92.3%, 79.0% and 70.5%, respectively in young group ($p<0.001$). Although OS rates after surgery and TACE were comparable between the two groups, elderly group showed lower 1-, 3-, and 5-year OS rates than young group after RFA. In addition, 1-, 3-, and 5-year recurrence-free survival (RFS) rates of elderly subgroup were lower than those of young group (63.2%, 30.5%, and 23.0% vs. 75.7%, 48.0%, and 36.6%, respectively, $p<0.001$).
One-, 3-, and 5-year RFS rates after surgery, RFA, and TACE were 74.4%, 61.5%, and 52.5% vs. 70.2%, 23.5% and 13.8% vs. 40.8%, 18.4%, and 16.3%, respectively in elderly group ($p<0.001$); 81.4%, 63.5%, and 51.5% vs. 75.1%, 41.4%, and 29.9% vs. 59.2%, 23.6%, and 11.7%, respectively in young group ($p<0.001$). RFS rates after surgery and TACE were comparable between the two groups, whereas elderly group showed lower 1-, 3-, and 5-year RFS rates than young group after RFA. Multivariate analysis showed that sex and initial treatment modality were the significant predictive factor for OS and RFS.
CONCLUSION: Although long-term outcomes after treatment of single small HCC in elderly group were lower than those in young group, adoption of curative treatment modality was an independent predictive factor for the better outcomes irrespective of age. Therefore, in elderly patients with well-preserved liver function and good performance status, curative treatment including surgery should be more positively considered for single small HCC.
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Disclosure of Interest: None declared

P0067 EFFICACY OF SORAFENIB ACCORDING TO THE NUMBER OF PRIOR TACE PROCEDURES IN HCC PATIENTS

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INTRODUCTION: It has been recently suggested that sorafenib should be initiated as early as possible in patients with hepatocellular carcinoma (HCC) who failed transarterial chemoembolization (TACE); however, the correlation

between the efficacy of sorafenib and the number of prior TACE procedures has not been documented. We analyze here the correlation between the efficacy of sorafenib and the number of prior TACE procedures in HCC patients included in the Nation-wide Italian database ITA. LI. CA.
AIMS & METHODS: The ITA. LI. CA. database contains data of 5136 HCC patients treated at 18 Italian Centers. All patients treated with sorafenib were included in this analysis. The following endpoints were considered: overall survival (OS), time to progression (TTP) and disease control rate (DCR). These endpoints were compared in patients with no TACE, one and ≥2 prior TACE procedures.
RESULTS: In total, 321 patients had received sorafenib (271 males; age 65±11 years; 225 in BCLC-C stage). Of these, 201 received no TACE (187 were in BCLC-C stage), 60 one TACE and 60 ≥2 TACE procedures. Median OS was significantly longer in patients who received one single TACE procedure, with respect to those with no or ≥2 TACE procedure(s) (19 months with one TACE versus 11 months with no TACE and 12 months for ≥2 TACE; $p<0.05$). No differences among groups were observed in TTP (one TACE: 4 months; no TACE: 4 months; ≥2 TACE: 5 months; p = not significant), but patients with only one TACE prior to sorafenib treatment had an improved DCR (one TACE: 34%; no TACE: 24%; ≥2 TACE: 28%; $p<0.05$).
CONCLUSION: Although with all the limitations of any observational study, this analysis, conducted in a large field-practice database, suggests that HCC patients who start sorafenib after one single TACE procedure present improved OS and DC with respect to those who received TACE ≥2 TACE procedures.
Disclosure of Interest: None declared

P0068 CORRELATION BETWEEN LDH LEVELS AND RESPONSE TO SORAFENIB IN HCC PATIENTS

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INTRODUCTION: Lactate dehydrogenase (LDH) is a predictor of clinical outcome in hepatocellular carcinoma (HCC) patients. However, the predictive role of LDH on the clinical outcomes of sorafenib treatment has been poorly documented. The correlation between LDH levels and clinical outcomes in HCC patients treated with sorafenib included in the Nation-wide Italian database ITA. LI. CA is investigated here.
AIMS & METHODS: The ITA. LI. CA. database contains data of 5136 HCC patients treated at 18 Italian Centers. All patients treated with sorafenib treatment and with available LDH values were considered. A ROC analysis was performed to find a suitable threshold for baseline LDH levels. Overall Survival (OS) and time to progression (TTP) were compared in patients with LDH above and below the identified threshold. Study endpoints were also evaluated according to different patterns of LDH levels during treatment.
RESULTS: Baseline LDH levels were available for 97 patients (85 males, 61 in BCLC-C stage); data on LDH levels during sorafenib were reported for 10 patients. Mean baseline LDH concentration was 324±141 U/L. The most accurate cut-off value for LDH concentration was 297 U/L. Both study endpoints were equal in patients with LDH values ≥297 U/L (n = 47) and in those with lower LDH concentrations (n = 52) (OS: 12.0 months in each population; TTP: 4.0 months in each group). During treatment, LDH values decreased in three patients (mean difference = -219 U/L). Patients with decreased LDH concentrations have a prolonged OS versus those with unmodified/increased values ($p = 0.0083$; all patients with decreasing LDH are alive, median OS for patients with increasing LDH was 8.0 months). Median TTP was 19.0 months in patients with decreasing LDH and 3.0 months in those with increasing values ($p = 0.008$).
CONCLUSION: The clinical benefits of sorafenib do not seem influenced by baseline LDH. However, a decreased LDH concentration during sorafenib might be associated with improved clinical outcomes.
Disclosure of Interest: None declared

P0070 SAFETY AND EFFICACY OF SORAFENIB IN ELDERLY PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

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INTRODUCTION: The average age of patients with hepatitis and hepatocellular carcinoma (HCC) in Japan is increasing. Sorafenib is approved for the treatment of advanced HCC; however, its safety and efficacy for elderly patients is not established by published studies. Therefore, we aimed to evaluate the safety and efficacy of sorafenib for elderly patients (≥80 years of age) included in the Saga Liver Cancer Study Group.
AIMS & METHODS: We conducted a retrospective study between July 2008 and August 2013 that included 134 patients with advanced HCC who received sorafenib in Saga, Japan until disease progression or treatment intolerance. We divided the patients into two groups comprising 36 patients 80 years of age or greater (≥80 group) and 98 patients less than 80 years of age (<80 group). We compared antitumour effect [objective response rate (ORR), disease control rate (DCR), time to tumour progression (TTP)], overall survival (OS), and adverse events (AEs) of the two groups.
RESULTS: Baseline characteristics were not significantly different between the two groups. The median ORRs were 6.9% and 8.3%, and the median DCRs were 37.9% and 46.4% in the ≥80 and <80 groups, respectively. These values were not significantly different between the two groups ($p = 0.81$, $p = 0.43$). The median TTPs were 2.9 months for both groups, and the median OSs were 14.7 and 9.2 months for the ≥80 and <80 groups, respectively, which were not significantly different. The frequencies of AEs were 97.2% and 96.6% in the ≥80 and <80 groups. The frequencies of grade 3 AEs between the ≥80 and <80 groups were significantly different (69.4% and 49.0% respectively, $p = 0.036$).
CONCLUSION: Sorafenib treatment is equally effective for elderly and non elderly patients with advanced HCC. However, the high frequency of AEs in elderly patients is problematic and requires close attention.
Disclosure of Interest: None declared

P0071 HEPATOCELLULAR CARCINOMA INCIDENCE IN CHRONIC HEPATITIS C PATIENTS ACCORDING TO SUSTAINED VIROLOGIC RESPONSE (SVR) AND FLUCTUATION OF ALFA FETO-PROTEIN LEVELS DURING ANTIVIRAL TREATMENT

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INTRODUCTION: Chronic hepatitis C (CHC) is an important risk factor for progression of liver disease to advanced fibrosis and hepatocellular carcinoma (HCC) and the published studies showed that the kinetics of alfa feto-protein (AFP) levels in cirrhotic patients are more valuable than single AFP values for predicting the HCC.
AIMS & METHODS: Our aim was to assess the HCC incidence in relation to antiviral treatment response and fluctuation of AFP levels during antiviral treatment in a large number of patients from a single institution. We retrospectively collected data of HCV patients, who were diagnosed and treated between 1989-2011. We analyzed the HCC incidence according to AFP fluctuation (baseline vs. end of treatment-EOT) in the entire Cohort of patients and in SVR and non-SVR patients.
RESULTS: We identified 2627 patients diagnosed with chronic hepatitis C. We excluded 975 patients because they did not receive antiviral therapy, 5 because they were diagnosed simultaneously with HCV/HCC and 321 patients due to lack

Table to abstract P0071
Table 1. HCC incidence in different groups, according to AFP levels at baseline and EOT (P0071 table)

Cohort	Group A: n=50 (3.8%) AFP > 10/ AFP > 10 (ng/ml,baseline/EOT)		Group B: n=81 (6.1%) AFP > 10 /AFP < 10 (ng/ml, baseline/EOT)		Group C: n=1167 (88%) AFP < 10 /AFP < 10 (ng/ml,baseline/EOT)		Group D: n=28 (2.1%) AFP < 10/AFP > 10 (ng/ml,baseline/EOT)		P value
All	24%		9.8%		1.8%		17.8%		A vs. B: p=0.004 Avs.C:p < 0.0001 A vs. D: p=0.72 B vs.C: p < 0.0001 B vs. D: p=0.42 C vs.D: p < 0.0001
SVR	30.7%	p=0.77	7.1%	p=0.83	0.5%	p < 0.0001	12.5%	p=0.93	A vs. B: p=0.12 A vs.C: p < 0.0001 A vs. D: p=0.67 B vs. C: p=0.003 B vs. D: p=0.81 C vs. D: p=0.04
Non-SVR	21.6%		11.3%		4.7%		20%		A vs. B: p=0.30 A vs.C: p=0.0002 A vs. D: p=0.84 B vs. C: p=0.10 B vs. D: p=0.56 C vs. D: p=0.01

of AFP values at baseline and EOT. We included in the final analysis 1326 patients. The median follow-up time was 10 years (0.2-25 years). The overall HCC incidence was 3.5% and the median time between HCV and HCC diagnosis was 7 years (0.5-15 years). According to baseline fibrosis stage, HCC incidence was: 0.9% in F(0-2) patients, 1.8% in F3 and 10.1% in F4 patients.
The HCC incidence was significantly higher in non-SVR as compared with SVR patients: 7.4% vs. 1.2%, $p < 0.0001$.
AFP values > 10 ng/ml at baseline, EOT and the increase of AFP values during the antiviral treatment are associated with high HCC incidence in both SVR and non-SVR patients (Table 1). The decrease of AFP values during the antiviral treatment is associated with reduced HCC incidence, comparative to the cases with high AFP at baseline and EOT. AFP levels < 10 ng/ml in both baseline and EOT are protective against HCC development exclusively in the SVR group.
CONCLUSION: The fluctuation of AFP levels during antiviral treatment plays an important role on HCC development. The patients with AFP > 10 ng/ml at both baseline and EOT had the highest risk to HCC, however they achieved SVR. Hence, an intensified HCC surveillance should be performed in these patients.
Disclosure of Interest: None declared

P0072 INFLUENCE OF HBV REACTIVATION ON THE RECURRENCE OF HEPATITIS B-RELATED HEPATOCELLULAR CARCINOMA AFTER CURATIVE RESECTION IN PATIENTS WITH LOW VIRAL LOAD

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INTRODUCTION: It is unclear whether the reactivation of hepatitis B virus (HBV) influences the prognosis of hepatocellular carcinoma (HCC) after resection in patients with chronic hepatitis B. The aim of this study was to identify the effect of HBV reactivation on the recurrence of hepatitis B-related HCC after curative resection in patients with low viral load (HBV DNA <2.000 IU/mL).
AIMS & METHODS: We retrospectively analyzed a total of 130 patients who underwent curative resection for HBV-related early-stage HCC (single nodule; <5 cm / two or three nodules; <3 cm) with preoperative HBV DNA level <2.000 IU/mL and serial check-up on HBV DNA. The predictive factors including HBV reactivation for the recurrence of HBV-related HCC after curative resection were investigated. HBV reactivation was defined as the reemergence or an increase of more than 10-fold in serum HBV DNA as compared with the level before resection.
RESULTS: Fifty-three patients (41%) had HBV reactivation after resection among 130 patients. HBV reactivation was observed in 22 of 53 patients with undetectable baseline HBV DNA and in 31 of 77 patients with detectable HBV DNA. Cumulative recurrence rates after resection at 1, 2, and 3 years were 17.0%, 23.3%, and 31.4%, respectively. The multivariable analysis demonstrated that the risk factors for the recurrence were the presence of microvascular invasion (hazard ratio (HR) 2.62, $p = 0.003$), multi-nodularity (HR 4.61, $p = 0.005$), HBV reactivation after resection (HR 2.03, $p = 0.032$), and HBeAg positivity (HR 2.06, $p = 0.044$).
CONCLUSION: HBV reactivation after curative resection was associated with the recurrence of HBV-related HCC in patients with low viral load. This study suggests that aggressive viral suppression by anti-viral therapy can help to reduce the recurrence of HCC after resection in chronic hepatitis B with low viral load.
Disclosure of Interest: None declared

P0073 A STUDY OF PLASMA PROLIDASE ACTIVITY IN CASES WITH AND WITHOUT HEPATOCELLULAR CARCINOMA IN THE SETTING OF UNDERLYING CIRRHOSIS

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INTRODUCTION: Cancer cell prolidase enzyme activity has been reported to be important for tumor invasiveness and metastasis. As far as we know, plasma prolidase activity (PPA) has not been studied in patients with hepatocellular carcinoma (hcc).
AIMS & METHODS: We aim to assess the correlation between the PPA and AFP levels in patients with hepatocellular carcinoma. A total of 51 patients with cytopathological diagnosis of HCC in the setting of cirrhosis, 31 patients with cirrhosis without HCC and 33 cases as healthy volunteers were enrolled in this study. There were no significant differences with respect to gender and age of the study cohort with the healthy group. The patients with HCC were divided into groups according to tumor size, number and presence of vascular invasion. Barcelona-Clinic Liver Cancer (BCLC) criteria was used for staging of patients with hcc. PPA was measured spectrophotometrically. AFP level was measured with immunoassay method.
RESULTS: PPA was significantly higher in cases with HCC than cases with cirrhosis without HCC and, healthy controls (1182 U/L versus 932 U/l and 880 U/l, respectively). Patients with cirrhosis had PPA similar to those of healthy controls ($p > 0.05$). PPAs differed significantly in the group of tumor diameters less than 3 cm (n:13), compared to the group of tumor diameters between 3-5 cm (n:9) and more than 5 cm (n: 29) (($p = 0.003$) According to the tumor number, a significant difference has been seen in the group which has more than two tumors compared to the group which has one ($p = 0.001$) and two tumors ($p = 0.027$). PPA also differed in patients with regard to BCLC staging classification ($p = 0.003$). However, prolidase levels showed no statistically significant difference with presence of macrovascular invasion in patients with HCC ($p = 0.898$). There was a significant positive correlation between PPA and serum AFP values ($r = 0.731$; $p < 0.001$)
CONCLUSION: To our knowledge, this is the first study reporting increased PPA in patients with HCC, and it was found to be significantly associated with size, number and BCLC stage of the tumor. This was not seen in patients with cirrhosis without HCC. Furthermore, PPA significantly associated with serum AFP levels. However, further studies should be done to clarify clinical significance and pathophysiological role of augmented prolidase activity in cases with HCC.
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Disclosure of Interest: None declared

P0074 VALUE OF ESOPHAGOGASTRODUODENOSCOPY IN PATIENTS REFERRED FOR CHOLECYSTECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Up to 33 percent of patients with symptomatic cholelithiasis report persisting abdominal pain after cholecystectomy, suggesting alternative causes for these symptoms. Esophagogastroduodenoscopy (EGD) may serve as a tool to identify additional symptomatic abdominal disorders beforehand, in order to avoid unnecessary gallbladder surgery. There is controversy whether routine EGD prior to cholecystectomy is appropriate.
AIMS & METHODS: We performed a systematic review and meta-analysis to assess the value of EGD prior to cholecystectomy. A systematic literature search was conducted in Pubmed, Embase, Web of Science, ClinicalTrials.gov, and the Cochrane library. All studies were included that reported the proportion of patients who were referred for cholecystectomy, but in whom surgery could be avoided after treatment of abnormalities detected with EGD. Pooled estimates were calculated using a random effects model.
RESULTS: Twelve eligible studies were included with a total of 6.317 patients with cholelithiasis receiving EGD. The pooled estimate of abnormalities detected with EGD was 36.3% (95% CI, 28.0-45.0). Treatment of these findings avoided cholecystectomy in 11.0% (95% CI, 3.9-21.1) of patients. In a total of 3.8% (95% CI, 1.4-7.6) of patients referred for cholecystectomy who underwent prior EGD, gallbladder surgery was avoided.
CONCLUSION: Our study indicated that the value of prior EGD in preventing gallbladder surgery is limited. EGD should only be considered selectively in patients with cholelithiasis referred for cholecystectomy.
Disclosure of Interest: None declared

P0075 REFERENCE RANGES OF SERUM BILE ACID IN CHILDREN AND ADOLESCENTS

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INTRODUCTION: Serum total bile acid (tBA) concentrations are prognostic and predictive markers for hepatic disorders. Due to the lack of data on normal value ranges of tBA in children and adolescents we aimed to determine such ranges as well as the composition of BA in this age group.
AIMS & METHODS: tBA concentration was measured in 194 healthy children and adolescents (0 - 19 years). Unconjugated and taurine or glycin conjugated BA were measured by using high performance liquid chromatography tandem mass spectrometry (HPLC MS/MS). Patients were classified in five groups according to their age: 0-5 months (n = 17), 6-24 months (n = 13), 3-5 years (n = 22), 6-11 years (n = 44), and >11 years (n = 98), respectively.
RESULTS: tBA values found in children were significantly higher compared to reference ranges in adults (0.28 – 6.50 µmol/l). Serum tBA increased constantly after delivery (0-5 months: 3.85 – 6.32 µmol/l) and reached a peak at the age of 6-24 months (6.61 – 9.43 µmol/l). Henceforward tBA decreased continuously (3-5 years: 4.27 – 6.43 µmol/l, 6-11 years: 3.61 – 5.14 µmol/l and >11 years: 3.10 – 4.12 µmol/l). In neonates levels of taurine conjugated BA were elevated; however, after 6 months glycine conjugated clearly predominated.
CONCLUSION: This study shows that serum tBA levels vary substantially in the first years of life indicating age-dependent reference ranges for tBA and the BA profile; the causes of the variations need further clarification.
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Disclosure of Interest: None declared

P0076 EUS-GUIDED DRAINAGE WITH A LUMEN APPOSING METAL STENT IS FEASIBLE FOR THE TREATMENT FOR ACUTE CHOLECYSTITIS IN HIGH RISK PATIENTS

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INTRODUCTION: Percutaneous gallbladder drainage is the treatment of choice in high-risk surgical patients with acute cholecystitis. However, it is associated with discomfort and risk of inadvertent drain removal which may lead to bile leakage and recurrent cholecystitis. Recently, EUS-guided drainage has been introduced as an alternative treatment option.
AIMS & METHODS: Our aim was to determine the feasibility and safety of EUS-guided gallbladder drainage with a lumen apposing metal stent (AXIOS) in patients with acute cholecystitis at high risk for surgery. We performed a prospective, multicenter study. Stent removal was scheduled after 3 months and patients were followed until 9 months after removal. Study endpoints included safety, recurrent symptomatic cholecystitis, clinical and technical success.
RESULTS: Between June 2012 and Feb 2014, 30 patients were included (11 men (37%), mean age 85±7 years). Median time between onset of symptoms and stent placement was 2 days (range 1-28 days). The majority of patients (87%) presented with calculous cholecystitis. In 11 patients (37%) a transgastric approach and in 19 patients (63%) a transduodenal approach was used. Stent placement was technically successful in all patients (100%), but in 4 patients (13%) a second stent was placed due to problems with stent deployment. Clinical success was achieved in all but one patient (97%) after a median of 3 days (IQR 3-5 days). In one patient with ongoing fever for 14 days, endoscopic irrigation was successfully performed through the stent to drain large amounts of pus from the gallbladder. Stent removal was successfully performed in 12 patients (40%) after a median of 91 days (range 15-133), of which one was evaluated as being difficult due to tissue overgrowth (125 days). In 18 patients (60%) no stent removal was performed, including 2 patients (2%) with significant tissue overgrowth (105 and 150 days), 5 patients (17%) with follow-up <3 months, 5 unrelated deaths <3 months (17%), 4 patients (13%) with a poor clinical condition, 1 patient (3%) with a polypoid lesion in the gallbladder and 1 patient (3%) with lingering stones. Causes of death included urosepsis (n=1), pneumonia (n=1), myocardial infarction (n=1) and progression of pancreatic adenocarcinoma (n=2). Major complications were reported in 4 patients (13%). One patient presented with melena due to mucosal gangrene of the gallbladder for which endoscopic irrigation of the gallbladder was performed. One patient developed fever due to food contents in the gallbladder for which stent removal was performed. This patient also developed acute biliary pancreatitis 21 days later. Two patients developed symptoms of cholestasis due to common bile duct stones for which ERCP was performed. During a mean follow-up of 212 days (95% CI 149-274) none of the patients developed recurrent cholecystitis.
CONCLUSION: EUS-guided gallbladder drainage with a lumen apposing stent was found to be feasible in high-risk surgical patients with a high clinical success rate. Difficulties with stent deployment was seen in approximately 15% of patients. The overall number of major complications was low, but tissue overgrowth may complicate stent removal.
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P0077 THE EFFECT OF PERIAMPULLARY DIVERTICULUM ON THE CLINICAL PRESENTATION OF CHOLEDOCHOLITHIASIS AND OUTCOME AFTER ERCP

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INTRODUCTION: Periampullary diverticulum (PAD) is an incidental finding in up to 20% of ERCPs. Its incidence increases with age. PAD is associated with CBD stones and is considered a risk factor for obstructive jaundice, cholangitis and pancreatitis even in the nascence of CBD stones. However, the impact of PAD on the presentation and consequences in patients with CBD stones is unclear.
AIMS & METHODS: The aim of our study was to investigate the effect of PAD on the clinical presentation and course of patients with suspectedcholedocholithiasis.
All ERCPs performed in our unit from 1/2010 to 7/2013 were reviewed. Studies performed for documented or suspected choledocholithiasis were included in the study. Patients were divided into two groups. Group I- patients without PAD and group II- with PAD. The following data were recorded: Age, gender, comorbidities, indication for ERCP, previous imaging studies, liver function tests, presence of gallbladder, prior sphincterotomy, CBD diameter,ERCP success and complications, as well as the presence, size and type of PAD.
RESULTS: Three hundred and two patients met the inclusion criteria. Mean age was 66.4 ± 20.5y (range 19-98), 173 (57.3%) women. Altogether, 86 patients (28.4%) had PAD. Ninety-nine percent of ERCPs were successful. Two hundred and fifty-three patients (83.8%) had CBD stones on ERCP. Significant complications (pancreatitis, perforation, death) were recorded in 14 patients (6.5,3, respectively) (4.6%). Patients with PAD were older (73.4±16.2y Vs 63.6±21.4y) and predominantly male (53.5% Vs 38.4%), $p<0.01$. Patients with PAD presented more often with cholangitis compared to those without PAD (58.1% Vs 34.6%, $p< 0.001$). There were no differences between the two groups regarding imaging findings, laboratory tests, presence of gallbladder, comorbidities, procedural success, prior ERCP, inadvertent pancreatic duct cannulation, presence of CBD stones, number and size of CBD stones, procedure related complications and their severity, or number of ERCPs for stone clearance.
CONCLUSION: PAD is a risk factor for infectious complications ofcholedocholithiasis. However, the presence of PAD does not predispose patients to misinterpretation of imaging studies, procedural difficulty, failure or complications of ERCP.
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Disclosure of Interest: None declared

P0078 MULTICENTER TRIAL FOR EFFICACY OF MAGNESIUM TRIHYDRATE OF UDCA AND CDCA (CNU®)FOR GALLSTONE DISSOLUTION

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INTRODUCTION: The gallstone is still a most prevalent medical issues in the pancreatobiliary system. Laparoscopic cholecystectomy is a treatment of choice; however, oral litholysis with bile acids has been an attractive alternative therapeutic option for asymptomatic or mild symptomatic subgroups. Ursodeoxycholic acid (UDCA) and chenodeoxycholic acid (CDCA) or both had been investigated for their effectiveness on stone dissolution. Recently, the prevalence of gallstones has increased due to the wide availability of sonographic examination and dietary habit modification. We conducted a prospective, multicenter, phase IV clinical study to evaluate the efficacy of magnesium trihydrate of UDCA and CDCA for gallstone dissolution at present.
AIMS & METHODS: The objects of this study are to evaluate the effects of CNU® on GB stone dissolution and to assess the improvement of stone associated symptoms and to find out predictive factors for gallstone dissolution.
In total 10 medical centers in Korea participated in the investigation from Jan 2011 to June 2013. Inclusion criteria were; GB stone (diameter <15mm) in sonography, GB EF ≥ 50% in DICIDA biliary scan, radiolucent on Plain X-ray and asymptomatic or mild symptomatic patients. Exclusion criteria were: age under 18 years, complicated GB stones, patients with severe co-morbidity, abnormal LFT (ALT >2x N). The treatment consisted of 1 tablet (114mg of UDCA and 114mg of CDCA) at morning and 2 tables at bedtime. Patients were followed up at 1Mo, 3Mo and 6Mo for LFT, symptom score and ultrasonography (6Mo)
RESULTS: Total 236 cases were enrolled and 196 cases (Male 87, Female 109, mean age 54.8+12.8)) were finished the study and were analyzed. Complete dissolution was achieved in 13.3% after 6 months administration of CNU. Partial dissolution (defined as reduction in volume more than 25%) was 32.1%. Overall response rate was 45.4%. Stone size and BMI are factors for predicting gallstone dissolution. Gallbladder ejection fraction is not a predictive factor for dissolution. CNU treatment showed significant symptomatic improvements regardless of stone dissolution.

CONCLUSION: Magnesium trihydrate of UDCA and CDCA (CNU) is a well tolerated and effective agent for gallstone dissolution. However, a substantial portion of gallstones are still ineffectively treated with CNU. This group may have pigment stones rather than cholesterol stones. Further study is needed to evaluate effect of longer Tx duration and recurrent rate after cessation of Tx. Development of methods for predicting chemical composition of gallstones is warrant for selecting good candidates for medical dissolution Tx.
Disclosure of Interest: None declared

P0079 SIZE OF RECURRENT SYMPTOMATIC COMMON BILE DUCT STONES AND FACTORS RELATED TO RECURRENCE

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INTRODUCTION: Common bile duct (CBD) stones can be treated successfully by endoscopic stone extraction. Unfortunately, 4% to 24% of patients have recurrent CBD stones after the initial extraction of CBD stones. Some patients even have multiple recurrences. Unfortunately, little information is available on the size and recurrence interval of recurrent symptomatic CBD stones or on ways to prevent recurrence.
AIMS & METHODS: Between January 2007 and December 2011, 481 consecutive patients undergoing endoscopic extraction of CBD stones at a single institute were enrolled. We selected 34 patients with recurrent symptomatic CBD stones and 63 patients who were followed up more than five years without recurrence. We evaluated the role of endoscopic papillary large-balloon dilation (EPLBD) ($\geq$ 10 mm) in preventing the recurrence of CBD stones while identifying risk factors related to recurrence. Furthermore, the characteristics of symptomatic recurrent CBD stones and the interval of recurrence were investigated in patients with the first, second, and third recurrences of CBD stones.
RESULTS: The sizes of the CBD stones increased during the recurrences: 10.1 $\pm$ 5.2 mm, 13.5 $\pm$ 7.3 mm, and 16.8 $\pm$ 7.8 mm at the initial presentation, the first recurrence, and the second recurrence, respectively ($P = 0.016$). Among CBD stone recurrences, 50% occurred within 2.3 years, and 80% occurred within 5.3 years. The recurrence group had a smaller proportion of patients under 50 years of age, larger CBD diameters, fewer histories of more than 10 mm EPLBD, and more type I periampullary diverticula, compared with the non-recurrence group ($P < 0.05$). Multivariate analysis revealed that EPLBD more than 10 mm and smaller CBD diameter were independently related to less recurrence of CBD stones ($P = 0.001$ and 0.012, respectively).
Table. Multivariate analysis of the factors related to the recurrence of common bile duct stones

Factors	OR (95% CI)	P value
Endoscopic papillary large-balloon dilation ($\geq$ 10 mm)	0.161 (0.055 – 0.473)	0.001
CBD diameter	1.126 (1.027 – 1.235)	0.012
Type I periampullary diverticulum	3.322 (0.608 – 18.17)	0.166
Age ($<$ 50)	0.314 (0.073 – 1.360)	0.122

CONCLUSION: The sizes of CBD stones increased during recurrences. EPLBD more than 10 mm and smaller CBD diameter were related to less recurrence of CBD stones.
Disclosure of Interest: None declared

P0080 A COMPARATIVE STUDY BETWEEN PTGBD AND ETGD AS A BRIDGE TO SURGERY IN PATIENTS WITH ACUTE CHOLECYSTITIS AND A SUSPICION OF CBD STONE

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INTRODUCTION: To compare the technical feasibility, clinical and surgical outcomes between a single-step approach of endoscopic removal of CBD stones with endoscopic transpapillary gallbladder drainage (ETGD group) and a two-step approach of endoscopic removal of CBD stones and percutaneous transhepatic gallbladder drainage (PTGBD group) as a bridge treatment before cholecystectomy, in patients with acute cholecystitis and a high suspicion of common bile duct (CBD) stones.
AIMS & METHODS: From March 2006 to May 2013, a total of 79 patients were enrolled in this study retrospectively. The PTGBD group (n = 39) was compared with the ETGD group (n = 40, ENGBD: 22, ERGBD: 18) in terms of technical and clinical success rates, adverse events, and surgical outcomes of surgery time and rate of conversion to open surgery in the non-inferiority analysis.
RESULTS: PTGBD and ETGD groups had similar outcomes in terms of technical success rate (97.4% 38/39 vs 92.5% 37/40; 95% 1-sided confidence interval (CI) lower limit, -14.6%; $p = 0.028$ for noninferior margin of 15%) and clinical success rate (94.7% 36/38 vs 91.9% 34/37; 95% 1-sided CI lower limit, -12.9%; $p = 0.045$ for noninferior margin of 15%). The two groups did not differ significantly in the rates of adverse events (5.1% 2/39 vs 7.5% 3/40; $p = 1.000$), surgery time (59.3 vs 55.7 min; $p = 0.361$), rates of conversion to open cholecystectomy (5.2% 2/38 vs 0% 0/37; $p = 0.135$). There was no significant differences in the technical, clinical, and surgical outcomes between ENGBD and ERGBD groups respectively.
CONCLUSION: In patients with acute cholecystitis and a high suspicion of CBD stones, the single-step approach through ERCP and simultaneous ETGD could be an effective alternative treatment modality to the two-step approach through PTGBD followed by ERCP.
Disclosure of Interest: None declared

P0081 VISCERAL ABDOMINAL FAT MEASURED BY CT SCAN IS ASSOCIATED WITH AN INCREASED RISK OF SYMPTOMATIC GALLSTONE DISEASE

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INTRODUCTION: Previous studies have shown that obesity measured as BMI is a causal risk of gallstone disease. Visceral fat promotes systemic inflammation by secreting adipokines and inflammatory cytokines.
AIMS & METHODS: This study aims to investigate whether visceral fat measured by computed tomography (CT) is a risk factor for symptomatic gallstone disease (cholangitis or cholecystitis). A total of 582 participants (451 without gallstone and 131 symptomatic gallstone disease) who underwent CT and abdominal ultrasonography were analyzed. The associations between body mass index (BMI), visceral adipose tissue (VAT) area, subcutaneous adipose tissue (SAT) area, and symptomatic gallstone disease were estimated using odds ratios (ORs) and 95% confidence intervals (CIs) adjusted for age, sex, dyslipidemia, and diabetes mellitus.
RESULTS: In multivariate analysis, symptomatic gallstone disease was significantly associated with VAT area and SAT area (P for trend <0.001, and 0.045, respectively), but not BMI (P for trend 0.40). When the obesity indices were considered simultaneously, symptomatic gallstone disease remained significantly associated with VAT area for both categorical data and trend (P for trend 0.003), but not BMI (P for trend 0.536). The adjusted ORs for the highest quartile of the VAT area in gallstone disease were 3.2, compared with the lowest quartile.
CONCLUSION: Abdominal visceral tissue measured by CT, rather than BMI, is a better predictor for risk of symptomatic gallstone disease.
Disclosure of Interest: None declared

P0082 POSITIVE PREDICTIVE VALUE OF ENDOSCOPIC ULTRASOUND (EUS) FOR THE DETECTION OF INTRALUMINAL FILLING DEFECTS IN THE COMMON BILE DUCT (CBD) IN A LARGE NON-ACADEMIC TEACHING HOSPITAL

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INTRODUCTION: In small academic studies, endoscopic ultrasound has been shown a reliable and safe method to assess the presence of common bile duct stones.
AIMS & METHODS: The aim of this study was to calculate the positive predictive value (PPV) for the presence of CBD stones with EUS. For this we retrospectively included all patients in whom CBD stones were detected with EUS and who subsequently underwent endoscopic retrograde cholangiography (ERC). This study was performed in a large non-academic teaching hospital in The Netherlands between November 2006 and January 2011. PPV was calculated by dividing the number of true positives by the total number.
RESULTS: EUS detected CBD stones in 99 patients who subsequently underwent ERC. The median time-interval between EUS and ERC was 5 days (interquartile range 1-15 days). The PPV for the total group was only 56% (57/99). However, the PPV depended on the time-interval between EUS and ERC, being: 80% (8/10) within 24 hours, 63% (32/51) within 1-6 days, and 47% (18/38) after one week. Moreover, the PPV differed substantially depending on the type and number of intraluminal filling defects in the CBD, namely sludge (10/21, PPV 48%), or one stone (29/51, PPV 58%), or more than one stone (18/24, PPV 75%), or more than one stone with acoustic shadow (8/10, PPV 80%).
CONCLUSION: EUS performed in a large non-academic teaching hospital has a lower PPV for detection of CBD stones than overall reported in literature. This seems to be explained at least in part by the large variation in time-intervals between EUS and ERC indicating that ERCP should promptly follow a positive EUS and may be delayed a few days after the onset of symptoms to allow for spontaneous stone passage. Sludge in the CBD as finding on EUS has the lowest PPV when compared with stones with or without an acoustic shadow.
Disclosure of Interest: None declared

P0083 WHICH IS A BETTER PROCEDURE: SINGLE SESSION VERSUS MULTIPLE SESSIONS OF ERCP FOR COMMON BILE DUCT STONES WITH OR WITHOUT ACUTE CHOLANGITIS?

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INTRODUCTION: Tokyo guidelines (TG13) for management of acute cholangitis (AC) and acute cholecystitis were revised and published in 2013. TG13 recommend the elective, early or urgent biliary drainage using endoscopic retrograde cholangiopancreatography (ERCP), followed by treatment of etiology such as common bile duct (CBD) stones after the resolution of AC. However,

the usefulness of completion of endoscopic clearance of CBD stones with biliary drainage in a single session, remains unclear.
AIMS & METHODS: The aim of this study is to clarify which of these, a single session or multiple sessions of ERCP, is better for the patients with CBD stones with and without AC. This is a retrospective study. Between August 2012 and March 2014, a total of 411 ERCPs were performed in 252 patients with biliary and pancreatic diseases in our hospital. The patients with CBD stones with or without AC treated with ERCP-related procedure were eligible for the study. The patients with recurrent disease were excluded. Finally 116 consecutive patients (56 males and 60 females) were included in the study. They were divided into two groups; Group A for the patients in a single session of ERCP, and Group B for those in multiple sessions of ERCP. Groups A and B were compared with each other for the clinical outcomes, namely total duration of hospitalization (DH) and frequency of adverse events. The grade of AC, Grade I (mild), Grade II (moderate) and Grade III (severe), were also taken into account. Wilcoxon/Kruskal-Wallis test and Kaplan-Meier analysis were used as statistics. This study was approved by the local committee of ethics.
RESULTS: Group A and Group B was consisted of 84 and 32 patients, respectively. Mean age was 72.4 in Group A and 78.8 in Group B. The sphincterotomy and the maneuver using retrieval basket or balloon were performed more frequently in Group A ($p < 0.001$). In total, 74 patients were complicated with AC; grade I in 44, grade II in 17 and grade III in 13, and 42 patients were without AC. In Group A, grade I in 35, grade II in 10 and Grade III in 5, and without AC in 34 patients, respectively. In Group B, grade I in 9, grade II in 7 and grade III in 8, and without AC in 8 patients, respectively. The mean DH was 12.7 days in total. It was significantly shorter in Group A (9.9 days), as compared with Group B (20.1 days) ($p < 0.001$). In total, DH was incrementally longer according to the degree of AC grade ($p < 0.0001$); it was significantly longer (32.0 days) in grade III, as compared with Grade I (11.3 days), grade II (15.6 days) and without AC (7.0 days). In the patients with AC grade III, DH was significantly shorter in Group A (18.0 days) as compared with Group B (40.75 days) ($p = 0.0437$). Also in the patients without AC, DH was significantly shorter in Group A (6.4 days) as compared with Group B (9.9 days) ($p = 0.033$). As for adverse events, post ERCP pancreatitis was occurred in 4 patients in Group A and in 1 patient in Group B, and there was no significant difference between both groups ($p = 0.69$).
CONCLUSION: A single session of ERCP for completion of clearance of CBD stones with biliary drainage is superior to multiple sessions of ERCP, especially for the patients complicated with AC grade III and those without AC.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
PANCREAS I – POSTER EXHIBITION – HALL XL

P0084 THE ROLE OF PROINFLAMMATORY CYTOKINES AND ADHESION MOLECULES IN VASCULAR DISORDERS AND ORGAN DYSFUNCTION IN ACUTE PANCREATITIS PATIENTS

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INTRODUCTION: The main component in the pathogenesis of acute pancreatitis is the transition from local to the system inflammation that causes the severity of disease. Changes of microcirculation and endothelial dysfunction are an important step from mild to severe disease.
AIMS & METHODS: The study involved 53 acute pancreatitis patients (28 - severe, 25 - mild). We measured interleukin-6, interleukin-18, ICAM-1 and E-selectin in the blood plasma. Flow in the visceral arteries was assessed with the help of the Doppler sonography.
RESULTS: A significant increase of both pro-inflammatory cytokines and adhesion molecules was determined only in severe acute pancreatitis. We determined that the level of IL-6 significantly correlated with the appearance of liver dysfunction. There was a significant correlation between the concentration of IL-18, ICAM-1, E-selectin and the appearance of multiple organ dysfunction syndrome. There was a significant direct correlation concentrations of IL-6 with peak systolic velocity in the superior mesenteric artery ($R = 0.502941$, $p = 0.047063$), with an index of resistance in common hepatic ($R = 0.532845$, $p = 0.033574$), splenic ($R = 0.511125$, $p = 0.043028$) and superior mesenteric ($R = 0.563200$, $p = 0.023107$) arteries. The level of IL-18 was significantly correlated with peak systolic velocity in the common hepatic artery ($R = 0.589102$, $p = 0.016342$), splenic artery ($R = 0.547865$, $p = 0.028022$) and superior mesenteric artery ($R = 0.504783$, $p = 0.046131$), as well as the resistance index in the common hepatic artery ($R = 0.524375$, $p = 0.037051$) and superior mesenteric artery ($R = 0.573230$, $p = 0.020271$). The level of ICAM-1 was significantly correlated with changes in blood flow in the visceral vessels, in particular, peak systolic velocity in the common hepatic artery ($R = 0.802061$, $p = 0.000186$), splenic ($R = 0.764581$, $p = 0.000,562$) and the superior mesenteric artery ($R = 0.768212$, $p = 0.000509$), as well as the resistance index ($R = 0.527422$, $p = 0.035770$; $R = 0.608824$, $p = 0.012315$; $R = 0.736152$, $p = 0.001148$, respectively) in them. The level of soluble E-selectin may also affect splanchnic flow in patients with acute pancreatitis, defined as a significant direct correlation between the concentration dependence of E-selectin and peak systolic velocity of blood flow in the common hepatic ($R = 0.838249$, $p = 0.000095$) and splenic ($R = 0.689902$, $p = 0.004424$) arteries and resistance index in the common hepatic ($R = 0.710321$, $p = 0.003002$) and superior mesenteric ($R = 0.759862$, $p = 0.001012$) arteries.
CONCLUSION: It was determined that the levels of proinflammatory cytokines and adhesion molecules increase in the blood of acute pancreatitis patients. Their level correlates with the organ dysfunction and disturbances in splanchnic blood flow.
Disclosure of Interest: None declared

P0085 TIMING OF INTERVENTION IN INFECTED NECROTIZING PANCREATITIS: AN INTERNATIONAL MULTIDISCIPLINARY SURVEY AND CASE VIGNETTE STUDY

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INTRODUCTION: It is unclear whether there is consensus regarding the timing of intervention in patients with infected necrotizing pancreatitis (INP).
AIMS & METHODS: We evaluated the current expert opinion regarding timing of intervention in INP. An anonymous digital survey was sent to 118 expert pancreatologists (surgeons, gastroenterologists, radiologists) from all continents. The survey consisted of 18 questions and 10 clinical cases including CECT images of varying disease stages. Diagnostic and therapeutic options included fine needle aspiration (FNA), antibiotics, (percutaneous or endoscopic) catheter drainage and necrosectomy.
RESULTS: Response rate was 74% ($N = 87$). The step-up approach, initial catheter drainage if needed followed by necrosectomy, was accepted by most experts (87%). Consensus was lacking regarding the use of FNA to diagnose INP: 0% used FNA routinely, 40% only in case of clinical suspicion, 45% rarely and 15% never. After definitively diagnosing INP, 55% would postpone an intervention and await the effect of antibiotics, whereas 45% would immediately perform an intervention. Walled-off necrosis was not considered a technical prerequisite for percutaneous catheter drainage by 88% of experts whereas 66% considered it essential for endoscopic transluminal drainage. More experts would intervene in case of proven INP (gas in the (peri)pancreatic necrotic collection on CECT) vs. clinical signs of INP: i.e. day 7: 34% vs 2%, day 14: 57% vs 25%, day 30: 89% vs 72%.
CONCLUSION: Although the step-up approach is well accepted as routine management strategy of INP, consensus regarding the timing of initiating this approach is lacking. Proof of infection and disease duration influence the timing of intervention. This study highlights the need for a randomized trial on timing of intervention in INP.
Disclosure of Interest: None declared

P0086 PREDICTION OF POST-ERCP PANCREATITIS BY 4-HOUR POST-ERCP SERUM AMYLASE AND LIPASE LEVEL

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INTRODUCTION: Acute pancreatitis is the most common and serious complication of endoscopic retrograde cholangiopancreatography (ERCP). Early prediction of possible post-ERCP pancreatitis (PEP) could allow for an earlier safe discharge of a patient on the same day after ERCP.
AIMS & METHODS: The aim of this study was to investigate a predictive cut-off value of 4-hour post-ERCP serum amylase and lipase levels for the PEP. In patients who underwent ERCP procedures and had tests for serum amylase and lipase levels of 4-hour post-ERCP and the next morning at Ajou Medical Center from January 2012 to August 2013, patient demographics, the procedure reasons, performance of pancreatograms, serum amylase and lipase levels were retrospectively evaluated.
RESULTS: PEP occurred in 16 (3.1%) after 516 ERCP procedures. Its severity was mild in 4 (25%), moderate in 9 (56.3%), and severe in 3 (18.8%). The mean 4-hour amylase level was significantly higher in patients with PEP, compared with those without PEP (965 U/L vs. 158 U/L, $p = 0.001$). There were no statistically significant differences in age, gender, and the procedure reasons between both groups. The sensitivity, specificity and negative predictive value (NPV) of a 4-hour post-ERCP amylase level with a cut-off value of 2.5 times of its normal upper limit (290 U/L) was 75.0%, 88.0% and 99.1%, respectively. The sensitivity, specificity and negative predictive value (NPV) of a 4-hour post-ERCP lipase level with a cut-off value of 8 times of its normal upper limit (480 U/L) was 75.0%, 91.3% and 99.1%, respectively. The patient group undergoing pancreatogram revealed high incidence of post-ERCP pancreatitis, but no significant difference in the 4-hour post-ERCP serum amylase and lipase level, compared to its counterpart group.
CONCLUSION: The 4-hour post-ERCP serum amylase level and lipase level with cut-off value of 2.5 times and 8 times of their normal upper limit have so far proven to be useful predictive values for an earlier safe discharge of a patient on the same day after ERCP.
Disclosure of Interest: None declared

P0088 PREDICTING SUCCESS OF CATHETER DRAINAGE IN INFECTED NECROTIZING PANCREATITIS

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INTRODUCTION: Catheter drainage as the first treatment step of infected necrotizing pancreatitis is successful in at least 30% of patients. It is currently not possible to predict which patients will also need necrosectomy. We evaluated predictive factors for success of catheter drainage in infected necrotizing pancreatitis.
AIMS & METHODS: We performed a post-hoc analysis of 130 prospectively included patients who underwent primary catheter drainage for (suspected) infected necrotizing pancreatitis. Using logistic regression we evaluated the association between success of catheter drainage (i.e. survival without necrosectomy) and 22 factors regarding demographics, disease severity (e.g. CRP, APACHE-II score and organ failure), morphologic characteristics on CT (e.g. percentage and distribution of necrosis and CTSI) and drainage criteria (e.g. timing of drainage and type of drain).
RESULTS: Drainage was performed percutaneously in 113 patients and endoscopically in 17 patients. Infection was confirmed in 116 patients (89%). Catheter drainage was successful in 45 patients (35%). In multivariable regression, the following variables were associated with success of drainage: female gender (odds ratio[OR] 4.84; 95% > confidence interval[CI] 1.89-12.4; $p = 0.001$), absence of multi-organ failure (OR 6.19; 95% > CI 1.50-25.53; $p = 0.012$), percentage of pancreatic necrosis (< 30%/30-50%/ > 50%: OR 2.29; 95% > CI 1.21-4.36; $p = 0.011$), primarily left-sided pancreatic necrosis (OR 13.35; 95% > CI 1-174; $p = 0.048$) and homogeneity of the collection (OR 5.23; 95% > CI 1.60-17.05; $p = 0.006$). A prognostic nomogram including these factors yielded probability of success ranging from 99% (all factors present) to 1% (none of the factors present).
CONCLUSION: Female gender, absence of multi-organ failure, low percentage of necrosis, left-sided pancreatic necrosis and a homogeneity of the collection are independent predictors for success of catheter drainage in infected necrotizing pancreatitis. The constructed nomogram can easily predict success in clinical practice.
Disclosure of Interest: None declared

P0089 FUNGAL INFECTION IN PATIENTS WITH WALLED-OFF PANCREATIC NECROSIS IS ASSOCIATED WITH A POOR PROGNOSIS

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INTRODUCTION: Patients with necrotizing pancreatitis and infected necrosis have a worse prognosis than patients with sterile necroses. While there is clear evidence that bacterial infection in pancreatic necrosis increases mortality and morbidity, studies on the influence of fungal infections have been conflicting.
AIMS & METHODS: To evaluate the impact of fungal infections in patients with walled-off pancreatic necrosis (WON) treated by endoscopic, transmural drainage and necrosectomy (ETDN). In addition, to evaluate the effect of antifungal treatment.
We retrospectively retrieved medical charts of 123 patients who underwent ETDN for WON in our department between November 2005 and December 2013.
RESULTS: Fifty-seven out of the 123 patients (46%) had fungus in their necrosis. The median time from the symptom debut to the first fungal finding was 61 days (range 8-195). In 20 patients (35%) the first fungal finding was at the index endoscopy, in 24 patients (42%) it was at the second endoscopy, and in 9 patients (16%) at the third endoscopy. The prevailing fungal finding at both the index and secondary endoscopy was Candida albicans (55% and 56%, respectively).
Ten of the 57 patients (18%) with fungal infection died during admission, and 18 (32%) developed organ failure. The mortality in patients infected with bacterial infection, only, was 6.5% ($p = 0.046$). Concomitant fungemia was found in 6 patients. Three patients with concomitant fungemia died, as opposed to seven with fungi in the necrosis, only (50% vs. 14%, respectively $p = 0.027$).
Thirty-nine of the 57 patients (70%) were treated with antifungals. There was no significant difference in mortality or occurrence of organ failure between this group and the group that was not treated with antifungals.
Culturing from the necrosis was repeated in 35 out of 57 patients (61%), of which 17 patients were positive for fungus. The same fungal species on both the first and the second culture was found in 15 out of the 17 patients (88%) despite adequate antifungal treatment based on the susceptibility pattern.
CONCLUSION: Fungal infection in WON, especially with concomitant fungemia, is associated with a poor prognosis. Whether the outcome may be explained by the fungal infection per se or it is merely a consequence of a prolonged disease course is, however, at present unknown. Only about one-third of all cases with fungal infection in necrosis were found at the index endoscopy, which is why continuous culturing should be mandatory throughout the disease course
Disclosure of Interest: None declared

P0090 EFFECT OF INTRAVENOUS FLUID RESUSCITATION ON INFLAMMATORY MARKERS OF ACUTE PANCREATITIS AND ITS CLINICAL OUTCOME

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INTRODUCTION: Early in the course of acute pancreatitis (AP) management revolves primarily around supportive care and fluid resuscitation remains the cornerstone. Inflammatory cytokines play a crucial role in extravascular fluid sequestration. Recent evidence shows the superiority of Ringer lactacte (RL) over normal saline (NS) as the fluid of resuscitation patients with AP.
AIMS & METHODS: To study the effect of two different types of resuscitation fluids viz. normal saline (NS) and Ringers lactate (RL) on inflammatory markers IL-6 and IL-10 and on the clinical course and outcome of patients with acute pancreatitis (AP).
Consecutive adult patients with AP who presented within 5 days of onset of symptoms between July 2012 and June 2013 were randomized to receive NS or RL. The patients were classified as having mild, moderate or severe AP and managed in a high dependency unit as per a uniform protocol. Intravenous fluid was infused initially as 20ml/kg bolus till a base line CVP of 8 cm of water and a urine output of > 0.5ml/kg/hr. was established. Further fluids were infused to maintain urine output as mentioned above. Serum samples were obtained at admission days 0, 3 and 7. IL-6 and IL-10 were estimated on the cryo-preserved serum samples using a Diaclone ELISA kit. Patients were monitored for the development of organ failure, sepsis, local complications, duration of hospital stay and final outcome till 28 days of admission. Data was recorded using Microsoft excel and analyzed using SPSS software v17.0.
RESULTS: 50 patients of AP with a mean age of 45.82±16.46 years (56% males) were included. NS and RL groups included 25 patients each who were well matched for age and sex. There was no significant difference in the severity of AP between the 2 groups ($p = 0.77$). IL-6 levels on day 0, day 3 and day 7 were significantly elevated in patients with severe AP (SAP) compared to those without severe disease [183.66±43.92, 178.20±36.28, 143.85±47.21 pg/ml vs 145.90±60.93, 119.99±58.86, 86.44±38.50 pg/ml ($p < 0.05$)] and remained persistently elevated at the end of first week in SAP group. No such correlation was seen with IL-10 level ($p > 0.05$). The cumulative fluid infused over first 7 days of admission was not statistically significant between the 2 groups (13.56±4.93 liters vs. 13.99±4.58 liters, $p > 0.05$). There was no statistically significant difference in the serum IL-6 levels noted between the NS and RL groups but among patients with severe disease ($n = 29$), those who received RL had significantly lower serum IL-6 levels at the end of first week than those in RL group; $p = 0.043$. Patients receiving NS had significantly longer duration of hospitalisation (22±12.45 days versus 14±7.17 days; ($p = 0.015$), higher incidence of infective complication ($p = 0.037$) and a higher need for intervention ($p = 0.050$). Patients receiving RL were found to show a greater magnitude of reduction in their organ failure score on day 3 and 7 in comparison to those receiving NS ($p = 0.012$ and 0.001).
CONCLUSION: There was no significant reduction in cytokine levels among patients resuscitated with RL or NS. However, patients receiving RL had an early organ failure resolution, fewer infections and shorter hospital stay, making RL the preferred fluid for resuscitation.
Disclosure of Interest: None declared

P0091 A C-REL/NFTAC2/COX-2 PATHWAY CONFERS TRAIL RESISTANCE IN PANCREATIC CANCER

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INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) represents one of the deadliest malignancies with an overall life expectancy of six months despite current therapies. NF-kB signalling has been shown to be critical for this profound cell-autonomous resistance against chemotherapeutic drugs and death-receptor induced apoptosis, but little is known about the role of the c-Rel subunit in solid cancer and PDAC apoptosis control.
AIMS & METHODS: In the present study, by analysis of genome-wide patterns of NF-kB dependent gene expression we investigated the role of c-Rel in apoptosis resistance of PDAC.
RESULTS: TRAIL resistant Panc1 and Patu8988 cells exhibited a strong TRAIL inducible NF-kB activity, whereas TRAIL sensitive MiaPaca2 cells displayed only a small increase in NF-kB binding activity. Transfection with siRNA against c-Rel sensitized the TRAIL resistant cells in a comparable fashion to siRNA targeting the p65/RelA subunit. Gel shift analysis revealed that c-Rel is part of the TRAIL inducible NF-kB complex in PDAC. Array analysis identified NFATc2 as a c-Rel target gene amongst the 12 strongest TRAIL inducible genes in apoptosis resistant Panc1 cells. By database search and chromatin immunoprecipitation we were able to funcionally characterize one regulatory element for c-Rel in the NFATc2 promoter. In line, siRNA targeting c-Rel strongly reduced TRAIL induced NFATc2 activity in TRAIL resistant PDAC cells. Furthermore, siRNA targeting NFATc2 sensitized these PDAC cells against TRAIL induced apoptosis. Finally, TRAIL induced expression of COX-2 was diminished

through siRNA targeting c-Rel or NFATc2 and pharmacological inhibition of COX-2 with celecoxib enhanced TRAIL apoptosis.
CONCLUSION: In conclusion, we were able to delineate a novel c-Rel, NFATc2 and COX-2 dependent anti-apoptotic signalling pathway in PDAC with broad clinical implications for pharmaceutical intervention strategies.
Disclosure of Interest: None declared

P0092 THE MICROARRAY TISSUE ANALYSIS OF GENES INVOLVED IN PANCREATIC ADENOCARCINOMA

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INTRODUCTION: The pathogenesis of pancreatic ductal adenocarcinoma involves the multi-stage development of molecular aberrations affecting signaling pathways that regulate cancer growth and progression. Tissue microarray analysis of pancreatic tumors allows simultaneous assessment of genetic disorders, which can lead to identification of biomarkers of poor prognosis.
AIMS & METHODS: To characterize the gene expression of pancreatic adenocarcinoma compared to normal tissue from the same patient. We investigated sixteen samples of T3 pancreatic adenocarcinoma obtained intraoperatively and compared them to normal pancreatic tissue from the same patients. RNA was extracted and assessed qualitatively and quantitatively, followed by amplification of cDNA using reverse transcriptase, cRNA synthesis, and hybridization of microarray slides. For each sample 1000 ng of total RNA was available. The overexpressed and underexpressed genes were classified by their known function in the cell. We selected genes over- or underexpressed three times compared to normal adjacent tissue some described previously in pancreatic pathology, and used RT-PCR for validation.
RESULTS: On microarray tissue analysis 41 genes were overexpressed and 402 were underexpressed in the pancreatic adenocarcinoma samples. There were selected genes involved in transcription process as ZNF 428, MIXL1, SEPT 1, genes involved in intracellular signaling as FLJ21865, AGRP and genes involved in transmembranar and intracellular transport as CCDC88, UTP14A,VPS11, LLRC21,CHRM3, Marveld3. Validation by qRT-PCR confirmed the involvement of AGRP and MIXL1 gene in pancreatic adenocarcinoma tissue.
CONCLUSION: Microarray tissue analysis of pancreatic adenocarcinoma showed more underexpressed than overexpressed genes. After validation, the overexpressed gene AGRP was shown to be one possible factor responsible for anorexia and perineural invasion. The possible role in pancreatic cancer of MIXL1, known to play a role in cellular proliferation and differentiation, should be further clarified.
Disclosure of Interest: None declared

P0093 CCK-B RECEPTOR GENE VARIANT IS NOT ASSOCIATED WITH INCREASED RISK, NOR WITH DECREASED SURVIVAL IN PANCREATIC ADENOCARCINOMA

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INTRODUCTION: Cholecystokinin-B (CCK-B) receptor is often overexpressed in pancreatic ductal adenocarcionoma (PDAC); stimulation of the receptor promotes tumor growth. An intronic mutation (c.811+37C>A) in the *CCKBR* gene causes retention of intron-4, resulting in a new spliceform, which was previously shown to correlate with higher PDAC risk and a more aggressive phenotype.
AIMS & METHODS: Our aim was to test the effect of the c.811+37C>A mutation on PDAC risk and prognosis in a Hungarian population. 122 subjects with PDAC (cases) and 106 subjects with no pancreatic disease (controls) were recruited from the Hungarian National Pancreas Registry. Genomic DNA was isolated from peripheral blood. Intron-4 of the CCKBR gene, including exon-intron boundaries, was amplified and sequenced.
RESULTS: We found the c.811+37C>A intronic mutation in 35 heterozygous and 5 homozygous cases and in 32 heterozygous and 3 homozygous controls (allele frequency 18.4% and 17.9% respectively). One case subject carried a p. R319Q and one control subject a p. R319W missense mutation. Survival analysis showed no significant difference in median survival between wild type cases and carriers for the mutation (8.7 months and 6.9 months respectively)
CONCLUSION: In our cohort, the c.811+37C>A intronic mutation was not associated with increased risk for PDAC. Also, the mutation was not associated with shorter survival, indicating that this genetic variant is not a clinically relevant prognostic factor. Supported by TÁMOP and OTKA.
Disclosure of Interest: None declared

P0094 HYPOXIA AND NEUROINFLAMMATION LEAD TO AN INTERLEUKIN-6-INDUCED SCHWANN CELL ACTIVATION IN PANCREATIC CANCER

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INTRODUCTION: Pancreatic cancer (PCa) is characterized by prominent intrapancreatic neuropathy and neuropathic pain. Up to now, the impact of glia cells on the development of the pancreatic neuropathy has not yet been investigated.
AIMS & METHODS: We studied whether there is an activation of peripheral glia cells (Schwann cells, SC) in PCa and what signalling pathways might be responsible for intrapancreatic glial activation. SC were cultured under hypoxia, in pancreatic cancer cell (PCC) supernatants or co-coltured with PCC and T-lymphocytes and investigated via immunoblotting, MTT viability assay, Multiplex-Luminex-ELISA® and cell area measurement. Nerves in PCa and normal pancreas (NP) were analysed for their immunoreactivity for glial fibrillary acidic protein (GFAP), hypoxia inducible factor 1 alpha (HIF-1α) and carboanhydrase IX (CA-IX). The SC distribution and frequency in conditional PCa knock-out mice was assessed after in-vivo blockade of the IL-6 signalling pathway.
RESULTS: Hypoxia leads to upregulation of the intermediate filaments GFAP, Nestin and Vimentin and pro-inflammatory cytokines in SC. The nerves in PCa were immunoreactive for HIF-1α and CA-IX, and the extent of neuro-immunoreactivity for HIF-1α and CA-IX correlated to the intraneural GFAP amount. PCC supernatants led to upregulation of GFAP and Nestin in SC, cellular hypertrophy (stellation) and higher proliferation rate. The serverity of pancreatic neuritis correlated with the intraneural GFAP amount. The blockade of IL-6, but not of IL-1β in PCC supernatants abolished the upregulation of GFAP and Nestin. GFAP/SOX10 double positive SC were found around pancreatic intraepithelial neoplasia (PanIN) of Ptf1a-Cre;$Kras^{G12D}$, but not around PanINs of Ptf1a-Cre;$Kras^{G12D}$;$IL6^{-/-}$ mice. The blockade of IL-6 *trans*signalling in Ptf1a-Cre;$Kras^{G12D}$;$sgp130^{tg}$ mice had no influence on the SC distribution around PanINs.
CONCLUSION: SC in PCa show typical features of reative gliosis, which is induced via the classical IL-6 signalling.
Disclosure of Interest: None declared

P0095 DIAGNOSTIC EFFICIENCY OF CELL-BLOCK WITH IMMUNOSTAINING, SMEAR CYTOLOGY, LIQUID-BASED CYTOLOGY IN EUS-FNA ON PANCREATIC LESIONS: AN INSTITUTION'S EXPERIENCE

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INTRODUCTION: The diagnostic efficiency of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) cytology varies largely depending on the processing methods of specimens.
AIMS & METHODS: The present study aimed to evaluate the diagnostic efficiency of cell block (CB) with methods of immunostaining, smear cytology (SC) and liquid-based cytology (LBC) without on-site cytopathologist in patients with pancreatic lesions. 72 patients with pancreatic lesions were prospectively enrolled in this study. After EUS-FNA, specimens were determined by SC, LBC and CB with immunostaining, respectively. Diagnostic efficiency of SC was compared with that of LBC and CB. The final diagnosis was confirmed by surgically resected specimens, diagnostic imaging and clinical follow-up.
RESULTS: 60 malignant and 12 benign pancreatic lesions were determined. The diagnostic sensitivity, negative predictive value and accuracy (90.0%, 66.7% and 91.7%) of CB with immunostaining were significantly higher than those of SC (70.0%, 30.0% and 75.0%, $P < 0.05$), LBC (73.3%, 31.6% and 77.8%, $P < 0.05$). The combination of CB and SC, or CB and LBC did not significantly increase the efficiency compared to CB with immunostaining alone ($P > 0.05$). Table: Diagnostic efficiency of SC, LBC and CB methods in pancreatic lesions

	SC	LBC	CB	SC+CB	LBC+CB
Sensitivity,% (n)	70.0 (42/60)	73.3 (44/60)	90.0 (54/60)*	91.7 (55/60)	93.3 (56/60)
Spcificity, % (n)	100 (12/12)	100 (12/12)	100 (12/12)	100 (12/12)	100 (12/12)
PPV, % (n)	100 (42/42)	100 (44/44)	100 (54/54)	100 (55/55)	100 (56/56)
NPV, % (n)	30.0 (12/40)	31.6 (12/38)	66.7 (66/72)*	70.6 (12/17)	75.0 (12/16)
Accuracy, % (n)	75.0 (54/72)	77.8 (56/72)	91.7 (66/72)*	93.1 (67/72)	94.4 (68/72)

CONCLUSION: The CB with immunostaining technique presents a higher diagnostic efficiency than both of SC and LBC without on-site cytopathologist in patients with pancreatic lesions who had undergone EUS-FNA.

Disclosure of Interest: None declared

P0096 EFFECT OF TELOMERASE PEPTIDE VACCINATION, GV 1001 COMBINED WITH GEMCITABINE IN PANCREATIC DUCTAL ADENOCARCINOMA

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INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) shows dismal prognosis due to early metastasis, frequent recurrence and chemo-resistance. However, there is no effective treatment to overcome these problems. GV1001 is a telomerase-based cancer vaccine made of a 16-mer TERT peptide and human telomerase reverse transcriptase (hTERT), the rate-limiting subunit of the telomerase complex, is therefore an attractive target for cancer vaccination.
AIMS & METHODS: AIMS: The aim of this study was to evaluate the combination benefit of telomerase peptide vaccination, GV1001 combined with Gemcitabine in PDAC.
METHODS: Human PDAC cell lines (Panc-1 and AsPC-1) and PDAC stem cells (CD133+) were used in in vitro experiments. Also, a PDAC xenograft mice model was established using PDAC cell lines (Panc-1 and AsPC-1) and PDAC stem cells (CD133+). Treatment groups were divided as follows; control, Gemcitabine alone, GV 1001 alone and Gemcitabine and GV 1001 combination. The changes of weight and tumor size were evaluated in regular intervals before and after the treatment. The inflammatory cytokines (IL-6, TNF-α, INF-γ), leptin and ghrelin were measured from the serum of xenograft PDAC mice model.
RESULTS: ***In vitro experiments:*** GV1001 alone did not affect the proliferation of PDAC cells.
Almost 100% of the population of each PDAC cell line was positive for Epithelial Specific Antigen (ESA, Epithelial Cellular Adhesion Molecule). The positive results in PDAC cells ranged from as few as 0.5% to as many as 3% for ESA+CD133+ cells.
In vivo experiments: Mean tumor volume and size were decreased in treatment of Gemcitabine only group and Gemcitabine with GV 1001 group, and there were no significant differences between the two groups. However, Gemcitabine only or Gemcitabine with GV 1001 treatment groups had significantly small tumor size and volume compared to control group ($P < 0.001$). Interestingly, there was significant difference in mean body weight between the groups with Gemcitabine only vs. Gemcitabine with GV 1001 combination groups. Mice of Gemcitabine with GV 1001 treatment group did not have significant weight loss compared to Gemcitabine only group although they have decreased tumor size and volume. There was no mortality of mice until the end of the treatment.
CONCLUSION: GV1001 showed beneficial effects combined with Gemcitabine in the PDAC xenograft mice model, preventing emaciation and increasing anti-inflammatory effects. Moreover, GV 1001 combined with Gemcitabine treatment showed significant loss of fibrosis in tumor tissue. Therefore, further investigation of GV1001's effect may give us useful insights to understand the biology of PDAC progression and the synergistic effects of anti-cancer drug delivery in PDAC treatment.
Disclosure of Interest: None declared

P0097 PRDX1 PROMOTES PANCREATIC CANCER CELL MOTILITY AND INVASION BY MODULATING P38 MAPK ACTIVITY

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INTRODUCTION: Previous reports describe that Prdx1 is an antioxidant enzyme that participates in the regulation of hydrogen peroxide-mediated signal transduction, and is also implicated in the immune response, cell proliferation, differentiation, and apoptosis. Prdx1 interacts with apoptosis signal-regulating kinase 1 (ASK1), a member of the mitogen-activated protein kinase kinase kinase (MAPKKK) family that activates both MKK4/MKK7-JNK and MKK3/MKK6-p38 MAPK signaling cascades, via the thioredoxin-binding domain of ASK1; the redox-sensitive catalytic activity of Prdx1 is required for the interaction with ASK1.
AIMS & METHODS: Pancreatic ductal adenocarcinoma (PDAC) is among the deadliest cancers because PDAC cells are highly invasive, they easily invade surrounding tissues, and they metastasize at an early stage. Since the role of Prdx1 in migration and invasion of cancer cells, including pancreatic cancer cells, has not been reported, the aim of this study was to investigate the role of Prdx1 in invasiveness of pancreatic cancer cells. This study describes new and unique findings regarding the molecule Prdx1.
RESULTS: Prdx1 plays a role in promoting cell motility and invasion by regulating the activity of p38 MAPK, a member of the MAPK family protein. Prdx1 interacts with active forms of p38 MAPK, and complexes of Prdx1 and phosphorylated p38 MAPK localize at the leading edges of migrating PDAC cells. Suppression of Prdx1 decreases active p38 MAPK and inhibits cell motility and invasion. Treatment of PDAC cells with a p38 MAPK inhibitor decreases invasiveness. The peroxidase activity of Prdx1 was likely not associated with cell motility and invasion in PDAC. Thus, Prdx1-dependent promotion of cell motility and invasion is likely associated with increased active p38 MAPK. Suppression of Prdx1 inhibits membrane ruffling and protrusions and decreases peripheral actin structures in membrane protrusions. The p38 MAPK inhibitor also inhibits the formation of membrane protrusions via inhibition of accumulation of Prdx1 in cell protrusions.
CONCLUSION: Prdx1 regulates actin-cytoskeleton rearrangements at membrane protrusions through modulation of the activity of p38 MAPK, which in turn promotes pancreatic cancer cell motility and invasion. Inhibition of binding of Prdx1 with active p38 MAPK may be effective for targeted molecular therapy, because any such therapy would inhibit the formation of cell protrusions and consequently limit cell motility and invasion of pancreatic cancer cells.
Disclosure of Interest: None declared

P0098 TIME-RESTRICTED ACTIVATION OF PROTEIN KINASE D2 DIRECTS VASCULOGENESIS DURING MOUSE EMBRYONIC STEM CELL DIFFERENTIATION

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INTRODUCTION: The protein kinase D (PKD) isoenzymes PKD1, -2, and -3, are prominent downstream targets of PKCs and phospholipase D in various biological systems. Recent data from our laboratory identified PKD isoforms as novel, essential mediators of tumour cell-endothelial cell communication but also as regulators of tumour cell motility and metastasis formation. The role of PKD isoforms during vascular development remains elusive.
AIMS & METHODS: In the current study, we aimed to dissect the contribution of PKDs to vasculogenesis and angiogenesis in early embryonic development using mouse embryonic stem (ES) cells as bona fide tool.
RESULTS: First, we identified Protein Kinase D2 as the predominant isoform in undifferentiated ES cells leading us to particularly focus on this isoform. Time-restricted PKD2 activation using an inducible knock-in allele in differentiating mouse ES cells prevented cardiac mesoderm but activated a vascular differentiation program as shown by gene and protein regulation. Interestingly, the proliferative capacity is strongly diminished as a consequence of forced PKD2 expression. Finally, we aimed to underpin our findings in two independent *in vivo* models: First, embryoid bodies were transplanted on the chorioallantois membrane (CAM) of fertilised chicken eggs, a widely used model to study pro- and anti-angiogenesis. In line, with our *in vitro* data pronounced vessel formation was evident in the tumour-like structures arising at day 4 of the CAM assay. Second, we used the teratoma assay and induced PKD2 in immunodeficient mice during teratoma formation. While there was no difference in teratoma weight or size, a strong increase of CD31 expression as an indicator of vasculogenesis was observed in teratoma lysates.
CONCLUSION: Our data obtained in murine ES cells demonstrate that PKD2 contributes to the regulation of angiogenesis during early development and ascribes a vascular fate in two independent embryonic tumorgenesis models.
Disclosure of Interest: None declared

P0099 GENISTEIN POTENTIATES THE ANTITUMOR EFFECT OF 5-FLUOROURACIL BY INDUCING APOPTOSIS AND AUTOPHAGY IN HUMAN PANCREATIC CANCER CELLS

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INTRODUCTION: Although 5-fluorouracil (5-FU)-based combination chemotherapy (e.g. FOLFIRINOX) has demonstrated effectiveness against pancreatic cancer, novel therapeutic strategies must be developed to enhance increase the therapeutic window of these cytotoxic agents. Genistein is a soy-derived isoflavone with pleiotropic biologic effects that can enhance the antitumor effect of chemotherapeutic agents.[1-3]
AIMS & METHODS: To understand how genistein potentiates the antitumor effects of chemotherapeutic agents, we examined apoptosis and autophagy in the MIA PaCa-2 human pancreatic cancer cell line and subcutaneous pancreatic tumor xenograft model. Apoptosis was evaluated using DNA fragmentation assay and Western blot of poly (ADP ribose) polymerase and caspase-3. Meanwhile, autophagy was evaluated using Western blot of microtubule-associated protein light chain 3 (LC3)-I/II and fluorescent microscopy observation of green fluorescent protein-LC3B puncta and acidic vesicular organelle formation. In animal study, induction of apoptosis and autophagy was assessed by TUNEL assay and immunohistochemistry staining of LC3B, respectively.
RESULTS: We observed that genistein enhanced 5-FU-induced apoptosis by down-regulating B-cell lymphoma 2 (bcl-2). Moreover, genistein enhanced 5-FU-induced autophagy and triggered autophagic cell death by decreasing bcl-2 while inducing beclin-1. In vivo treatment studies demonstrated that the combination of 5-FU and genistein significantly decreased final tumor volume comparing to genistein alone or 5-FU alone by inducing apoptosis as well as autophagy.
CONCLUSION: Genistein can potentiate the antitumor effect of 5-FU by inducing apoptotic cell death as well as autophagic cell death. These results demonstrate the potential of genistein as an adjuvant therapeutic agent to enhance the antitumor effects of current first-line cytotoxic agents against pancreatic cancer.
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Disclosure of Interest: None declared

P0100 CHARACTERIZATION OF THE NERVE-STELLATE CELL INTERACTIONS IN PANCREATIC CANCER

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INTRODUCTION: Pancreatic stellate cells (PSC) emerged in recent years as the main actor for the generation of pancreatic fibrosis in pancreatic cancer (PCa). Subsequent to their activation, PSC start to proliferate, migrate, and produce several extracellular matrix (ECM) components as well as cytokines. In this context, neural invasion and pancreatic neuroplasticity is most prominent in the desmoplastic areas.
AIMS & METHODS: The present study aims at elucidating the characterisation of the interactions of nerves, carcinoma cells and PSC and the potential impact of PSC during the generation of neuropathic alterations in PCa.
PSC were isolated from Wistar rats and cultivated under hypoxia, stimulated with TGFβ or left untreated as controls. After cell lysis, the expression of neurotrophic factors and their receptors (GFRα) was determined by Immunoblotting and by qRT-PCR. For neuroplasticity assays, dorsal root ganglia (DRG) were isolated from newborn Wistar rats and treated with supernatants of quiescent and activated PSC. Changes in neurite length, axonal branching, perikaryonal diameter and glial density were determined.
RESULTS: PSC produce neurotrophic factors as well as their receptors and alter the expression pattern of neurturin and artemin after activation towards their active forms, whereas the GFRα expression remains unchanged. After treatment of PSC with hypoxia or TGFβ, PSC are activated. Cell culture supernatants of activated PSC lead to an increased neurite and glial density in isolated DRG.
CONCLUSION: Activated PSC alter their expression pattern of neurotrophic factors, influence neuroplasticity of isolated DRG and therefore may play a seminal role in the generation of pancreatic neuropathy and pain in PCa.
Disclosure of Interest: None declared

P0101 THE METASTASIS-PROMOTING ROLES OF EXTRAVASATED PLATELET AGGREGATION IN PANCREATIC CANCER AND STROMA

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INTRODUCTION: The last decade has focused attention on the central role of platelets interacting with tumor cells and the immune system in promoting tumor progression and distant spread through release of growth factors, such as transforming growth factor beta (TGF-β), vascular endothelial growth factor A (VEGF-A) and plasminogen activator inhibitor-1 (PAI-1), into the tumor microenvironment. We focused on the potential metastasis-promoting role of extravasated platelet aggregation (EPA) in pancreatic cancer and stroma.
AIMS & METHODS: Resected pancreatic cancer specimens from 40 patients were used in this study. To examine the expression and localization of platelet aggregation in the epithelial-mesenchymal transition (EMT) region in cancer and stroma, CD42b, Snail1 and E-cadherin were assessed using immunohistochemistry. We determined the correlation of these expressed proteins with clinical features and overall survival.
RESULTS: CD42b expression was detected at the invasive front of the tumor, which was in 73% of the EMT portion, but not in the region of tubular formation. Increased Snail1 and loss of E-cadherin expression were noted in 85% and 75% of the EMT portion, respectively. There was a significant correlation between CD42b and Snail1 expression ($p = 0.02$) and CD42b and loss of E-cadherin expression ($p = 0.008$). No prognostic impact of CD42b, Snail1 or loss of E-cadherin expression on overall survival was identified using Kaplan–Meier survival analysis.
CONCLUSION: We demonstrate that EPA is associated with the first step in the formation of the EMT. These data suggest a potential role for antiplatelet agents to suppress EMT and metastasis by changing the tumor microenvironment.
Disclosure of Interest: None declared

P0102 CATHEPSIN B AND D DRIVE THE FIBROGENIC POTENTIAL OF PANCREATIC STELLATE CELLS AND MODULATE THE STROMAL COMPARTMENT IN PANCREATIC DUCTAL ADENOCARCINOMA (PDAC)

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INTRODUCTION: Remodelled extracellular matrix (ECM) has been implicated in the resistance of cancer cells to chemotherapy. Stromal-cell-derived proteases, e.g. cathepsins, are involved in tumorigenesis and tissue invasion but their role in regulating pancreatic stellate cells (PSCs) and thus ECM formation is unknown. We studied whether cathepsin B and D, lysosomal proteases both highly expressed in pancreatic cancer, contribute to fibrogenesis by activating PSCs.
AIMS & METHODS: Cathepsin B and D activity was measured in serum of PDAC patients. PSCs were isolated by Nycodenz-gradient from mouse pancreas for immunoblotting and immunofluorescence staining. TGFβ1 was measured using ELISA and LC/MS-mass-spectroscopy.
RESULTS: Serum cathepsin D activity was increased and correlated with poor survival of patients with PDAC. Expression of cathepsin B and D was negligible in quiescent PSCs but increased in parallel with PSC trans-differentiation to myofibroblasts. Silencing or inhibition (Pepstatin, CA074Me) of cathepsin B and D decreased phenotypic markers of PSC activation. Moreover, latent TGFβ1 was cleaved to TGFβ1 leading to an increase in the PSC fibrogenic potential in a time-dependent manner. Cathepsin D activated cathepsin B and both acted directly on latent TGFb1. TGFb1 increased proliferation, invasion and extracellular matrix remodedelling of PSCs.
CONCLUSION: We show that Cathepsin D activity correlates with poor survival in PDAC patients. Cathepsin B and D expression increases during PSC activation *in vitro* and both modulate ECM-formation via proteolytic cleavage of latent TGFβ1. Via PSC activation cathepsins B and D regulate fibrogenesis and stroma development in pancreatic cancer and therefore represent a promising treatment target.
Disclosure of Interest: None declared

P0103 SRC/STAT3 SIGNALING PATHWAYS ARE INVOLVED IN KAI1-REDUCED VEGF-C DOWN-REGULATION IN PANCREATIC CANCER

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INTRODUCTION: To investigate the signaling pathways involved inKAI1-reduced vascular endothelial growth factor C (VEGF-C) down-regulation and lymphatic metastasis in MIA PaCa-2 pancreatic cancer cells.
AIMS & METHODS: MIA PaCa-2 pancreatic cancer cells were transfected with KAI1 by liposomes. The expression level of VEGF-C was assessed by Western blot. Levels of vascular endothelial growth factor (VEGF)-C secreted by cells measured by enzyme-linked immunosorbent assay (ELISA). Src and STAT3 phosphorylation was detected by Western blot. Signaling transduction inhibitors, PP2 and AG490, were used to block Src and STAT3 signaling pathways, respectively.
RESULTS: KAI1 overexpression decreased VEGF-C expression and inhibited Src and STAT3 phosphorylation. PP2 pretreatment efficiently reversed the upregulation of Src and STAT3 phosphorylation and VEGF-C expression. AG490 pretreatment efficiently reversed the upregulation of STAT3 phosphorylation and VEGF-C expression, but not the upregulation in Src phosphorylation.
CONCLUSION: This study identified that Src/STAT3 signaling pathways were involved in KAI1-reduced VEGF-C down-regulation and suggested their important roles in lymphatic metastasis in pancreatic cancer.
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Disclosure of Interest: None declared

P0104 TP53 CODON 72 AND MDM2 SNP309 POLYMORPHISMS IN PANCREATIC CANCER

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INTRODUCTION: Single-nucleotide polymorphisms (SNPs) of TP53 gene (codon 72, rs1042522) and mouse double minute 2 (MDM2) promoter (SNP309, rs2279744), have been associated with increased risk of various human cancers. However, few studies have analyzed these polymorphisms in pancreatic cancer.
AIMS & METHODS: We investigated TP53 codon 72 and MDM2 SNP 309 polymorphisms in 32 patients with pancreatic ductal carcinoma (PDAC) and 21 patients with controls (non-neoplastic pancreatic epithelium attached to resected specimens without pancreatic disease), using paraffin-embedded tissue sections.

RESULTS: The frequencies of TP53 codon72 arginine (Arg)/Arg, Arg/proline (Pro), and Pro/Pro were 6, 28, and 66% in PDAC and 29, 52, and 19% in controls, respectively. The ratio of Pro/Pro genotype to Arg/Arg genotype was significantly higher in PDAC than controls [p = 0.004, adjusted odds ratio (OR) = 15.75; 95% confidence interval (CI) 2.30-107.9]. On the other hand, those of MDM2 SNP309 TT, TG, and GG genotypes were 22, 44, and 34% in PDAC and 38, 33, and 29% controls, respectively. There were no significant differences among them.
CONCLUSION: This is the first study to evaluated the significance of TP 53 codon 72 and MDM2 SNP 309 polymorphism using paraffin-embedded pancreas tissue. The proportion of Pro/Pro genotype was significantly higher in PDAC, while the proportion did not differ in MDM2. This finding indicates that TP53 codon 72 polymorphism is likely to be correlated with increased risk for pancreatic cancer.
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Disclosure of Interest: None declared

P0105 POSTRANSCRIPTIONAL REGULATION OF HO-1 AND COX-2 EXPRESSION AS NOVEL THERAPEUTIC TARGETS IN PANCREATIC CANCER

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INTRODUCTION: Pancreatic cancer is a rapidly invasive, metastatic tumor, which is resistant to standard therapies, thus only 10–15% of patients are candidates for potentially curative surgery. None of the currently available chemotherapeutic agents have an objective response rate of over 10%. Recent studies show that RNA binding proteins regulate post transcriptional gene expression and play a critical role in RNA stability andtranslation, thus they potentially could become an important group of new therapeutic targets.
AIMS & METHODS: We examined the association of this postranscriptional regulation pathway (CUGBP2 and HuR) and the expression of COX-2 and HO-1, which are known to be associated with inhibition of apoptosis, increased tumor invasiveness and resistance to oxidative stress and/orchemotherapy, and promotion of angiogenesis. Western blot analysis, immunohiostochemistry and quantitative RT-PCR were employed to show the expression of mRNA and protein in normal pancreas (from organ donors), cancer tissue (surgical specimens).
RESULTS: RT-PCR analysis showed 10.3 and 14 fold lower HuR and CUGBP2 mRNA levels in pancreatic cancer compared to normal tissue ($p < 0.05$), COX-2 levels were 1.5 times higher and HO-1 expression on average was upregualted 6-fold in the pancreatic cancer samples, compared to the normal pancreatic tissue ($p < 0.05$). Western blot analysis showed very low levels of HuR and CUGBP2 in pancreatic cancer compared with the normal tissue ($p < 0.05$). Expression of COX-2 protein levels was 2-fold higher in pancreatic cancer. Western blot analysisrevealed 3.5 times higher ($p < 0.017$) expression of HO-1 in pancreatic cancer.
CONCLUSION: The decreased or altered activity of CUGBP2 and HuR could be associated with high chemoresistance and early dissemination of pancreatic cancer through the HO-1 and COX-2 mediated cytoprotective and carcinogenesis pathways. These results mandate further functional studies and evaluation of postranscriptional regulation as a new potential therapeutic target.
Disclosure of Interest: None declared

P0106 DIAGNOSTIC VALUE OF A PANCREATIC MASS ON COMPUTED TOMOGRAPHY IN PATIENTS UNDERGOING PANCREATODUODENECTOMY FOR PRESUMED PANCREATIC CANCER

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INTRODUCTION: Preoperative differentiation between malignant and benign pancreatic tumors can be difficult. Consequently, some 5-14% of patients undergoing pancreatoduodenectomy for suspected malignancy are ultimately diagnosed with benign disease.
AIMS & METHODS: We aimed to determine the diagnostic value of a pancreatic mass on computed tomography (CT) in patients with presumed pancreatic cancer and the additional value of reassessment by expert-radiologists.
We performed a multicenter retrospective cohort study in 1629 consecutive patients undergoing pancreatoduodenectomy for suspected malignancy (2003-2010). All patients with unexpected benign disease at postoperative pathological diagnosis were included in a 1:3 ratio with random patients with (pre)malignant disease. The preoperative CT scan was reassessed by two expert-radiologists separately and subsequently (after defining a mass as *'a measurable space occupying soft tissue density, except for an enlarged papilla or focal steatosis'*) in consensus.
RESULTS: 86 patients with benign and 258 patients with (pre)malignant disease were included. A mass was reported in the original CT report in 66% of patients versus 48% and 50% on reassessment by the two expert-radiologists, respectively. Interobserver agreement among expert-radiologists was moderate (kappa = 0.47, 95%CI 0.38-0.56); they disagreed on the presence of mass in 29% of patients. The incidence of mass decreased to 44% after consensus reading ($P < 0.001$ vs. original report). 167/212 (79%) masses identified in the original report proved to be malignant after pancreatoduodenectomy versus 139/150 (93%) masses identified by expert-radiologists in consensus ($P < 0.001$). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of masses identified in the original CT report were 68%, 42%, 79%, 7%, and 67%, respectively. For masses identified by expert-radiologists in consensus these were 54%, 87%, 98%, 12%, and 56%, respectively.
CONCLUSION: In patients with presumed pancreatic cancer, the diagnostic value of a pancreatic mass on CT is high, whereas the absence of a mass cannot rule out malignancy. Expert-radiologists less frequently identified a pancreatic mass as compared to the original CT-report, with doubled specificity for malignancy.
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P0107 FARNESOID X RECEPTOR (FXR) EXPRESSION IN HUMAN PANCREATIC ADENOCARCINOMA: ASSOCIATIONS WITH CLINICOPATHOLOGICAL PARAMETERS, TUMOR PROLIFERATIVE CAPACITY, PATIENTS' SURVIVAL AND RETINOID X RECEPTORS (RXRS) EXPRESSION

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INTRODUCTION: Farnesoid X Receptor (FXR) belongs to the group of nuclear receptors (NRs). As a transcription factor, it binds to DNA either as a monomer or as an heterodimer with Retinoid X Receptor (RXR). FXR affects several metabolic pathways, including development of atherosclerosis, intestinal bacterial growth and liver regeneration. Additionally, FXR is involved in the pathogenesis of cholestatic diseases, non-alcoholic fatty liver disease, inflammatory bowel disease and cancer. Although many studies have investigated FXR expression in various cancer types, a few data exist, so far, on the clinical significance of this receptor in pancreatic cancer.
AIMS & METHODS: The expression levels of FXR and its heterodimeric partners RXR-α, -β and -γ were assessed immunohistochemically on histopathological samples obtained from pancreatic adenocarcinoma patients, and associated with various clinicopathological parameters, tumor proliferative capacity (Ki-67 labeling index), and patients' survival.
RESULTS: Moderate/strong FXR expression was noted in 27 (49.1%) out of 55 pancreatic adenocarcinoma cases, being at borderline level associated with earlier histopathological stage ($p = 0.054$). Moderate/strong FXR/RXR-α expression was significantly correlated with low tumour histopathological grade of differentiation ($p = 0.017$). Moderate/strong FXR/RXR-β and FXR/RXR-γ expression was significantly correlated with smaller tumor size ($p = 0.037$, $p = 0.005$, respectively) and earlier histopathological stage ($p = 0.017$, $p = 0.004$, respectively), while moderate/strong FXR/RXR-γ expresssion was also significantly correlated with the absence of lymph node metastases ($p = 0.018$). Furthermore, patients presenting moderate/strong FXR expression showed significantly longer survival times compared to those with negative/weak (log-rank test, $p = 0.013$). In multivariate analysis, FXR expression and histopathological stage were identified as independent prognostic factors for patients' survival (Cox-regression analysis, $p = 0.044$ and $p < 0.001$). Patients presenting moderate/strong FXR/RXR-β or FXR/RXR-γ expression showed significantly longer survival times compared to those with negative/weak (log-rank test, $p = 0.021$, $p < 0.001$, respectively).
CONCLUSION: FXR, FXR/RXR-α, FXR/RXR-β and FXR/RXR-γ expression levels in pancreatic cancer are associated with important histopathological parameters and better patients' outcome.
Disclosure of Interest: None declared

P0108 CLINICAL SIGNIFICANCE OF PREGNANE X RECEPTOR (PXR) AND RETINOID X RECEPTORS (RXRS) EXPRESSION IN HUMAN PANCREATIC ADENOCARCINOMA: AN IMMUNOHISTOCHEMICAL STUDY

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INTRODUCTION: Pregnane X Receptor (PXR) is a member of the nuclear receptor (NR) superfamily, expressed mainly in the liver and intestine, exerting its transcriptional regulation by binding to DNA response elements as an heterodimer with Retinoid X Receptor (RXR). PXR is involved in the homeostasis of numerous endobiotics, as well as in inflammatory bowel disease, bone homeostasis, liver steatosis and antifibrogenesis. Additionally, PXR has a multifactorial impact on cancer, either by directly affecting cell proliferation and apoptosis or by inducing chemotherapy resistance. Even though many studies have investigated PXR implication in various types of cancer, data on the clinical significance of this receptor in pancreatic cancer are still very limited.
AIMS & METHODS: The expression levels of PXR and its heterodimeric partners RXR-α, -β and -γ were assessed immunohistochemically on histopathological samples obtained from pancreatic adenocarcinoma patients, and associated with various clinicopathological parameters, tumor proliferative capacity (Ki-67 labeling index), and patients' survival.
RESULTS: Moderate/strong PXR expression was noted in 24 (43.6%) out of 55 pancreatic adenocarcinoma cases, being positively correlated with tumour histopathological grade of differentiation ($p = 0.023$). Moderate/strong PXR/RXR-β and PXR/RXR-γ expression was significantly correlated with smaller tumor size ($p = 0.005$, $p = 0.012$, respectively) and earlier histopathological stage ($p = 0.003$, $p = 0.014$, respectively). Additionally, pancreatic adenocarcinoma patients presenting moderate/strong PXR/RXR-β or PXR/RXR-γ expression showed longer survival times compared to those with negative/weak, at non significant levels though (log-rank test, $p = 0.278$, $p = 0.053$, respectively).
CONCLUSION: In our study, PXR and PXR/RXRs expression was for the first time examined in human pancreatic cancer cases, being correlated with favourable histopathological parameters and associated with longer patients' survival.
Disclosure of Interest: None declared

P0109 UROKINASE-TYPE PLASMINOGEN ACTIVATOR (UPA)-POSSIBLE PANCREATIC CANCER DIAGNOSTIC AND PROGNOSTIC MARKER?

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INTRODUCTION: Urokinase-Type Plasminogen Activator (uPA) is a serine proteinase, which transforms inactive plasminogen to the active plasmin. UPA is involved in cancer progression, growth and metastasis through degradation of extracellular matrix (ECM), growth factors FGF, IGF, VEGF release and cellular migration activation. UPA overexpression was confirmed in many human cancers including pancreatic cancer and was connected to the poor survival. UPA expression was found in the vessels of tumor stroma, which suggests that it can be detected in serum.
AIMS & METHODS: The aim of this study was to evaluate the uPA serum concentration in patients with pancreatic cancer (PC) and chronic pancreatitis (CP) in order to determinate it's possible diagnostic and prognostic value.
The study group included 90 patients: 40 with pancreatic cancer, 30 with chronic pancreatitis and 20 healthy individuals (control group). Serum level of uPA was analyzed using an enzyme-linked immunosorbent assay (ELISA). Pancreatic cancers were classified according to the TNM classification. Criteria for resectability included: absence of distant metastases, lack of evidence of tumor involvement of major arteries, and (if there is venous invasion) a suitable segment of portal vein (above) and superior mesenteric vein (below) the site of venous involvement to allow for venous reconstruction.
RESULTS: We revealed threefold increase in uPA serum level in patients with pancreatic cancer (3.23ng/ml) and twofold increase in patients with chronic pancreatitis (2.18ng/ml), with was significant higher than in control group (1.01ng/ml) ($p < 0.05$ PC vs CP; PC vs control; CP vs control). We observed significantly higher level of uPA in patients with pancreatic cancer and CA19-9 > 500 IU/l compared to patients with CA19-9 <500 IU/l – 3.98 ng/ml vs 2.8 ng/ml ($p < 0.03$). We noticed lower level of uPA in patients with resectable pancreatic cancer: 2.28 ng/ml vs 3.4 ng/ml in patients with unresectable pancreatic cancer but difference was not significant ($p = 0.14$). In addition there was no correlation between uPA level and pancreatic cancer stage. We found the significant correlation between high serum uPA concentration and shorter survival ($p < 0.05$); mean survival in patients with uPA > 2 was 181 days ±155.11 and in patients with uPA < 2 ng/ml- 335 days ±313.75 ($p = 0.04$).
CONCLUSION: The results suggest the possible use of serum uPA in pancreatic cancer diagnosis and differentiation from chronic pancreatitis. Significant correlation between serum uPA concentration and decreased survival, may indicate on the role of uPA as a prognostic marker in pancreatic cancer.
Disclosure of Interest: None declared

P0110 PARTIAL COVERED BILIARY METALLIC STENT WITH/WITHOUT DUODENUM METAL STENT AND NEOADJUVANT CHEMORADIATION THERAPY PROVIDES SYMPTOMATIC BORDERLINE RESECTABLE PANCREATIC HEAD CANCER WITH A CHANCE FOR R0 SURGERY

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INTRODUCTION: Neoadjuvant chemradiationtherapy (NACRT) may lead to successful margin-negative resection (R0) in pts with borderline resectable pancreatic head cancer (BRPHC). NACRT using a covered metallic biliary stent has been attempted in pts with BRPHC, however, the efficacy of this therapy with/without metallic duodenal stent (MDS) and the influence of using partially covered metallic stent (PCMS) for its delivery in the treatment of BRPHC has not been evaluated.
AIMS & METHODS: To evaluate the efficacy of and complications associated with the use of PCMS with/without MDS during NACRT and the surgical period.
We reviewed the outcomes of consecutive pts with BRPHC had histopathologically proven pancreatic adenocarcinoma, who presented with symptomatic biliary obstruction, and divided the patients chronologically, in terms of the period of stent placement into two groups: group A; plastic stent (PS) deployment plus NACRT between August 2009 and October 2010; group B; prospectively PCMS deployment with/without MDS plus NACRT between November 2010 and December 2013. The pts were categorized as having borderline resectable cancer based on the NCCN clinical practice guideline established in 2013. Data on the pts demographics, complications, non re-intervention rate (NRR), surgical time, operative blood loss, length of hospital stay, complications after resection, the rate of R0 and prognosis were studied. Safe R0 surgery was defined as R0 surgery without the need for re-intervention or postoperative complications.
RESULTS: There were a total of 57 pts with LAPHC (group A and B: 29 and 28 pts, respectively). The median time from stent placement to surgery in the overall subject population were 130.5 Days in group A and 130.7 days in group B. MDS was deployed in one pts with group A and three pts with group B. NPR for the 1st 30 days in group A (PS) and B (PCMS) were 48% and 96%, respectively. NPR for the 2nd 30 days in group A and B were 23% and 92%, respectively. NPR for the 3rd 30 days in group A and B were 15% and 92%, respectively. Regarding NPR, PCMS is superior to group using PS ($p < 0.05$). No severe complications including gastrointestinal bleeding after irradiation were noted in any pts. There were no significant differences between groups regarding surgical time, operative blood loss, length of hospital stay. The rates of achievement of R0 surgery in groups A and B were 68.9% (20/29) and 89.3% (25/28), respectively. The PCMS and MDS did not interfere with the conduct of the NACRT and pancreaticoduodenectomy in any patients. The rates of achievement of safe R0 surgery in groups A and B were 10.3% (3/29) and 70.4% (20/28), respectively ($p < 0.05$). Multivariate analysis showed that odds ratio for safe R0 surgery was 18.426 ($p < 0.0001$) for PCMS placement.
CONCLUSION: Insertion of PCMS should be considered for the relief of biliary and/or duodenum obstruction in pts with BRPHC scheduled to receive NACRT, in view of the minimize need for re-intervention for recurrent biliary obstruction, and a potentially high rate of achievement of safe R0 surgery, as compared to the results obtained with PS deployment.
Disclosure of Interest: None declared

P0111 BRANCH DUCT INTRADUCTAL PAPILLARY NEOPLASMS WITH CYSTS LARGER THAN 3 CM WITHOUT HIGH-RISK STIGMATA: SHOULD WE RESECT THESE NEOPLASMS OR NOT?

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INTRODUCTION: In 2012, revised international consensus guidelines were published, and they suggested a more conservative approach for the management of BD-IPMN with cysts larger than 3 cm without other ''high-risk stigmata''. But, several recent studies have challenged the safety of this guideline. The aim of this study is to compare the prognosis in patients who underwent surgical resection because of the cyst size and the prognosis in patients who chose close observation.
AIMS & METHODS: We retrospectively reviewed the data of 48 BD-IPMN patients with a cyst size ≥ 3cm, without any other suspicious features, between March 1995 and October 2013. We divided the patients into 2 groups (21 patients underwent surgery, and 27 patients chose close observation), and compared the patients' characteristics and prognosis.
RESULTS: The patients in the observation group were older than the patients in the surgery group and they had severe co-morbidities (≥2 ACE-27 co-morbidity score (moderate)). None of the patients developed new ''worrisome features'' or ''high-risk stigmata'' during the follow-up period, and the causes of death were not related to IPMN. Among the 21 patients who underwent resection; 4 patients (19%) were diagnosed with invasive carcinoma, and 1 patient (4.8%) was diagnosed with intestinal type of invasive carcinoma. No surgery-related death and major postoperative complications were noted.
CONCLUSION: While making a decision regarding the management of BD-IPMN with a cyst size ≥ 3cm in the absence of high-risk stigmata, we should consider the risk of surgery in patients, but we should not hesitate to perform resection in surgically fit patients especially in high-volume centers with experienced surgeons.
Disclosure of Interest: None declared

P0112 FOLLOW UP HIGH-RISK INDIVIDUALS FOR EARLY DETECTION OF PANCREATIC CANCER

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INTRODUCTION: For the detection of pancreatic cancer in early stage, it is important to identify high-risk individuals and follow up those patients periodically. We have started an early detection system for pancreatic cancer since 1998, and revealed that individual with either pancreatic cyst (>5mm) or dilated main pancreatic duct (>2.5mm) is high-risk for pancreatic cancer. Follow up of high-risk individuals (HRIs) with imaging tests, such as trans abdominal ultrasound which is specialized to pancreato-billiary area (pancreatic US: pUS), endoscopic ultrasound (EUS) and computed tomography (CT) or magnetic resonance imaging (MRI), can lead to the detection and treatment within asymptomatic patients, however usefulness of the optimal imaging approach is not known.
AIMS & METHODS: Between June 2007 and January 2014, 535 asymptomatic HRIs were examined periodically at single center, using pUS (every 3 or 6 month) and CT or MRI (once a year). EUS was performed when any changes such as hypoechoic mass, new nodule or rapid change in cyst size were detected by pUS. ERCP was recommended for cytology when the size of cyst become bigger than 3cm or main pancreatic duct was dilated bigger than 3mm or a newly narrowed part appeared, or the size of cyst or main pancreatic duct changed rapidly. EUS-FNA was performed when an invasive nodule or hypoechoic mass was detected. Contrast harmonic pUS/EUS was also performed if necessary.
RESULTS: Sixteen patients with pancreatic cancer have been confirmed as malignancy during follow up (2.99% incidence rate), 8 males and 8 females (mean age = 69.1 yrs). Eight patients had an intraductal papillary mucinous neoplasms (IPMNs) with an associated carcinoma (2: invasive, 6: non-invasive), six had an invasive ductal adenocarcinoma, and two had ductal carcinoma in situ (PanIN3). Mean total follow up period until the detection of cancer was 34.8 months (range 6.6 - 64 mo). Fourteen patients were asymptomatic. The number of patients with cancer stage of 0, IA, IIA, IIB, III, was 7, 4, 2, 1 and 2, respectively. Ten cases were brought to further examination by the findings detected by pUS, two with symptoms such as abdominal pain, one with tumor marker elevation, one with MRI finding, one with CT finding and one with EUS finding which was found by chance during further examination for another lesion. All invasive pancreatic cancers (smaller than 10mm) were detected only by either pUS or EUS but not by CT nor MRI. Invasive cancer showed hypo-vascularity in pUS/ CE-EUS. Three cases were comfirmed as malignant by EUS-FNA and twelve cases by ERCP. Thirteen cases had surgical resection and three cases had chemotherapy.
CONCLUSION: Periodical examination of asymptomatic HRIs frequently detects small pancreatic cancer with early stage. EUS and pUS could detect invasive pancreatic cancer in early stage better than CT or MRI and are thought to be important modalities in surveillance.
Disclosure of Interest: None declared

P0113 THE INFLUENCE OF NEURAL INVASION ON SURVIVAL AND TUMOR RECURRENCE IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA – A SYSTEMATIC REVIEW AND META-ANALYSES

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INTRODUCTION: The aim of this study is to assess the true impact of perineural invasion/Pn on survival and tumor recurrence in pancreatic ductal adenocarcinoma/PDAC.
Pn is a histopathological hallmark of PDAC, which affects overall survival/OS and tumor recurrence. Until now, recent studies could demonstrate that Pn influences disease-free-survival-time/DFS and progression-free-survival-time/PFS. However, at this time point, there is still no consensus on the real impact of Pn in PDAC.
AIMS & METHODS: Pubmed, Cochrane library, Ovid and Google Scholar were scanned for the terms "pancreatic ductal adenocarcinoma", "pancreatic cancer", "survival", "tumor recurrence" and "perineural invasion". Using the *P*referred *R*eporting *I*tems for *S*ystematic review and *M*eta-*A*nalysis/PRISMA guidelines, a systematic review/SR and meta-analyses was performed. All articles meeting the predefined criteria were critically analyzed on relevance and meta-analyses were performed by pooling univariate and multivariate hazard ratios/HR.
RESULTS: 23 studies for the influence of Pn on tumor recurrence and a total of 101 studies analyzing the influence of Pn on survival were identified by the SR. The performed analyses revealed the prognostic influence of Pn on PDAC patients. The pooled HR of the univariate (1.86; CI 1.67-2.08; $p < 0.00001$) and multivariate analyses (1.50; CI 1.36-1.65; $p < 0.00001$) showed a strong negative impact of Pn on OS in PDAC. Interestingly, Pn was also closely linked to decreased DFS (HR: 2.23, CI 1.13-4.41; $p < 0.05$) and PFS (HR: 2.82; CI 1.97-4.04; $p < 0.00001$) in the pooled multivariate analyses.
CONCLUSION: This is the first systematic review and meta-analyses focusing on the prognostic impact of Pn on OS, DFS and PFS in PDAC. Here we could demonstrate that Pn is an independent prognostic factor among PDAC patients, which decreases OS, PFS and DFS. Therefore, Pn should receive increased attention for improved patient stratification and be considered much more intensively in the development of novel therapeutic algorithms in PDAC.
Disclosure of Interest: None declared

P0114 OBESITY IS A RISK FACTOR FOR PANCREATIC PRECANCEROUS LESIONS

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INTRODUCTION: Obesity was described as a risk factor of pancreatic cancer in combination with metabolic abnormalities. The respective roles of intravisceral and subcutaneous fat are unknown and the prevalence of precancerous lesions in obese patients was never evaluated.
AIMS & METHODS: To characterize the frequency and severity of pancreatic intraepithelial neoplasia (PanIN) in patients with fatty pancreas, to correlate pathological findings with metabolic abnormalities, tobacco intake and type of fat. Consecutive pancreatic specimens of patients operated on for benign neuroendocrine tumors were analyzed. The pancreatic parenchyma was analyzed at least 2 cm apart from the tumor. Fatty infiltration and fibrosis of the parenchyma in intra- and extralobular locations were assessed. Dysplastic lesions were described according to the PanIN classification. General characteristics of the patients were collected, including body mass index (BMI), diabetes and tobacco intake. Liver steatosis was assessed by CT scan (mean of 3 regions of interest, threshold >58UH). The subcutaneous and intravisceral fat (% of the total area) was estimated on CTscan by the ImageJ software (1.47, NIH, USA).
RESULTS: 110 patients (males: 57%) were included (median surface of pancreatic specimen: 7.5 cm2). Median age at surgery was 53.8 [17-85] years. Arterial hypertension, diabetes, tobacco intake were found in 19, 9 and 23%, respectively. Median BMI was 24 [16-37], (BMI < 25: 45%, 25-< 30: 24%, > 30: 11%). Overall, PanIN lesions were found in 65% of the patients, Type 1, 2 and 3 PanIN were observed in 62, 38 and 1% of the cases, respectively. Fibrosis and fatty pancreas (intra- and extralobular locations) were found in 1% and 24% and in 30% and 51%, respectively. Liver steatosis was observed in 27%. A correlation was observed between the presence of PanIN lesions on one hand and fatty pancreas [extra- (0.01) and intralobular (< 0.0001)], intralobular fibrosis (0.003), high BMI ($p = 0.02$), liver steatosis ($p = 0.03$) and subcutaneous ($p = 0.02$) and intravisceral fat ($p = 0.02$) on the other. Presence of PanIN was not influenced by tobacco intake or diabetes. The number of PanIN lesions was correlated with the severity of liver steatosis ($r = -0.25$, $p = 0.02$), the percentage of intravisceral fat ($r = 0.22$, $p = 0.04$) but not with the percentage of subcutaneous fat ($r = 0.14$, $p = 0.22$) or patient age at surgery.
CONCLUSION: Obesity -and especially android obesity with increased intravisceral fat- is a risk factor for precancerous lesions of the pancreas. These results suggest that fatty infiltration *per se* plays a specific role in pancreatic oncogenesis.
Disclosure of Interest: None declared

P0115 MUCIN PHENOTYPE PREDICTS THE SITE OF METASTASIS AFTER RESECTION OF PANCREATIC DUCTAL ADENOCARCINOMA

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INTRODUCTION: Prognosis after surgical resection of pancreatic ductal adenocarcinoma remains poor because of the high incidence of recurrence. Some studies have described the sites of metastasis after resection of pancreatic ductal adenocarcinoma, but little is known about the relationship between clinicopathological features of the primary carcinoma and site of recurrence. Both normal and malignant epithelial cells of a variety of organs contain mucous substances that are rich in very high molecular weight glycoproteins called mucins, which contain many serine- and threonine-linked carbohydrate chains. However, few studies examine the relationship between mucin phenotype of primary pancreatic ductal adenocarcinoma and the site of metastasis.
AIMS & METHODS: The current study focused on clinicopathological features, including mucin phenotype, in primary pancreatic ductal adenocarcinoma and their relationship to sites of metastasis after surgical resection. A total of 323 patients underwent pancreatic resection in our hospital from 1982 to 2003. Seventy-four patients died from a known cause. Patients with intraductal papillary mucinous neoplasm were excluded. The follow-up period was 61 to 288 months. Clinical data were obtained from patients' charts, and pathological factors were assessed according to the WHO classification. A control group comprised 13 patients who had survived more than 10 years after surgery for carcinoma of the pancreas (10 group). Sections were stained with hematoxylin and eosin and high iron diamine blue stain for detection of sulfomucin and sialomucin. The staining pattern was classified into three groups: pure sialomucin type (Si type), pure sulfomucin type (Su type), and mixed type. With regard to immunohistochemical staining for MUC1, MUC2, MUC5AC and MUC6, staining of more than 10% of the carcinoma was defined as positive. Neurovascular invasion was deemed to be present if involvement of more than five sites on a typical section was seen.
RESULTS: Of the 74 patients with an obvious cause of death, 45 died of peritonitis carcinomatosa following local recurrence (P group), 25 died of liver metastasis (L group), 2 died of lung metastasis, and 2 died of bone metastasis. We compared the clinicopathologic features between the L group, P group, and 10 group. Clinicopathologic features of each group are as follow: L group: frequent

Si type of carcinoma (vs. P group, $p < 0.0001$; vs. 10 group, $p = 0.0002$), high rate of venous invasion (vs. P group, $p < 0.0001$; vs. 10 group, $p < 0.0001$), and shorter prognosis (3–34 months, vs. P group, $p = 0.0257$). P group: advanced pT factor (vs. 10 group, $p = 0.0015$) and high rate of R1 status (vs. L group, $p = 0.0370$; vs. 10 group, $p = 0.0243$). 10 group: lower grade of pT factor (vs. L group, $p = 0.0086$; vs. 10 group, $p = 0.0015$) and lower stage (vs. P group, $p = 0.0037$).
CONCLUSION: We might be able to predict the occurrence of liver metastasis by preoperative histochemical mucin staining of carcinoma cells that were classified as Si type preoperatively using EUS-FNA or biopsy.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
ENDOSCOPY AND IMAGING I – POSTER EXHIBITION – HALL XL

P0116 EUS-FNA FOR SMALL GASTROINTESTINAL SUBMUCOSAL LESIONS: USEFULNESS OF FORWARD-VIEWING ECHOENDOSCOPE ATTACHED WITH CAP DEVICE

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INTRODUCTION: Previous reports demonstrated endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNA) for gastrointestinal submucosal lesion (SML) is feasible and safe with high diagnostic yield. On the other hand, since it is difficult to perform EUS-FNA for small SML especially less than 15mm, almost small SMLs are observed without EUS-FNA. However, because SMLs include malignant lesions even though a tumor is small, it is desirable to perform EUS-FNA when possible.
AIMS & METHODS: The aim of this study is to evaluate feasibility and safety of EUS-FNA using forward-viewing echoendoscope attached with a cap device to the tip of scope for the small SML. Eight patients who had small SML less than 15mm I upper GI were enrolled in this study. EUS-FNA was done using forward-viewing EUS scope (XGIF-UCT160J-AL5; Olympus, Tokyo, Japan) and needle devices (22G, 25G), with rapid on-site evaluation. To fix the SML at the needling, a cap device was attached to the tip of scope. We evaluated the rate of sampling, accuracy, and complication.
RESULTS: Mean diameter of SMLs was 10.6 mm±2.94mm (mean±SD, range 8-15mm). The puncture could be done in all 8 cases, and mean number of FNA passes was 4.6±1.59 (mean±SD, range 3-7). The adequate materials were obtained in 6 (87.5%) for cytology, in 4 (50%) for histological examination with immunostaining. In 1 (12.5%) patient, adequate sample for both cytology and histology was not obtained. As final diagnosis, 6 patients were gastrointestinal stromal tumor (2 in definition, 3 in suspicion), 2 patients were leiomyoma. No complication was noted.
CONCLUSION: Although the rate of definitive diagnosis was 50%, EUS-FNA using forward-viewing echoendoscope attached with a cap device for small SML was feasible and safe.
Disclosure of Interest: None declared

P0117 ENDOSCOPIC CHARACTERISTICS OF EARLY GASTRIC CANCERS MIXED WITH WELL AND POORLY DIFFERENTIATED ADENOCARCINOMA

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INTRODUCTION: The risk of lymph node metastasis of superficial gastric cancer depends on histological type, invasion depth and the size. Sometimes, well differentiated gastric adenocarcinoma has poorly differentiated component partially. And, the incidence of lymph node metastasis is higher than that of the well differentiated type. Therefore, endoscopic diagnosis of histological type is important. However, the endoscopic characteristics of such a histologically mixed gastric adenocarcinoma are unknown.
AIMS & METHODS: The aim of this study is to investigate the endoscopic characteristics of early gastric cancers partially with poorly differentiated type. One hundred eighty-two gastric adenocarcinomas from 172 patients treated by ESD from January to December 2012 were enrolled in this study. All of the examination was performed by Olympus H260Z with Lucera. And, narrow band imaging (NBI) magnified observation was performed after white light imaging (WLI) observation. Magnified endoscopic findings were divided into surface and vascular pattern. Surface pattern was divided into villous, pit and unclear. The gross type was classified into 0-I, 0-IIa, 0-IIb and 0-IIc type, and the number was 9, 67, 7, and 99, respectively. The histology was classified into well and poorly differentiated type. When the cancer had only well differentiated type, it was classified as pure well differentiated type. And, when the well differentiated adenocarcinoma had a poorly differentiated component, it was classified as mixed type. And when the cancer was composed of only poorly differentiated adenocarcinoma, it was classified as pure poorly differentiated type.
RESULTS: 1. The numbers of pure well differentiated type, mixed type and pure poorly differentiated type were 157, 23 and 2, respectively.
2. 0-I type: Seven of 9 lesions were pure well differentiated type, and two of 9 lesions were mixed type. The size of these two lesions was more than 20mm.
3. 0-IIa type: Sixty three and 4 of 67 lesions were well differentiated and mixed type, respectively. The incidence of mixed type has relationship with the size. When the lesions were divided three groups depends on the size such as 1-9, 10-19, 20-29, 30mm or bigger, the incidence of mixed type was 0% (0/15), 8% (2/24) and 0% (0/15), 15% (2/13), respectively.
4. 0-IIb type: All of seven lesions were pure well differentiated type.
5. 0-IIc type: 80, 17 and 2 of 99 lesions was pure well, mixed and pure poorly differentiated type, respectively. And when the size was subclassified into four groups 2-9, 10-19, 20-29, 30mm or bigger, 0% (0/30), 25% (12/48), 27% (4/15) and 50% (3/6) were mixed type.
6. The surface pattern of well differentiated adenocarcinoma observed by magnified endoscopy showed irregular villous or pit pattern. However, the surface pattern of mixed type was unclear in some cases. However, sometimes the surface was covered by thick mucus, and magnified endoscopic observation was impossible.
CONCLUSION: The incidence of mixed type depends on the size and macroscopic type of the superficial gastric cancer. Magnified endoscopy was sometimes useful to detect mixed type from the surface pattern.
REFERENCES
NONE
Disclosure of Interest: None declared

P0118 SUBMUCOSAL FIBROSIS AFFECTS THE OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR GASTRIC NEOPLASMS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is an effective treatment for gastric neoplasms. However, because of its technical difficulty, it takes longer, and there is a greater risk of complications such as bleeding and perforation. The success of ESD depends on the technical proficiency of the endoscopist and the condition of the gastric tumor. Even for a skilled endoscopist, however, submucosal fibrosis can be an obstacle to success of ESD. Submucosal fibrosis, which usually results from inflammation or tumor invasion, makes it harder to lift the tumor tissue from the muscle layer. This in turn lengthens the procedure time, creates risk of complications such as perforations, and reduces the success rate of complete en bloc resection. Despite its importance, there has been little investigation of the relationship between the degree of submucosal fibrosis and outcomes of ESD in early gastric tumors. Accordingly, the aims of this study were 1), to examine the association between endoscopic and pathologic findings and submucosal fibrosis in gastric neoplasms; 2), to examine the association between degree of submucosal fibrosis and outcomes of ESD.
AIMS & METHODS: Two hundred forty six patients with gastric neoplasms (52 cases of adenomas and 194 cases of early gastric cancers) were treated by ESD from November 2008 to September 2013. Endoscopically, the degree of submucosal fibrosis was classified as follows, based on the findings obtained after a solution including indigo carmine was injected under the submucosal layer: F0, no fibrosis, which appeared as a blue transparent layer; F1, mild fibrosis, which appeared as a white web-like structure in the blue submucosal layer; and F2, severe fibrosis, which appeared as a white muscle-like structure without a blue transparent layer.
RESULTS: The presence of endoscopic submucosal fibrosis was not significantly related to tumor size, ulceration, histological findings, submucosal invasion, and en bloc resection rates in univariate analysis. However, posterior walls of the stomach harbored higher frequency of submucosal fibrosis compared with anterior wall regardless of upper, middle or lower portion of the stomach ($p < 0.05$). The procedure time according to the degree of endoscopic submucosal fibrosis were as follows (mean ±SD): F0, 82.1±42.1 minutes; F1, 146.6±81.6 minutes, and F2, 171.4±106.7 minutes, showing significant difference between groups ($p < 0.01$). The severity of endoscopic submucosal fibrosis was associated with abundant immediate bleeding which required hemostasis using hemoclips during ESD procedure ($p < 0.05$). However, delayed bleeding was not significantly related to the degree of submucosal fibrosis.
CONCLUSION: Submucosal fibrosis of gastric neoplasms is closely related to tumor location, procedure time, and severe bleeding during ESD. Moreover, the more advanced the endoscopic submucosal fibrosis, the longer the time required for ESD and the higher the frequency of immediate bleeding. Further development of endoscopic devices and peripheral equipments are needed for safe and complete resection of lesions with severe fibrosis.
Disclosure of Interest: None declared

P0119 NEW ENDOSCOPIC TECHNIQUE FOR SECONDARY PLACEMENT OF VOICE PROSTHESIS

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INTRODUCTION: The functional speech rehabilitation in laryngectomized patients after total laringectomy remains as one of the most challenging matters for head and neck surgeons and speech therapists.
The use of voice prostheses has been considered the gold standard in voice rehabilitation for the last 25 years. Insertion can be performed either as a primary procedure during laryngectomy or as a secondary procedure with rigid esophagoscope or trocar. In some patients these procedure became technically impossible due to some post treatment cervical abnormalities such as necks reduced hyperextension (post surgery or radiotherapy) anastomotic reduced diameter (post surgery), trismus and other impairments situations.
AIMS & METHODS: Objective: To present an endoscopic technique for secondary placement of Provox prosthesis using the flexible endoscope, a plastic

pliable overtube (to keep the virtual esophageal lumen open so the traqueoesophageal puncture could be performed safely, avoiding unexpected lesions on the posterior esophageal wall), a 14 gauge intravenous catheter to perfomed the puncture, and a flexible guidewire. Furthermore, using the flexible endoscope instead of the rigid esophagoscope we can avoid some of the major complications of the classical technique i.e.: mediastinitis, cervical cellulitis, fracture of cervical vertebra, and esophageal perforation
Methods: 7 patients referred to voice rehabilitation with Provox II vocal prosthesis in a secondary placement, in which the classic technique could not be performed, underwent a new surgical technique, performed with a flexible endoscope, a plastic pliable overtube, a 14 gauge intravenous catheter and a flexible guidewire,
RESULTS: The procedure was successfully performed in all seven patients. There were no complications related to the surgical technique.
CONCLUSION: In patients where the classic technique for secondary insertion of the Provox prosthesis is technically impossible, this new technique could be a good alternative
Disclosure of Interest: None declared

P0120 ARE OUTCOMES FOLLOWING ENDOSCOPY FOR EMERGENCY UPPER GI BLEEDING WORSE AT NIGHT AND WEEKENDS?

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INTRODUCTION: Patients admitted out of hours or at weekends may have an excess mortality due to the fact that they undergo emergency endoscopy by junior staff. We retrospectively looked at the predictors of mortality in patients undergoing emergency endoscopy for severe bleeding in Leeds.
AIMS & METHODS: The survival of patients with the most significant upper GI bleeding lesions who underwent emergency endoscopy in Leeds between end of April 2008 and middle of June 2012 were selected for retrospective analysis using data from our endoscopy reporting system and hospital records.
RESULTS: A total of 509 significant emergency gastroscopies were carried out with the finding of 197 duodenal ulcers, 105 gastric ulcers, 161 oesophageal varices, 26 gastric varices, 12 Dieulafoy's and 9 other bleeding lesions (bleeding biopsy site, bleeding EMR site, gastric lymphoma, 3 PHG, 3 angioectasia).
After 22% of procedures (114/509), the patient died within 30 days. As expected, patients who died had a significantly higher Rockall score (7.6 vs. 6.0 $p < 0.0001$), a higher ASA level (3.5 vs. 2.7 $p < 0.001$) and a lower systolic BP at the time of the examination (94.8 vs 103 $p = 0.025$). Patients who died following endoscopy for bleeding ulcers were significantly older than those who survived (77.7 vs. 67.5 yrs, $p = 0.006$). There was no significant difference in mortality with the type of bleeding lesion, Hb (8.0 vs. 7.8) or heart rate (100 vs. 102 bpm) at the time of the endoscopy between those who survived and those who died. Patients who died, were transfused significantly more blood than those who survived (5.9 units vs 3.8). Of the patients who suffered a re-bleed, 52 patients died and only 62 survived. A total of 28 patients required emergency angiography and embolisation of a bleeding vessel. This small group had suffered a significantly greater blood loss (21 had suffered a re-bleed) and had an average Hb of only 6.9 in spite of having received an average of 12.9 units of blood. In spite of this, 22 patients survived following embolisation.
Undergoing an emergency gastroscopy at night or during the weekend or a bank holiday was not associated with an increased risk of death ($p = 0.50$, $p = 0.32$ respectively). Whether the examination was carried out by a SpR or a Consultant made no difference to the survival of the patient ($p = 0.40$).
CONCLUSION: Our study had the statistical power to detect all the recognised risk factors for death following admission with an acute upper GI bleed including advancing age, increasing comorbidity, hypotension, re-bleeding and transfusion requirement. We found no evidence that undergoing an emergency endoscopy at night or during the weekend or a bank holiday had any adverse effect on outcomes. Similarly, the level of seniority of the endoscopist did not affect outcomes.
Disclosure of Interest: None declared

P0121 LONG-TERM OUTCOMES OF PATIENTS WITH MALIGNANT DYSPHAGIA THAT HAVE UNDERGONE STENTING

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INTRODUCTION: Oesophageal stenting with fully covered self-expanding metal stents (SEMS) has transformed the care of patients with malignant dysphagia. SEMS are easily removable and have fewer reported long-term complications of tumour ingrowth although possibly more migration. However, predictive factors for favourable outcomes are yet to be fully defined for those with malignant dysphagia.
AIMS & METHODS: The aim of this retrospective study was to evaluate the complications, the re-intervention rate and the survival after insertion of fully covered SEMS for malignant dysphagia and to identify any predictive factors for outcomes other than tumour stage. All SEMS procedure data were retrieved from Royal Liverpool University Hospital patient database retrospectively in a 2-year inclusion period and analysed regarding SEMS characteristics, procedural events, re-interventions and survival on a standard proforma.
RESULTS: A total of 96 fully covered SEMS were inserted in 74 patients (47 males) with a median age of 73 (range 36-89) years. Technical success was 99% (95/96), with no complications of perforation or bleeding. Minor ($n = 6$) complications included chest pain, vomiting & severe GORD. The 30-day mortality was 12% but was not directly related to the SEMS insertion. The 7-day readmission rate following SEMS placement was 5% as result of symptoms caused by SEMS including pain & vomiting. The median survival was 125 (range 4-910) days. 26 (35%) of the patients needed re-intervention due to recurrence of dysphagia due SEMS migration or tumour overgrowth. The SEMS migration rate was 18% ($n = 14/96$) occurring after a median of 120 (range 10-365) days. 87% of the migrated SEMS were from tumours of the lower oesophagus and GOJ. Tumour overgrowth occurred in 16% ($n = 15/96$) at a median of 120 (range 28-210) days. In 19/26 (73%) cases palliation was successfully achieved with re-intervention; further SEMS placement in 17 & APC in 2. Interestingly, the patients with recurrence of dysphagia had significantly ($p \leq 00.5$) prolonged survival (median 156 (range 30-790) days) compared to patients who did not need any intervention (median 125 (range 4-910) days).
CONCLUSION: Fully covered SEMS are safe and offer extremely effective palliation of malignant dysphagia for up to 3-4 months. Re-intervention beyond this point is for recurrence of dysphagia due to SEMS migration and/or tumour overgrowth that may be due to increased patient survival. The majority of patients can be re-palliated successfully with further endotherapy.
Disclosure of Interest: None declared

P0122 HIGH DIAGNOSTIC YIELD OF EUS-ASSISTED SINGLE INCISION-NEEDLE KNIFE (SINK) BIOPSY FOR HISTOLOGICAL ANALYSIS OF UPPER GASTROINTESTINAL STROMAL TUMORS

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INTRODUCTION: Gastrointestinal stromal tumors (GIST) are the most frequent type of mesenchymal neoplasms of the upper gastrointestinal tract and may be malignant regardless their echopattern or size, therefore, histologic and immunohistochemical (IH) analysis are crucial for diagnostic and pronostic purposes. EUS- guided FNA provides a low diagnostic yield, specially for smaller GIST. EUS - assisted SINK biopsy is an alternative method with promising preliminary results.
AIMS & METHODS: We aimed to evaluate the diagnostic yield of SINK samples for IH analysis and mitotic index (MI)assessement.
Retrospective evaluation of a prospectively-mantained database, including all patients with upper gastrointestinal subepithelial tumors (SETs) who underwent EUS-assisted SINK biopsy since April 2010 to March 2014. All patients underwent previous radial/linear EUS for size measurement and morphological characterization; then a needle-knife was used in blended current at 30W to 60W settings and a 6 to 12 mm linear incision was made along the highest convexity zone of the lesion. Then, 3 to 5 biopsy samples were obtained from the exposed tissue with a standard biopsy forceps and included in formalin. When histologic analysis revealed features of mesenchymal origin (spindle cells), specific IH markers for GISTs (cKit- CD 117, CD 34) and mitotic count per 50 high- power fields (HPF) to assess malignant potential were performed.
RESULTS: 72 patients (M/F: 38/34) were included (mean age 63.66, range 22-89). There were 27 mesenchymal lesions (27/72: 37.5%); GIST 23, leiomioma 4. Median size: 3.53 mm (1.34-5.90). IH analyses for SINK samples was positive in 25/ 27 GISTs (92.59%) and MI determination was feasible in 21/ 27 (77.77%). 16/21 showed < 5 mitoses per 50 HPF and were categorized as 'very low risk' according to the NIH classification-all these lesions with diameters under 30 mm. There were no procedure-related complications.
CONCLUSION: EUS-assisted SINK-biopsy of upper GISTs appears to be an easy and safe technique and provides sufficient tissue samples for IH diagnosis and assessment of malignancy by means of an accurate MI calculation.
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Disclosure of Interest: None declared

P0123 PENTAX I-SCAN™ WITH MAGNIFICATION FOR THE IDENTIFICATION OF UNDERDIAGNOSIS ORGANIC ESOPHAGEAL LESIONS (BARRET ESOPHAGUS AND ESOPHAGITIS) IN PATIENTS WITH FUNCTIONAL DYSPEPSIA: A PROSPECTIVE STUDY

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INTRODUCTION: Functional dyspepsia (FD) is a highly prevalent gastrointestinal disorder characterized by symptoms originating from the gastroduodenal region in the absence of underlying organic disease as defined by Roma III criteria. Upper endoscopy (UE) associated to digital chromoendoscopy (DC), magnification (M) and high definition (HD) had shown excellent results for

the diagnosis of Barret esophagus (BE) and esophagitis. However, not all patients are investigated with this kind of technology, where UE results are considered as absence of organic lesions, thus diagnosed as FD.
AIMS & METHODS: Based on the hypothesis that HD UE associated to DC and M can detect more mucosal details than standard UE, we evaluate the effectiveness of i-Scan^{TM} (HD UE+DC+M) in patients with functional dyspepsia for the identification of organic esophageal lesions. After approval by the ethics committee and signing of an informed consent, a prospective study was performed in consecutive patients undergoing for UE from Nov 2012 to June 2013. Inclusion criteria: Criteria of FD in accordance to ROMA III criteria, normal standard UE in the last 3 months previous to the inclusion in this study. Exclusion criteria: age <18, pregnancy, history of: gastritis, GERD, gastrointestinal cancer, H pylori infection, pancreatic disease, choledocolitiasis, alcohol or smoke abuse, use of medications (IBP, NSAIDs, Antibiotics). HD UE+DC and M was performed using the EPK-i processors with i-Scan^{TM} from Pentax. Under sedation patients underwent HD UE, analyzing all the mucosa aspects using initially white light (WL), with especial regard in the Z-line at the level of the cardia. Then DC was performed using i-Scan. Any alteration in the mucosa pattern (color, pitt or vascular pattern) was analyzed and then classified as inflammation or BE using Los Angeles and Prague classifications respectively. Finally acetic acid was performed and a target biopsy was done as the gold standard method to confirm i-Scan findings.
RESULTS: 491 patients were included. 48% were men with a mean age of 47 (ranges: 18-87). 151/491 patients (30.7%) had an organic esophageal lesion detected at i-Scan. 45/151 patients were detected initially by HD-UE-WL. Biopsy confirm the esophageal lesions in 125 cases. i-Scan detect 94 cases of short BE (C<1,M<1), 25 cases of esophagitis (Grade A), and 6 cases where considered to have a mixed disease (BE and esophagitis). The accuracy to predict BE for i-Scan was 95% and 100% for esophagitis.
CONCLUSION: HD UE+M+DC (i-Scan^{TM}) could detect an important number of organic esophageal lesions as BE and esophagitis in patients initially overdiagnosed as a functional disease.
Disclosure of Interest: C. Robles-Medranda Consultancy for: Pentax Medical, MaunaKea technologies, R. Del Valle: None declared, M. Soria: None declared, G. Bravo: None declared, H. Lukashok: None declared, C. Robles-Jara: None declared

P0124 COMPARATIVE STUDY OF ESD AND SURGICAL RESECTION FOR GASTRIC SETS ORIGINATED FROM MUSCULARIS PROPRIA

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INTRODUCTION: Endoscopic resection for gastric subepithelial tumors (SETs) originated from the muscularis propria (GSET-PM) has offered less invasive alternatives to surgical resection. The aims of this study were to compare endoscopic subtumoral dissection (ESD) with surgical resection for the removal of GSET-PM.
AIMS & METHODS: This study involved 17 patients with GSET-PM removed by ESD and 76 patients who underwent curative surgical resection. ESD was attempted in GSET-PM with well marginated tumors which was below 5cm and showed an endoluminal growth pattern according to endoscopic ultrasound (EUS) finding.
RESULTS: ESD group were more likely to have upper portion (10/17, 58.8%) and surgery group were more likely to have mid portion (41/76, 53.8%) (p=0.039). ESD group had smaller median tumor size (25.6 mm vs 35.9 mm, p=0.037) and higher endoluminal ratio (58.5±9.1% vs 45.8±15.4%, p=0.002). ESD group mostly had Yamada type III (10/17, 58.8%) and the surgery group were mostly Yamada type I (52/76, 68.4%) (p<0.001). Complete resection by ESD was lower than by surgical resection (82.4% vs 100%, p<0.001). In ESD group, 3 performed surgical resection after ESD (1 incomplete resection and 2 uncontrolled bleeding) and 1 showed perforation which was completely resected with endoscopic closure. In the surgery group, complications occurred in 6 patients (1 leakage, 1 stricture, 1 hernia and bowel obstruction, 1 wound infection and 2 worsened general condition after surgery). Although surgery group were lower in complication rate than ESD group (p=0.006), severity of complications were higher in the surgery group and there were no mortalities in the ESD group compared with 2 in the surgery group. There was no statistical difference of recurrence and the follow-up period between the two groups.
CONCLUSION: ESD can be a good option for the resection of endoluminal GSET-PM and could replace treatment by surgical resection in Yamada type III with a high endoluminal ratio.
Disclosure of Interest: None declared

P0125 NON-CURATIVE ENDOSCOPIC RESECTION DOES NOT ALWAYS LEAD TO GRAVE OUTCOMES IN SUBMUCOSAL INVASIVE EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been widely performed for the treatment of early gastric cancer (EGC).
AIMS & METHODS: The aim of this study is to confirm the effectiveness of ESD in submucosal invasive gastric cancers (SM-GC), with a special focus on patients who underwent non-curative resection.
Data for 1,246 patients who underwent ESD for treatment of EGC at six medical centers in Daegu-Gyeongbuk, Korea, between February 2003 and May 2010 were collected. After retrospective analysis of ESD databases, 118 patients were enrolled in the study. The corresponding EGC lesions were classified into three groups based on the results of pathological examination: 1) gastric cancers with submucosal invasion less than 500μm (SM1-GC) that met the expanded criteria (EC) (SM1 EC group, n=42); 2) SM1-GC that did not meet the EC (SM1 non-EC group, n=38); and 3) gastric cancers with submucosal invasion greater than 500μm (SM2-GC group, n=38).
RESULTS: The en bloc resection rate (SM1 EC group/SM1 non-EC group/SM2-GC group: 85.7%/94.7%/97.4%, respectively) and complete resection rate (SM1 EC group/SM1 non-EC group/SM2-GC group: 81.0%/81.6%/71.1%, respectively) did not differ significantly among the three groups. However, the curative resection rate was significantly better in the SM1 EC group (69.0%) compared to that in SM1 non-EC and SM2-GC groups (0% in both cases). Out of a total of 118 patients, 89 (75.4%) underwent non-curative resection. Cancer recurrence was observed in 9 patients (9/89, 10.1%) during the median follow-up period of 40 months (range: 3-99). We analyzed the overall survival and disease-free survival in non-curative patients that underwent or did not undergo additional surgery. The overall survival and disease-free survival did not differ significantly between patients that were treated with additional surgical resection and those that were simply followed up after ESD.
CONCLUSION: Non-curative resection in SM-GC does not always lead to cancer recurrence. Thus, if additional surgery cannot be performed because of the patient's unsuitable condition (due to age, underlying disease, etc.) or refusal, a close follow-up with endoscopy can be considered as an alternative for carefully selected patients. Moreover, as the ESD technology continues to evolve, it might be possible to expand the criteria for curative ESD in patients with SM-GC.
Disclosure of Interest: None declared

P0126 PROSPECTIVE LONG-TERM OBSERVATION TRIAL OF ARGON PLASMA COAGULATION (APC) FOR SHORT-SEGMENT BARRETT'S ESOPHAGUS IN AN OUTPATIENT SETTING

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INTRODUCTION: Barrett's esophagus (BE) is the only known precursor lesion to esophageal adenocarcinoma of the distal esophagus. There are various endoscopic treatments to ablate BE to generate a neo-squamous epithelium such as radiofrequency ablation (RFA), cryotherapy and argon plasma coagulation (APC). However, there is limited data available for APC in an outpatient setting.
AIMS & METHODS: Prospective long-term observation trial of Argon Plasma Coagulation in an outpatient setting.
Patients of a gastroenterology practice were considered for entry into this trial. At the initial endoscopy a chromoendoscopy was undertaken and biopsies were taken (bioptic mapping). Then the patients were treated with a high frequency pulsed APC (16 boosts/sec) in order to ablate BE completely. One session was necessary for tongue-shaped and complete covering epithelium, more than two sessions for distal circular BE. Follow-ups were scheduled after six weeks, six months, one and two years.
RESULTS: 73 patients (17% women, median age: 71 years, range: 34 -82 years) were enroled but only 70 patients were finally included in this trial. Other than rare minor retrosternal pain after large ablations there were no other treatment-associated complications. Of all patients treated with APC-ablation 87.5% showed a stable complete eradication with regenerated neo-squamous epithelium in the follow up. During the 2-year follow up 4.3% showed a macroscopic and histological recurrence. However, the clinical role of residual or recurrent BE in form of so called "Buried glands" (10%) is still uncertain and worth discussing.
CONCLUSION: In this trial it was shown the first time that APC was a safe and efficient endoscopic treatment to ablate short-segment non-dysplastic BE especially in an outpatient setting.
Disclosure of Interest: None declared

P0127 FUNCTIONAL ESOPHAGOSCOPY VIA TRANSNASAL ACCESS ALLOWS NEW INSIGHTS IN PATIENTS WITH NEUROGENIC DYSPHAGIA

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INTRODUCTION: Patients suffering from neurogenic dysphagia often get caught in the trap: they find themselves somewhere in the space between different specialists. This dilemma might be due to a lack of pathophysiological knowledge of the complex swallowing process from the oral cavity to the stomach and an inability to directly visualize the esophageal phase of deglutition.

AIMS & METHODS: In a multidisciplinary setting, 31 consecutive patients with suspected neurogenic dysphagia were evaluated by transnasal access applying an ultrathin video endoscope with an outer diameter of 3.8 mm (BF-3C160, Olympus Europe). Patients were examined in sitting position while ingesting water and food of different consistencies. Diagnostic was completed by videofluoroscopy and high-resolution manometry. The study was approved by the local Ethics Committee.
RESULTS: Functional endoscopy was successfully performed in all patients. We were able to show that functional endoscopy is a feasible and safe method; no adverse events were noted. Endoscopic findings correlated well with the clinical signs of the patients and the other diagnostic modalities. A variety of disorders was documented by functional endoscopy and recorded as video files: Incomplete and delayed closure of the upper esophageal sphincter (in retroflex view), clearance disturbance of tubular esophagus, esophageal hyperperistalsis and hypomotility. The most common findings in the oral and pharyngeal phase were bolus leakage, delayed swallowing reflex, vallecular residues, and, aspiration during food intake.
CONCLUSION: By interdisciplinary cooperation with additional assessment of the esophageal phase of deglutition using the innovative method of functional endoscopy, the diagnostic of neurogenic disorders including dysphagia may be tremendously improved leading to a better clinical understanding of complex dysfunctional patterns. To our best knowledge, this is the first study to show that a retroflex view of the ultrathin video endoscope within the esophagus may be safely performed. This diagnostic comprehensive approach should be helpful to apply focused prophylactic and therapeutic actions.
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P0128 REPEATED BOLUS INJECTION VERSUS SLOWLY CONTINUOUS INFUSION OF PROTON PUMP INHIBITOR FOR THE MANAGEMENT OF BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Elevated intra-gastric pH is important in management of bleeding and healing the artificial ulcer after endoscopic submucosal dissection. The Proton Pump Inhibitor (PPI) has powerful acid suppression. At present, the standard treatment of choice for the prevention of gastric ulcer bleeding is continuous infusion of PPI after intravenous bolus loading.
AIMS & METHODS: Our aim is to compare the effects of repeated bolus injection and slowly continuous infusion of PPI for the management of delayed bleeding after gastric ESD.
From March 2012 to Feb 2013, 273 patients with gastric superficial epithelial neoplasm were enrolled. The group was divided into two. One is the repeated bolus group, the other one the slowly continuous-infusion group. All patients are undergod ESD. In slowly infusion group After initial pantoprazole 80mg bolus loading for 30 min before ESD, 8mg/hr continuous infusion for 72 hours is done after initial 80mg bolus loading for continous infusion group. For repeated bolus group (n = 136), pantoprazole 40mg bolus is injected q 12 hours for 72 hours. After 72 hours, Oral pantoprazole 40 mg daily for 4 to 8 weeks. Follow-up endoscopy is performed 2 days and 4 weeks after ESD. (In case of incomplete ulcer healing, 8 week endoscopy and pantoprazole 8 wk medication was done.)
RESULTS: No difference on clinical characteristics were seen between two treatment groups. Bleeding events occurred in 8.4% (23/273) of all patients. In follow up endoscopic findings, high risk of stigma was found in 15.8% (43/273) of all patients. No difference in bleeing event was seen between repeated bolus group and slowly continous infusion group. Submucosal invasive, gross type of lesion and coronary disease were significant risk factors for rebleeding events rather than the method of PPI administration.
CONCLUSION: The method of PPI administration was not significantly different to predict post ESD delayed bleeding. Submucosal invasive, gross type of lesion and coronary disease were more important to predict post ESD delayed bleeding.
Disclosure of Interest: None declared

P0129 A NOVEL STRATEGY IN THE ENDOSCOPIC TREATMENT OF REFRACTORY UPPER GI-BLEEDING IN ANTICOAGULATED PATIENTS WITH THE OVER-THE-SCOPE-CLIP (OTSC) – ARE WE ENTERING TO A NEW ARA IN THE TREATMENT OF UPPER GI-BLEEDING?

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INTRODUCTION: The OTSC (OVESCO, Germany) is a novel endoscopic device successfully applied for severe GI bleedings, perforations, fistulas and experimental NOTES procedures.
We performed a retrospective analysis of all OTSC applications for acute gastrointestinal bleeding from February 2009 to March 2014 using our endoscopy database and individual patient records.
AIMS & METHODS: Over a 5 year period 55 patients [median 73 y (29-97) 17 w, 38 m, ASA 2-4] with acute severe upper gastrointestinal bleeding (hemoglobin < 7 g/dl at admission for acute bleeding or as emergency endoscopy for hospitalized patients) using 56 OTSCs (n = 54 T-type 12/6 17.5 mm OD; n = 2 T-type 14/6 21 mm OD).
RESULTS: In 48/55 cases (87.2%) acute bleeding was related to peptic ulcer disease, in 2 cases due to bleeding from a malignant ulcer (1x gastric AC, 1x gastric lymphoma), 2 cases due to recurrent bleeding after polypectomy and clip in the stomach. In 1 case a heavily bleeding Mallory Weiss tear and in 1 case a bleeding ulcer at a gastro-jejunal anastomosis was treated. One patient bled heavily from a deep muscle laceration after balloon dilatation for achalasia. 18/55 (32.7%) were treated due to a failure of a previous hemostasis methods (standard hemoclips, injection or radiologic embolization).
Of the 55 patients 44 (80%) were on pre-existing anticoagulation, 9/55 (16.4%) took warfarin, 24/55 (43.6%) aspirin, 10/55 (18.2%) heparin/enoxaparin and 1 (1.8%) was anti-coagulated with a combination of aspirin plus clopidogrel.
In 46/55 of all cases, primary treatment with the OTSC was successful (83.6%), in all the cases without re-bleeding events. In 7/55 (12.7%) surgical treatment was necessary due to insufficient hemostasis. However, 4 of those 7 patients died during the hospital stay. 2 multi-morbid patients not fit for surgery passed away.
CONCLUSION: The OTSC system is a promising new tool for the management of acute severe GI-bleeding. Especially patients with pre-existing anticoagulation and multi-morbidity seem to profit from this system.
Disclosure of Interest: None declared

P0130 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR GASTRIC NEOPLASMS IN THE PYLORUS

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INTRODUCTION: Endoscopic resection (ER) for gastric neoplasms in the pylorus is a technically difficult procedure.
AIMS & METHODS: We investigated clinical outcomes to determine the feasibility and effectiveness of ER for gastric neoplasm in the pylorus. Subjects who underwent ER for gastric neoplasm in the pylorus at Asan Medical Center between January 1997 and February 2012 were eligible. The clinical features of patients and tumors, histopathologic characteristics, adverse events, results from ER, and survival were investigated.
RESULTS: A total of 227 subjects underwent ER for 228 gastric neoplasms in the pylorus. Median age was 62 years (interquartile range [IQR]: 53-68 years), and the male to female ratio was 2.2:1. Median tumor size was 14 mm (IQR: 10-22 mm), and median procedure time was 23 minutes (IQR: 15-33 minutes). En bloc resection was achieved for 193 lesions (84.6%), including complete resection (CR) of 195 lesions (85.5%), and curative resection (CuR) of 167 lesions (73.2%). Rates of CR and CuR were significantly lower for pyloric and postpyloric lesions than for prepyloric lesions ($p = 0.002$ and $p = 0.006$). Adverse events occurred in 19 patients, including delayed bleeding in 12 (5.3%) and stricture in 7 (3.1%). During a median follow-up period of 79.0 months, local tumor recurrence was detected in 2.6%. The 5-year overall and disease-specific survival rates in the 83 patients with gastric cancer were 81.5% and 96.9%, respectively.
CONCLUSION: ER appears to be a feasible and effective method for the treatment of gastric neoplasms in the pylorus, on the basis of these favorable clinical outcomes.
Disclosure of Interest: None declared

P0131 THE ROLE OF NONCONTRAST COMPUTED TOMOGRAPHY (CT) PRIOR TO THE ENDOSCOPIC INTERVENTION FOR THE SUSPICIOUS ESOPHAGEAL FISH BONE (FB)

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INTRODUCTION: Accidental foreign body ingestion is not uncommon among patients of all ages. The immediate risk to the patient ranges from negligible to life threatening. In Asian countries, fish bones (FB) are the most prevalent esophageal foreign bodies and they are usually ingested accidentally together with food. The FBs have sharp polygonal or pin-like pointed structure and they can perforate or tear the esophageal wall. Therefore, endoscopic intervention should be performed if FB is impacted in the esophagus. However, it is difficult to diagnose esophageal FB with symptom, sign or plain radiography in most cases. Computed tomography (CT) has been proven to be accurate and noninvasive technique for evaluating the structures of esophagus. There are few reports or practical guidelines for using CT scan for the diagnosis of esophageal FB till now.
AIMS & METHODS: The aim of this study was to evaluate the usefulness of CT scan for the diagnosis of esophageal FB. Between March 2009 and March 2014, consecutive patients with suspected esophageal FB at Jeju National University Hospital were identified. Among those, patients with normal plain radiography were included, and medical records were abstracted for CT scan and endoscopy with outcomes. In some patients, noncontrast neck CT scan was performed prior to endoscopic intervention. We evaluated the outcome in two groups (pre-endoscopic CT or No CT).
RESULTS: During the study period, 134 patients (M:F = 55:79) who were strongly suspected of FB ingestion with normal plain radiography were enrolled. The mean age was 54.5±15.6. Of those 134 patients, 91 (68%) underwent CT

scan, and 43 (32%) underwent endoscopic intervention without CT scan. Among 91 patients with pre-endoscopic CT scan, 57 patients had positive CT findings of FB. The subsequent endoscopic procedure showed FB in 56 (98%), and FB was removed in all patients successfully. Among 34 patients who had negative finding of FB on the CT scan, 20 patients underwent endoscopy because of patients' request. However, FB was found in only 2 (10%) patients at the inlet of esophagus. In these two patients, artifacts which were made by dental prosthesis interfered with detecting FB on the CT scan. Among 43 patients without pre-endoscopic CT scan, 31 patients (72%) had esophageal FB in endoscopic examination. The sensitivity, specificity, positive predictive value, and negative predictive value of CT scan for the detection of FB was 98.2%, 90.1%, 96.5%, and 94.7%, respectively.
CONCLUSION: Pre-endoscopic CT scan is accurate and noninvasive diagnostic modality for the detection of ingested esophageal FB. Moreover, CT scan prior to endoscopic procedure is very useful to avoid unnecessary endoscopic procedure. Further studies are needed about the advantages of pre-endoscopic CT scan for the evaluation of pre-endoscopic complication and for the planning of endoscopic removal method.
Disclosure of Interest: None declared

P0132 ENDOSCOPIC THERAPY IN UPPER GI BLEEDING: ARE WE FOLLOWING THE GUIDELINES?

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INTRODUCTION: Acute upper gastrointestinal bleeding (UGIB) is a common medical emergency that carries a 10% inpatient mortality. Acute peptic ulcer disease is the most common aetiology followed by variceal bleeding. Mortality has not significantly improved over the last 50 years, highlighting the need to follow best practice guidelines in order to improve outcomes.
Upper GI endoscopy allows us to diagnose and treat the cause of UGIB as well as to help prevent re-bleeding. The 2012 NICE guidance on the management of non-variceal UGIB states that adrenaline as monotherapy should be avoided. It suggests that only mechanical therapy (e.g clips) be used as monotherapy and that adrenaline should always be used as dual therapy with either clips or thermal coagulation (APC).
The aim of our study was to audit our practice and compliance with NICE guidance in delivering appropriate endoscopic therapy for non variceal UGIB and to ascertain the rate of re-bleeding.
AIMS & METHODS: A retrospective analysis of all patients who underwent upper GI endoscopy for melaena or haematemesis as a primary symptom over an eight year period (2006-2013) was performed within a large district general North London NHS trust. Data was obtained from the Unisoft Endoscopy reporting software. The therapies used at endoscopy for UGIB were scrutinized.
RESULTS: 3759 patients were referred for upper GI endoscopy with melaena or haematemesis. 594 patients received endoscopic therapy (102 for variceal bleeds and 492 for non-variceal bleeds).
Table 1: Therapies in non-variceal upper GI bleeding:

Therapy	Number of patients (%)
Adrenaline monotherapy	172 (34.9%)
Adrenaline + Endoclip*	117 (23.8%)
APC monotherapy	94 (19.1%)
Adrenaline + APC*	53 (10.8%)
Endoclip monotherapy*	32 (6.5%)
Adrenaline + APC + endoclip*	18 (3.7%)
Endoclip + APC	6 (1.2%)
Total	**492**

A total of 26 patients (5.3%) diagnosed with non-variceal upper GI bleeding experienced re-bleeding (defined as the re-appearance of melaena/haematemesis with repeat endoscopy within 7 days). Of these patients 14 (53.8%) had received optimal (NICE recommended) therapy whilst 12 (46.2%) had received sub-optimal therapy (7 had adrenaline monotherapy and 5 had APC monotherapy). There was no associated increase in mortality compared to the national average.
CONCLUSION: This study demonstrates poor adherance to current NICE guidance on dual therapy in non variceal UGIB as only 45% of patients received optimal intervention. Endoscopic monotherapy for acute UGIB– either with adrenaline (35%) or APC (19%), though no longer recommended was still evident within our trust. The type of therapy given did not influence the risk of re-bleeding in our population and our overall mortality rates fell within expected levels.
Disclosure of Interest: None declared

P0133 PRIMARY OBESITY SURGERY ENDOLUMENAL METHOD FOR THE TREATMENT OF 162 OBESE PATIENTS WITH A FOLLOW UP TIME OF 1 YEAR

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INTRODUCTION: Obesity is at epidemic proportions and rising[1]. Bariatric surgical procedures have demonstrated better durable weight loss than diet and exercise. However risk may limit adoption of these procedures[2]. Endoscopic procedures like the Primary Obesity Surgery Endolumenal (POSE), may offer less risk and satisfactory results, however, limited safety and outcome data is available[3].
AIMS & METHODS: The objective of the study was to describe the POSE procedure, perioperative care, one year safety and weight loss outcomes for a single center.
Methods: 162 patients undergoing the POSE procedure between July 2011 and April 2013 were followed for one year. Overall patient status and weight data was collected at baseline and at 1 year (n = 130). Outcomes included adverse events, change in total body weight (TBWL), percentage of TBWL (%TBWL) and percentage of excess weight loss (%EWL).
RESULTS: Patients tolerated the procedure well with no serious short or long term adverse events. All but one patient was discharged within 24 hours of procedure. Mean age was 43.7±11.0 years and baseline BMI was 38.0 ± 4.9 kg/m^2. Initial body weight (106.7± 18.0 kg) was significantly reduced at 1 year: mean TBWL was 16.0±10.2 kg and mean % TBWL was 14.4±8.2%. At 1 year of follow up %EWL was 43.4±25.6%
CONCLUSION: The POSE method can be considered an effective, safe and well tolerated for the treatment of patients with obesity, at least at 1 year of follow-up.
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Disclosure of Interest: None declared

P0134 A KOREAN MULTI-CENTER STUDY TO EVALUATE THE EFFICACY OF THE OTSC SYSTEM FOR TREATMENT OF GI FISTULA, PERFORATION AND NOTES ENTRY SITE CLOSURE

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INTRODUCTION: Recently, a new over-the-scope clip (OTSC) (Ovesco Endoscopy, Tuebingen, Germany) system has been developed and used for the primary non-surgical closure of GI tract perforations and fistulas.
AIMS & METHODS: The aims of this study were to investigate the therapeutic yield of endoscopic management by the OTSC system. We performed a multicenter prospective study. In total six experts (five centers) performed OTSC procedure.
RESULTS: This study involved in total 17 patients (median age 55 years (range 32-77 years), 12 men) with GI leaks from anastomotic dehiscence, fistulas, and esophageal perforation due to Boerhaave's syndrome: Three gastrojejunostomy site, three esophagojejunostomy site, three esophagogastrostomy site, two Boerhaave' syndrome, two gastrobronchial fistula, one gastrocolonic fistula, one endoscopic full thickness resection site closure, one jejuno-jejunal fistula, one colonopseudocyst fistula. The diameter of leaks ranged between 5 and 20 mm. Mean procedure time was 18.3 min. Technically, all procedures were succssful. Complete sealing of leaks was achieved by using OTSC alone in 14 of 17 patients. For one OTSC fail patient, closure was completed by placing one additional covered stent. Two fistula cases required surgical repair.
CONCLUSION: The OTSC system is very useful in the management of GI leaks especially in case of anastomotic leakage after bowel surgery.
Disclosure of Interest: None declared

P0135 THE TISSUE EFFECT OF ARGON-PLASMA COAGULATION WITH PRIOR SUBMUCOSAL INJECTION (HYBRID-APC) VERSUS STANDARD APC: A RANDOMIZED EX-VIVO STUDY

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INTRODUCTION: Thermal ablation for Barrett's esophagus has widely been established in gastrointestinal endoscopy during the last decade. The mainly used methods of radiofrequency ablation (RFA) and argon-plasma coagulation

(APC) carry a relevant risk of stricture formation of up to 5-15%. Newer ablation techniques that are able to overcome this disadvantage would therefore be desirable.
AIMS & METHODS: The aim of the present study was to compare the depth of tissue injury of the new method of Hybrid-APC versus standard APC within a randomized study in a porcine esophagus model. Using a total of 8 explanted pig esophagi, 48 esophageal areas were ablated either by standard or Hybrid-APC (APC with prior submucosal fluid injection) using power settings of 50 and 70W. The depth of tissue injury to the esophageal wall was analysed macroscopically and histopathologically.
RESULTS: Using 50 W, mean coagulation depth was 937±469μm during standard APC, and 477±271μm during Hybrid-APC ($p = 0.064$). Using 70 W, coagulation depth was 1096±320μm (standard APC) and 468±136 μm (Hybrid-APC; $p = 0.003$). During all settings, damage to the muscularis mucosae was observed. Using standard APC, damage to the submucosal layer was observed in 4/6 (50 W) and 6/6 cases (70 W). During Hybrid-APC, coagulation of the submucosal layer occurred in 2/6 (50 W) and 1/6 cases (70 W). The proper muscle layer was only damaged during conventional APC (50W: 1/6; 70W: 3/6).
CONCLUSION: Hybrid-APC reduces coagulation depth by half in comparison with standard APC, with no thermal injury to the proper muscle layer. It may therefore lead to a lower rate of stricture formation during clinical application.
Disclosure of Interest: H. Manner: None declared, A. Neugebauer Other: Employee of Erbe Elektromedizin, M. Scharpf: None declared, K. Braun: None declared, C. Ell: None declared, F. Fend: None declared, M. Enderle Other: Employee of Erbe Elektromedizin

P0136 EVALUATION OF GASTRIC SUBMUCOSAL TUMORS BY ENDOSCOPIC VISUALIZED FEATURES ON SUBMUCOSAL ENDOSCOPY

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INTRODUCTION: Although the macroscopic characteristics of submucosal tumors (SMTs), such as gastrointestinal stromal tumors (GISTs), have been characterized, the assessment of SMTs by their endoscopic visualized features (EVF; which are observed by endoscopic imaging under direct view) remains unevaluated.
AIMS & METHODS: The aim of the present study was to investigate the potential of endoscopic diagnostics for SMTs using EVF. The EVF of 26 gastric SMT cases, in which the final pathological diagnosis was obtained by bloc biopsy using the submucosal endoscopy with mucosal flap method, were retrospectively reviewed. Each type of SMT was classified according to the following five EVF: Color, clarity, shape, tumor coating and solidity. Additionally, the EVF of 13 low-risk GISTs and 13 benign submucosal tumors (BSTs) were comparatively evaluated for the five abovementioned EVF.
RESULTS: Similar trends were identified between the low-risk GISTs, granular cell tumors and the schwannoma with regard to EVF. While these tumors exhibited cloudy EVF, leiomyomas tended to exhibit clear EVF. Among SMTs of the heterotopic pancreas type, the EVF demonstrated particularly small nodules of the pancreatic tissue itself. Although the sample size included in the present study is small, a classification system for gastric SMTs was proposed according to the EVF. When compared with the BST group, the GIST group demonstrated a significantly higher frequency of tumors that exhibited a combination of three EVF (white, cloudy and rigid) that are consistent with all gastric GISTs ($P < 0.05$).
CONCLUSION: Gastric SMTs may be classified based on the EVF, which indicates that the EVF possess potential diagnostic value for the differentiation of GISTs from BSTs.
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Disclosure of Interest: None declared

P0137 MIXED HISTOLOGICAL-TYPE (INTESTINAL AND DIFFUSE TYPE) EARLY GASTRIC CANCER PATIENTS TENDED TO BE NON-CURATIVE RESECTION BY ENDOSCOPIC SUB-MUCOSAL DISSECTION

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INTRODUCTION: It is well known that the histological types of gastric cancer are intestinal and diffuse type (by Lauren[1]). Intestinal type mucosal gastric cancer will be cured by ESD. However, Diffuse type gastric cancers have lymph node metastasis and even intramucosal cancer. Intestinal type was divided into well (tub1) differentiated adenocarcinoma and moderately (tub2) differentiated adenocarcinoma according to their structure abnormality by Japanese Classification of Gastric carcinoma (JCGC). Intestinal type is equal to differentiated adenocarcinoma and Diffuse type is equal to undifferentiated adenocarcinoma by JCGC. Mixed-histological type (Intestinal and Diffuse) early gastric cancer sometimes yields different results in pre-endoscopic submucosal dissection (ESD) biopsy diagnosis and post-operative ESD diagnosis. This complicates the diagnosis of the cancer region using narrow band imaging (NBI).
AIMS & METHODS: The purpose of this study is to evaluate the clinical characteristics and tendencies of mixed-histologic-type early gastric cancer, and bring up points of consideration of pre-operative ESD diagnosis. 1259 patients who were diagnosed with predominantly differentiated early gastric cancer (M: 1026 cases, SM: 233 cases) and who were treated with ESD between 2005 and 2012 without previously being treated at the Cancer Institute Hospital were retrospectively studied. The histological type of the cancer tissue, the criteria used to determine the stump, and the degree of SM invasion were determined based on the Japanese Classification of Gastric Carcinoma (JCGC). The Chi-square test and logistic regression analysis were used as univariate and multivariate analysis respectively to statistically compare the test groups.
RESULTS: Mixed-histologic-type early gastric cancer was defined as showing 10% or more undifferentiated adenocarcinoma in the post-operative ESD diagnosis. 94.6% of well (tub1) differentiated adenocarcinoma diagnosed by biopsy accorded with final ESD specimens pathology. However, 68.2% of moderately (tub2) differentiated adenocarcinoma diagnosed by biopsy accorded with ESD specimens. Mixed-histologic-type adenocarcinoma tended to be bigger in size and had a higher positive rate of sub-mucosal invasion than pure differentiated adenocarcinoma. (Size: 23.2 mm (±13.2) vs14.7 mm (±9.8), $p < 0.05$ SM: 45% vs 26%, $p < 0.05$) The rates of lateral margin involvement (LM), Lymphatic invasion (ly) and Lymph node metastasis (LN) were significantly different between groups of pure differentiated adenocarcinoma and mixed-histologic-type adenocarcinoma.(LM: 5.4% vs 1.0%, $p = 0.003$ ly: 18% vs 3.1%, $p < 0.05$ LN: 3.6% vs 0.3%, $p = 0.003$) In the multivariate analysis, all the above factors are significantly different between groups.
CONCLUSION: If pre-operative histological diagnosis using biopsy specimens before ESD shows tub2, there is the possibility that it is mixed-histologic-type early gastric cancer. We consider it necessary in such a case to conduct a careful pre-operative diagnosis of the cancer region using NBI or a biopsy of the surrounding area, while keeping in mind the clinical characteristics of mixed-histologic-type adenocarcinoma avoiding non- curative resection by ESD.
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Disclosure of Interest: None declared

P0138 A MORPHOLOGICAL CLASSIFICATION OF WHITE OPAQUE SUBSTANCE WITHIN GASTRIC NEOPLASIA VISUALIZED BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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INTRODUCTION: White opaque substance (WOS) identified within gastric neoplasias is a unique finding visualized in magnifying endoscopy with narrow-band imaging (ME-NBI) and represents intramucosal accumulation of lipid droplets. The morphological classification of WOS within gastric neoplasia has not been investigated in detail.
AIMS & METHODS: The aim of the current study was to establish the morphological classification of WOS and investigate whether it can be used to discriminate between adenoma and early carcinoma. This study retrospectively investigated two hundred twenty-seven patients with 242 gastric neoplasias (29 adenomas and 213 early carcinomas) who underwent ME-NBI before endoscopic resection in our hospital between January 2010 and December 2013. We studied the frequency of WOS within gastric neoplasias and identified the following morphological patterns: 1) dotted pattern, scattered and distributed as dots; 2) linear pattern, shaped like a line composed of aggregated dots; 3) reticular pattern, shaped like a honeycomb composed of connected lines; 4) speckled pattern, mottled and composed of aggregated dots; and 5) diffuse pattern, diffusely distributed by dense WOS in the intervening part. We also investigated the irregularity of WOS within adenomas and early carcinomas. We defined irregular WOS as disorganized and asymmetrical distribution of WOS in all patterns.
RESULTS: WOS was more frequently observed in adenomas (13/29: 44.8%) than in early carcinomas (62/213: 29.1%). WOS within adenomas showed a symmetrical distribution with a regular reticular pattern because the intervening part has no severe structural abnormalities. The WOS within carcinomas showed an asymmetrical distribution with an irregularly dotted or speckled pattern because the intervening part has severe structural abnormalities.

	Adenoma (13)	Carcinoma (62)	*P value*
Dotted pattern	2 (15.4%)	30 (48.4%)	<0.05
Linear pattern	5 (38.5%)	13 (21.0%)	NS
Reticular pattern	8 (61.5%)	9 (14.5%)	<0.01
Speckled pattern	4 (30.8%)	40 (64.5%)	0.053
Diffuse pattern	1 (7.69%)	8 (12.9%)	NS
Irregular WOS	3 (23.1%)	60 (96.8%)	<0.01

CONCLUSION: In gastric neoplasias containing WOS, the morphological classification of WOS is useful in discriminating between adenoma and early carcinoma.
Disclosure of Interest: None declared

P0139 ESTABLISHMENT OF AN ENDOSCOPIC DIAGNOSIS FOR GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE (CHIEF CELL PREDOMINANT TYPE) USING MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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INTRODUCTION: Gastric adenocarcinoma of the fundic gland (chief cell predominant type, GA-FG-CCP) has recently been proposed as a new and rare variant of gastric adenocarcinoma. We previously described the clinicopathological and endoscopic features of GA-FG-CCP using conventional endoscopy (CE) in 2010 and 2014[1-2]. If this tumor type is not recognized by a physician, it may be misdiagnosed as a submucosal tumor or fundic gland polyp or it may be overlooked. Therefore, the endoscopic diagnosis of GA-FG-CCP using magnifying endoscopy with narrow-band imaging (ME-NBI) may be useful; however, this technique has not been investigated in detail.
AIMS & METHODS: The aim of the current study was to evaluate the endoscopic features of GA-FG-CCP using ME-NBI. A total of 17 GA-FG-CCPs were evaluated retrospectively between January 2008 and December 2013. The endoscopic and clinicopathological features of the lesions were analyzed to provide information of diagnostic value.
RESULTS: A total of 17 patients [median age 66 y (57-75), 10 men, 7 women] with 17 lesions were treated as follows: 12 were treated with ESD, 3 were treated with EMR, and 2 underwent surgery. Except for 2 cases that underwent additional surgery, all of the cases underwent an endoscopic removal without further treatment. Twelve of the lesions were detected in the upper stomach, 4 in the middle stomach, and 1 in the lower stomach. Macroscopically, 9 lesions were submucosal tumors in shape, whereas 5 were depressed, 1 was flat-elevated, 1 was protruded and 1 was flat in shape. The mean tumor size was 11.8 (3-39) mm. Histopathologically, there were 5 intramucosal cancers and 12 submucosal invasive cancers. The mean depth of the submucosal invasion was 337.5 (50-1200) μm. Lymph node metastasis was observed in one case (25%, 1/4). The most common features of the 17 lesions with CE were 1)submucosal tumor shape in 10(58.8%) cases, 2) whitish color in 12(70.6%) cases, 3)dilated vessels with branching architecture in 9(52.9%) cases and 4)background mucosa without atrophic change in 15 (88.2%) cases. The endoscopic findings for a GA-FG-CCP using ME-NBI did not meet the criteria for carcinoma. However, we detected the four most frequently occurring features using ME-NBI to be 1)an indistinct line of demarcation between the lesion and the surrounding mucosa 8/8(100%), 2)a dilatation of the crypt opening 7/8(87.5%), 3)a dilatation of the intervening part between the crypts 5/8(62.5%) and 4)the presence of microvessels without distinct irregularities 7/8(87.5%).
CONCLUSION: GA-FG-CCP has distinct endoscopic characteristics, especially in terms of its shape, color, vessels and background mucosa using CE and in its demarcation lines, the shape of the crypt opening, the shape of the intervening part between the crypts and the microvessels observed with ME-NBI. Further investigations should include collecting cases using CE and ME-NBI based on these endoscopic features.
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P0140 DIAGNOSTIC AND THERAPEUTIC EFFICACY OF ENDOSCOPIC ENUCLEATION FOR SMALL GASTRIC MUSCULARIS PROPRIA LAYER TUMOR

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INTRODUCTION: Gastric subepithelial tumors originated from muscularis propria (MP) are partly benign tumors, but some gastric stromal tumors have malignant potential, especially gastrointestinal stromal tumors (GISTs). PM tumors are usually treated by surgical intervention and endoscopic treatment remains controversial. The aim of this study was to retrospectively evaluate the utility of endoscopic enucleation for diagnosis and treatment of MP tumors.
AIMS & METHODS: From January 2010 to June 2013, forty patients with gastric MP tumor ($\leq$ 20 mm) underwent endoscopic enucleation. Before endoscopic resection, all patients performed endoscopic ultrasound to determine the layer of origin and the accurate size. Small PM tumor ($<$12 mm) was resected by using band ligation method and PM tumor (range 12-20 mm size) was enucleated by endoscopic submucosal resection (ESD) technique using various endo-knifes. Tumor characteristics, tumor size, procedure technique, complete resection rate and recurrence were analyzed.
RESULTS: A total 40 patients (16 men, 24 women; mean age 50.3 years) were eligible for inclusion in this study. The histologic diagnosis was leiomyoma (n = 24), GIST (n = 15) and schwanoma (n = 1). Band ligation method was used in 20 patients. Median procedure time was 8 min (5-26) and complete resection rate was 95% (19/20). Two patients developed perforation, which was closed by endoscopic methods with metallic clips. ESD method was used in 20 patients. The mean procedure time was 41.1 minutes (range 10 – 260) and complete resection rate was 60% (12/20). Four cases were complicated by perforation, and the perforations were closed with metal clips. The mean follow-up time was 9.8 months (range 3-35). No recurrence was developed during follow-up period.
CONCLUSION: Endoscopic enucleation appears to be effective method for the histologic diagnosis and removal of small MP layer tumors ($<$2cm). Although there is a risk of perforation which has become manageable endoscopically.
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P0141 COMPARISON OF DEXMEDETOMIDINE VERSUS MIDAZOLAM FOR PROCEDURAL SEDATION DURING ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC TUMOR

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is nowadays commonly performed as a treatment for gastric tumor. However, the sedation with midazolam (MDZ) often did not reach a satisfactory sedation during the procedure and the drug could suppress respiration and blood pressure also.
AIMS & METHODS: To investigate the safety and efficacy of dexmedetomidine (DEX) in comparison with midazolam (MDZ) as a sedative during an endoscopic submucosal dissection (ESD) of gastric tumor.
Design: Prospective, randomized, double-blind study.
Setting: Tertiary-care institution.
Patients: Scheduled patients undergoing ESD of gastric tumor.
Main Outcome Measurements: The depth of sedation by using a MOAA/S score (Modified Observers Assessment alertness/sedation), interfering actions of patients, sedation related-adverse events, and the satisfaction degree of the doctors.
RESULTS: Eighty patients were randomly assigned to one of two treatment regimens (40 patients of each). There was no statistically significant difference between the two groups regarding age, sex, body mass index, ASA classification, and tumor characteristics. Appropriate sedation rate and the satisfaction degree of the doctors were significantly high in the DEX group. There were more movements of patient leading to an interruption of the procedure in the MDZ group than in the DEX group. There was no difference in the adverse events between the two groups.
CONCLUSION: DEX for the sedation during gastric ESD is as safe as MDZ and the sedation effect of DEX is superior to that of MDZ.
Key words: Procedural sedation; Endoscopic submucosal dissection; Sedative agents; Dexmedetomidine; Midazolam
Disclosure of Interest: None declared

P0142 A NEW METHOD TO PERFORM DIRECT PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY USING DOUBLE BALLOON ENTEROSCOPY AND FLUOROSCOPY

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INTRODUCTION: Direct percutaneous endoscopic jejunostomy (DPEJ) is usually performed using traditional push enteroscopes or pediatric colonoscopes. The success rate of DPEJ in expert hands is about 68%. Herein we present a new method to perform DPEJ using DBE and fluoroscopy.
AIMS & METHODS: To report on the efficacy and safety of DBE-assisted DPEJ with simultaneous use of fluoroscopy.
The DBE was performed by using the standard push-pull-technique after the balloon enteroscope was advanced beyond the ligament of Treitz. During advancement, a site in the jejunum was sought for PEJ tube placement by transillumination and finger indentation. In addition we confirmed the site of indentation by placing a radio-opaque marker on the skin and verifying that the small bowel loop was closed to the skin. After a suitable site was identified, DPEJ placement was performed by using the Ponsky-method (pull-type-percutaneous gastrostomy tube technique and 20 Fr PEG-kit.
After placing the DPEJ we administered water soluble contrast through the tube to clearly confirm intraluminal jejunal positioning.
RESULTS: The study included 24 patients (11 females, 13 males, mean age 55 years, age range 31-79). The indications for DPEJ were feeding in 23 patients and venting for malignant small bowel obstruction in one. The technical success was 91.6%. In two patients no transillumination was possible. The mean distance of DPEJ was 74 cm (range 50 to 90 cm) past the pylorus or the anastomosis. One jejunostomy site got infected (4.1%). There were no major complications associated with the procedure.

CONCLUSION: DBE-DPEJ using fluoroscopic assistance seems an efficacious, safe and successful approach for patients requiring jejunal enteral feeding. Nevertheless, studies comparing the double balloon enteroscopy technique to the standard push enteroscopy technique are needed to establish potential advantages of this technique.

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P0143 ENDOSCOPIC CLOSURE OF COMPLEX FISTULAS IN POST-BARIATRIC SURGERY PATIENTS USING THE OVER-THE-SCOPE-CLIP (OTSC) SYSTEM

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INTRODUCTION: The novel over-the-scope-clip (OTSC) allows for excellent apposition of tissue, potentially permitting closure of various types of GI defects.
AIMS & METHODS: To evaluate the usefulness and safety of OTSC for endoscopic closure of fistulas and leaks and perforations in patients with post-obesity surgery altered upper GI anatomy
Case series of all patients with post-obesity surgery altered upper GI anatomy referred for attempted endoscopic closure over a 14-months period. Data analysis included clinical characteristics, demographics, indication, and type of bariatric surgery, primary closure, recurrence, complications, and long-term follow-up clinical outcome.
RESULTS: Seven consecutive patients with fistulas and leaks associated with previous bariatric surgery, four men, three women, were included. The mean age was 50.3 years (range 29-66), mean ASA score of 3 (range 2-4). The most common surgery was gastric sleeve (n = 4), followed by gastric bypass (n = 3). Four patients had a gastropleural fistula; three patients had a gastro-peritoneo-cutaneous fistula. Endoscopic closure was achieved in 6/7 (85.7%). Whereas 4 patients had resolution of the fistula after one endoscopic session, two patients required two sessions and one patient required three sessions. On long-term follow-up there was one recurrence, which was treated with another OTSC. There were no complications associated with OTSC-applications.
CONCLUSION: This is the largest series reported so far on the utility of OTSC for closure of fistulas associated with bariatric surgery. OTSC represents an effective, easy to perform and safe endoscopic therapeutic modality for various types of fistulas. This therapy should be added to the armamentarium of therapeutic endoscopists.

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P0144 IMPROVING OUTCOMES FROM UPPER GASTROINTESTINAL BLEEDING IN ENGLAND BETWEEN 2001 AND 2012

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INTRODUCTION: Upper gastrointestinal bleeding (UGIB) is a common medical emergency with significant mortality. UGIB management has changed in recent years with early therapeutic endoscopy and interventional radiology (IR) rather than surgery for uncontrollable bleeding. We have therefore examined outcomes for patients with UGIB over the last decade in England.
AIMS & METHODS: Hospital attendances in England are collated using Hospital Episode Statistics (HES). ICD-10 coding was used to identify admissions to hospital with UGIB between 2001 and 2012. Death in hospital, 30 day mortality, emergency readmission within 30 days, median time to endoscopy, need for surgery or IR and length of stay were examined.
RESULTS: 679,505 episodes were examined involving 378057 men and 301448 women. 51.9% were coded as undergoing inpatient endoscopy. The overall in-hospital mortality and 30-day mortality for UGIB was 12.2% and 16.1% respectively. Both in hospital and 30-day mortality fell over the 10 year period examined (2001-2003 14.4% and 18.1% vs. 2009-2012 10.2% and 14.3%, $p < 0.001$). There has been a large fall in age-adjusted in-hospital mortality (81.7 per 1000 (95% CI 79.1-84.3) in 2001-2002 vs. 56.5 (95% CI 56.5-58.3) in 2011-2012). Age-adjusted 30-day mortality has also fallen from 102.9 per 1000 (95% CI 99.9-105.9) in 2001-2002 to 79.9 (95% CI 77.7-82.1) in 2011-2012. In-hospital mortality for bleeding varices has fallen by 21.8% from 235.6(95% CI 207.8-265.5) per 1000 in 2001-2003 to 184.3 (95% CI 165-205) in 2009-2012 and for bleeding peptic ulcer it has fallen by 18% from 82.2 per 1,000 in 2001-2003 (95% CI 76.7-88) to 67.4 (95% CI 62.4-72.7) in 2009-2012. For patients who were not coded as undergoing endoscopy, overall in-hospital and 30-day mortality was higher (16.4% and 21% respectively) but also fell over the decade. During the same period there has been a significant fall in the number of patients undergoing surgery (2001-2003 1.84% vs. 2009-2012 0.75%, $p < 0.001$) and a rise in the proportion of patients undergoing an IR procedure (2001-2003 0.04% vs. 2009-2012 0.18% $p < 0.001$). Median time to endoscopy did not change significantly (2001-2003 1(IQR 1-3) days vs. 2009-2012 1(IQR 0-3)days) and the percentage of patients undergoing endoscopy within 48 hours of admission remained 55% over the same time period. Average length of stay fell from 5 (range 2-12) days in 2001-2003 to 4 (range 1-9) days in 2009-2012 but rates of emergency readmission within 30 days have significantly increased (2001-2003 18.2% vs. 2009-2012 27.8% $p < 0.001$).
CONCLUSION: Outcomes for patients with UGIB have improved over the past decade with significant reductions in associated mortality and age-adjusted mortality. There has been a reduction in surgery and increase in IR for UGIB.

Disclosure of Interest: None declared

P0145 ROUTINE CONFOCAL ENDOMICROSCOPY IN A CLINIC SPECIALIZED IN THE MANAGEMENT OF THE DIGESTIVE PATHOLOGY WITH MUCOSECTOMY, SUBMUCOSAL DISSECTION, PROSTHESIS AND PUNCTURE: RESULTS OF THE FIRST MONTHS OF USE

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INTRODUCTION: Probe-based Confocal Laser Endomicroscopy (pCLE) is an imaging technique that allows the achievement of an extemporaneous microscopic exam of a lesion before the treatment or to control the quality of the endoscopic treatment.
The aim of the study is to appreciate the real indication of Cellvizio in routine in a clinic specialized in the management of the digestive pathology.
AIMS & METHODS: In 5 months of practice (from May 16th until November 23rd 2013) during 436 endoscopies, 51 procedures of pCLE were performed. In all cases, the pathologist exam supports the conclusions of the probe-based microscopic exam.
Among these 51 procedures, 6 are presented:
- One in the esophagus showing the utility of pCLE to find a dysplasia area on a Barrett's Esophagus before mucosectomy followed by a BARRX destruction.
- One in the colon showing the utility of pCLE to differentiate serrated polyps from hyperplasic polyps so as to realize an immediate resection.
- One in the stomach showing the utility of pCLE to find a gastric dysplasia area inside relief abnormalities and treat it by submucosa dissection.
- One in the duodenum showing the utility of pCLE to differentiate an inflammatory granuloma from an adenomatous residue which would justify an ARGON treatment and/or a mucosectomy on a duodenal scare or a right colic that could initiate major complications.
- One in the biliary duct showing the utility of pCLE for the immediate diagnosis of cholangiocarcinoma (1) allowing to choose the most appropriate prosthesis.
- One in the pancreas showing the utility of pCLE for the differential diagnosis of pancreas cysts (serous, mucinous, pseudocysts, cystic forms of neuroendocrine tumors)

RESULTS: For the first 51 procedures the repartition was: 2 cases in the esophagus (4%), 3 in the cardia (6%), 3 in the stomach (6%), 2 in the duodenum (4%), 1 in the small bowel (2%), 3 in the biliary duct (6%), 3 in the Vater papillia (6%), 1 in the pancreas and 33 in the colon (64%).
In 43 cases (84%), the pCLE diagnosis was consistent with those of the pathologist. In 6 cases (12% of cases, 1 in cardia BE, 1 in the stomach, 1 in colonic mucosectomy scares, 1 at the Vater papillia and 2 colonic polyps). pCLE over evaluated the lesion. In 2 cases (4% of cases, 2 cases with colon polyp) pCLE didn't concur with the diagnosis of the pathologist.
CONCLUSION: Optical biopsies have been useful in the management of the lesions in the whole digestive tract in 51 cases out of 436 (11.7% of cases) before E. M. R, E. S. D., installation of biliary prosthesis, pancreatic cysts treatment and to control the nature of potential residues on an E. M. R or E. S. D. scares.

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Disclosure of Interest: None declared

P0146 HIGH-PRESSURE INJECTION OF GLYCEROL WITH HYBRIDKNIFE FOR ESD IS FEASIBLE AND INCREASES THE EASE AND SPEED OF THE PROCEDURE: AN IN VIVO STUDY IN PIGS

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INTRODUCTION: The HybridKnife water-jet system (ERBE, Tubingen, Germany) has been shown to increase dissection speed and decreased the risk of perforation during endoscopic submucosal dissection (ESD). Glycerol mixture is a viscous, long-lasting solution preferentially used by Japanese ESD experts. The combination of the HybridKnife system with a glycerol solution has not been evaluated to date.
AIMS & METHODS: A prospective non-randomised comparative study of ESD with HybridKnife injecting of either a glycerol mixture or normal saline was performed. Twenty dissections (ten per group) were performed on four anaesthetised domestic mini-pigs. Dissection speed (mm^2/min), size of the specimen (mm^2), duration (min), en bloc resection rate, and bleeding and perforation rates were prospectively recorded. An evaluation of operator comfort and perception of safety (dissection score) was performed using a visual analogue scale with 0 being the worst score and 10 the best.
RESULTS: High-pressure injection of the glycerol mixture and dissection with the HybridKnife was feasible without complications. Dissection was significantly more rapid (1.67-fold) with glycerol injection than normal saline injection (27.44 vs. 16.44 mm^2/min; $p<0.001$). The dissection score was significantly higher in the glycerol group than in the normal saline group (5.9 vs. 2.9; $p<0.001$) indicating that both operators felt more comfortable and safe performing ESD with the glycerol mixture injection. No differences were observed in the rates of en bloc resection, bleeding and perforation.
Table 1: Results

Solution	Glycerol (n = 10)	NaCl 0.9% (n = 10)	p
Mean surface (mm^2)	1495 (+/- SD 430.3)	976 (+/- SD 117.8)	0.0127
Mean time (min)	54 (+/- SD 9.43)	62.6 (+/-SD 17.08)	0.082
Mean speed (mm^2/min)	27.44 (+/- SD 5.70)	16.44 (+/- SD 3.43)	<0.001
Perforation	0%	0%	NS
Bleeding	20%	20%	NS
En bloc resection	100%	100%	NS
Dissection score	5.9 (+/- SD 0.7)	2.9 (+/- SD 0.78)	<0.001
Preliminary incision	5	4	NS

CONCLUSION: In an in-vivo pig model, high-pressure jet injection of glycerol with HybridKnife for ESD is feasible and increases the speed and safety of the procedure compared with use of normal saline.
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Disclosure of Interest: None declared

P0147 VALIDATION OF A FRENCH TRAINING PROGRAM OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN LIVE PIGS AIMING TO START EFFICIENT AND SAFE HUMAN RECTAL ESD

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INTRODUCTION: ESD is a beneficial procedure that allows higher rates of en bloc and *complete* resection for large precancerous lesions or superficial cancer. However, training in ESD requires numerous sessions to become efficient, and so takes time and patience especially in Western countries. A well-structured training program is essential, because the outcome of ESD is dependent of the experience of the endoscopist. European experts recommend structured training programs with animal models to overcome the initial learning curve. Afterwards, constant practicing of ESD is required to increase success and decrease the procedure time and complications. We report the sucessful experience of a standardized local training program for ESD in a french tertiary center with a starting recruitment.
AIMS & METHODS: Between March and December 2013, 31 pig gastric ESD were performed by two operators. After the 11 initial pig gastric ESD, operators began human rectal ESD and 8 rectal human ESD were performed during the same period. The 20 next animals ESD were performed in parallel in order to keep a constant exposure to ESD cases. All procedures were performed with a hybridknife type T (Erbe medical, Erlangen, Germany). Glycerol mixture and physiologic serum were used for submucosal injection. Live, 20 kg, domestic mini-pigs, fasted for 48h prior to the procedure, were used. The duration of the procedure, size of the specimen, speed of the dissection, en bloc resection rate, complete resection rate and complications rate were prospectively recorded.
RESULTS: In the pig model, the en bloc resection rate was 96.7% (29/30). The speed of dissection increased with the experience of the operator to reach a plateau (30 mm^2/min) after 10 dissections. The speed of dissection for the 15 last ESD was significantly higher than the 16 first ESD (16.6 vs 28.2 mm^2/min; $p<0.001$). The mean size of the resected specimen was 1072.8 mm^2, the mean dissection time was 47.9 min and the mean speed of dissection was 22.4 mm^2/min. Only 1 perforation occurred and 6 (19.3%) per procedure bleedings imposed the use of a coagulation forceps.
In human rectal ESD, en bloc and complete resection rate were 100%. The mean specimen size was 1909.2 mm^2, the mean procedure time was 256 min. The average speed of dissection was 8.6 mm2/min: 5.8 mm^2/min for the first 4 cases vs 10.9 mm^2/min for the last 4 cases ($p=0.03$) No perforation occurred and 2 patients presented per procedure bleeding considered as a complication. 2 patients presented post procedure bleeding at day 7 and day 17 successfully treated with hemoclips.
CONCLUSION: A local training program with a pig model allows starting human dissection with high safety and efficiency. Initial training accelerates the learning curve and the continuous practice in pig model allows maintaining constant training until the recruitment of patients becomes sufficient.
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P0148 BURIED BUMPER SYNDROME - MANAGEMENT BASED ON ACCURATE STAGING

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INTRODUCTION: Buried bumper syndrome (BBS) is one of the major complications of percutaneous endoscopic gastrostomy (PEG). Until now there is no universal diagnostic and therapeutic algorithm based on the degree of disc submersion.
AIMS & METHODS: to assess safe and effective algorithm for diagnosis and therapy of BBS based on easy-to-use classification of severity. Methods: retrospective analysis of an endoscopic database, composition and evaluation of BBS severity scale
RESULTS: We have identified 40 cases of BBS in 38 patients (pts.) out of 1248 procedures of PEG performed from 01.01.2002 to 31.12.2012 at our endoscopy unit. The cohort consisted of 27 men and 11 women of 22-84 years of age (mean age 64 years). The most frequent indications for gastrostomy were neoplasma (18 cases) and neurological impairment (16 cases). Duration of gastrostoma to the diagnosis of BBS varied from 2 weeks to 64 months (mean 13 month). The incidence of BBS was 3.2% and it has almost tripled between subsequent five-year intervals - from 1.8% in group A (year 2003-2007) to 5% in group B (year 2008-2012). Potential reasons for the increase we found in more frequent detection of asymptomatic BBS (0 in group A, 8 in group B, $p=0.05$), often in patients with already minimal or no use of the stoma (0 in group A, 9 in group B, $p=0.03$). New classification of the depth of disc migration was composed based on clinical examination, gastroscopy and abdominal ultrasound (Table). Endoscopic component of this classification was validated with a high inter-rater agreement ($\kappa=0.93$) and abdominal ultrasound showed favourable parameters in the localisation of the buried bumper inside the stomach (sensitivity, specificity, positive and negative predictive value were 100%, 90%, 92% and 100%, respectively). Spectrum of severity in our cohort according to this classification was: grade 1 - 6 pts., grade 2 - 5 pts., grade 3 - 15 pts., grade 4 - 0 pt., grade 5 - 13 pts., grade 6 - 1 pt. 13 patients with grade 3 were treated endoscopically by various techniques of dissection, only one case was complicated by pneumoperitoneum. From 13 patients with BBS grade 5, six underwent laparotomy - bumper was localized outside the stomach in all cases.

STAGE	gastroscopy/abdominal ultrasound (US)/clinical finding
0	normal
1	ulcer below the disc and/or partial overgrowth of the disc (less than a half of disc area covered)
2	disc components still visible (more than a half of disc area covered)
3	disc completely covered, guide wire can be introduced; US: disc localized inside the stomach
4	disc completely covered, guide wire cannot be introduced; US: disc localized inside the stomach
5	disc completely covered; US: disc localized out of the stomach
6	disc protrudes out of the skin or palpable just below the skin

CONCLUSION: Incidence of BBS in our series was 3.2% with significant rise during 11 year period. New BBS severity classification based on gastroscopy and abdominal ultrasound is easy tool for stratification of patients for surgical and endoscopic therapy. Acknowledgement: Supported by the project PRVOUK 37-08.
Disclosure of Interest: None declared

P0149 ENDOSCOPIC SUBMUCOSAL RESECTION FOR METACHRONOUS TUMOR IN THE REMNANT STOMACH AFTER SUBTOTAL GASTRECTOMY

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INTRODUCTION: Subtotal gastrectomy is one of the most common procedures to resect gastric cancer curatively. However, if the patients have a remnant stomach after the surgery, the risk of metachronous gastric tumor remains. Because early gastric cancer (EGC) patients have a good prognosis after curative surgery, the incidence of metachronous tumor in the remnant stomach is now problematic. When the metachronous gastric tumor is detected, endoscopic submucosal dissection (ESD) can be considered as an alternative treatment option than an additional operation.
AIMS & METHODS: Little information exists concerning the optimal treatment of metachronous tumor in the remnant stomach. The aim of this study was to assess the clinical outcomes and safety of ESD for this lesion. We retrospectively enrolled patients who had undergone ESD for metachronous tumor in the remnant stomach after subtotal gastrectomy from December 2007 to January 2013 at the Samsung Medical Center in Seoul, Korea. A total of 18 lesions in 12 patients with EGC and 6 patients with high grade dysplasia (HGD) were treated by ESD. The patient characteristics, endoscopic findings and histopathological features and technical outcomes of ESD were investigated.
RESULTS: A total of 18 patients had previously undergone 17 Billoth-I (94%), 1 Billoth-II (6%) gastrectomies. The median period from the previous gastrectomy to the subsequent ESD for metachronous tumor in the remnant stomach was 71months (range 13-207 months), the median tumor size was 13mm (range 4-22mm). En block resection with curative resections achieved for 16 lesions (88.9%). Adverse events showed 1 case of perforation (5.6%) and there was neither case of requiring emergent surgery nor treatment-related mortality during this study period. The patients who requiring additional surgery for curative treatment due to deep submucosal invasion were 2 (11.2%).
CONCLUSION: ESD for the metachronous tumor in a remnant stomach after subtotal gastrectomy showed a high en bloc resection rate and very low complication rate. Therefore, we suggest that ESD is an effective and safe treatment method for metachronous tumor in the remnant stomach if it is performed by highly qualified experts. It is less invasive than additional surgery. Therefore, it can give a better quality of life to the patients, and the treatment outcome is excellent, with no treatment-related mortality in this study.
Disclosure of Interest: None declared

P0150 EFFICACY OF REBAMIPIDE IN THE HEALING OF IATROGENIC ULCERS POST ENDOSCOPIC SUBMUCOSAL DISSECTION: A META-ANALYSIS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is a treatment option for early gastric cancer (EGC). It is less invasive, however, it is associated with larger, deeper ulcers post-procedure. Combined use of mucosal protective anti-ulcer drugs such as rebamipide and proton pump inhibitors (PPI) was reported to promote ulcer healing.
AIMS & METHODS: The study aims to determine the efficacy of rebamipide in the healing of post ESD associated ulcers.
PubMed, Cochrane Database and bibliographies of retrieved articles were searched for eligible articles. Randomized controlled trials involving patients with EGC who underwent ESD and were given rebamipide monotherapy or as adjunct to PPI were included in this meta-analysis. 2 reviewers extracted the data and assessed the quality of the studies included. Review Manager 5 software was used to analyze data from the studies included. Random effects model was used for combining quantitative data.
RESULTS: 6 studies with a total population of 758 were included in the review. 356 patients were randomized to the treatment group (rebamipide alone or as an adjunct to PPI). 354 patients were randomized to the control group (PPI or H2-RA). Rebamipide monotherapy or as an adjunct to a PPI compared to placebo (PPI or H2-RA) significantly improved healing with a p value of 0.0002 (RR 1.50, 95% CI 1.21-1.87).
CONCLUSION: Rebamipide improves the healing of post ESD associated ulcers especially when administered with PPI for 4 weeks.
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Disclosure of Interest: None declared

P0151 ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE TREATMENT OF GASTROINTESTINAL NEOPLASIAS: INITIAL RESULTS IN 31 PATIENTS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is an advanced technique used for en-bloc curative resection of early neoplasms of the gastrointestinal tract. Main advantages are high rate of curative resection and low recurrence rate, avoiding in most cases the need of surgery.
AIMS & METHODS: Initial training on Animal Research facilities was carried out for 2 years before starting ESD in humans. Prospective analysis of ESD performed for suspected early neoplasia of GI tract. The interventions were performed mostly in the endoscopy suite, full equipped to provide general anaesthesia in selected cases (all cases on the oesophagus and stomach, as selected colorectal cases). Flush knife BT® (Fujifilm Co. Japan) was the main knife used, both in versions BT 1.5mm (oesophagus, colon and rectum) and 2.0mm (stomach); occasionally other knifes were applied, such as Hook-knife®and Dual-Knife® (Olympus Co, Japan)
RESULTS: From January 2012 to February 2014 ESD was completed in 31 patients. The mean age was 64.4 years (SD12), with a male proportion of 55%. Over 60% of the cases were performed in colorectal location (colon 12 (39%); rectum 7 (22%)); other locations were stomach (9 (29%)) and oesophagus (3 (10%)). Initial success of ESD was 93.5%, with 2 cases requiring surgery due to failure or severe complication (both colonic cases). The en-bloc resection rate was 96.5%, the average specimen size 18.1 cm2 (max. length on average 46.4mm), with a median of 114 minutes (34-256) to complete the procedure. Regarding the morphology, 16 cases were 0-IIa, 5 cases 0-Is, 3 cases 0-IIa/0-IIc, 2 cases 0-IIb, 2 cases 0-Is/IIa 1 case 0-IIa/0-IIb and 1 case 0-IIb/0-IIc. Lateral spreading tumors (LSTs) distribution was: LST granular mixed type 5 cases, LST granular homogeneous type 7 cases, and 1 case of LST non-granular type. The R0 resection rate for successful ESD was 90% (26 cases). There were 12 cases (39%) with perforation (38%), of which 10 (80%) were managed successfully with local endoscopic treatment (closure with clips). There were 2 cases of late complications (splenic rupture and mild lower gastrointestinal bleeding), with no mortality associated. We analyzed the population according to chronological inclusion and divided into 3 similar periods. The average dissection speed during the initial phase was 0.36mm/min, compared to 0.49mm/min and 0.44mm/min during the intermediate and the final phase respectively, with no statistically significant differences ($p = 0.2$) due to the small sample size.
CONCLUSION: ESD is an effective technique in the treatment of early neoplastic lesions in the digestive tract, particularly in cases of flat-depressed morphology, with a size greater than 20mm and/or the presence of submucosal fibrosis. The technical difficulty, along with the prolonged time of endoscopy and the risk of serious complications (essentially perforation) are the main constraints of ESD. However, in our own experience, high en-bloc and R0 resection rate can be achieved, along with remarkable technical progress during the learning curve and successful endoscopic management of perforation. Our results demonstrate the possibility of successful adoption of ESD in Europe after completing proper training.
Disclosure of Interest: None declared

P0152 ENTONOX DURING COLONOSCOPY; HOW SHOULD IT BE USED?

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INTRODUCTION: Entonox can be used to ease the discomfort associated with colonoscopy but the optimal mode of administration is unknown. We have compared continuous and as required Entonox use during screening colonoscopy examinations.
AIMS & METHODS: Patients attending for screening colonoscopy were invited to participate. Eligible patients were randomised to using Entonox as required or continuously. Procedural and demographic details including HADS score were collected. Examinations were performed by three experienced colonoscopists. Patients rated pain on a 10 point numerical ratings scale (0 = no pain and 10 = extreme pain) every 2 minutes during colonoscopy, prior to discharge and 1-3 days following colonoscopy. The colonoscopist and specialist screening practitioner (SSP) also rated the patient's overall pain severity and the technical difficulty of colonoscopy.
Continuous and categorical data were compared using a *t* test and chi-squared test respectively. Correlations were assessed using Pearson's correlation coefficient and the agreement between observers was assessed using the intra-class correlation coefficient (ICC).
RESULTS: 157 patients were screened and 49 were excluded (34 opted for intravenous sedation, 13 declined and 2 had a cardiac pacemaker). 108 patients were randomised and 8 patients were withdrawn (7 had a cancer and 1 was unable to activate Entonox). Study participants had a mean age of 67 years and 75% were male. 46 patients were randomised to continuous and 54 to as required use.
15/54 (27.7%) patients in the as required group did not use Entonox and 7/46 (15.2%) of patients in the continuous group reverted to as required use due to side effects. The number of patients requiring additional analgesia was not significantly different between continuous use and as required use (4/46 vs 3/54, $p = 0.54$).

There was no significant difference in the overall pain scores given by patients who used Entonox continuously and as required (mean score = 2.4 vs 3.2, p = 0.08 and peak score = 4.2 vs 4.8, p = 0.26). Overall patient satisfaction was high with the continuous and as required methods (mean = 9.9 vs 9.7, p = 0.23) as was willingness to undergo a repeat examination (mean = 9.2 vs. 9.7, p = 0.09). A HADS anxiety score of ≥7 was associated with higher overall pain scores (mean score = 2.1 vs 3.6, p = 0.004 and peak scores = 3.7 vs 5.6, p = 0.003). Patient with a HADS anxiety score <7 who were allocated to continuous rather than as required use had lower pain scores (mean = 1.4 vs 2.5, p = 0.045) but there were no significant differences between strategies in the patients with a HADS score ≥7 (3.3 vs 3.8, p = 0.6) There was no significant difference in the pain ratings according to gender.

Patients overall rating of pain prior to discharge correlated highly with the mean intra-procedural pain score (r = 0.84) and peak rating of pain (r = 0.84). There was also a very high correlation between the patients overall pain rating prior to discharge and 1-3 days later (r = 0.94). There was good agreement between the patients and the SSPs (ICC = 0.79) and endoscopists (ICC = 0.76) overall pain rating.

CONCLUSION: Overall, the method of Entonox administration did not influence pain ratings. However, continuous Entonox use was more effective in patients with a low anxiety level.

Disclosure of Interest: None declared

P0153 NON-ANAESTHESIOLOGIST ADMINISTERED PROPOFOL IN COLONOSCOPY – INTERIM ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Propofol allows the best sedation in colonoscopy. There is only one Randomized Controlled Trial (RCT) comparing Non-Anaesthesiologist Administered Propofol (NAAP) with sedation by an anaesthesiologist.

AIMS & METHODS: Our goal was to compare the incidence of sedation-related adverse events (AE), colonoscopy quality, and patient satisfaction between NAAP and anaesthesiologist sedation. We performed a single blinded RCT with two parallel intervention groups (group A – NAAP; group B – anaesthesiologist sedation). In group A, a 40-60 mg propofol bolus was administered followed by 10-20 mg bolus as needed. In group B propofol was administered under the anesthesiologist indication. The primary endpoint was the incidence of AE as defined by the World SIVA International Task Force on Sedation. Secondary endpoints were propofol dose, patient satisfaction, and pain assessed by a 10-point visual analogue scale, procedure and recovery time, and colonoscopy quality indicators (cecal intubation rate, withdrawal time, adenoma detection rate). A sample size of 330 (1:1) cases was calculated for a power of 90% at a 5% level of significance, and based on the AE incidence in our preliminary experience. Patients aged 18-80 with low anaesthetic risk (ASA I-II) were included (patienťs characteristics presented in table 1). Herein we present the interim analysis of the first 100 cases. Statistical analysis was performed with SPSS version 21. Chi-square, Fischer's exact, t-tests and logistic regression were used as appropriated.

RESULTS: The incidence of AE was 34.3% on group A and 42.4% on group B (odds ratio 0.709; 95% CI 0.302-1.668; p = 0.43). There were no severe (sentinel) AE events. The following interventions were necessary: atropine administration (0% vs 6.1%); airway repositioning (14.9% vs 9.1%); increase in O2 administration (8.9% vs 6.1%); increase in fluids rate (4.5% vs 0%). Mean propofol dose: group A 222 ± 84 mg vs group B 245 ± 118mg (p = 0.276). Procedure times were 22.24 ± 13.12 and 21.39 ± 10.78 min (p = 0.75), withdrawal time was 11.97 ± 10.36 vs 11.84 ± 6.15 min (p = 0.949) and recovery time was 62 ± 44 vs 61 ± 22 min (p = 0.856) in group A and group B respectively. Patients had no pain (0) in 84.5% vs 88.5% (p = 0.946) and reported complete satisfaction with the sedation in 84.8% vs 81.2% (p = 0.58). Procedural amnesia was reported in 88 vs 93.8% (p = 0.49). All the patients were willing to repeat the colonoscopy under propofol sedation. Cecal intubation rates were 95.5% vs 93.9% (p = 1.0), adenoma detection rates were 30.4% vs 31.3% (p = 0.93).

Patient characteristics	Group A(n = 67)	Group B(n = 33)	p
Male sex, n (%)	24(35.8)	14(42.5)	n.s.
Mean age, years (sd)	57(14)	51(18)	n.s.
ASA I/II, n	6/61	7/26	n.s.
Cardiovascular disease, n (%)	10(14.9)	5(15.2)	n.s.
Smoking, n (%)	15(22.4)	5(15.2)	n.s.
Snoring history, n (%)	4(8.0)	2(6.0)	n.s.

CONCLUSION: In the interim analysis NAAP was equivalent to anaesthesiologist sedation in the rate of adverse events in a low risk population. Clinicaltrials.gov (NCT02067065).

Disclosure of Interest: None declared

P0154 MACROSCOPIC COLONOSCOPY FINDINGS OF COLLAGENOUS COLITIS; A THREE-CENTRE EXPERIENCE

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INTRODUCTION: Microscopic colitis (MC) encompasses 2 entities, collagenous colitis (CC) and lymphocytic colitis (LC).[1] Although (by definition) a histopathological diagnosis, there are occasions when colonoscopy reveals findings such as alteration of the vascular mucosal pattern/innominate grooves, mucosal nodularity and a sequence of mucosal changes from defects/lacerations to cicatricial lesions that are thought to be characteristic of MC, and especially CC.[1,2] The aim of this study was to evaluate the frequency and type of endoscopic findings in patients diagnosed with CC in two University Hospitals.

AIMS & METHODS: Retrospective study. The database of the Pathology Department of 2 university hospitals in Edinburgh (Scotland) and Malmo (Sweden), and a district general hospital in Spain (general Hospital de Tomelloso) were searched for patients who have been diagnosed with CC between May 2008 and August 2013. Endoscopy reports & endoscopic images were retrieved and reviewed; data on lesions, sedation, bowel preparation (type and effect) and endoscopists' experience were abstracted. Categorical data are reported as mean ±SD. The Fischer's exact, the *chi-square* and the *t* (unpaired) tests were used to compare datasets. A two-tailed *P* value of <0.05 was considered statistically significant.

RESULTS: A total of 416 patients' (96M/320F; mean age: 67.1±12.1 years) case notes, who were diagnosed with CC, were collected and reviewed.

The colonoscopies had been carried out by senior medical/surgical staff (consultants or associate specialists) in 331 (79.6%). A total of 81 (19.5%) patients had a mix of findings, previously described as being suggestive of CC in endoscopy, such as mucosal erythema/oedema (mosaic pattern): **65**, colonic mucosa linear defects (lacerations, tears, ulcers/fractures, mucosal furrows): **10**, cat-scratch mucosa: **4,** and cicatricial lesions: **3**.

Although the use of polyethylene glycol (PEG) offer superior quality of bowel prep effect (as compared to other pre-colonoscopy preparations; $P<0.0001$), this was not associated with higher detection rate of (all types) macroscopic findings and/or colonic mucosal defects in specific ($P=1.0$). Furthermore, mucosal colonic defects had no association with either the experience of the colonoscopist ($P=0.812$), or the use of general anaesthesia/propofol ($P=0.53$), and/or the use spasmolytic (hyoscine butylbromide/glucagon), $P=0.568$.

CONCLUSION: A substantial minority of patients with CC (19.5%) had endoscopic findings indicative of CC. The presence of these findings is not associated with procedural factors such as endoscopist's experience, quality of bowel prep, and/or use of spasmolytic during colonoscopy.

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P0155 A TAILORED SEDATION FOR COLONOSCOPY BY NON-ANESTHESIOLOGISTS: USE OF PROPOFOL TARGET CONTROLLED INFUSION FOR SAFELY ERASE PATIENTS' PAIN

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INTRODUCTION: Pharmacokinetics and pharmacodinamic of both Midazolam(M) and Pethidine(P) (the most common drugs for procedural sedation) don't allow during colonoscopy to rapidly adjust dosage according to patient response and to the complexity and length of the procedure. As result patients may be too much or not enough sedated. Propofol sedation overcomes these limitations but may expose the patient to dangerous side effetcs such as hypotension and respiratory depression.

AIMS & METHODS: Demonstrate that Propofol Target Controlled Infusion (PTCI) enables properly modified infusion rate (ie total drug dose) in order to perform a zero pain colonoscopy and without affecting safety. 3 types of sedation were utilized in this trial: PTCI, M+P, Propofol titration (PT). Propofol infusion was controlled by a TCI pump set on Schnider protocol. Propofol administration and monitoring was performed by a nurse trained on recognizing adverse effects and on basic resuscitation maneuvers; an anesthesiologist was always on call. Colonoscopy started 1 min after infusion was begun. Initial Effect Site Target Concentration was 2.5 μg/ml, increments of 0.5 μg/ml/min were allowed until total pain relief. We monitored pts' $ETCO_2$, SpO_2, NIBP, ECG. At the end of the procedure pts were transferred to recovery room only when Observer's Assessment of Altertness/Sedation (OAA/S) scale was > 3 and then discharged when ALDRETE score was > 8. Satisfaction was established by Numeric Visual

Scale (NVS, pain evaluation from 1 to 10). A control group (treated with M+P) followed the same protocol.
RESULTS: 721 consecutive pts undergoing both diagnostic and operative colonoscopy were included. No exclusion critheria were stipulated. 345 pts PTCI at an average drug dosage (ADD) of 156.8±69.6 mg; 376 pts M+P at an ADD, respectively, of 4.18±1.3 mg and 47.5±5.5 mg; The 2 groups were clinically homogeneus (M = 55.4%; F = 44.6%; ASA 1-2 = 90%, ASA 3 = 10%) *Adverse events:* Hypoxemia (So2 < 90%): PTCI = 0.M+p = 8 (p < 0.05); Apnea: PTCI = 3, M+p = 26 (p < 0.001); Hypotension (SBP < 90mmHg): PTCI = 44, M+p = 36 (p = ns); Bradycardia (<40 bpm) PTCI = 5, M+p = 11 (p = ns). Apnea was treated successfully with neck extension. *Outcome and satisfaction:* mean NVS (all procedures) PTCI 0.36±1.2 vs 1.07±2.1 M+P (p < 0.001); mean NVS (only difficult proceures) PTCI 0.24±1 vs 1.97±2.8 M+P (p < 0.001); mean cecal intubation time (intubation rate was 98.4%) PTCI 6.14±3.6 min vs M+P 7.52±4.8 min (p < 0.01), mean time for the entire procedure (colonoscopy + recovery time): PTCI 38.76±15.1 min vs M+P 53.95±14.6 min (p < 0.001). PTCI total mean dosage was compared with the mean dosage of 50 colonoscopies in propofol titration, at the univariate analysis less total propofol (adjusted for BMI, Sex, Age, Endoscopist, Abdominal surgery) was administered using PTCI than the titration method: 156.85±69.63 vs 212.50±85.70 (p < 0.0001).
CONCLUSION: Propofol TCI provide a extremely flexible technique which ensures a sedation tailored to the individual patient and gives the possibility to guarantee an effective sedation for long lasting procedures without affecting recovery time. The final results are the opportunity to totally relieve pain, high performance (time length and quality of recovery) and less operator-dependent process.
Disclosure of Interest: None declared

P0156 HOW WELL DOES RADIOLOGY PREDICT COLITIS? CORRELATING IMAGING WITH ENDOSCOPY; A RETROSPECTIVE STUDY

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INTRODUCTION: A common indication for endoscopic assessment of the large intestine is to clarify an abnormal finding on either cross sectional or contrast radiological imaging. Our aim was to assess how often a positive diagnosis of colitis of any form was made following either CT scanning or barium enema. We then aimed to correlate these radiological findings with those seen at a subsequent endoscopy.
AIMS & METHODS: The endoscopy database at Gloucestershire Hospitals NHS Foundation Trust was reviewed for procedures performed between January 2008 and June 2013. Cases where endoscopy was performed for the indication of ''abnormal radiological findings'' were selected. The patients' radiology reports were reviewed and the cases where ''colitis'' or ''inflammation'' was described as possible differentials were selected. We then compared these radiological findings with those seen on endoscopy for positive correlation. The endoscopic finding of diverticular disease was taken as a positive correlation where relevant. Histology reports from the biopsies taken during the endoscopic procedures were also reviewed to confirm the endoscopic findings.
RESULTS: Between January 2008 and June 2013, 562 colonoscopies or flexible sigmoidoscopies were performed as a result of an abnormality seen on radiological imaging. In 168 (30%) a positive diagnosis of colitis was mentioned on the radiology report. Demographics showed a fairly even sex distribution with 53% of patients female, 47% male. The ages ranged from 22-98 with a mean age of 60.9 years. A total of 5 cases were excluded, with the colonoscopy failing to reach the region of interest in 4 cases.
Endoscopy confirmed mucosal inflammation in 60 of the 163 cases (37%) whereas the endoscopy was reported as normal in the remaining 103 cases (63%). In patients with positive endoscopic correlation, biopsies were taken in 34 (57%) of cases. Biopsies were not taken in cases where diverticular disease was identified and considered a positive diagnosis.
In those with histological specimens 28 of the 34 (82%) showed histology consistent with an inflammatory process. Of these the majority (57%) showed Crohn's disease. 6 specimens showed no inflammatory change on histology despite a macroscopic impression of inflammation.
Interestingly 2 biopsy series were taken despite negative endoscopic correlation, of which 1 was confirmed as lymphocytic colitis on histology. Another showed features of Crohn's on histology (this patient had known Crohn's).
CONCLUSION: 37% of the cases in our series referred for endoscopic evaluation after the finding of ''colitis'' on radiological imaging were confirmed to have colonic inflammation at endoscopy. This suggests that there is a limited correlation between radiological and endoscopic imaging when a diagnosis of colitis is being considered.
Further studies are required to determine whether a number of parameters considered together to create a scoring system would increase the likelihood of a positive pick up at endoscopy following colitis identified on radiological imaging, thereby improving diagnostic yield and reducing the number of unnecessary procedures. Interestingly, with one diagnosis of lymphocytic colitis made on samples from endoscopically normal colon, an argument could be made for taking biopsy series in all cases to exclude microscopic colitis.
Disclosure of Interest: None declared

P0157 SHORT MESSAGE SERVICE (SMS) IN COLONOSCOPY PREPARATION - PERICLES-I -A FEASIBILITY STUDY

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INTRODUCTION: High quality preparation is essential for colonoscopy. A sufficient colon cleaning improves adenoma detection rate and reduces rates of necessary re-colonoscopies due to invalid preparation. Several studies showed importance of patients education and correct pre-colonoscopy diet. Only few studies have evaluated feasibility of using new media such as SMS in high quality preparation. The ***PERICLES***-project (*prospective studies for improvement of colonscopy preparation by optimized visualisation*) aims to optimize patient guidance by reminding the most important steps during colonoscopy preparation.
AIMS & METHODS: Objective: To assess the feasibility of colonoscopy preparation using SMS (short message service) starting 4 days prior colonoscopy appointment and to assess sufficient colonoscopy preparation.
Design: A feasibility study Setting: Tertiary care center, university hospital.
Subjects: Patients scheduled for out-patient colonoscopy at a university hospital.
Interventions: Patients enrolled in the SMS study group get SMS information at different timepoints according to the next step of colonoscopy preparation and diet information. Data of out-patient colonoscopies with regular preparation procedure were collected as control group during time of SMS study.
RESULTS: Colonoscopy could be performed in all patients included in the study. Overall patient satification receiving SMS based information was high. Asked if the SMS reminder system was helpful to get the colonoscopy preparation done (1 not helpful to 10 very helpful) an average score of 7.8 was counted (n = 18). On the contrary asked if the SMS reminder system was inhibitory (1 not inhibitory to 10 very inhibitory) an average of 1.1 was counted (n = 19). The average total BBPS was significantly higher than in the control group (Mean±SEM 7.316 ± 0.2967 (SMS-group), Mean±SEM 6.269 ± 0.1925 (control group); good bowel preparation for colonoscopy ≥5). BBPS calculated for the different colon regions. LC = Left colon (Mean±SEM 2.500±0.1357 (SMS group) Mean±SEM 2.138±0.06530 (control group)), TC = transverse colon (Mean±SEM 2.400±0.1124 (SMS group) Mean±SEM 2.115±0.06875 (control group)), RC = right colon (Mean±SEM 2.400±0.1124 (SMS group) Mean±SEM 2.015±0.07325 (control group)) were higher than in the control group.
CONCLUSION: A SMS (short message service) system in colonoscopy preparation works is stable and effective. Quality of colonoscopy preparation was higher than in regular preparation procedure. Patients were highly satisfied by using the SMS system during colonoscopy preparation.
Disclosure of Interest: None declared

P0158 WHY DON'T WE RETRIEVE ALL THE ENDOSCOPIC RESECTED POLYPS?

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INTRODUCTION: Colonoscopy is able to diagnose, resect and retrieve colonic polyps. The latter is of major importance to allow an accurate histological evaluation. Factors associated with failed polyp retrieval are not yet clear.
AIMS & METHODS: To evaluate the prevalence of failed polyp retrieval; to define factors associated with polyp retrieval failure.
A single center retrospective study that considered all the resected polyps by snare in consecutive colonoscopies performed between September 2011 and December 2012. Eleven gastroenterology specialists and 3 residents were considered as endoscopists. Demographic and endoscopic data obtained through the colonoscopy report.
Statistical analysis (SPSS v.19): Chi-square, t-student.
RESULTS: 496 colonoscopies were evaluated, corresponding to 484 patients (male gender 66.1%, mean age 63.4 years [±10.2]). Considering a total of 1111 resected polyps, 52 (4.7%) were not retrieved. A deficient bowel preparation (p = 0.0006), a coloretal surgery history (p = 0.008), a higher number of resected polyps (p < 0.0001), a smaller size of resected polyps (p < 0.0001), a right-side location (p = 0.0006) and a cold snare resection versus current snare resection (p = 0.0007) were factors associated with failed polyp retrieval. Colonoscopy performed by a resident (p = 0.81), under deep sedation (p = 0.94) or with diverticulum (p = 0.44) were not related with failed polyp retrieval.
CONCLUSION: In our study the polyp retrieval failure prevalence was 4.9%. A 1) deficient bowel preparation, 2) a colorectal surgery history, 3) a greater number of resected polyps, 4) a smaller size of the resected polyps, 5) a righ-side location and 6) a cold snare resection were associated with polyp retrieval failure.
Disclosure of Interest: None declared

P0159 FUSE COLONOSCOPY YIELDS HIGHER DETECTION OF ADVANCED AND MULTIPLE ADENOMAS AS COMPARED TO STANDARD FORWARD VIEWING COLONOSCOPY: A POST-HOC PER PATIENT ANALYSIS FROM A RANDOMIZED COMPARATIVE TRIAL

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INTRODUCTION: As compared with Standard Forward Viewing (SFV) colonoscopy, Full Spectrum Endoscopy (Fuse) colonoscopy has been shown to significantly increase the yield of adenomas detected (per lesion analysis) [1].

However, the accuracy of FUSE based upon a per-patient analysis has not fully been addressed.
AIMS & METHODS: We performed a post-hoc analysis of the data from a recently completed international, multicentre, randomized trial (NCT01549535) in which 197 patients underwent same-day, back-to-back tandem colonoscopy with SFV- and FUSE-colonoscopes. The per-patient detection rate of polyp/advanced adenoma was calculated for each of the two colonoscopy techniques according to polyp size and multiplicity (≥3 polyps). The relative detection rate was defined as the ratio between the number of patients classified by either SFV or FUSE colonoscopy in each lesion category and the cumulative detection with both of the colonoscopy techniques (SFVor FUSE) for the same lesion category. Statistical analysis was performed by Chi-square test.
RESULTS: We found 111, 23 and 9 patients presenting with at least one ≤5mm, 6-9mm, or ≥10mm polyp respectively, while 22 and 27 additional patients had as their most severe lesion an advanced adenoma or multiple adenomas, respectively. The relative sensitivity of SFV and FUSE for each type of lesion is shown in Table 1. In detail, the sensitivity of FUSE was statistically significantly superior to SFV for all categories except for polyps ≥10mm. As compared to SFV colonoscopy, FUSE detected an additional 9 patients with multiple adenomas, resulting in a relative per-patient sensitivity of 94%, as compared with 27% for SFV colonoscopy.
CONCLUSION: As compared to SFV colonoscopy, FUSE colonoscopy appears to be more effective in identifying patients with multiple polyps and polyps up to 9 mm in size, including 6-9mm advanced adenomas. These data appear to further demonstrate the clinical relevance of the additional adenoma detection of FUSE as previously shown at a ''per lesion'' level [1].
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Disclosure of Interest: None declared

P0160 DISCRETE DYSPLASTIC LESIONS IN ULCERATIVE COLITIS MAY BE ADEQUATELY MANAGED ENDOSCOPICALLY: A LONG TERM FOLLOW-UP STUDY

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INTRODUCTION: While there is evidence to support endoscopic resection of adenoma-like mass (ALM) occurring in patients with ulcerative colitis (UC), its long-term follow up data is currently limited. The aim of this study is to evaluate the long-term outcomes of patients with UC who have had an endoscopic resection of dysplasia within segment of bowel affected by colitis.
AIMS & METHODS: All patients who had their dysplastic lesions resected endoscopically between 1998 and 2008 were retrospectively identified from the endoscopic and histology databases. Patients who were immediately referred to colectomy were excluded. Medical records, endoscopy and histology reports were reviewed to determine the primary study outcome, which was defined as no further dysplasia episode, recurrence of dysplasia, or development of colorectal cancer (CRC).
RESULTS: A total of 100 patients underwent endoscopic resection for 121 discrete dysplastic lesions during the study period (table 1). The median follow-up duration from the time of dysplasia resection was 70 months (interquartile range (IQR), 53 – 89 months). The Paris classifications of the resected lesions were: Ip (60 lesions, 50.4% of 121 lesions), Is (36, 29.8%), IIa (3, 2.5%), IIb (4, 3.3%), IIa/c (1, 0.8%), and lateral spreading tumour (1, 0.8%). Remaining 16 lesions (13.2%) were described as ''appearance suspicious for dysplasia associated lesion or mass (DALM)'', where Paris classification was not recorded. Median size of the resected lesions was eight millimetres (IQR, 4 – 15 millimetres). Lesions were removed using snare polypectomy (66 lesions, 54.5% of 121 lesions), EMR (30, 24.8%), hot biopsy (21, 17.4%) or ESD (4, 3.3%) techniques. Histology showed low-grade dysplasia (LGD) in 111 (91.7% of 121 lesions) and high-grade dysplasia (HGD) in 10 lesions (8.3%). Pathologist's interpretations on the lesions were as follows: histological features favour DALM (36 of 121 lesions, 29.8%) favour sporadic adenoma (56, 46.3%), or ''distinction not possible on histological grounds alone (29, 23.9%)''. Overall, 23 patients (23% of study population) had developed recurrent episode of dysplasia in median of 41 months since the time of resection (IQR, 16 – 55 months). Seven of these patients underwent colectomy: cancer was detected in two patients (Duke's A and C), but no other patients had HGD or CRC in surgical specimen. The patient who developed Duke's C cancer did not have surveillance colonoscopy for five years prior to the cancer diagnosis. The cumulative incidence of recurrent episode of dysplasia following endoscopic resection was 3.1% in 1 year, 7.4% in 2 years, 11.9% in 3 years, 16.7% in 4 years and 22.0% in 5 years.

Table to abstract P0160

Patient demographics	
Sex (%)	
Male	66 (66%)
Female	34 (34%)
Disease extent (%)	
Extensive	87 (87%)
Left-sided	13 (13%)
Disease duration (years) (Median, interquartile range)	24 (13 – 33)
Age at the time of dysplasia diagnosis (years) (Median, interquartile range)	61 (54 – 69)

CONCLUSION: Patients with endoscopically resectable, well-circumscribed dysplastic lesions within the segment of colitis may be appropriately managed with endoscopic resection. However, close surveillance is necessary given the relatively high rate of recurrence.
Disclosure of Interest: None declared

P0161 LOW-GRADE DYSPLASIA IN ULCERATIVE COLITIS: IMPACT OF LESION SHAPE AND SIZE ON PROGRESSION TO HIGH-GRADE DYSPLASIA OR COLORECTAL CANCER

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INTRODUCTION: One of the most challenging aspects of managing low-grade dysplasia (LGD) in ulcerative colitis (UC) is the identification of patients who will progress to high-grade dysplasia (CRC) or colorectal cancer (CRC). The aim of this study was to identify risk factors associated with progression to HGD or CRC in UC patients diagnosed with LGD.
AIMS & METHODS: Patients with UC who were diagnosed with LGD between 1990 and 2012 were identified from the UC surveillance database of a large tertiary centre in the UK and followed up to 1st January 2013. Data on patient demographics, endoscopic and histological variables at the time of the first LGD episode were collected and correlated with progression to HGD or CRC, our primary outcome measure. Time to event analysis was performed using Cox proportional hazards methods with a Bonferroni adjusted significance level ($p = 0.0022$).
RESULTS: A total of 189 patients were evaluated during 1,100 patient-years of follow up from the date of the first LGD diagnosis (median, 53 months; interquartile range, 19 – 92 months). Overall, 38 (20.1% of study population) had progressed to HGD (16 patients) or CRC (22 patients). Table 1 shows the variables significantly associated with progression to HGD or CRC on univariate analysis. A statistically non-significant trend towards the progression to HGD or CRC was observed in those patients with history of primary sclerosing cholangitis (hazard ratio (HR), 3.54; $p = 0.018$), a shortened colon (HR, 2.75; $p = 0.024$), multiple episodes of dysplasia (HR, 2.59; $p = 0.005$), and histological active inflammation in the segment of LGD (HR, 2.20; $p = 0.025$). At the multivariate level, only non-polypoid shape (HR, 7.3; 95% confidence interval (CI), 2.4 – 21.8; $p < 0.001$), lesion size one centimeter (cm) or bigger (HR, 4.2; 95% CI, 1.3 – 13.3; $p = 0.015$) remained significant variables contributing to HGD or CRC.

Variables	Categories	Hazards ratio (HR)	95% confidence interval (CI)	P
Lesion shape	Polypoid §	1	10.0 – 58.1	<0.001
	Non-polypoid¶	24.1	1.5 – 22.6	
	Invisible‡	5.8		
Lesion size	<1cm	1	4.8 – 41.3	<0.001
	≥1cm	14.1		
Stricture	No	1	2.4 – 21.1	<0.001
	Yes	7.1		
Previous indefinite dysplasia	No	1	1.9 – 8.4	<0.001
	Yes	4.0		
Pathologist's interpretation on histological features	Adenoma more likely	1	1.4 – 109.4	<0.001
	Distinction not clear	12.2	5.1 – 273.6	
	UC associated dysplasia more likely	37.2		
Multifocal dysplasia	No	1	1.6 – 6.0	.001
	Yes	3.1		

Table 1: Results of Univariate Analysis (only significant variables are shown). §: Discrete pedunculated or sessile polyps (Paris classification type I). ¶: Flat, depressed (Paris type II), irregular, diffuse, plaque-like or lesions with poorly defined edges. ‡: LGD with no evidence of endoscopic abnormality.
CONCLUSION: Low-grade dysplastic lesions that are non-polypoid or large (≥1cm) have a high-risk of progression to HGD or CRC in patients with UC. Patients harboring these lesions require careful counseling of management options including colectomy. Conversely, small polypoid low-grade dysplastic

lesions may be appropriately managed with endoscopic resection and close surveillance.
Disclosure of Interest: None declared

P0162 A PILOT STUDY OF FLUORESCENT IMAGING OF COLORECTAL TUMOR USING Γ-GLUTAMYL-TRANSPEPTIDASE (GGT) FLUORESCENCE ACTIVITY PROBE

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INTRODUCTION: New endoscopic technologies improve visibility of early colorectal cancers. However, flat lesions especially in lateral spreading tumor of the non-granular type (LST-NG) are sometimes hard to detect even with such modalities. γ-glutamyl-transpeptidase (GGT) is poorly expressed in normal tissue, but overexpressed on the cell membrane of various cancer cells in vivo. The use of γ-glutamyl hydroxymethyl rhodamine green (gGlu-HMRG) has been reported to show specific and immediate fluorescence activity with overexpressed GGT in tumor. This fluorescence active probe is expected to be applied to a new modality for cancer-selective fluorescence imaging[1].
AIMS & METHODS: This pilot study aimed to evaluate ex-vivo fluorescent imaging of colorectal tumor using the GGT fluorescence activity probe. 30 endoscopically resected colorectal tumors from March 2013 to March 2014 were included in this study. 1000μl of gGlu-HMRG in a concentration of either 50μM or 500μM was sprayed on the freshly resected specimen fixed on a black board. Fluorescent images of the resected specimen were taken after spraying gGlu-HMRG every 30 seconds for 15 minutes using a dedicated imaging machine providing 550nm of blue excitation light (Discovery; INDEC Inc.). The fluorescence image 7 minutes after spraying (when fluorescence activity had almost reached equilibrium) was evaluated by 3 endoscopists. The fluorescence activity was judged positive or negative. Lesions showing partial fluorescence activity were considered positive. This pilot study assessed the proportion of lesions positive for fluorescence and correlation with their clinicopathological characteristics.
RESULTS: The clinicopathological features were; mean age was 68±7, male/female = 15 /15, mean tumor size: 39±13mm, macroscopic type: lateral spreading tumor of the granular type (LST-G)/LST-NG = 20/10, adenoma/ carcinoma in adenoma = 13/17. 20 (67%) of images after 7 minutes were positive for fluorescence activity and 10 (33%) were negative. The mean tumor size of lesions positive for fluorescence activity was 42mm and that of negative was 32mm. Of 13 adenoma, 7 (54%) lesions were positive and 6 (46%) were negative. Of 17 carcinoma in adenoma, 13 (76%) lesions showed positive and 4 (24%) were negative. 16 LST-G lesions (80%) and 4 LST-NG lesions (40%) revealed positive. 18 (75%) of 24 lesions in 50μM gGlu-HMRG and 2 (33%) of 6 lesions in 500μM revealed positive.
CONCLUSION: Topically spraying gGlu-HMRG to identify GGT activity in ex vivo colorectal tumors provides rapid and selective fluorescent imaging.
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Disclosure of Interest: None declared

P0163 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GIANT COLORECTAL LATERAL SPREADING TUMORS LARGER THAN 10 CM: IS IT FEASIBLE?

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INTRODUCTION: Colorectal endoscopic submucosal dissection (ESD) has recently been used for the resection of large colorectal neoplasms that could not be completely resected by conventional endoscopic mucosal resection (EMR). The colorectal ESD technique has an advantage of high en bloc resection rates, but is not accepted as a standard procedure due to several limitations, such as relatively high perforation rate and very high technical difficulty. However, ESD was applied to the lesions such as the giant colorectal lateral spreading tumor (LST) larger than 10 cm by some expert ESD-endoscopist. Thus, we investigated the feasibility and safety of ESD of giant colorectal LST over 10 cm.
AIMS & METHODS: A total of 133 patients received colorectal ESD between March 2009 and August 2013 by a single expert ESD-endoscopist at Gangnam Severance Hospital, Seoul, Korea. Among them, 7 patients had giant colorectal LSTs larger than 10cm. The tumor features, complete resection rate, and complications of ESD of giant colorectal LST were evaluated. We compared the clinicopathologic factors of ESD between giant colorectal LSTs and others. All patients underwent regular follow-up to evaluate for any local recurrence or distant metastasis.
RESULTS: The colorectal LSTs larger than 10cm were categorized as the giant colorectal LST. The locations of the 7 giant colorectal LST lesions as follows: cecum (n = 1), sigmoid colon (n = 2), and rectum (n = 4). The average maximal diameter of the giant colorectal LST lesions was 124.3 mm (range: 110-160 mm), and the procedure time was 294.3 min (range: 146-570 min). 2 lesions were whole nodular types and 5 lesions were focal nodular lesions by the Japanese Classification of Colorectal Carcinoma. According to the World Health Organization classification system, histologic diagnosis determined that 1 lesion was low grade dysplasia, 2 lesions were high grade dysplasia, and 4 lesions were carcinoma. Profound bleeding occurred in 1 patient with whole nodular type LST, who changed to piecemeal resection and was needed transfusion during ESD. Perforations developed in 2 patients after ESD, which were managed by endoscopic clipping treatment. The duration of hospitalization in the giant colorectal LST was 5.6 day (range: 2-12 day). During a mean follow-up period of 18.5 mo (range: 5.9-27.4 mo), no local recurrence and distant metastasis occurred. The complication rate was higher in giant colorectal LST than others (42.9% vs 8.7%, $p = 0.026$). The en-bloc resection and curative resection rate of ESD for the giant colorectal LST was 85.7% and 100%, respectively, and these rates were comparable with that of ESD for LST smaller than 10 cm. (en-bloc resection rate 92.1%, and curative resection rate 92.9%)
CONCLUSION: The ESD of giant colorectal LSTs appears to be a feasible and curative treatment, even if, it endure the higher complication rate, higher technical difficulty and longer procedure time.
Disclosure of Interest: None declared

P0164 ANALYSIS OF THE BLEEDING AFTER THE ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) AND THE ENDOSCOPIC MUCOSAL RESECTION (EMR) OF COLORECTAL NEOPLASMS FOR THE PATIENTS TAKING ANTI-THROMBOTIC AGENTS

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INTRODUCTION: Recently, EMR and ESD for the patients with many complication has been increasing. Anti-thrombotic therapy is usually provided to prevent cerebro-cardiovascular events. In 2012, the endoscopic treatment guidelines for the patients taking anti-thrombotic agents were published from Japan Gastroenterological Endoscopy Society. Thereafter, in our institution, we perform endoscopic treatment in accordance with the guidelines. Delayed bleeding is one of the major complications of EMR and ESD, but little is known about the influence of anti-thrombotic therapy.
AIMS & METHODS: In this study, we analyzed the delayed bleeding rate after colorectal EMR and ESD for the patients taking anti-thrombotic agents. This is a retrospective study for the consecutive patients treated in our center from February 2014 to January 2013. Furthermore, we divided the patients taking anti-thrombotic agents into three groups, and compared the bleeding rate and the clinical background with control group. [A]: anti-coagulant continuation group, [B]: heparin or anti-coagulant single agent replacement group, [C]:anti-coagulant discontinuation group. Statistical analysis was made by Chi-squared test (significance: $p < 0.01$).
RESULTS: We treated 328 patients with 633 colorectal neoplasms by EMR, and the delayed bleeding rate was 1.9% (12/633). Male/Female ratio was 237:91 and the mean age was 64.5 years. 63 patients (19.2%) with 129 neoplasms (20.4%) received anti-thrombotic therapy and divided into three groups, [A]:16/28, [B]:21/45, [C]:26/56 (patients/neoplasms). Patients taking the anti-coagulant agents were significantly older than control group ($P < 0.01$). The delayed bleeding rate was 1/28(3.6%) in group A, 2/45(4.4%) in group B and none (0/56) in group C. We found no significant differences about the delayed bleeding rate when we compared each group with the control group (9/504; 1.9%). On the other hand, we treated 47 patients with 47 neoplasms by ESD. Male/Female ratio was 32:15 and the average age was 68.7 years. 11 patients (23.4%) received anti-thrombotic agent and divided into three groups, [A]:4, [B]:2, [C]:5. In ESD, patients taking anti-thrombotic agents were significant older ($P < 0.01$), and the delayed bleeding was not recognized in all cases. In addition, cerebro-cardiovascular events did not occur in all cases during the clinical course of EMR and ESD.
CONCLUSION: We found no significant differences about the delayed bleeding rate between patients taking anti-thrombotic agents and control group. Although this is a single institutional study, we thought that EMR and ESD for the patients taking anti-thrombotic agents could be performed without increased risk of delayed bleeding in accordance with the guidelines.
Disclosure of Interest: None declared

P0165 SESSILE SERRATED ADENOMA (SSA): QUALITATIVE ENDOSCOPIC IDENTIFICATION USING ACETIC ACID, FICE AND IMAGE MAGNIFICATION

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INTRODUCTION: Sessile Serrated Adenoma may be the precursor of 30% of colorectal cancers. The colonoscopy finding and identification of this type of lesion can reduce the incidence of colorectal cancer.
The correct approach on the search of this specific type of lesion is known to be a true challenge for the colonoscopists nowadays, and the precise identification, in number and type, of these lesions is associated to the quality of the colonoscopy exam.
Not much can be found in the literature about the combined use of acetic acid, FICE and image magnification in the identification of this specific type of lesion.
AIMS & METHODS: 150 lesions in the right colon were prospectively evaluated: the lesions were larger than 10mm, had a mucus cap and their morphology suggested sessile serrated adenoma, by the analysis of these lesions, crypts pattern. The study was performed by an endoscopist with extensive experience in chromoendoscopy and magnification and a single pathologist with extensive experience in this type of lesion. The lesions were classified into three types of Pits: type II Classic (Pit II - C), Pit II Open Shape (Pit II - O), and Pit II Fat

Shape (Pit II - F). The crypts were evaluated after instillation of acetic acid, chromoscopy (FICE), and image magnification.
RESULTS: From all the 150 lesions, 122 were classified as SSA. The Pit pattern II –C was found in all of the lesions analyzed, revealing a low specificity in the association of this pattern with SSA. However, the Pit II – O pattern was found in 120 lesions, and 118 of these were classified as SSA form, showing a stronger association of this pattern and SSA than the Pit II- C pattern. When it comes to the Pit II –F, it was found in 122 lesions, and 120 of these were classified as SSA. All lesions containing the association of Pit II- O and Pit II –F pattern, were classified as SSA.
CONCLUSION: The strong correlation between the colonoscopic findings of SSA with the use of acetic acid, FICE and image magnification and histological/molecular alterations of the suspicious lesions, reveals the importance of this technique in this type of lesions' management decision and in the participation on the colorectal cancer prevention.
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Disclosure of Interest: None declared

P0166 THE USEFULNESS OF INTRAVENOUS CIMETROPIUM BROMIDE ON POLYP/ADENOMA DETECTION DURING COLONOSCOPY WITHDRAWAL

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INTRODUCTION: Colorectal cancer can be prevented effectively by colonoscopy, because it can detect polyps and adenoma. It can miss from 5 to 32% of polyps, and proximal colon cancers are not efficiently prevented by colonoscopy screening. Cimetropium bromide has antispasmodic activity and improves polyp detection, especially in the right side colon.
AIMS & METHODS: We studied the effect of cimetropium bromide on detection of adenoma in colonoscopy.
Patients undergoing colonoscopy for screening and diagnostic examinations were included and received 5 mg cimetropium bromide at cecal intubation in Pusan National University Yangsan Hospital during 2 months in 2013 and 2014, respectively. We studied retrospectively polyp detection rate (PDR), adenoma detection rate (ADR), advanced adenoma detection rate (AADR), and sessile serrated adenoma detection rate (SADR) in right side colon as well as in whole colorectum.
RESULTS: A total of 1025 patients were analyzed in this study. Cimetropium group consisted of 214 patients and control group consisted of 811 patients. ADR, AADR in whole colorectum were significantly higher in cimetropium group, respectively (38.2% vs 28.4% ($p=0.03$), 10.5% vs 5.3% ($p=0.026$)). Also, PDR, ADR, and AADR in right side colon were significantly higher in cimetropium group, respectively (25.6% vs 19.4% ($p=0.015$), 23.4% vs 15.6% ($p=0.023$), 7.2% vs 3.5% ($p=0.024$)). But, PDR in whole colorectum and SADR in right side colon between two groups were not different. In non-right side colon, PDR and ADR were not significantly higher in cimetropium group, respectively (31.6% vs 27.8% ($p=0.487$), 25.0% vs 21.0% ($p=0.154$)).
CONCLUSION: Cimetropium bromide can improve ADR and AADR in right side colon as well as colorectum in colonoscopy.
Disclosure of Interest: None declared

P0167 CORRELATION BETWEEN ENDOSCOPIC AND ENDOMICROSOPIC SCORES IN CROHN'S DISEASE PATIENTS IN DETECTING RELAPSE AFTER SURGERY

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INTRODUCTION: As clinical relapse risk is well correlated with the endoscopic appearance in operated Crohn's disease (CD) patients, it's recommended to perform an endoscopy in the year following the surgery in order to adapt treatment. In endoscopy, the relapse is based on Rutgeerts score superior to i2 defined by the presence of more than 5 ulcerations. Confocal Laser Endomicroscopy (CLE) can detect inflammation on a macroscopic healing mucosa (whereas macroscopically the mucosa appears normal). Inflammation is evaluated by CLE according to percentage of gaps reported to total villous perimeter and to Watson's score based on shedding and luminal signal.
AIMS & METHODS: Aim: To evaluate inflammation with CLE into the ileum above the anastomosis (ileocolic anastomosis) and compare with Rutgeerts score.
Patients and methods: In the year following the surgery, under sedation, an endoscopy with CLE (EC3870K Pentax, Tokyo) was performed after 3 ml fluorosceine injection. Relapse was scored endoscopically with Rutgeerts score and endomicroscopically with percentage of gaps and Watson's score, which were quantified as calprotectine in stools, urinary neopterine and C-reactive protein (CRP). We compared Harvey Bradshaw score, Watson's score, calprotectine, neopterine, CRP and histology (Gomes score) with Rutgeerts score.
RESULTS: 26 patients (12 men, mean age 36 ± 11 years (± SD)) were included prospectively. The endoscopy was performed in 9 ± 3 (range 6 to 13) months after the surgery. 9 patients relapsed with a mean Rutgeerts score 2.7 ± 0.8 after 10 ± 2.5 months and 17 patients did not relapse with a mean Rutgeerts score 0.4 ± 0.5 after 8 ± 3 months. 5, 2 and 2 patients presented a Rutgeerts score i2, i3, i4, and 10 and 7 presented a Rutgeerts score i0 and i1, respectively. The mean percentage of gaps was 11.5 ± 17 (range 0 to 55). Watson score was 1.7 ± 0.9 (range 0 to 3). The mean HB was 1 ± 1.1 (range 0 to 4). Mean Gomes score was 1.1 ± 0.9 (range 0 to 3). Mean CRP, calprotectine and neopterine were 5.4 ± 9.3 (range <2 to 44 mg/l), 811 ± 2207 (range 35 and 9200) and 553 ± 287 (range 142 and 992), respectively. The correlation was significantly positive between Rutgeerts and Watson score and percentage of gaps (Rho 0.65). The correlation was positive but not significantly with CRP, Gomes and calprotectine (Rho 0.47, 0.35 and 0.27, respectively). However, in 5/10 and 2/7 patients with i0 and i1 Rutgeerts score, respectively, CLE detected inflammation (Watson score 2).
CONCLUSION: There is a good correlation between CLE score and Rutgeerts but CLE detected inflammation in 5 patients without endoscopic relapse. The follow-up of these patients would be interesting to evaluate CLE in predicting relapse in CD patients.
Disclosure of Interest: None declared

P0168 ENDOSCOPIC SELF-EXPANDABLE METAL STENTS IN ACUTE MALIGNANT LARGE BOWEL OBSTRUCTION – SINGLE CENTER EXPERIENCE

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INTRODUCTION: Endoscopic self-expanding metal stents (SEMS) may be used in acute malignant large bowel obstruction (AMLBO) emerging as an alternative to surgery.
AIMS & METHODS: Characterize the population of patients with AMLBO that placed endoscopic SEMS in clinical practice. Cross-sectional study of patients with AMLBO that placed SEMS in a tertiary center in a 3 year period.
RESULTS: We placed SEMS in 47 patients, with a mean age of 71±13 years. The distal top of the tumor was located in the descending colon in 12.8%, in the sigmoid colon in 61.7% and in the rectum in 25.5%. Eighty-one percent of patients had lymph node invasion and 68.1% had metastasis. The location of the tumor did not influence the presence of lymph node involvement ($p=0.764$), metastasis ($p=0.885$) nor the extent of the stent used ($p=0.511$). Fluoroscopy was used in 57.4% of the procedures. There was need for placement of a second stent in 6.4% of patients due to migration during the opening. The rate of early complications was 11% and late complications was 4.6%. The use of fluoroscopy did not influence the occurrence of immediate complications ($p=0.385$), early complications ($p=0.950$) or late complications ($p=0.057$). Thirty-three percent of patients underwent surgery at a later time, with neo-adjuvant therapy in 17.8%. The median time of follow-up was 150 days (P25-75: 23 – 437), with a mortality rate at first year of 60.6%. The survival was significantly higher in patients submitted later to combined therapy in relation to chemotherapy, surgery or symptomatic treatment (838.5 days [± 35.0] *vs* 387.6 days [± 87.7] *vs* 354.3 days [± 80.2] days *vs* 222.3 [± 104.6 therapy], $p<0.001$).
CONCLUSION: The majority of patients with AMLBO had advanced disease. SEMS have a high success rate with a low complication rate, reducing the high morbidity and mortality associated with emergency surgery and creation of a stoma.
Disclosure of Interest: None declared

P0169 COLONIC CHICKEN SKIN MUCOSA IS AN INDEPENDENT ENDOSCOPIC PREDICTOR OF DISTALLY LOCATED ADVANCED COLORECTAL ADENOMA

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INTRODUCTION: Chicken skin mucosa (CSM) surrounding colorectal adenoma is described as an endoscopic finding with pale yellow-speckled mucosa and aggregations of lipid-filled macrophages in the lamina propria noted on histopathology. However, its clinical significance is unknown.
AIMS & METHODS: The aim of this study was to evaluate the prevalence, clinical characteristics of CSM, and association between colorectal carcinogenesis and CSM. This cross-sectional study was performed on 733 consecutive patients who underwent endoscopic polypectomy for colorectal adenoma after screening colonoscopy at the Asan Health Promotion Center between June 2009 and December 2011. The colonoscopic and pathological findings of colorectal adenoma including number, size, location, dysplasia, and morphology, and clinical parameters were reviewed.
RESULTS: The prevalence of CSM was 30.7% (225 of 733 patients), and most CSM-related adenomas were located in the distal colon (93.3%). Histological analysis revealed lipid-laden macrophages in the lamina propria of the mucosa. According to multivariate analyses, CSM was significantly associated with advanced pathology, including villous adenoma, high-grade dysplasia, and carcinoma *in situ* (OR 2.078, 95% CI 1.191-3.627, $p=0.010$), multiple adenomas (i.e., ≥ 2 adenomas; OR 1.692, 95% CI 1.143-2.507, $p=0.009$), and a protruding morphology (OR 1.493, 95% CI 1.027-2.170, $p=0.036$). There were no significant differences found in terms of polyp size or clinical parameters between patients with and without CSM.
CONCLUSION: CSM-related adenoma was mainly observed in the distal colon. CSM was associated with advanced pathology and multiple adenomas. CSM may be a potential marker of the carcinogenetic progression of distally located colorectal adenomas.
Disclosure of Interest: None declared

P0170 PREVALENCE OF COLORECTAL POLYPS IN A GROUP OF SUBJECTS WITH AVERAGE-RISK OF COLORECTAL CANCER UNDERGOING COLONOSCOPIC SCREENING IN TEHRAN, IRAN BETWEEN 2008 AND 2013

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INTRODUCTION: Colorectal cancer (CRC) is one of the leading causes of death in different countries. Due to slow progression of GC, detection of CRC in early stage is important issue. There have been no high quality studies from the Middle East.
AIMS & METHODS: We aimed to investigate the prevalence of preneoplastic and neoplastic lesions of the colon in the average risk population.
Eligible asymptomatic, average risk adults between 2008 and 2012, aged older than 40 years old, in Firoozgar general hospital were involved. They underwent screening colonoscopy. All polypoid lesions were removed and examined by an expert gastrointestinal pathologist. The lesions were classified by size, location, numbers and pathologic findings. Size of lesion was also measured by endoscopists.
RESULTS: One thousand and eight subjects were enrolled in this study. The mean age of participants was 56.45 ± 9.59 years and 51.6% subjects were male. Overall polyp detection rate was 199/1208 (16.5%). Of them 26 subjects had non-neoplastic polyps including hyperplastic polyps, and 173/1208 (14.3%) subjects had neoplastic polyps of which, 26 (2.15%) were advanced neoplastic lesion. The prevalence of colorectal neoplasia was more common among 50-59 years old (p =); although, prevalence of adenoma was noticeable in 40-49 years old group. The advanced adenoma was also more frequent among age over 50 years old. Majority of adenomas were detected in distal colon, but a quarter of advanced adenomas were detected in proximal colon. Most colorectal adenoma was detected beyond sigmoid. The increasing age and male gender were associated with presence of adenoma.
CONCLUSION: It seems that CRC screening among average-risk population might be recommended in countries such as Iran. However, sigmioidoscopy alone would have missed many colorectal adenomas. Furthermore, the 50-59 age group could be considered as an appropriate target population for this purpose.
Disclosure of Interest: None declared

P0171 STANDARD QUALITY ENDOSCOPY REPORT: DELPHI CONSENSUS TO IDENTIFY QUALITY MEASURES FOR UPPER AND LOWER GI ENDOSCOPY

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INTRODUCTION: Efforts to improve quality in endoscopy are ongoing and quality measures determined by examining the procedure report have been proposed as a mechanism for meeting this goal. Complete documentation is necessary for patient care and appropriate use of endoscopy. However, quality measures are very numerous and it is undetermined which are really critical for quality of cure.
AIMS & METHODS: To identify the quality measures to be included in the upper and lower GI endoscopy report of standard quality. Quality measures were extracted from the Quality Assurance Task Groups of the US Gastroenterology Societies (ASGE, AGA, ACG). Measures included in the questionnaire were divided in three categories: 1) pre-procedural with patient demographics (n. 15); 2) procedural (n. 27); 3) post-procedural (n. 9). A Rand Delphi method was used to reach the consensus. Participants were asked to label each measure using a 6 point Likert scale from 0 (not required) to 5 (absolutely required). The questionnaire was iteratively proposed to via a web-based application with a feedback of the results observed at the preceding round (median value; % of patients expressing the median value). Consensus was reached when no significant change was observed between values of the last two rounds (median, IRQ range, P value by Wilcoxon test). Measures with a score-5 were considered to characterize the standard (minimum) quality.
RESULTS: A total of 72 participants completed the 3 Delphi rounds required to reach the consensus: mean age 48; working experience (yrs) 11; n. endoscopy/week >15 in 61%; public employment 61%. A strong consensus was obtained for 33 (61%) out of 51 metrics. A score-5 was achieved for the following measures: patient name and birth date; exam indication; date and findings of the previous endoscopy for follow-up; anti PLT/coagulants use; informed consensus collection; assistants/anesthesiologist names; sedation drugs and doses; antibiotic prophylaxis use; causes of incomplete examination; stricture lumen according to the endoscope diameter; photographic documentation of landmark and findings; findings localization and biopsies; operative interventions: description of technique and completeness; definition of complete EGD retroversion manouvre; definition of complete colonoscopy: ileoscopy and retroversion in the rectum; indications after endoscopy in case of adverse events and follow-up.
CONCLUSION: The availability of a huge number of measures may be one of the causes of the poor report quality. The identification of the list of measures defining the endoscopy report of standard quality could provide endoscopists with an improvement tool and referring physicians with a report that use standard terms and provide follow-up recommendations. The identification of mandatory quality measures within their long list will ensure a fair accounting of the procedure and may encourage broader adoption of quality improvement efforts.
Disclosure of Interest: None declared

P0172 SELF-EXPANDABLE MESH METAL STENTS (SEMS) FOR ACUTE COLONIC OBSTRUCTION - EXPERIENCE OF A UK CENTRE

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INTRODUCTION: Acute intestinal obstruction occurs in up to 30% of patients with colorectal carcinoma. Historically, emergency surgical decompression was the treatment of choice. Self-expandable mesh metal stents (SEMS) have been increasingly used for malignant colonic obstruction. Several studies showed its efficacy in relieving obstruction, offering good palliation, avoiding emergency surgery and reducing the need for stoma creation.
AIMS & METHODS: A password-protected database of prospectively recorded endoscopic activity in our UK centre was analysed. Endoscopic records of patients undergoing SEMS for colonic obstruction from April 2007 to April 2014 were assessed. Data parameters included: patient demographics; site and pathology of obstruction; SEMS details; technical success of SEMS placement (correct placement of the stent across the stricture); clinical success (colonic decompression, with relief of obstructive symptoms and no significant complication); complications and the need for further intervention.
RESULTS: 107 SEMS insertion procedures were performed on 95 patients during the study period. M: F 46%:54%; median age 70 years (range 20 – 95); 50% were tertiary referrals. Causes of obstruction were primary colorectal cancer (CRC) (78%), extrinsic compression (18%) due to other malignancy mainly gynaecological; unspecified (4%). Obstruction occurred in left colon (distal to mid transverse) in 87% of cases. The majority of patients (97%) had sedation and only 3% were done under general anaesthesia. 3 stent types were used: 98% uncovered (Boston Wallflex (n = 27), Cook Evolution (n = 78)), 2% fully covered (Taewoong Medical (n = 2)). The median length of SEMS was 80mm (range 60mm – 120 mm). A single SEMS was inserted in 92% of patients, with 2 SEMS in the same session in 8 patients, and 3 SEMS in one patient. All SEMS were inserted under combined endoscopic and fluoroscopic guidance. Technical success was achieved in 98% of patients, with clinical success in 76%.

Complication	Number (%)	Post perforation management
Perforation	5/107 (5%)	4/5 (80%)-emergency laprotomy 1/5 (20%)- palliated
Obstruction due to 'flat valving'	2/107 (2%)	
stent migration	6/107 (6%)	
Stent occlusion	3/107 (3%)	

Median time to perforation from stent insertion was 4.5 days (range 1 – 15 days). Median time to death from stent insertion was 8.5 months; 6/107 (6%) died < 30 days from stent insertion, with one attributed to stent-related perforation. Stent migration noted to occur more in non-CRC extrinsic obstruction (2/19 (11%)) than primary CRC (4/88 (4.5%)).
CONCLUSION: Our data demonstrate that SEMS insertion for acute colonic obstruction is technically highly successful. However, technical success does not guarantee clinical success in all cases, and non-CRC extrinsic compression may be associated with higher rates of SEMS migration. The 5% perforation rate was similar to other reported studies, and needs to be considered in conjunction with the risks of emergency surgery in this patient group. The results of large randomised multicentre trials of SEMS vs surgery in palliating acute colonic obstruction are awaited.
Disclosure of Interest: None declared

P0173 LEARNING CURVE IN MUCOSAL HEALING (MH) AND INFLAMMATORY ACTIVITY ASSESSMENT BY USING THE ERLANGEN MH SCORE FOR CONFOCAL LASER ENDOMICROSCOPY (EMHS) IN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Confocal laser endomicroscopy (CLE) is a modern imaging technique that enables real time histology in vivo, during endoscopy, providing new insights of mucosal pathology. Monitoring histological activity to assess

MH is important in evaluating the therapy response and management of inflammatory bowel diseases (IBD). Our group has recently validated an endomicroscopic mucosal healing score (eIBD-MHs), which has to be interpreted by skilled endoscopists.
AIMS & METHODS: Our first aim was to analyze the learning curve (LC) of MH assessment by CLE in endoscopists naïve to the CLE technique. Secondly, we comparatively investigated the LC between endoscopists and residents (i.e. physicians acquainted neither to endoscopic nor to CLE techniques).
Therefore, 4 study groups were established: a.) senior endoscopists (n = 3), board certified (>2000 procedures, >2 years of experience); b.) junior endoscopists (n = 3) (significant endoscopic skills, <2 years of experience); c.) internal medicine residents (n = 4) without endoscopic experience, and d.) a skilled endomicroscopist (n = 1). Initially, all attendees received a random set of 20 CLE images from 10 IBD patients with different inflammatory activity and a table with the eIBD-MHs (9 criteria) for a spontaneous offline assessment (based only on histologic knowledge from medical school and interdisciplinary medical-histopathology meetings). Thereafter, all physicians participated in a short training session including explanation of the CLE technique, terminology, elementary CLE lesions, and assessment of IBD cases based on the eIBD-MHs before and after therapy). Subsequently, the same set of 20 CLE pictures was re-assessed (in a modified, paired succession, grouped per patient, before and after therapy). All physicians were blinded regarding patients' identity, diagnosis and disease activity. Assessment scores and duration from the pre- and post-teaching evaluation were statistically analyzed.
RESULTS: The average evaluation times before and after training for the groups a; b; c and d were: 25 vs. 12,33; 23 vs. 15; 24,5 vs. 15,25; 14 vs. 9 minutes, respectively). Overall, the evaluation time before the CLE instruction session was significantly longer ($p < 0.001$) compared to second evaluation times. No significant differences were observed between the physicians with or without endoscopic experience regarding assessment duration and quality. Interobserver agreement of the MH evaluation in the groups (compared to the assessment results of the skilled endomicroscopist) for group a; b and c were: 0.72; 0.52 and 0.75, respectively.
CONCLUSION: In conclusion, the LC for MH and inflammatory activity assessment by CLE is fast, can be easily learned and is independent of basic or advanced endoscopic skills or experience.
Disclosure of Interest: None declared

P0174 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION: RESIDUAL/RECURRENT LESIONS VERSUS PRIMARY LESIONS

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INTRODUCTION: Residual/locally recurrent lesions may occur after endoscopic resection: endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) or after transanal endoscopic microsurgery (TEM) for rectal lesions. ESD may be useful for resection of scar-embedded lesions, not lifted by standard injection of saline solution, but may be more technically difficult. We evaluated the feasibility and safety of ESD, as a salvage therapy for residual/locally recurrent lesions compared to primary lesions.
AIMS & METHODS: From January 2012 to March 2013 we performed 30 colonic ESD. Fifteen patients were on the first endoscopic treatment and the remaining fifteen had residual/recurrent lesions (median diameter of 21 mm) and have received at least an attempt at endoscopic resection using standard techniques including snare polypectomy, EMR or argon plasma coagulation, or TEM (5/15). The tumor size, the procedure duration, complications and early recurrence rate were compared between the two groups.
RESULTS: Procedure time was similar between groups (70±22 min vs 72±35 min). The lesions were significantly smaller (23±9 mm vs 35± 15 mm; $P < 0.05$) in the residual/ locally recurrent group, compared with primary lesions. Immediate bleeding rate was significantly higher in primary lesions group (46.6% vs 6.6%; $P < 0.05$). However, there were no cases of delayed bleeding in both groups. Intraprocedural perforations were observed only in residual/ locally recurrent group (3/15: 20%): surgery was needed in one patient, while two patients were managed using endoclips. Early recurrence, evaluated at three months, was similar between groups (20%)
CONCLUSION: Endoscopic submucosal dissection for residual/locally recurrent lesions was more difficult with higher risk of perforation due to presence of scar. However, the presence of lesions of smaller size and the low risk of intraprocedural bleeding, may recommend this procedure for scar-embedded lesions instead of surgical resection.
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Disclosure of Interest: None declared

P0175 THE USE OF DOUBLE CHANNEL GASTROSCOPE REDUCED THE PROCEDURAL TIME IN LARGE LEFT-SIDED ENDOSCOPIC MUCOSAL RESECTIONS

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INTRODUCTION: Endoscopic mucosal resection (EMR) of large colorectal lesions is associated with an increased procedural time. Usually the ''inject and cut'' EMR technique is applied for large sessile or flat colorectal lesions. The use of double channel gastroscope (DCG) might reduce the procedural time in the rectosigmoid area.
AIMS & METHODS: To evaluate the effect of DCG use in the procedural time of injection-assisted EMR performed in the rectosigmoid area. To the best of our knowledge this is the only comparative study on this subject. All EMRs for sessile or flat rectosigmoid lesions larger than 2cm performed from July 2012 to September 2013 were retrospectively analyzed. The use of DCG was mainly dependent on the availability.
RESULTS: There were 55 lesions 2cm or larger in the rectosigmoid area in 55 patients, of which 26 were removed by EMR using a DCG (DC group) and 29 by using an ordinary colonoscope or gastroscope (OS group). The mean size of the removed polyps was not statistically different between the two groups (4.3cm ±1.86 & 3.9 cm ± 1.9 in DC and OS group respectively). The Paris classification was similar between the two studied groups. The mean procedural time in the DC group (24.4±18.3 min) was significantly lower compared to that of OS group (36.3±24.4 min) ($p < 0.05$). Moreover, in the subgroup of patients with polyps larger than 40mm the statistical difference in the mean procedural time between the DC group (33±21min) and OS group (58.7±20.6 min) ($p < 0.01$) was even more pronounced. Outcome parameters such as recurrence rate (12 months follow-up), post-procedural bleeding rate and hospital stay were similar between the two groups. No case of perforation was observed. Multivariate linear regression analysis revealed that the polyp size ($b = 0.92$, $p < 0.001$) and use of DCG ($b = 15.5$, $p < 0.001$) were significantly associated with the procedural time.
CONCLUSION: Our data suggest that the use of DCG for large sessile or flat rectosigmoid lesions significantly reduces the procedural time. The use of DCG seems to be more effective in larger polyps. These results should be confirmed in a prospective study.
Disclosure of Interest: None declared

P0176 ADENOMATOUS HISTOLOGY IN COLONIC POLYPS: INFLUENCE OF POLYP LOCATION, SIZE AND PARIS-CLASSIFICATION

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INTRODUCTION: Published data on the likelihood of a polyp being an adenoma in relation to its location in the colon, size and form are incomplete.
AIMS & METHODS: To evaluate these factors in a consecutive patient group all histologically verified colonic adenomas which were removed by one endoscopist between 01-01-2011 and 31-12-2013 were included into this analysis. Before polypectomy polyps were classified as protruded (Paris classification type I) or flat (Paris type II), their size was estimated as compared to an open biopsy forceps, and the location in the colon was noted. Polyps were grouped according to their diameter using groups of sizes published in the literature. In the study period 698 patients were colonoscoped by one of the authors (mean patient age 62 years, 392 female). Visibility was reduced by fecal residues in 43 patients (6.2%). In 12 patients (1.7%) the cecum was not reached. In 8 patients (1.1%) the polyp could not be retrieved.
RESULTS: 1877 polyps were removed and histologically assessed. In 8 patients (1.1%) the polyp could not be retrieved for histological analysis. In 7 patients (1.0%) the location of the polyp was not described. In 34 polyps (6% of polyps) the estimated diameter was not described. Carcinoma of the sigmoid colon was detected in one patient. Adenoma was detected in 565 polyps (n = 222 Paris type I lesion; n = 343 Paris type II lesion). 13% of all adenomas were located in the coecum (18 Paris I; 56 Paris II), 23% in the ascending colon (52 Paris I; 79 Paris II), 27% in the transverse colon (71 Paris I; 79 Paris II), 7% in the descending colon (19 Paris I; 22 Paris II), 22% in the sigmoid colon (43 Paris I; 80 Paris II) and 8% in the rectum (19 Paris I; 27 Paris II). The table shows the total number of adenomas in 5 groups according to lesion diameter, and the likelihood of a polyp having adenomatous histology in % of all removed polyps, again in relation to diameter and to Paris-classification of the lesion.
Table to abstract P0176

Diameter	"minute" <5 mm	"small" 6-7 mm	8-9 mm	"large" >10 mm		Total
Number of adenomas	270	189	40	10-19 mm 27	≥20 mm 5	531
Adenoma, % of all polyps	23%	39.5%	51.3%	82%	100%	—
Adenoma in Paris I	58%	61%	64%	91%		62%
Adenoma in Paris II	20%	29%	32%	75%		23%

CONCLUSION: Summary: 63% of adenomas are located oral to the left colonic flexure. 61% of adenomas are flat lesions. Both in the right and in the left colon the majority of adenomas are flat. However, in polyps of all sizes protruding lesions have a significantly higher likelihood of being adenomatous as compared to flat lesions. In flat and protruding lesions the likelihood of a polyp being adenomatous increases with polyp size, from 58% to 91% in protruding and from 20% to 75% in flat lesions. **Conclusion:** Almost two thirds of colonic adenomas are flat or are located oral to the left colonic flexure. Although only a minority of small and flat polyps are adenomatous, they comprise the majority of adenomas. The high number of lesions in the right sided colon has not been reported before and may be related to excellent colonoscopy preparation with only 6% of colonoscopies having been influenced by fecal residues. The clinical role of the right sided and the small polyps needs to be determined.
Disclosure of Interest: H. Hammer: None declared, J. Klein: none, M. Okcu: none, K. Preisegger: none

P0177 A HAND-HELD METAL DETECTOR IS AN ACCURATE, LOW COST ASSESSMENT OF FLEXIBLE SIGMOIDOSCOPY COMPLETION TO THE SPLENIC FLEXURE

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INTRODUCTION: Flexible sigmoidoscopy (FS) is a validated screening test to reduce the incidence of colorectal cancer. Bowel scope screening is due to be implemented in the UK by 2016. There is variability in FS performance between operators; internal colonoscopic markings are unreliable for colonoscope position. Three dimensional (3D) magnetic imaging systems eg Scopeguide™ (Olympus, UK) represent real time instrument position but are not widely available. Hand-held metal detectors (HHMD) can easily localise metal objects within the body. We assessed use of HHMD to confirm flexible endoscopic tip placement at the splenic flexure (SF).
AIMS & METHODS: Adult subjects undergoing outpatient FS/colonoscopy were eligible and gave consent. When the operator judged examination complete to the SF, an independent observer placed the HHMD at the left 10th intercostal space, anterior-axillary line (corresponding to the internal fixation of the colon at the SF). A positive result was recorded if the HHMD beeped. Position was then assessed by Scopeguide™. If the SF could not be reached, the patient was excluded. We evaluated 3 different HHMD from different manufacturers. Patient experience was also studied. Ethical review NREC Ref no 13/LO/1065; IRAS Project ID 121224.
RESULTS: 44 subjects were recruited consecutively: mean age 64 years (range 17-74), 50% male (n = 22), mean BMI 27 kg/m^2 (range 20-41 kg/m^2). Endoscopic confirmation of position at SF showed concordance with Scopeguide™ in 95% (42/44). Subjects 1-6 were examined using BDS200 (Black & Decker) HHMD. Despite promising results on colonoscopic training models, this proved insensitive in humans and was abandoned. For subjects 7-30 (n = 24) studied with GMS120 (Bosch) HHMD, positive reading at the correct anatomical marking was recorded in 88% of examinations with Scopeguide™ validation. Of the 3 failures, 2 had a BMI of >30 kg/m^2. Use of an X-Ray screening trolley improved specificity. For subjects 31-44, n = 14, a detector with increased sensitivity and directional capabilities, GPP (Garrett Metal Detectors USA), was used on standard endoscopy trolleys. This showed concordance with 3D imaging in 100% of cases (n = 14) including 4 patients with BMI >30kg/m^2. There was one true negative versus endoscopic assessment confirmed by Scopeguide™. The technique was further validated by loss of signal on scope withdrawal. Patient questionnaires showed high acceptability.
CONCLUSION: Use of HHMD in FS has shown excellent concordance with ScopeguideTM for colonoscope localisation at SF. Specificity and sensitivity are improved by adapting the specifications of the HHMD. A HHMD is an accurate and very cheap (€100 per unit) means of assuring quality during FS and further studies may confirm its role as a useful training tool especially during future service expansion.
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Disclosure of Interest: None declared

P0178 CONFOCAL LASER ENDOMICROSCOPY (CLE) DEMASKS SUBTLE MUCOSAL CHANGES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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INTRODUCTION: IBS is a symptom-based diagnosis characterized by chronic abdominal pain, bloating, and alterations of the bowel habits without any organic cause. CLE allows in vivo visualization of microscopic features of the intestinal epithelium in real time during endoscopy.
AIMS & METHODS: To assess whether CLE is able to demask microscopic alterations of the small and large bowel mucosa in patients with established diagnosis of IBS.
Patients with established diagnosis of IBS according to Rome-III criteria and control patients underwent ileocolonoscopy. Fluoresceine guided CLE was performed in the terminal ileum and random optical biopsies were additionally performed in the colon and rectum. Attention was paid to presence or absence of epithelial gaps, intramucosal bacteria, crypt and vessel morphology, goblet cells and cellular infiltrate within the lamina propria. Physical biopsies were additionally taken for histopathological analysis.
RESULTS: Epithelial gap density and the microvascular pattern were increased in a subgroup (44%) of patients with IBS according to Rome-III as compared to control patients suggesting an altered intestinal permeability. No differences were observed regarding the presence of intramucosal bacteria, colonic crypt morphology, presence of goblet cells or the cellular infiltrate within the lamina propria ($P > 0.05$).
CONCLUSION: Confocal imaging revealed subtle changes of the mucosa in patients with IBS. These findings were not visible in every patient with IBS according to Rome-III criteria suggesting that some IBS patients may have an organic cause of the disease.
Disclosure of Interest: None declared

P0179 IN VIVO ASSESSMENT OF PORTAL HYPERTENSIVE COLOPATHY AND CLINICAL OUTCOME OF PATIENTS WITH LIVER CIRRHOSIS WITH CONFOCAL LASER ENDOMICROSCOPY (CLE)

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INTRODUCTION: Recent data has highlighted the role of mucosal integrity for bacterial translocation in the gut which is also discussed as a major cause for development of spontaneous bacterial peritonitis (SBP) and/ or hepatic encephalopathy (HE) in patients with liver cirrhosis. CLE has emerged as a valuable tool for real time diagnosis of mucosal integrity and allows in vivo imaging of commensal bacteria in the gut.
AIMS & METHODS: To prospectively assess the value of CLE for in vivo diagnosis of portal hypertensive colopathy and its association to Child-Pugh class, Model for End Stage Liver Disease (MELD), HE and development of SBP. Patients with established diagnosis of liver cirrhosis and portal hypertension were prospectively included. Clinical, biochemical, and ultrasound criteria, including portal vein thrombosis, ascites and collateral portosystemic vessels were assessed in addition to endoscopic criteria (e.g. esophageal varices, portal gastropathy) and beta-blocker intake. Fluoresceine aided CLE was performed in every patient in the sigmoid colon, rectosigmoid junction, and rectum. Afterwards biopsies were taken, unless contraindicated, for corresponding histopathological analysis.
RESULTS: Overall, more than 14,700 CLE images were collected. Confocal imaging revealed dilation and/or ectasia of microvessels, congestion of blood flow, edema, and a non-specific increase of the cellular infiltrate within the lamina propria. These findings were directly correlated to Child-Pugh class and MELD score with patients at higher scores showing more distinct changes of the microarchitecture. Of note, disturbed mucosal integrity, as observed by CLE, was strongly correlated with occurrence of HE and SBP, even in the follow-up of the patients. The procedure was well tolerated by the patients, and no adverse events were observed.
CONCLUSION: Fluoresceine guided CLE in patients with liver cirrhosis and portal hypertensive colopathy is safe and well tolerated. In vivo imaging revealed similar microscopic changes of portal colopathy as conventional histology without the need of physical biopsies. Of note, confocal imaging corresponds to clinical outcome parameters, including development of HE and/or SPB.
Disclosure of Interest: None declared

P0180 HIGH-DEFINITION ENDOSCOPY WITH COMPUTED VIRTUAL CHROMOENDOSCOPY FOR PREDICTION OF FOOD ALLERGY IN REAL-TIME – A PROSPECTIVE, RANDOMIZED STUDY WITH CROSS-OVER DESIGN

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INTRODUCTION: Food allergy is mediated via IgE and non-IgE mediated mechanisms. White-light endoscopy is not feasible to detect any specific mucosal alterations in patients with intestinal food allergy.
AIMS & METHODS: To access the value of advanced endoscopic imaging using high-definition colonoscopy with computed virtual chromoendoscopy (CVC) for prediction of mucosal changes in patients with suspected food allergy.
Patients suffering from recurrent abdominal pain and diarrhea were consecutively included. At baseline, patients underwent a standardized clinical interview in order to contain the diagnosis. Afterwards, patients underwent ileocolonoscopy with high-definition white-light endoscopy alone followed by CVC or the reverse. The mucosa of the terminal ileum, caecum and at the rectosigmoid junction was carefully inspected with or without CVC. Following the endoscopic inspection, a diagnostic lavage examination was performed at the above mentioned locations and analysed by measuring 13 different allergic markers, including TNF-alpha, IgE, and eosinophilic cationic protein. Finally, biopsies were obtained for additional histopathological analysis of the tissue.
RESULTS: 46 patients were randomized of which 39 patients (31 female, mean age 50 years; Range 21-78 years) completed the study protocol. Based on the clinical presentation, histopathological results and the lavage diagnosis 61% (24/39) of patients were diagnosed with intestinal food allergy. High-definition imaging with CVC visualized lymphoid hyperplasia, slight mucosal edema and

blurred mucosal vascular pattern. No mucosal changes were observed with high-definition endoscopy alone. CVC allowed correct diagnosis in 21 of 24 intestinal food allergy cases as compared with the criterion standards, giving a sensitivity, specificity and accuracy of 88%, 87%, and 87%, respectively. Positive and negative predictive value of CVC to predict food allergy was 91% and 81%, respectively.
CONCLUSION: High-definition endoscopy with CVC could mimic slight mucosal changes in patients with intestinal food allergy which were highly predictive for the disease. Therefore, advanced endoscopic imaging could add valid new criteria for diagnosis of intestinal food allergy.
Disclosure of Interest: None declared

P0181 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL LESIONS IN A SWEDISH CENTRE

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INTRODUCTION: Underwater endoscopic mucosal resection (UEMR) without submucosal injection has recently been reported to be a useful to remove large colorectal polyps in one single institution (1). The aim of this study was to examine if UEMR is a safe and effective procedure for removing large colorectal lesions in our institution.
AIMS & METHODS: Two experienced interventional endoscopists performed all UEMR cases after observing UEMR procedures. UEMR was performed by use of a colonoscope with hood and the polyp was fully immersed in water during the entire procedure. All polyps were removed by en bloc or piecemeal resection and without submucosal injection. The size of the snare (15 or 33 mm) depended on lesion size. Patient data were collected prospectively.
RESULTS: A total of 13 consecutive patients (8 men, mean age 74 years, range 52-84) referred for polyp removal of colorectal lesions underwent UEMR. Totally 16 lesions with a mean size of 17 mm (range 7-30) were removed by UEMR. Lesions were located in the cecum (n = 8), ascending colon (n = 2), transverse colon (n = 4) and rectum (n = 2). 56% of the polyps were removed en bloc and the rest by piecemeal technique. All lesions were radically removed as judged endoscopically. Minor bleeding events occurred during three procedures which were easily managed with coagulation forceps and clips. No complications, such as perforation or delayed bleeding, occurred.
CONCLUSION: UEMR seems to be an effective and safe method for removing colorectal polyps and should be incorporated into the therapeutic arsenal of institutions managing large colorectal lesions.
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Disclosure of Interest: None declared

P0182 A PREDICTOR OF THE DIFFICULTY OF COLORECTAL ESD FROM THE STANDPOINT OF DISSECTION SPEED

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been applied to the treatment of large colorectal tumors in Japan. However, the rate of complications is still higher than conventional endoscopic resection. For a management of complications, it is so important that we try to predict the difficulty of ESD in advance. Dissection speed during ESD will be related to the stability of the intraoperative visual field or ESD procedure itself.
AIMS & METHODS: To evaluate the difficulty of ESD from the dissection speed, we retrospective analyzed 94 patients who underwent colorectal ESD in Omori Red Cross Hospital from 2012 April to 2014 March. Because the mean dissection speed of total cases was 29.4±15.5(mm^2/min), we divided the patients into two groups: a low speed group (≦14 mm^2/min) (group A) and a control group (≧15 mm^2/min) (group B). The two groups were compared with respect to their clinical background and tumor characteristics predicted as a difficult case. In this study, for keeping uniform the quality of ESD, ESD procedure with a needle type device was done by one experienced ESD physician who under took more than 150 colorectal ESD before this study. In addition, the degree of submucosal fibrosis was classified into three types (F0–2) [(1)] (F0: no fibrosis, F1: mild fibrosis, F2: whitish submucosa or severe fibrosis). Independent and significant predictors were determined by multivariate analysis.
RESULTS: 94 lesions (male/female: 51/43) underwent ESD procedures; 14 in group A and 80 in group B. In a low speed group (group A), tumor location was C1/A2/T3/D3/S4/R1, and the mean tumor size was 25.3±9.8mm (15-50), and 5 cases had a fibrosis (F1; 2 cases and F2; 3 cases), and the rate of en bloc and curative resection was 100% and 13/14 (92.9%), and the mean operation time was 73.3min. The mean age, sex, the number of having antithrombotic agents was similar between two groups. The statistical analysis showed that severe fibrosis (F2) was predictor of a low speed (OR = 36.0; 95%CI = 2.46-527.1; p = 0.009), but tumor size (≧30mm), depressed tumor (IIc or LST-NG-PD), total fibrosis, location of tumors in the rectum or cecum, and the straddle of the fold did not have any significant differences. With respect to the postoperative course, there was also no differences in WBC, CRP, a number of having a high fever (≧38°C), using antibiotic agents, taking a painkiller, and a hospital period. Otherwise, there was one complication case in all lesions. This case (group A) had a thick fibrosis (F2) after severe radiation colitis and resulted in a delayed perforation the following day.
CONCLUSION: The size or location of tumors will not be related to dissection speed. This study showed a severe fibrosis was only a predictor, which was independent of the tumor size, of decelerating a dissection speed during colorectal ESD. In a case with severe fibrosis, an operation will take much time because of the difficulty, so an experienced physician should perform ESD. Additional cases, while considering dissection speed, will probably be a good reference for a predictor of the difficulty of colorectal ESD.
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Disclosure of Interest: None declared

P0183 PREDICTIVE FACTORS OF AN INCOMPLETE EN BLOC RESECTION IN ENDOSCOPIC MUCOSAL RESECTION FOR COLORECTAL TUMORS

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INTRODUCTION: *En bloc* resection by the procedure of endoscopic mucosal resection (EMR) for colorectal tumors over 2 cm in diameter is difficult according to previous reports. However, predictive factors of difficulty of *en bloc* resection are not indicated in colorectal EMR.
AIMS & METHODS: The aim of this study is to clarify predictive factors of an incomplete *en bloc* resection in EMR for colorectal tumors. From January 2012 to December 2013, a total of 277 patients with 370 colorectal tumors larger than 10 mm in diameter except pedunculated type tumors underwent EMR at Izumiotsu Municipal Hospital (Osaka, Japan). Age (mean): 70 years, sex: male 169 / female 108, location: right hemicolon 183 / left hemicolon (including the rectum) 187, macroscopic type: protruding type including sessile (Is) 43 / semi-pedunculated (Isp) 151 / flat-elevated type (IIa) 156 / IIa+Is 20. DRAGONEA bipolar snare (ZEON Medical Co., Tokyo, Japan) was used and selected width of snare 13 mm or 26 mm in diameter in reference to the lesion size in EMR procedures. Standard saline solution was injected into the submucosa in all cases. We retrospectively analyzed predictive factors of an incomplete *en bloc* resection on age, sex, tumor size, location, macroscopic type, and histological findings by multivariate analysis.
RESULTS: With crude-OR, location was 1.98 (95% Confidence Interval (CI), 1.12 to 3.48) and tumor size 1.11 (95% CI, 1.05 to 1.18) were associated with the incomplete *en bloc* resection. Regarding the location, the multivariate-adjusted OR of the incomplete *en bloc* resection for the right hemicolon was 1.9 (95% CI, 1.06 to 3.38) compared with the left hemicolon. Regarding the tumor size, the multivariate-adjusted OR of the incomplete en bloc resection for the highest tertile was 2.97 (95% CI, 1.53 to 5.75) compared with the lowest tertile (p for trend < 0.01, cutoff value: 16 mm).
CONCLUSION: Size (cutoff: 16 mm in diameter) and location (right hemicolon) of the colorectal tumors are indicated to be predictive factors for an incomplete *en bloc* resection by EMR. Especially, when lesion over 16 mm in diameter or located in right hemicolon is treated by EMR, the consideration of EMR-precutting technique or endoscopic submucosal dissection may be needed.
REFERENCES
Disclosure of Interest: None declared

P0184 SUBMUCOSAL DISSECTION IN THE COLORECTUM: LOW RATE OF PIECEMEAL RESECTION AND RECURRENCE

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for colorectal neoplasms was developed in Japan but is now spreading rapidly. The technique was started in our institute in the year 2010.
AIMS & METHODS: The aim of this study is to evaluate the results of colorectal ESD procedures for the first 4 years. The subjects are 205 consecutive lesions in 180 patients which were treated with ESD technique. The indications for ESD in our hospital are; 1. Neoplasms larger than 20mm but confined to the mucosa or invading minimally to the submucosal layer, 2. Those smaller than 20mm but unable to be lifted by injection due to fibrosis. The instruments used are PCF-Q260AZI or JI (Olympus), Short ST Hood and Flush Knife (Fujifilm) and VIO 300D (Erbe).
RESULTS: Male: female ratio was 86:94 and the average age was 68.0 (39-90) years old. The location was the cecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum in 36, 51, 48, 6, 24 and 40 of the lesions, respectively. The final pathological diagnosis was sessile serrated adenoma/polyp (SSA/P) in 18, adenoma in 63, mucosal cancer in 101, minimally invasive cancer (SM1) in 15 and deeply invasive cancer (SM2) in 7, and neuroendocrine tumor in 1. The gross appearance of the adenomas and cancers was flat or laterally spreading tumor (LST) in 174, sessile or 0-Is in 9, and depressed or 0-IIc in 3. The LSTs were subdivided into 53 lesions of homogeneous granular-type (LST-GH), 41 mixed-nodular type (LST-GM), 41 flat-elevated type (LST-NGF), and 39 pseudo-depressed type (LST-NGPD). The average size in LST-GH, LST-GM, LST-NGF, LST-NGPD, 0-Is, 0-IIc, and SSA/P was 41.1mm, 39.7mm, 30.7mm

and 25.7mm, 36.4mm, 10.3mm, and 23.9mm respectively. Invasive rates in these subtypes in order was 1.9%, 14.6%, 9.8%, 20.5%, 22.2%, 33.3%, and 0%. Post-procedure bleeding occurred in 2 cases (0.98%). Minor intra-procedure perforation was encountered in 6 cases (2.93%), but no emergency operation was required. Delayed pneumoperitoneum was witnessed in one case, but it was attributable to the ileus caused by anal stricture. If we divide the cases into 1st, 2nd, 3rd, and 4th fifty lesions, the en bloc resection rate was 78%, 88%, 98% and 98%. Local recurrence was witnessed in 3 cases (1.46%) in all of which the ESD procedure had resulted in piecemeal resection due to fibrosis, but the recurrent lesions were all small and removed endoscopically.
CONCLUSION: Submucosal dissection in the colorectum was successful with low rate of piecemeal resection and recurrence, but without serious complications.
Disclosure of Interest: None declared

P0185 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) PERFORMED BY EXPERTS IN COLONOSCOPY WITH LITTLE EXPERIENCE OF GASTRIC ESD

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INTRODUCTION: The efficacy of colorectal endoscopic submucosal dissection (ESD) has been reported mainly from Japanese referral centers. However, it is technically difficult and is associated with a higher risk of adverse events than endoscopic mucosal resection (EMR), especially for novices in colorectal ESD with little experience in gastric ESD.
AIMS & METHODS: We aimed to evaluate the results of colorectal ESD during the clinical learning curve. Colorectal ESD was performed by 2 endoscopists who had expertise in colonoscopy and colonic EMR but had experience of fewer than 5 cases of gastric ESD. A total of 120 cases consisting of the first 60 cases of each endoscopist were retrospectively investigated. The main outcome measurements were procedural time, en bloc resection rate with tumor-free margins (R0 resection rate) and adverse events rate. From among the clinical characteristics obtained before the ESD procedure, factors that affected the main outcome measurements were identified.
RESULTS: (Clinical characteristics) Tumors were located at the rectum, left colon, right colon and junction (dentate line, SD junction, hepatic flexure, splenic flexure, ileocecal valve) in 22, 19, 51 and 28 cases, respectively. With regard to the macroscopic type, 44, 23, 5 and 8 cases were granular-type laterally spreading tumor (LST), nongranular-type LST, depressed and protruding type, respectively. Of the 120 cases, 20 cases had factors which reflected fibrosis of the submucosal layer (sporadic localized lesions with ulcerative colitis, local residual tumors after EMR, etc.). The mean tumor diameter was 38.5±18.3 mm. The histological analysis showed 59 adenocarcinomas and 61 adenomas. (Outcomes) The mean procedural time was 101.7±65.9 min. A total of 113 cases (94.2%) were resected en bloc, and the R0 resection rate was 80.0% (96/120). Perforation and postoperative hemorrhage occurred in 8 (6.7%) and 2 (1.7%) cases, respectively. Multivariate analyses revealed that lesions in junction and lesions with factors reflecting fibrosis were significantly associated with longer procedural time (≥90 min) and a lower en bloc resection rate. Larger lesions (≥40 mm) and lesions resected in the first half (up to 60 cases) were also associated with longer procedural time.
CONCLUSION: Colorectal ESD is feasible and safe when performed by experts in colonoscopy with little experience of gastric ESD. For novices in colorectal ESD, beginning with lesions in junction and lesions with factors reflecting fibrosis may not be advisable.
Disclosure of Interest: None declared

P0186 A VALIDATION STUDY OF 4 TYPE BOWEL CLEANSING SCALE: ARONCHICK, BOSTON BOWEL PREPARATION, OTTAWA, HAREFIELD SCALE

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INTRODUCTION: Total colonoscopy is a potent tool for assessing the large bowel. There are various bowel preparation scale, but few bowel preparation scale have been validated. Diversity in bowel preperation scales can cause a lot of confusion on decisions in the clinical environment and much confounding of results within clinical studies. However there have been no clinical trials that compared 4 types of bowel preparation scales. The aim of this study is to assess the compatibility and reliability of 4 different types of bowel preparation scales.
AIMS & METHODS: This study compared 4 types of bowel preparation scales: Aronchick scale (AC), Boston bowel preparation scale (BBPS), Ottawa scale (OS), Harefield cleansing scale (HCS). 5 trainees read 20 total colonoscopy studies twice, with an interval of 1 month. We used Intraclass correlation coefficient (ICC) to evaluate Intra-observer (test-retest) consistency and inter-observer reliability of the BBPS and the OS. The unweighted kappa statistic was used to assess the reliability of the AC and the HCS.
RESULTS: Total 400 ratings were completed in this study. Inter-observer and intra-observer reliability were assessed by ICC and kappa statistic. ICC for OS was 0.73 (95% CI, 0.52-0.87, $p < 0.0001$), BBPS 0.76 (95% CI, 0.59-0.88, $p < 0.0001$), inter-observer kappa for AC was 0.29 (95% CI, 0.19-0.42, $p < 0.0001$), HCS 0.27 (95% CI, 0.15-0.41, $p < 0.0001$). Intra-observer scores for OS, ICC was 0.79-0.96, BBPS, 0.73-0.89. Intra-observer kappa for AC was 0.51-0.79 and for HCS, 0.36-0.92.
CONCLUSION: Inter-observer agreement values were high in OS and BBPS. This validation analysis showed that OS and BBPS are reliable, coherent scales so that they can provide better standardization to evaluate bowel preparation in both study and clinical practice.
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Disclosure of Interest: None declared

P0187 MANAGEMENT OF LARGE COLONIC POLYPS IN A BOWEL CANCER SCREENING PROGRAMME

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INTRODUCTION: Bowel cancer is the third most common cancer in the United Kingdom forming up to 13.6% of all newly diagnosed cancers(1). Bowel cancer screening colonoscopy allows early polyp detection at a curable stage. Complete resection and follow-up of large polyps is crucial to prevent malignant progression.
AIMS & METHODS: The aim of this study was to review the management of polyps with diameters ≥ 2 cm, particularly of sessile polyps, to assess the enbloc resection rates, completeness of resection using endoscopic mucosal resection (EMR) vs surgery and the incidence of malignant polyps.
Patients were identified retrospectively from a regional bowel screening programme database. Details of index colonoscopy including polyp characteristics, method of resection and complications were recorded. Histology results were reviewed for all polyps. Outcomes from follow-up endoscopic surveillance were analysed.
RESULTS: One hundred and fifty-eight patients (102 males, 56 females, mean age 66.2 years) with polyps ≥ 2 cm were identified from 2182 screening colonoscopies from January 2010 to August 2013. Caecal intubation rate was 96.8% in this group.
Largest polyp size for each patient ranged from 20 to 60 mm (mean 26.6 mm). The incidence of adenocarcinoma was 11.9% (n = 19), all located within the left colon, with 12 requiring surgical resection.
One hundred thirty nine patients (n = 139) had 155 non-malignant large polyps, mostly tubulovillous or villous histology (n = 110, 79%).
Thirty-six patients had 37 sessile polyps which underwent primary resection by EMR (n = 26) or surgery (n = 11).
Polyp diameter was larger in the surgery group with mean polyp diameter of 40.4 mm vs 28.0 mm ($p < 0.05$).
EMR enbloc resection rate was 11.5% (n = 3 out of 26). Completeness of excision was 38.4% (n = 10) at 3 months and 92.3% (n = 24) at 1 year. EMR complications included 1 perforation, 1 post polypectomy syndrome and 1 bleed.
Surgical resection included: anterior resection in 2, TEMS excision in 7 and right hemicolectomy in 3.
CONCLUSION: Sessile polyps ≥ 2 cm are relatively uncommon in an asymptomatic bowel cancer screening programme (37 in 2182 colonoscopies). They can be successfully resected by EMR without recurrence in 92.3% at 1 year providing a 3 month site check is performed in all piecemeal polypectomies.
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P0188 ARE THERE ANY PARAMETERS TO PREDICT BILE DUCT STONES IN BILIARY PANCREATITIS BEFORE ERCP

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INTRODUCTION: The role of endoscopic retrograde cholangiopancreaticography (ERCP) for the management of acute biliary pancreatitis (ABP) remains a controversial topic. Pre-ERCP detection of biliary stones in patients with ABP may strengthen the indication for a subsequent ERCP.
AIMS & METHODS: The aim of this study was to determine the value of several clinical and laboratory parameters as non-invasive pre-ERCP indicators of bile duct stones. Patients presenting to Türkiye Yüksek İhtisas Teaching and Research Hospital (TYIH) between 1 January 2010 and 31 August 2011 with ABP, who underwent ERCP within 72 hours of the onset of symptoms were screened, and eligible patients were enrolled in the study. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value of several parameters, such as AST, ALT, GGT, ALP, bilirubin, common bile duct (CBD) width on USG and duration of syptoms, with the highest sensitivity and specificity for predicting the presence of CBD stones.
RESULTS: A total of 59 patients [20 (33.89%) males and 39 (66.1%) females] were included in the final analysis. Areas under the curve for CBD width, timing of ERCP, AST, ALT, GGT, ALP and bilirubin were 0.753, 0.630, 0.548, 0.370, 0.577, 0.568 and 0.495, respectively. As a predictor of the presence of a biliary stone(s), CBD width was found to have the highest sensitivity, specificity,

negative predictive value (NPV), positive predictive value (PPV) and general accuracy. With a cut-off value of 8.55 mm for CBD width, sensitivity and specificity were 75% with a NPV of 47.4%, PPV of 90.9% and general accuracy of 75. A summary of ROC analyses for the other parameters is provided in table 1.
Table 1. ROC analysis for the value of several labortory and clinical parameters as pre-ERCP indicators of the presence of bile duct stones.

	Cut-off	AUC	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Accuracy
CBD width (mm)	8.55	0.753	75	75	47.4	90.9	75
Duration (hours)	25.5	0.630	60.9	61.5	30.8	84.8	61
AST (u/L)	224.5	0.548	56.5	53.8	25.9	81.3	55.9
ALT (u/L)	156.2	0.370	43.2	40.0	13.8	76	42.6
GGT (u/L)	263	0.577	69.8	70	35	90.9	69.8
ALP (u/L)	153	0.568	56.8	60	24	86.2	57.4
Bilirubin (mg/dl)	1.54	0.495	54.8	50	20.8	82.1	53.8

CBD, common bile duct; AST, Aspartat Aminotransferase; ALT, Alanin Aminotransferase; GGT, Gama-Glutamyl Transferase; ALP, Alkaline phosphatase; AUC, area under the curve; NPV, negative predictive value; PPV: positive predictive value
CONCLUSION: Determination of CBD width on ultrasonography and serum GGT levels are important parameters that may help predict the presence of biliary stones prior to endoscopic intervention.
Disclosure of Interest: None declared

P0189 PROCEDURAL DESCRIPTION AND CLINICAL OUTCOMES OF A NOVEL COMBINED RETROGRADE-ANTEGRADE ENDOSCOPIC APPROACH USING ERCP AND EUS FOR THE MANAGEMENT OF POSTOPERATIVE BILE-DUCT TRANSECTIONS

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INTRODUCTION: Postoperative Bile-duct Transections (POBT) are not amenable to endoscopic therapy. Preliminary data from combined percutaneous-endoscopic approaches are encouraging. Isolated reports of successful retrograde canalization are intriguing. We hypothesized that aggressive retrograde (ERCP) and/or antegrade (EUS) attempts at recanalization may salvage POBTs for endotherapy, and subsequent serial stenting would induce remodeling and durable resolution as seen in partial strictures.
AIMS & METHODS: To assess the feasibility, safety and efficacy of an endoscopic treatment algorithm of POBTs and to characterize the heterogeneous techniques used to attempt recanalization.
Since September 2010, 248 consecutive ERCPs were performed at a tertiary Unit for postoperative complications (strictures/leaks) in 150 patients (69 Liver Transplant, 81 Other). POBTs were identified in 17 patients (9 Female; age = 59.6 [43-79] years) following liver transplant (LT) /cholecystectomy (CCx) /Other in 7/7/3. Clinical records were retrospectively reviewed for procedural data (success, antegrade Vs retrograde, technique) and clinical outcome (immediate POBT remodeling and mid-term clinical resolution).
RESULTS: Recanalization was achieved in 12/17 POBT (70%), by means of ERCP alone in 5 (4 LT, 1CCx), of ERCP combined with EUS-guided antegrade approach in 6 (2 LT, 3CCx, 1 Other), and EUS alone in 1. Lack of upstream biliary dilation precluded EUS attempts in 4, and recanalization failed in 1 despite EUS-hepaticogastrostomy (EUS-HG). 5 initial failures underwent surgical repair with/without interval external PTBD. 10/12 recanalizations required forced antegrade/retrograde techniques: using the hard end of a stiff guidewire, needle-knife, puncture with intraductal hollow needles, transhepatic peritoneoscopy or magnetic compression anastomosis. A mean (range) of 1.5 (1-5) ERCPs were needed to achieve recanalization. Coincidental bilomas were drained in 2 POBTS (one transpapillary by ERCP and one transmural by EUS each). 11 Patients have completed 12 treatment courses of serial stenting (2 plastic alone & 10 covered metal with/without plastic) after 323(180-503) days of stents in place. After a mean follow-up of 353(30-900) days, there were 3 recurrences (1 surgery, 1 currently undergoing stenting, 1 successfully remodeled endoscopically). Post-procedural or stent related mild cholangitis ensued in 4, and moderate post-sphincterotomy bleeding in 1.
CONCLUSION: 70% of POBTs can successfully be recanalized endoscopically by means of forced mechanical (guidewires, needles), thermal or magnetic techniques. Antegrade EUS approaches allow salvage of 60% of ERCP failures. Mid-term treatment ouctomes using this algorithm for POBTs appear comparable to those seen with partial postoperative strictures.
Disclosure of Interest: None declared

P0190 VALIDATION OF A RISK SCORE FOR PREDICTING POST-ERCP PANCREATITIS BASED ON THE EUROPEAN GUIDELINE

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INTRODUCTION: Post-ERCP pancreatitis (PEP) is an important complication in biliopancreatic endoscopy, associated with morbidity and mortality. While clinical and technical risk factors for PEP have been elucidated, the identification of a simple and valid risk score to predict PEP remains a challenge.
AIMS & METHODS: To develop a model to predict the risk of PEP in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP).
Methods: A risk score was created based on the prognostic factors for PEP identified on the basis of the ESGE Guideline (1) and validated on 1823 ERCPs from an independent, prospectively assembled database (''validation cohort''). The predictive performance of the models was tested by ROC analysis to identify patients at low and high risk of PEP.
RESULTS: A score proportional to its regression coefficient was assigned to each independent prognostic factor: suspected sphincter of Oddi dysfunction (SOD) (4.1 points), female sex (2.2 points), previous pancreatitis (2.5 points), young age (2 points), no chronic pancreatitis (1.9 points), normal serum bilirubin (1.9 points), precut sphincterotomy (2.7 points), pancreatic injection (2.2 points), large number of cannulation attempts (2.9 points), pancreatic sphincterotomy (3.1 points), biliary balloon sphincter dilation (4.5 points), failure to clear bile duct stones (3.4 points). The AUC of the ROC curve showed a predictive score performance of 0.9268 (95% C. I. 0.90-0.95 $p < 0.0001$). We identified 9.5 as the cut-off between low- and high-risk classes, with 88.5% specificity, 81.6% sensitivity. Considering only severe PEP ($n = 12$), there was a significant difference between the two risk classes ($p = 0.001$).
CONCLUSION: We developed and validated a simple risk score to predict PEP. It could be useful to clinicians for predicting the individual risk of PEP and directing prophylactic measures, to researchers for designing and interpreting clinical trials, and to policy-makers for saving healthcare resources.
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Disclosure of Interest: None declared

P0191 MONITORING RADIATION EXPOSURE IN HEALTH PROFESSIONALS DURING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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INTRODUCTION: Use of radiation in endoscopic procedures has been increasing in Gastroenterology, particularly during endoscopic retrograde cholangiopancreatography (ERCP). Safety radiation limits have been defined for persons with occupational exposure to ionizing radiation. Monitoring the efficacy of protection measures and quality of x-ray systems are recommended.
AIMS & METHODS: The objectives of this study were to measure occupational radiation doses during ERCP in a Gastroenterology department and evaluate the impact of a real time individual dosimeter system in staff behavior. A prospective study was performed, during three phases, in which radiation doses were measured with individual dosimeters in health professionals: gastroenterologist, endoscopy and circulating nurses, radiology technician and anesthesiologist. Phase 1 – 25 procedures, dosimeter placed under the protection apron, at thoracic level. Phase 2 – 18 procedures, dosimeter placed outside the protection apron, at cervical level, simulating absence of radiation protection. Phase 3 – 12 procedures, dosimeter placed in second phase position, but with real time exposure levels displayed in a monitor and staff being able to adapt their position.
RESULTS: In phase 2, the following doses were registered: gastroenterologist 6.78 ± 5.99 μSv, endoscopy nurse $7.63 \pm 12.88 \mu$Sv, radiology technician $6.86 \pm 6.27 \mu$Sv, anesthesiologist $6.58 \pm 11.75 \mu$Sv and circulating nurse $4.56 \pm 5.45 \mu$Sv. In phase 1, protection equipment allowed a significant reduction in exposure doses: gastroenterologist 3.37 ± 4.00 μSv, endoscopy nurse $0.09 \pm 0.16 \mu$Sv, radiology technician $0.70 \pm 1.55 \mu$Sv, anesthesiologist $0.43 \pm 0.95 \mu$Sv and circulating nurse $1.15 \pm 3.03 \mu$Sv ($p < 0.05$). In phase 3, with the change of health professionals' position, according to real time values, there was a reduction of 44-71% in radiation levels, except for the gastroenterologist whose change of position was limited by his role in ERCP.
CONCLUSION: The present study showed occupational exposure doses within the recommendations, proving the efficacy of radiation protective equipments. Real time knowledge of radiation doses may have a positive impact in professionals' behavior.
Disclosure of Interest: None declared

P0192 PALLIATIVE BILIARY DRAINAGE FOR KLATSKIN TUMORS: ENDOSCOPIC OR PERCUTANEOUS?

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INTRODUCTION: At the time of the diagnosis only 20% of patients with Klatskin Tumors have resectability criteria. Thus, the majority will require palliative procedures for maintenance of biliary drainage.
AIMS & METHODS: The aim of this study is to compare two palliative non-surgical methods (endoscopic and percutaneous approach) in terms of therapeutic efficacy and complications.
We performed a retrospective study of patients newly diagnosed with Klatskin Tumors, in the period betwen 2010-2012, undergoing endoscopic biliary drainage (EBD) and/or percutaneous transhepatic biliary drainage (PTHBD). We analyzed the patient characteristics, technical success (insertion of drain/stent through the stenosis), therapeutic success (total bilirubin $\leq$ 4mg/dL after the procedure), duration of patency, complications and need for reintervention.
RESULTS: We included 70 patients with a mean age of 71$\pm$11 years and a male predominance (67.1%), of which 32 were submitted exclusively to PTHBD, 30 to EBD and 8 at both. These eight were initially submitted to EBD, but by impossibility of access to the biliary tract they needed PTHBD, so we considerer 40 patients in the PTHBD group and 30 in the EBD group. The two groups differed regarding the mean age (PTHBD 68 years; EBD 74 years; $p=0.006$). No difference was found in the Bismuth Classification (Type III/IV: PTHBD 82.5%, EBD 70.0%) and technical success rate (PTHBD 75%; EBD 79%). The rate of therapeutic success was PTHBD 57.5%; ERCP 79.3% ($p=0.07$). The terapheutic failure was more common in Bismuth III/IV types, in both groups (PTHBD 48.5%; EBD 30.0%). The complication rate was in the PTHBD group 47.5% (cholangitis in eleven patients and hemorrhage in 8 patients) and in the EBD group 23.3% (cholangitis in four, pancreatitis in two and perfuration in one) $p=0.038$. The patency time was similar: PTHBD 136 days; EBD 133 days. The reintervention rate was 32.4% in the PTHBD group and 48.3% in the EBD group ($p=0.191$).
CONCLUSION: Palliative biliary drainage is possible by endoscopic or percutaneous route, although the success rate is limited, especially in patients with Bismuth types III/IV. Endoscopic biliary drainage seems to show a trend toward greater treatment success, and it is associated with fewer complications.
Disclosure of Interest: None declared

P0193 ERCP CANNULATION; EVALUATION OF A WIRE-LED TECHNIQUE FOR BILIARY ACCESS IN A TRAINING CENTRE

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INTRODUCTION: A range of techniques have been described to achieve successful cannulation at ERCP, and when training in ERCP it is often difficult to select the optimum approach [1]. There are potential advantages to a wire-led approach and we have evaluated this in our unit in a training setting.
AIMS & METHODS: To evaluate cannulation success rates for trainers and trainees using a wire-led technique as the default approach.
A prospective evaluation was done with 2 experienced trainers and 2 trainees (previous experience of 50-100 ERCPs each). The sphincterotome was pre-loaded with a hydrophilic wire (in limited cases loop tip wire was used) and cannulation started with the wire extending 3-5mm out of cannula. Attempts were then made to advance the wire deep into the bile duct before injecting any contrast or pushing the cannula through the ampulla. Trainees were allowed 6 minutes for cannulation attempts. If the wire-led approach failed then other techniques were used. Wire-led cannulation was considered successful only if no other techniques were required. Only cases with a 'virgin ampulla' were including in this study.
RESULTS: 100 cases were included over a 5 month period. Trainees were present in 62 (62%) cases. Overall biliary cannulation success was 93 (93%). Success rate was 54/62 (87%) if a trainee was present and 37/38 (97%), if no trainee was present. Independent success for trainees was 34/62 (55%), mostly using the wire-led technique 29/34 (85%). In cases where a trainer took over from a trainee, the wire-led approach was still successful in 14/28 (50%). Overall success with the wire-led approach alone was 31 (69%); other approaches used in remaining cases included pre-cut sphincterotomy, locked PD wire, and PD stent. A peri-ampullary diverticulum was the most common cause for failure of wire-led technique; other common causes included stricture, floppy ampulla, or an impacted stone. Median cannulation time was 6.5 minutes (IQR 4-10min) overall and 5 minutes (IQR 3-10min) for consultant-only cases. Immediate complications included false passage of wire (1 case, no further clinical events) and late complications: post ERCP pancreatitis (1 case, hospital stay 3 days, no further clinical events).
CONCLUSION: Wire-led biliary cannulation, with selective usage of additional techniques, may allow a cannulation rate of >90% in cases with a virgin ampulla. The technique appears to be a useful training tool and has a low complication rate.
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Disclosure of Interest: None declared

P0194 DOUBLE-BALLOON OVERTUBE-ASSISTED ENTEROSCOPY ERCP IN PATIENTS WITH BILLROTH II GASTRECTOMY: A LARGE SERIES REPORT

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INTRODUCTION: Data on double-balloon overtube-assisted enteroscopy to facilitate ERCP (DBE-ERCP) in patients with Billroth II gastrectomy is limited.
AIMS & METHODS: The primary aim was to evaluate DBE-ERCP success in patients with Billroth II gastrectomy and suspected pancreaticobiliary disease. The seconday aim was to examine the safety and efficacy of DBE-ERCP. Patients with Billroth II gastrectomy in whom standard ERCP techniques had failed underwent ERCP by using DBE with initial therapeutic intent were identified retrospectively. DBE success was defined as visualizing the papilla, while ERCP success as completing the intended pancreaticobiliary intervention. Clinical success was delineated as a greater than 50% reduction in abdominal pain or level of hepatic enzyme elevations or resolution of cholangitis or complete extraction of bile duct stone.
RESULTS: From April 2006 through December 2011, 77 patients (59-male, mean age 73.5 years, range 50-95 years) had 92 DBE-assisted ERCPs. Overall DBE-ERCP success was 69 of 77 (90%). DBE success was 73 of 77 (95%), of whom 69 of 73 (95%) achieved ERCP success. Reasons for DBE- ERCP failure ($n=8$): tumor obstruction within afferent limb ($n=2$), peritoneal adhesion ($n=2$), cannulation failure ($n=3$), and bowel perforation ($n=1$). Diagnosis in patients with DBE-assisted ERCP success ($n=69$): choledocholithiasis ($n=50$), biliary dilatation ($n=9$), malignant biliary stricture ($n=9$), normal study ($n=1$). Selective interventions included biliary sphincteroplasty (dilation $\pm$ cautery, $n=76$), stone extraction ($n=57$), stenting ($n=20$), nasobiliary drainage ($n=6$), and rendezvous ($n=3$). Complications occurred in 5 of 77 (6.5%). In those patients who underwent therapeutic ERCP ($n=68$), 66 patients (97%) achieved clinical success.
CONCLUSION: DBE permits diagnostic and therapeutic ERCP in patients with Billroth II gastrectomy with a high success and acceptable complication rates. DBE-assisted ERCP should be considered as an effective alternate when standard ERCP failed in such patients.
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Disclosure of Interest: None declared

P0195 OUTCOMES OF THE ENDOSCOPIC DRAINAGE OF PANCREATIC COLLECTIONS ACCORDING TO THE NEW ATLANTA CLASSIFICATION

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INTRODUCTION: Endoscopic drainage is considered a minimally invasive first-line treatment of pancreatic collections (PC). A revision of the Atlanta classification has been recently published but outcomes of endoscopic therapy according to this new classification are scarce.
AIMS & METHODS: Our objective was to evaluate the outcomes of the endoscopic drainage procedures of PC performed in our center during the last 5 years, assessing results with regard to morphological characteristics of the PC, technique used, and type of stent placed. A retrospective review of all endoscopically drained PC at our center from January 2009 to December 2013 was made. Indications for endoscopic drainage were symptomatic or complicated PC. PC were retrospectively classified according to the new Atlanta 2012 classification. Variables analyzed: 1) general variables: sex, underlying pancreatic pathology, PC type, 2) endoscopic technique: endoscopic intervention, type of stent, technical success (successful placement of draining stents), number of endoscopic interventions (including the session to retrieve the stents after PC resolution), complications, and 3) other variables: clinical success (symptom resolution), morphological success (resolution of the PC on computed tomography), and need for subsequent surgery. All drainage procedures were performed under endoscopic ultrasound guidance. Chi-squared and Fisher's exact test were used for analysis.
RESULTS: Endoscopic drainage was performed in 39 PC in 37 patients (33 men). 46.2% of PC developed in the setting of acute pancreatitis, 38.5% in chronic pancreatitis, and 12.5% after pancreatic surgery. PC included 17 pseudocysts (2 infected) and 19 walled-off necrosis (15 infected). We were unable to retrospectively classify 3 PC according to Atlanta 2012. The endoscopic approach was transgastric in 61%, transpapillary in 28%, and mixed in 7.7%. In 50% of transgrastric drainages a covered biliary metallic stent was deployed while the others underwent pigtail stents placement. The treatment approach and stent used were associated with the type of PC since walled-off necrotic PC were preferentially drained via a transgastric approach (17 of 19) and with metallic stents (13 of 19) ($p<0.05$). Nasocystic lavage was performed in 38.5% of drainages (13 infected walled-off necrotic PC and 2 infected pseudocysts). Endoscopic necrosectomy was required in 2 patients. Technical, clinical and morphological success was achieved in 94.9%, 76.9% and 66.7% of cases per

intention to treat analysis. Type, location, or etiology of PC, drainage technique and type of stent did not show a significant influence on technical, clinical, or morphological success. The median number of endoscopic sessions performed were 2 (range:1-6). There were 30% of complications after the endoscopic drainage including migration of the stents in 7 patients, infection in 2, and perforation in 1 case. 3 stent migrations and the perforation required surgery while the infections resolved after new endoscopic drainage procedure.
CONCLUSION: In our series, endoscopic treatment of PC achieved 95% technical success, 76.9% clinical success per intention to treat, and 66.7% morphologic success. The type of PC according to Atlanta classification determined the treatment approach and stent placed.
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Disclosure of Interest: None declared

P0196 CAN INITIAL PRECUT FISTULOTOMY IMPLEMENTATION REDUCE ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAPHY–RELATED COMPLICATION RISK?

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INTRODUCTION: Precut fistulotomy allows biliary access when standard cannulation methods fail. Precut fistulotomy is considered a risk factor for endoscopic retrograde cholangiopancreatography (ERCP)–related complications; however whether the complication risk is due to precut fistulotomy itself or to the prior prolonged attempts is still debated. We aimed at assessing success of cannulation and complications of an initial precut fistulotomy vs. a 'classic strategy' of precut fistulotomy after a difficult biliary cannulation.
AIMS & METHODS: We conducted a retrospective study from January 2011 to December 2012. A total of 152 patients without prior sphincterotomy were enrolled. The patients were classified into two groups: an initial precut fistulotomy (Group A, $n = 72$) or a late precut fistulotomy only after a failed difficult biliary cannulation (precut fistulotomy after $>$ 10 cannulation attempts, $>$ 10 minutes, and $>$ 3 accidental pancreatic duct cannulations, Group B, $n = 80$).
RESULTS: During the study period, total of 1412 ERCPs were performed. Of these, 152 cases (10.7%) underwent precut fistulotomy. Both groups were comparable, with no differences for age, gender or indications and findings. The overall success of cannulation for Group A and Group B was 95.9% vs 95%; mean cannulation time: 5.7 vs. 13.0 minutes ($p < 0.001$). The overall frequency of post–ERCP pancreatitis was 3 patients in Group A vs. 11 patients in Group B ($p = 0.041$). Other complications developed with 1 perforation and 2 bleeding presenting in the Group A and Group B, respectively. All resolved conservatively. Finally, the overall complication rates for Group A and Group B were 8.3% (6 cases out of 72 patients) and 17.5% (14 cases out of 80 patients), respectively.
CONCLUSION: Initial precut fistulotomy provides a higher cannulation success with significantly less time than late precut fistoltomy, although final overall success is similar. Initial precut fistulotomy implementation reduces post–ERCP pancreatitis risk but not the overall complication rate.
Disclosure of Interest: None declared

P0197 ENDOSCOPIC TREATMENT OF PANCREATIC FISTULAS DUE TO ETIOLOGIES OTHER THAN PANCREATITIS

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INTRODUCTION: Endoscopy is effective in the treatment of pancreatic fistulas due to pancreatitis.
AIMS & METHODS: We aimed to determine the effectivity of endoscopic treatment in patients with pancreatic fistulas due to etiologies other than pancreatitis.
RESULTS: The study group consisted of 44 patients (28 male, 6-80 years). Etiologies were surgery in 30 and trauma in 14 patients. Thirty-seven patients were presented with drainage through the drain, 5 with pancreatic ascites, and 2 with pseudocyst. Pancreatic fistulas were located in the blind end in 22 (50%)and lateral side of the pancreas in 9 (20.5%) patients. Pancreatic fistula could not be visualized during pancreatography in 6 (13.6%) patients. Six patients had disconnected pancreatic duct syndrome. Endoscopic treatments were pancreatic sphincterotomy (PES)+ stenting in 35, PES alone in 6, and PES + nasopancreatic drain insertion in 2 patients. The success of endoscopic treatment could not be determined in 9 patients due to lost to follow up in 6 and exitus in 1 patient. Endoscopic treatment was unsuccessfull in 7 patients due to disconnection in 6 and failure of cannulation in 1 patient. Endoscopic treatment was successfull in 29 patients (65%) and surgically placed drains were withdrawn after a mean time of 27.3 days (5-90) in fistulas located in the blind end, 11.9 (3-28) days in fistulas located in the lateral side, and 9.7 (3-18) days in fistulas with undefined location.
CONCLUSION: Endoscopy is effective in the treatment of pancreatic fistulas due to etiologies other than pancreatitis if the pancreatic duct is not disconnected.
Disclosure of Interest: None declared

P0198 THE RESULTS OF ERCP IN PATIENTS WITH A HISTORY OF FAILED CANNULATION

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INTRODUCTION: Cannulation of common bile or pancreatic ducts is a prerequisite for biliopancreatic interventions.
AIMS & METHODS: To determine the reasons of failed cannulations and suggest ways to increase the success rate.
We reviewed the data of the patients who were referred to our ERCP unit after failed cannulation at another center.
RESULTS: The study group included 71 patients (40 male, mean age:57.2 years). Sixty-nine patients had biliary and 2 pancreatic pathologies. On admission, 2 patients had retroperitoneal perforation, 1 patient had pancreatitis and cholangitis, each due to the previous ERCP attempt. The reasons of failed cannulation were unsuccessfull pre-cut in 31 (43.6%), failure to reach papilla due to apical stenosis in 8, presence of a peripapillary diverticula in 6, altered anatomy in 6 (3 with Billroth II), distal location of the papilla in 2, and failure to identify papilla in 1 patient. Fifteen patients had no reasons to explain failed cannulation. Cannulation was not attempted in the patient with retroperitoneal perforation. Of the remaining 70 patients, cannulation could be achieved in all of them (68/70, 97.1%) other than 2 with Billroth II gastroenterostomy. Cannulation could be achieved selectively in 50, after pre-cut in 14, dilation of the apical stenosis in 4, and by using either one channel two accessory method or leaving a guidewire in the pancreatic channel in 2 (2.9%) patients with peripapillary diverticula.
CONCLUSION: Performing pre-cut in the appropriate direction, realising the anatomic alterations and anomalies in the location of papilla, and applying advanced cannulation techniques are required to increase the success rate of cannulation.
Disclosure of Interest: None declared

P0199 PREVENTION OF POST-ERCP PANCREATITIS: A RANDOMIZED CLINICAL TRIAL USING RECTAL DICLOFENAC

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INTRODUCTION: Pancreatitis is one of the commonest post ERCP complications. Preliminary research has evaluated several pharmacologic agents for prevention of post-ERCP pancreatitis (PEP) but none has been proven to be effective. Non steroidal anti-inflammatory drugs (NSAIDs) have been shown to reduce the incidence of PEP via inhibition of phospholipase A2. There were various trials using different routes and dosages of NSAIDs. Meta analysis of these trials was carried out but the results were inconsistent. Hence, we conducted a clinical trial to evaluate the efficacy of prophylactic rectal diclofenac for the prevention of PEP in high-risk patients.
AIMS & METHODS: This was a randomized, open-label, two-arm, prospective clinical trial.
Only patients at high risk of developing PEP were selected. This was determined by validated patient- and procedure-related risk factors. All procedures were performed by gastroenterology trainees under the supervision of senior consultants. They were then assigned to either receive 100mg rectal diclofenac or no intervention immediately after ERCP. After the procedure, the patients were admitted to the ward for further observation.
The primary outcome of the trial was the development of PEP, which consisted of new onset of upper abdominal pain, an increase in pancreatic enzymes to at least three times the upper limit of the normal range after the procedure, and requiring at least 2 nights of hospital stay. The patients were also reviewed 1 month after discharge to exclude the occurrence of any adverse event related to the study drug and ERCP procedure. The difference in incidence of post-ERCP pancreatitis between the 2 study groups was analysed using Fisher exact test (2-tailed), with $P < 0.05$ indicating a significant difference.
RESULTS: Among 107 patients who were enrolled and completed follow-up, 62 (57.9%) received diclofenac and 45 (42.1%) were in the control group. Among all the patients, 4 (3.7%) developed PEP, in which 3 were in the diclofenac group (a pancreatic stent was deployed for 1 of the patient in this group) and 1 was in the control ($p = 0.31$). Every cases of PEP was mild. After ERCP, 5 (4.7%) developed cholangitis and 1 (0.9%) had a perforation in which they were treated conservatively. No drug related complications or adverse event were noted for both groups of patients.
CONCLUSION: Among patients at high risk for developing PEP, rectal diclofenac did not significantly decrease the incidence of PEP.
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Disclosure of Interest: None declared

P0200 EUS AND ERCP COMBINED WITH IDUS IN THE DIAGNOSIS OF BILE DUCT STRICTURE

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INTRODUCTION: A variety of cholongioscopes have been emerged as a new tools for diagnosis of different biliary strictures. But these new techniques are not widely applied clinically because of high price and too easy to damage.
AIMS & METHODS: We evaluated the value of endoscopic ultrasonography (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) combined with intraductal ultrasonography (IDUS) in the diagnosis of bile duct stricture. 36 patients with bile duct stenosis were recruited. The findings by endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography combined with intraductal ultrasonography and the results of bile duct brushing cytology and liquid-based cytology of these patients were analyzed. The final diagnosis was based on clinical data, histopathology and follow-up results (≥6 months).
RESULTS: All of the 36 patients, in whom 21 were diagnosed malignant biliary diseases, including 9 biliary tract carcinomas, 4 duodenal papilla carcinomas, 4 pancreatic cancers infiltrating common bile duct and 4 liver cancers infiltrating common bile duct; 15 were diagnosed as benign biliary diseases, including 9 bile duct stones, 4 liver fluke diseases, 1 cholangitic stenosis and 1 external compression, were shown to have bile duct stricture. The accuracy rate of EUS, ERCP, IDUS and EUS+ERCP+IDUS in the differential diagnosis of bile duct stricture disease were 77.8%, 88.9%, 91.7% and 94.4%, respectively. The accuracy rates of differential diagnosis of bile duct stricture disease between EUS and ERCP were similar; while the accuracy rate of EUS and ERCP combined with IDUS was significantly higher than both EUS and ERCP ($P<0.05$). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of EUS+ERCP+IDUS were 95.2%, 93.3%, 95.2%, 93.3%, respectively; the sensitivity, PPV, NPV in EUS +ERCP +IDUS were higher than that of EUS, ERCP and IDUS. All of the 36 patients received bile duct brushing cytology and the liquid-based cytology tests, 19 of which were diagnosed as malignant biliary diseases, while 17 were diagnosed as benign biliary diseases. The sensitivity, specificity and accuracy of differential diagnosis of bile duct stricture disease were 90.5%, 100% and 94.4%, respectively.
Table. Comparison of ERCP and EUS in the diagnosis of bile duct stricture

	EUS	ERCP	IDUS	EUS+ERCP+IDUS
sensitivity	71.4%(15/21)	85.7%(18/21)	90.5%(19/21)	95.2%(20/21)
specificity	86.7%(13/15)	93.3%(14/15)	93.3%(14/15)	93.3%(14/15)
PPV	88.2%(15/17)	94.7%(18/19)	95%(19/20)	95.2%(20/21)
NPV	68.4%(13/19)	82.4%(14/17)	87.5%(14/16)	93.3%(14/15)
diagnosis	28	32	33	34
misdiagnosis	8	4	3	2
Accuracy rate (%)	77.8	88.9	91.7	94.4

CONCLUSION: EUS and ERCP combined with IDUS can improve the diagnostic accuracy of bile duct disorders. IDUS is carried out under the guidance of a guide wire, and the operation is simple. It can also make up for the inadequacy of EUS. With the help of ERCP and IDUS, the bile duct could be directedly brushed, which could improve the diagnostic positive rate.
Disclosure of Interest: None declared

P0201 ENDOSCOPIC PANCREATIC INTERVENTIONS USING SHORT DOUBLE-BALLOON ENDOSCOPE IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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INTRODUCTION: In patients with surgically altered anatomy, endoscopic treatment of pancreatic disease such as pancreaticojejunostomy stricture, pancreatic fistula, and pancreatic duct stones can be challenging.
AIMS & METHODS: We evaluated the efficacy and safety of endoscopic pancreatic interventions using short double-balloon endoscope (DBE) for the treatment of pancreatic disease in patients with surgically altered anatomy.
Between October 2009 and April 2014, we performed endoscopic pancreatic interventions in 12 patients using a short DBE (152 cm in length with a 2.8 mm working channel; EC-450BI5/EI-530B, Fujifilm Medical, Tokyo, Japan), enabling conventional ERCP accessories. Previous surgeries included pancreaticoduodenectomy with Billroth II reconstruction (n = 7), pancreaticoduodenectomy with Roux-en-Y reconstruction (n = 3), and Roux-en-Y gastrectomy (n = 2). Indication for pancreatic interventions were anastomotic stricture (n = 8; with pancreatic duct stones [n = 5]), pancreatic fistula (n = 3), and pancreatic duct stones (n = 1).
RESULTS: Access to the papilla or the end of afferent loop successful in all 12 patients, but anastomosis site could not be identified in 3 patients. Pancreatic duct cannulation was achieved using a straight cannula (0.025-inch ERCP-catheter, MTW Endoskopie, Wesel, Germany) and a 0.035-inch hydrophilic guidewire (Radifocus, Terumo, Tokyo, Japan), or a metal tip cannula (PR-132Q, Olympus, Tokyo, Japan). Pancreatic interventions were successful in 9 patients (75%). Three of 6 patients with anastomotic stricture were treated successfully with balloon dilation, and the remaining 3 patients required repeated balloon dilation and long-term pancreatic stent placement. Two patients with pancreatic fistula were treated successfully with endoscopic nasopancreatic drainage. Pancreatic duct stones were successfully removed in 4 patients. Complications occurred in 3 (25%) patients, including retroperitoneal air (n = 1) and hyperamylasemia (n = 2), but all were asymptomatic.
CONCLUSION: Endoscopic pancreatic interventions using short DBE, although technically demanding, are effective and safe in patients with surgically altered anatomy.
Disclosure of Interest: None declared

P0202 "SHORT" SINGLE-BALLOON VERSUS DOUBLE-BALLOON ENDOSCOPE FOR PANCREATICOBILIARY INTERVENTIONS IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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INTRODUCTION: With the advent of short double-balloon endoscope (DBE), therapeutic pancreaticobiliary interventions are possible with surgically altered anatomy. However, because the channel diameter of short DBE is 2.8 mm, only limited ERCP devices are available and the exchange of devices is both time-consuming and cumbersome. Recently, a prototype short single-balloon endoscope (SBE) with passive bending and high force transmission, which has a 3.2 mm working channel and a 152 cm in length, was specifically developed for ERCP (SIF-Y0004-V01; Olympus Medical Systems, Tokyo, Japan).
AIMS & METHODS: The aim of this study was to compare the insertability and procedural efficiency of short SBE and short DBE for pancreaticobiliary interventions in patients with surgically altered anatomy. Between March 2013 and Jan 2014, we performed endoscopic pancreaticobiliary interventions using a short SBE in 20 patients who have successfully undergone short DBE-assisted ERCP. Previous surgeries included Roux-en-Y (R-Y) gastrectomy (n = 7), hepaticojejunostomy (n = 5), pancreaticoduodenectomy with R-Y reconstruction (n = 3), Billroth II (B-II) gastrectomy with Braun's anastomosis (n = 2), pancreaticoduodenectomy with B-II reconstruction and Braun's anastomosis (n = 2), and liver transplantation with hepaticojejunostomy (n = 1).
RESULTS: Access to the papilla or anastomosis with SBE failed in 3/20 patients (15%). Among successful patients, the median time (IQR) required to reach the target orifice was 26 min (11–32.5 min) with SBE and 16 min (11–21 min) with DBE ($P = 0.10$). Pancreaticobiliary interventions with SBE were successful in 17/17 patients (100%). Therapeutic procedures using SBE included stone extraction (n = 11), biliary plastic stenting (n = 5), papillary large balloon dilation (n = 3), balloon dilation of anastomotic stricture (n = 3), pancreatic stenting (n = 3), biliary metallic stenting (n = 1), balloon dilation of biliary stricture (n = 1), and endoscopic naso-pancreatic drainage (n = 1). Although almost the same procedures with prior DBE, the median ERCP procedure time (IQR) was shorter with SBE than with DBE [29 min (23–55.5 min) vs 63 min (46.5–93.5 min), $P = 0.03$]. Aspiration pneumonia as procedure-related complication occurred in 1 patient.
CONCLUSION: Insertability of a short SBE is slightly inferior to that of a short DBE. However, a short SBE with a 3.2 mm working channel allows most conventional ERCP devices to be used and reduces ERCP procedure time compared to a short DBE with an only 2.8 mm working channel.
Disclosure of Interest: None declared

P0203 INTER-OBSERVER AGREEMENT AND ACCURACY OF PREOPERATIVE EUS-GUIDED BIOPSY FOR HISTOLOGIC GRADING OF PANCREATIC CANCER

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INTRODUCTION: Post-surgical poor differentiation/high grade of pancreatic cancer (PADC) appears to accurately predict an early unfavourable outcome, these patients possibly deserving neo-adjuvant treatment. EUS-guided pancreatic tissue core biopsy (EUS-PTCB) may in theory allow a pre-operative assessment of PADC-grading. To assess inter-observer pathological agreement and accuracy of preoperative PADC-grading based on EUS-PTCB.
AIMS & METHODS: 42 post-surgical PADC-cases with preoperative EUS-PTCB were chosen. Four expert pathologists independently reviewed the EUS-PTCB slides, reporting tumour grading (well-/moderate-/poor-degree of differentiation). Agreement among pathologists for reporting PADC-grading on pre-operative EUS-PTCB material was expressed by using Cohen's/Fleiss' kappa statistic, as appropriate. Post-surgical PADC-grading was used as gold-standard to assess the cumulative accuracy of EUS-PTCB in preoperatively predicting PADG grade.
RESULTS: The k values for PADC-grading on EUS-PTCB material ranged from 0.09 to 0.41. The total agreement among the four pathologists was only fair (k = 0.27; 95% CI: 0.14-0.38). When tumor grades were grouped as well-/

moderately differentiated versus poorly differentiated, kappa values ranged from 0.19 to 0.50, with only a fair overall agreement (k = 0.27; 95% CI: 0.21-0.49). Preoperative EUS-PTCB-based accuracy of preoperative staging was 56% (75/134 readings; 95% CI: 40-65%), with mean sensitivity and specificity to detect a high grade poorly differentiated tumor of 41% (95% CI: 19-54%) and 78% (53/68 readings; 95% CI: 60-99%), respectively.
CONCLUSION: Preoperative EUS-PTCB-based pathological grading of PADC is unreliable, arguing against the use of this information in clinical practice. This appears to be related with both a suboptimal inter-observer agreement among pathologists and an overall low accuracy in predicting post-surgical staging.
Disclosure of Interest: None declared

P0204 PERFORMANCE OF THE PROCORE® 25 GAUGE NEEDLE IN OBTAINING SAMPLES FOR HISTOLOGICAL EXAMINATION IN A LARGE AND HETEROGENOUS COHORT OF PATIENTS: A TWO CENTERS STUDY

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INTRODUCTION: A new 25-gauge Procore® biopsy needle has become recently available. Scanty data on its performance are available. We evaluate the yield of this needle in obtaining samples for histologic evaluation (EUS-FNB), its diagnostic accuracy and inter-observer agreement between three pathologists in a large cohort of patients with heterogenous indication.
AIMS & METHODS: Consecutive patients who underwent EUS-FNB using the Procore 25G were retrospectively retrieved. The collected material was placed directly in formalin or in cytolit and sent for histologic evaluation. All samples were independently reviewed by three pathologists and scored for: (i) presence of an histologic, cytologic specimen or no specimen; (ii) presence or absence of neoplasia; (iii) diagnostic or not diagnostic. Diagnostic accuracy and inter-rater concordance among pathologists in the evaluation of the above mentioned parameters were calculated.
RESULTS: 94 patients (median age 71 years; 55 male) underwent EUS-FNB of 101 sites. Mass lesions were located in the pancreas (49 patients), abdomen (6), liver (8), common bile duct (3 masses and 3 wall thickening), stomach (1 sub-epithelial lesion and 2 wall thickening), mediastinum (2), lung (1), and adjacent to the rectum (1). All the remaining 25 sampled lesions were mediastinal (14) and abdominal (11) lymph nodes. The median lesion size was 30 mm (range, 15-67 mm) and a mean of 2.5 FNA passes (range, 1-6; median, 3; IQR, 2-3) per lesion was done. A total of 41 (40.6%) lesions were classified as having a histologic specimen either by at least two of the three pathologists. A presence of a cytologic specimen was found by at least two of the three pathologists in 29 (28.7%) cases. In the remaining 31 lesions no specimen was present according to all three pathologists. There was good agreement among pathologists in determining if EUS-FNB provided cytologic vs. histologic samples (kappa index, 0.82; 95% CI:0.74-0.90). When considering non-diagnostic samples as false negative, the pooled sensitivity of the EUS-FNB for neoplasia was 65% (154 of 237 readings; 95% CI: 54.8-75.1%), whereas specificity was 98% (50 of 51 readings; 95% CI: 89-100%). The pooled accuracy of the procedure was 70.8 (204 of 288 readings; 95% CI: 62.1-79.6%). In the per-protocol analysis, the overall sensitivity and accuracy of the procedure for malignancy was 93.8 (150 of 160 readings; 95% CI: 88.8-96.9) and 93.9% (170 of 181 reading; 95% CI: 89.3-96.9%), respectively. Substantial agreement on the presence (or absence) of neoplasia resulted (kappa index, 0.94; 95% CI: 0.83-1.00). Substantial agreement was seen across the three reviewers in describing diagnostic accuracy, with an overall kappa value of 0.95 (95% CI: 0.85-1.00). At multivariate analysis, histologic samples were more likely than cytologic one to lead to a correct diagnosis (OR, 4.1; 95% CI: 1.2, 15.0; p = 0.027).
CONCLUSION: EUS-guided FNB with the Procore 25G needle provided samples for histologic examination in about 40% of the cases and showed excellent results in term of interobserver variability.
Disclosure of Interest: None declared

P0205 COMBINED ENDOBRONCHIAL AND TRANSESOPHAGEAL APPROACH OF AN ULTRASOUND BRONCHOSCOPE FOR TISSUE DIAGNOSIS OF MEDIASTINAL LYMPHADENOPATHY

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INTRODUCTION: Morphological evaluation of mediastinal masses is essential for diagnostic confirmation and treatment planning of patients (pts) with mediastinal abnormalities. EBUS-TBNA and EUS-FNA is a safe and efficacy method to obtain tissue for morphological diagnosis. The combined approach reduces the need for additional equipment, the operating costs, and the duration of the procedure. However it could be difficult to select the order of preference if both of the techniques are available.
AIMS & METHODS: The aim was to determine the diagnostic value of EBUS-EUS combined approach by using single ultrasound bronchoscope for evaluation mediastinal lymphadenopathy. EUS−FNA and EBUS−TBNA (Olympus Exera II BF-UC160F, Olympus 21g needles) were compared in 166 patients for tissue diagnosis from enlarge (>0.9cm) 7 and 4L group lymph nodes. 110 lesions were sampled from the respiratory tract under moderate sedation as first step. For 56 lesions fine needle aspiration was performed initially from the esophagus under local anesthesia. Cytology examination of the fine needles aspirates was made on site. If EUS-FNA (8pts) gives a negative result (8pts) in the on-site cytological analysis, EBUS-TBNA was performed once.
RESULTS: Diagnosis was proved in 87.3% of cases in EBUS-TBNA group and in 85.7% of cases in EUS-FNA group. Definitive morphology diagnosis was made in 96.4% by the combined approach with rapid on-site evaluation of the fine needles aspirates.
CONCLUSION: Two procedures can be performed with single ultrasound bronchoscope and the combined approach with cytology examination on site has better diagnostic value than either alone. But EUS-FNA with ultrasound bronchoscope is easy, safe and doesn't request moderate sedation. Therefore it can be performed for patients for tissue diagnosis from enlarge 7 and 4L group lymph nodes as the first step of examination.
Disclosure of Interest: None declared

P0206 RESULTS AND LEARNING FROM A THERAPEUTIC ENDOSCOPIC ULTRASOUND PRACTICAL WORKSHOP ON A SWINE LIVING MODEL

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INTRODUCTION: Therapeutic endoscopic ultrasound (T-EUS) has been undergoing extensive development in recent years. Although previous experience on EUS-FNA and ERCP is considered to be needed, data on learning curves and the potential benefit of animal models training are lacking.
AIMS & METHODS: To train some different T-EUS techniques and to estimate their difficulties and the potential benefit of the swine model in this context.
Prospective data analysis from a T-EUS practical workshop on a biliary obstruction porcine model by OTSC clip®, addressed to endoscopists with previous EUS-FNA and ERCP experience. There were four different T-EUS procedures trained: common bile duct drainage (CBDD), cholecysto-gastrostomy (CGS), transrectal urinary bladder drainage (TUBD), simulating a fluid collection drainage, and gastro-jejunostomy (GJS). All animals were sacrificed after T-EUS procedures and necropsy studies were performed. Local Ethics Committee approval was obtained.
RESULTS: Thirty three procedures were analyzed (11 CBDD, 5 CGS, 7 TUBD, 10 GJS), performed by 12 endoscopists in 10 pigs (2.83 ± 0.58 proc./endoscopist; 3.3 ± 1.42 proc./animal). Main results are shown in Table 1. Together TUBD and GJS were the procedures more frequently and successfully completed versus CBDD and CGS (100% vs. 62.5%, p = 0.007 and 82.4% vs. 37.5%, p = 0.011). Among the different procedural steps, guidewire management (31.8%), stent insertion (25%) and cystotome use (20%) were the most troublesome ones.
Table 1. Results by procedure

	CBDD	CGS	TUBD	GJS	Total	*p
N	11	5	7	10	33	
Mean time duration (min.)	51.3 ± 14.5	48 ± 7.6	31.3 ± 5.9	21.2 ± 17.2	34.7 ± 18.5	*0.000*
Completed	63.6%	60%	100%	100%	81.8%	*0.007*
Final succes	45.5%	20%	85.7%	80%	60.6%	*0.011*
Trainer intervention needed	18.8%	20%	14.3%	20%	18,8%	*0.608*
Inmediate complications	10%	40%	14.3%	10%	15.6%	*0.437*

CONCLUSION: Our model appears to mirror the challenges of T-EUS even for endoscopists experienced in EUS-FNA and ERCP.
Ethical and cost concerns can be minimized by optimizing the number of T-EUS drainage procedures, up to 4 per animal.
CGS and CBDD, both longer and with higher number of steps and instrument requirements, are more challenging than TUBD or GJS, which suggests more demanding training is needed.
This kind of training based on animal model simulation may allow a safer and probably quicker learning curve on T-EUS.
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P0207 COMPLICATIONS AND HISTOPATHOLOGICAL ASSESSMENT OF THE PANCREAS IN A PORCINE MODEL AFTER EUS RADIOFREQUENCY ABLATION

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INTRODUCTION: Treating pancreatic cancer represents a major objective in research, as it still remains the fourth leading cause of cancer deaths among men and women, with approximately 6% of all cancer-related deaths. Radiofrequency ablation uses electromagnetic energy deposition causing thermal lesions and overheating tissue which leads in a final stage to necrosis.
AIMS & METHODS: We studied the assessment of an EUS-guided RFA probe through a 19-gauge needle, in order to achieve a desirable necrosis area in the pancreas. Radiofrequency ablation of the head of the pancreas was performed using a RITA Medical System device on 10 Yorkshire pigs with a weight between 25 to 35 kg. Using an EUS-guided RFA experimental probe we ablated an area of 2 to 3 cm wide at 5-10-15-20 watts for one minute a time.
RESULTS: No major complications were noted. High levels of amylase, lipase, aspartate transaminase and alanine transaminase were found within 3 days from the ablation. Necropsy pointed out a very well limited area with minimal invasion and inflammatory tissue at about 2 cm surrounding the lesion. No nearby fibrosis or adhesions were found and no major vessel injuries or adjacent organ damage was produced. The pathology examination revealed coagulative necrosis, a local acute inflamatory reaction with structured necrosis of the glandular parenchyma, steatonecrosis, and recent thrombosis of blood vessels.
CONCLUSION: EUS-Guided RFA of the pancreas may be a feasible procedure, however more studies are necessary.
Disclosure of Interest: None declared

P0208 ROLE OF ENDOSCOPIC ULTRASONOGRAPHY IN THE SELECTION FOR NEOADJUVANT TREATMENT OF GASTRIC ADENOCARCINOMA

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INTRODUCTION: Gastric remains one of the most common causes of cancer-related death. Recent studies reveal that neoadjuvant treatment of locally advanced gastric cancer improves survival of these patients. Endoscopic ultrasonography (EUS) staging is recommended in several guidelines, particularly in the assessment of the T and N stages. However, its role in identifing patient candidates to neoadjuvant therapy is not known.
AIMS & METHODS: The purpose of the study was to evaluate the accuracy of EUS in selecting patients for neoadjuvant therapy of gastric adenocarcinoma. We conducted a retrospective analysis of patients with gastric adenocarcinoma who underwent EUS staging and were submitted to primary gastrectomy between 2011 and 2013. We determined the agreement (kappa – k) between EUS and pathological TNM staging and the accuracy (AUROC, sensitivity and specificity) of EUS to identify patients with indication for neoadjuvant therapy (defined as stages II and III in the pathological analysis of the surgical specimen).
RESULTS: Between 2011 and 2013 were performed 141 USE, of which 66 were excluded (37 patients did not undergo underwent gastrectomy, 16 patients underwent neoadjuvant therapy, 7 USE were re-staging examinations and 6 cases weren't adenocarcinomas). Of the 75 patients enrolled, the median age was 66 years, 65% were male and 60% had intestinal type adenocarcinoma. The distribution of patients according to the EUS and pathological staging was: 50.7% and 46.6% for stage I, 31.1% and 33.3% for stage II, 16% and 21.3% for stage III. The agreement between EUS and pathologic stages for T, N and TNM was good (k = 0.61), moderate (k = 0.44) and fair (k = 0.36), respectively, while for stages II + III was good (k = 0.63). The accuracy of EUS for stages II + III was high (AUROC 0.82, sensitivity 78% and specificity 86%), especially for intestinal type adenocarcinoma (AUROC 0.84, sensitivity 86% and specificity 85%).
CONCLUSION: Endoscopic ultrasonography has an important role in the staging of gastric cancer, showing a good performance in the selection of patients for neoadjuvant treatment, especially in intestinal type adenocarcinoma.
Disclosure of Interest: None declared

P0209 ENDOSCOPIC ULTRASONOGRAPHY-GUIDED DRAINAGE OF HEPATIC ABSCESSES AND BILOMAS BY USING SELF-EXPANDABLE METAL STENTS (SEMS). A PILOT STUDY

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INTRODUCTION: Liver abscesses and bilomas are conventionally managed by means of percutaneous drainage or surgical approach. However, both procedures have been reported on high morbi-mortality rates. Transgastric EUS-guided drainage of both entities with plastic stents or nasocystic catheters have been exceptionally performed. We describe our experience using self expandable metal stents (SEMS) – tubular and lumen–apposing metal stents (LAMS) in this setting.
AIMS & METHODS: The aim of the study was to assess the technical feasibility and clinical outcomes of EUS-guided drainage of liver abscesses and bilomas using SEMS under mixed fluoroscopic, endoscopic and ultrasonographic guidance.
Retrospective analysis involving eight consecutive patients (March'12 to Oct '13) with liver abscesses/bilomas not accesible to percutaneous approach and/or discarded for surgery by means of age or comorbidities (Table 1). Procedures were performed by using linear echoendoscopes, 19G needles under EUS & fluoroscopic control, 0.035" guidewires, 8.5F cystotome and tract dilation with 4 mm biliary balloon. Aspiration of fluid was routinely performed for culture. Finally, cSEMS were placed, either tubular or lumen-apposing metal stents (LAMS: AXIOS^{TM}- Xlumena Inc).
RESULTS: Six patients with liver abscesses and 2 bylomas were included (Table 1) EUS-guided transgastric approach was performed in 6/8 cases (75%) in correspondence with abscesses located on the left hepatic lobe. 6 patients were managed with LAMS (5 abscesses, 1 biloma). Median diameter of abscesses was 80.05 mm (range 52.70 - 99). Drainages were successful in all cases and there were no procedure-related complications. Stents were removed after a mean of 7 weeks (range 4-12). There were no relapses after a mean follow-up of 7.5 months (range 1-18)
CONCLUSION: EUS-guided drainage of hepatic abscesses and bilomas by means of SEMS appears to be a safe, effective and useful procedure in patients not suitable for radiologic drainage or surgery. However, larger, prospective and multicenter studies are needed.
Disclosure of Interest: None declared

P0210 COULD QUANTITATIVE AND QUALITATIVE EUS-ELASTOGRAPHY RESULTS BE AFFECTED BY THE COMPRESSION RATE AND THE DIAMETER OF THE REGION OF INTEREST?

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INTRODUCTION: EUS-elastography (EUS-e) is an alternative method to evaluate tissue stiffness (elasticity-index) of solid pancreatic masses, which may be related to histopathology tissue features (hard = blue = neoplastic / soft = red-yellow-green = non-neoplastic). Recently publications show different results using EUS-e and a lack of data exist regarding the compression rate of the probe (CRP) and the diameter of the region of interest (d-ROI) under analysis.
AIMS & METHODS: Based on the hypothesis that EUS-e could be affected by CRP and the d-ROI this study aimed to evaluate the quantitative strain ratio (q-SR) and qualitative color (q-C) EUS-e results determined by the CRP and the d-ROI in normal pancreatic tissue (NPT). After approval by the ethics committee and signing of an informed consent, a prospective study was performed in 45 patients undergoing for upper-EUS from Oct-Nov 2013. Inclusion criteria: EUS for evaluate submucosal tumors. Exclusion criteria: age < 18 or > 55; pregnancy, history of: pancreatic disease, choledocolitiasis, symptoms of maldigestion, alcohol abuse, increased serum levels of pancreatic enzymes, smokers and EUS signs of chronic pancreatitis (Rosemont classification). EUS–e was performed using linear Pentax-EUS and Hitachi-Avius. The q-SR and q-C EUS-e was measured in the body of the pancreas taking in consideration the curve of the CRP high: +0.4 (H-CRP), middle: 0 (M-CRP), low: -0.4(L-CRP) in the largest (LROI) and smaller ROI (SROI) diameters. Analysis for q-C was obtained by the predominant color of the pancreatic area studied. Pictures where recorded and q-SR data

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	Collection type	Age/ Sex	Size (mm)	Approach	Stent type	Complications	Retrieval (weeks)	Follow-Up (months)	Outcome
1	Abscess	71/M	74	Transgastric	AXIOS 15 x 10	NO	8	6	Resolution
2	Abscess	92/M	91,6	Transgastric	AXIOS 15 x 10	NO	12	14	Resolution
3	Abscess	65/M	85	Transgastric	HotAXIOS 15 x 10	NO	9	3	Resolution
4	Abscess	34/M	99	Transgastric	AXIOS 10 x 10	NO	4	2	Resolution
5	Abscess	84/F	52,7	Transgastric	AXIOS 10 x 10	NO	6	1	Resolution
6	Abscess	49/F	78	Trans-duodenal	Tubular SEMS 60 X 10	NO	9	3	Resolution
7	Biloma	74/F	72	Trans - duodenal	AXIOS 15 x 10 + Plastic pig-tail	NO	4	13	Resolution
8	Biloma	53/F	69.4	Transgastric	Tubular SEMS 60 x 10 + Plastic pigtail	NO	4	18	Resolution

were calculated comparing EUS-e of pancreatic tissue with soft tissue (normal mucosal layer: red). Finally, a comparative analysis was performed between the results with the mean normal value (NV) of 1.68 for q-SR previously published for NPT, and between the different CRP.
RESULTS: 60 images were analyzed and 10 patients were included, 6 females, mean age 50 (ranges: 32-55). LROI q-C analysis: showed a predominant green (G) color in H-CRP in 90%, M-CRP in 50% and L-CRP in 70% of cases. SROI q-C analysis: showed a predominant G-color in H-CRP in 100%, L-CRP in 50% and M-CRP in 66.6% of cases. In LROI-quantitative showed a mean SR of 7.2 (range: 2.7-24) for H-CRP, 11.03 (range: 3.3-42) for M-CRP and 8.8 (range: 2.6-36) for L-CRP being $p<0.05$ for H-CRP and L-CRP when compared with NV q-SR, and for H-CRP when comparing with M-CRP. For SROI q-SR analysis showed a mean SR of 6 (range: 5.5-6.6) for H-CRP; 8 (range: 5-12) for M-CRP and 77 (ranges: 2.3-224) for L-CRP, being $p<0.05$ in all cases when compared with NV q-SR.
CONCLUSION: EUS-e (q-C and q-SR) results in NPT could be affected by CRP and d-ROI. These data suggest that a standardization of the measurements parameters is required to determine the best results and application of this technology in pancreatic diseases.
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P0211 ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA) IN PANCREATIC LESIONS: PREDICTIVE FACTORS OF ACCURATE DIAGNOSIS

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INTRODUCTION: Endoscopic ultrasound (EUS) has taken on an important role in the diagnosis of benign and malignant pancreatic disease. Due to the proximity of the transducer and reduced acoustic interference, EUS provides high-resolution ultrasound images of the pancreas with subtle anatomical detail and has the unique ability to obtain specimens of the pancreas and peripancreatic structures for cytohistological diagnosis.
AIMS & METHODS: The aim of this study is to identify the predictive factors for an accurate EUS-FNA diagnosis. **Methods:** Retrospective analysis of medical records of patients submitted to an EUS-FNA for evaluation of a pancreatic mass, from January of 2008 to December of 2013. All procedures were performed by 2 operators, using a linear echoendoscop Pentax® EG3870UTK and Hitachi HI Vision Preirus or EUB-6000 US. Collection of demographic data, ultrasonographic characteristics, technical information on EUS-FNA and cytohistological results.
RESULTS: A total of 1420 EUS examinations were performed during the period. 88 patients (with a mean age of 64±14 years; 54.5% female) diagnosed with pancreatic masses underwent EUS-FNA. 81.8% of them had this symptoms: epigastric pain (34%), weight loss (23.9%) and jaundice (23.9%). 51.5% of the lesions were located in head of pancreas and 67% were solid masses. The median size of the lesion was 31.8±12.5mm. The mean number of passages was 2.35±0.97. EUS-FNA was performed with 19 G needle in 7.1% of patients, 22G needle in 70.6% and with 25G needle in 22.4% of patients. The overall diagnostic accuracy was 82.9%. In 10 patients procore needle (19G-1;22G-1;25G-5) was used and the diagnostic accuracy was 100%, although not a statistically significant difference. Adenocarcinoma was the most common cytological diagnosis (62.9%), followed by inflammatory pancreatic disease (21%), endocrine neoplasm (6.5%), mucinous neoplasm cystic (6.5%) and IPMN (1.6%). There were no procedure-related complications. The predictors of diagnostic accuracy ($p< 0.05$) were: appearance of lesion (solid mass 90.6% vs. cystc mass 54.4%), size of lesion (diagnostic 32.6 mm vs non diagnostic 23.6 mm) and location of the lesion (body 100% vs. head 86.6% vs. neck 70.2% vs. tail 40%). The size of needle and number of passages did not significantly influenced the diagnostic accuracy of the procedure.
CONCLUSION: EUS-guided FNA is a safe and reliable technique for establishing a diagnosis in pancreatic mass lesions, especially in solid mass, located in body or head and with a greater dimension.
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Disclosure of Interest: None declared

P0212 LEARNING CURVE FOR ENDOSCOPIC ULTRASONOGRAPHY IN GASTRIC CANCER T STAGING USING CUMULATIVE SUM METHOD

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INTRODUCTION: One of the most studied tools for the loco-regional staging of gastric cancer is endoscopic ultrasonography (EUS). The American Society for Gastrointestinal Endoscopy guideline set 75 examinations as a minimum number of EUS procedures for mucosal cancer including esophageal, gastric, and rectal cancer before competency can be determined. The learning curve in the staging of gastric cancer, however, has not been evaluated.
AIMS & METHODS: We retrospectively reviewed the clinical records of patients who underwent EUS examinations for gastric cancer, which were performed by trainees, at Severance Hospital, Seoul, Korea, between March 2011 and February 2012. Cumulative summation analysis was applied to assess the learning curve for EUS T staging in each trainee.
RESULTS: A total of 553 initial EUS examinations for naïve gastric cancer performed by 4 trainees were enrolled in the study. Final EUS T staging was determined by experts in 332 gastric cancers, while EUS T staging of other 221 lesions was determined by trainees. Accuracies of EUS examinations performed by trainees and experts were 72.6% and 84.3%, respectively. Required EUS examinations for reaching a 1st plateau in each trainee were 20, 41, 60, and 65, respectively. In addition, poor predictive factors for accurate T staging of gastric cancer were 20–30 mm and 30–50 mm of size compared to 20 mm or less of size, pT2–pT4 stages compared to pT1 stage, and EUS T staging by trainees.
CONCLUSION: A threshold number of 75 which is suggested by guidelines may be acceptable for achieving competency of gastric cancer T staging by EUS.
Disclosure of Interest: None declared

P0213 PROGNOSTIC SIGNIFICANCE OF EUS NON-TRAVERSABILITY IN PATIENTS WITH LOCALLY ADVANCED SQUAMOUS ESOPHAGEAL CANCER RECEIVING PREOPERATIVE CHEMORADIOTHERAPY

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INTRODUCTION: Although endoscopic ultrasonography (EUS) is the most accurate loco-regional staging modality for squamous esophageal cancer (EC), approximately 30% of patients cannot complete EUS due to malignant stenosis (EUS non-traversability). Malignant stenosis has reportedly been associated with advanced tumor stage. However, to date, no study has assessed clinical implications of EUS non-traversable EC stenosis in patients with locally advanced EC receiving preoperative chemoradiotherapy (CRT).
AIMS & METHODS: This study aimed to examine the clinical implications and prognostic significance of EUS non-traversability in locally advanced EC patients treated with preoperative CRT. Data from 89 consecutive patients with locally advanced and resectable EC (stage II or III) planning preoperative CRT followed by esophagectomy were retrieved. Relevant clinical and cancer-specific parameters were reviewed retrospectively. Univariate and multivariate analysis with a Cox model were performed to determine significant factors for survival.
RESULTS: EUS scope could not pass through EC in 26 of 89 (29.2%) patients. Between EUS non-traversable and traversable group, dysphagia (88.5% vs. 52.4%; $P=0.001$), need for stent insertion (30.8% vs. 1.6%; $P<0.001$), median serum albumin level (3.6 vs. 3.9 g/dL; $P=0.028$), tumor length (6.0 cm vs. 4.0 cm; $P=0.002$), and percentage of stage III disease (65.4% vs. 38.1%; $P=0.019$) were significantly different. 79 (88.8%) patients completed preoperative CRT; 22 (84.6%) in non-traversable group and 57 (90.5%) in traversable group ($P=0.426$). 70 (78.7%) attained CR or PR. CRT response rates were not different between non-traversable and traversable group (76.9% vs. 79.4%; $P=0.798$). 53 (59.6%) patients underwent esophagectomy; 16 (61.5%) in non-traversable and 37 (58.7%) in traversable group ($P=0.806$). Median OS of all patients was 32.8 months (95% CI, 0–68.2 months) with 5-YSR of 43.8%. Stage III ($P=0.079$), non-response to preoperative CRT ($P<0.001$), incompletion of esophagectomy ($P<0.001$), weight loss ≥10% ($P=0.047$), serum albumin level <3.8 g/dL ($P=0.035$), EUS non-traversability ($P=0.025$) and tumor length ≥5 cm ($P=0.069$) were negative prognostic factors on univariate analysis. Weight loss ≥10% ($P=0.042$), EUS non-traversability ($P=0.007$), non-response to preoperative CRT ($P=0.003$), and incompletion of esophagectomy ($P=0.002$) remained significant negative prognostic factors of survival in multivariate analysis. EUS non-traversable EC patients had a significantly lower 5-YSR than those with EUS traversable EC (30.8% vs. 49.3%, $P=0.023$). 5-YSR was 50.0% for EUS non-traversable EC patients who attained a clinical response to CRT and also underwent esophagectomy (vs. 64.5% in EUS traversable EC patients; $P=0.153$).
CONCLUSION: EUS non-traversability is a significant negative prognostic factor in patients with locally advanced, resectable EC receiving preoperative CRT. The clinical implication may arise from incomplete loco-regional EC staging and larger tumor burden. We suggest that treatment should not be discontinued for the patients with EUS non-traversable EC stenosis, given the acceptable compliance to multimodality therapy and the survival of the patients who attained a clinical response to CRT and underwent surgery.
Disclosure of Interest: None declared

P0214 IS THE CORE BIOPSY NEEDLE (PROCORE TM COOK NEEDLE) THE ALMIGHTY SOLUTION FOR EUS-GUIDED TISSUE ACQUISITION? A COMPARISON WITH STANDARD EUS-FNA NEEDLES

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INTRODUCTION: Fine Needle Aspiration (FNA) under Endoscopic UltraSound (EUS) guidance is an efficient and safe method to obtain tissue samples from gastro-intestinal tract and from the nearest structures. Whereas EUS-FNA provides samples of cells without any tissue structure information, EUS-Fine Needle Biopsy (FNB) has the theorethical advantage to collect tissue specimens for histological evaluation. The aim of this study is to compare feasibility and diagnostic yield of the newly-developed FNB device (Cook EchoTip ProCore) with the standard FNA needles.
AIMS & METHODS: 134 patients (75/59 M/F; 62±13.5 years) were consecutively enrolled between April 2011 and June 2013, for a total of 137 lesions (mean size 33.5±16 mm, range: 6-100 mm): 81 pancreas, 31 lymph nodes, 8 stomach, 7 gut (including 1 papilla), 4 esophagus, 5 aspecific abdominal masses, 1 nervous ganglia. For each lesion EUS-guided tissue sampling was performed both with standard needle and with ProCore needle. An expert cytopathologist evaluated the material giving out a score (0-4) about the adequacy of the samples and assessing the feasibility of the diagnosis on the samples from the two types of needle.
RESULTS: A mean of 3.2±1.1 (range 1-6) and 2.8±1.1 (range 1-7) needle passes per lesion were performed with standard needles and ProCore respectively (p:ns). A core sample adequate for histological assessment from ProCore biopsy was achieved in 29% lesions (mean length 1.37±0.7 mm, range 0.5-3.0 mm), with no difference among the 22, the 19 and the 25 Gauge needle (25%, 46.7% and 33.3% respectively; p: ns). 37% of lesions however fitted for cytological evaluation, whereas 34% were inadequate. There were no statistical difference in the pathologists' adequacy score between the standard needle and the ProCore needle (2.3±1.4 and 2.3±1.4 respectively, p:ns). A final diagnosis was reached 84% cases; 66% of the ProCore samples and 67% of the standard needle samples (p:ns; Standard Echo alone versus both: p 0.009; ProCore alone versus both: p 0.005). In 16.5% the diagnosis was reached only on the ProCore sample. No complications were observed.
CONCLUSION: EUS-FNB is feasible and safe, but only in 29% of cases a core sample adequate for histological evaluation was obtained. The success rate in reaching the diagnosis is similar with standard needles and with ProCore needles. However the best results could be reached significantly better with the combination of the 2 type of needle than with EchoTip alone or with ProCore alone (p: 0.009 and p:0.005 respectively) and it seems that the ProCore needle could be useful especially on fibrotic or hard lesions.
Disclosure of Interest: None declared

P0215 NATURAL HISTORY OF PANCREATIC INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS: CLINICAL EVALUATION OF SENDAI CRITERIA IN A LARGE COHORT OF PATIENTS

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INTRODUCTION: Intraductal papillary mucinous neoplasms (IPMN) are mucin-producing, pancreatic cystic tumors, with a long-term potential for progression to adenocarcinoma. The revised "Sendai criteria", based on imaging features, can differentiate the lesions into high and low risk of progression, influencing the patient management. However, few data are still available about clinical management and a better understanding in natural history is critical.
AIMS & METHODS: To evaluate the natural history of IPMN throughout clinical follow-up. Second end-point was to assess the clinical correlation between endoscopic ultrasound features and malignant histology, in order to validate the "Sendai Criteria" in our clinical practice. All the patients with pancreatic IPMN, referred to our tertiary referral center between March 2003 and April 2013 were enrolled in the study. We divided patients into 3 groups, according to Sendai criteria: patients with cysts without signs of malignancy (1), patients with cysts with worrisome features (2) and patients with cysts with high risk stigmata (3). Data were analyzed using uni variate and multivariate logistic regression, to assess the risk factors of malignant progression at diagnosis (T0) and at 2 years of follow up (T2).
RESULTS: 371 patients were enrolled in the study period (171 M, mean age 67 years), with a mean follow up of 38 months from 1 up to 106 months (mean 38 mo). 191/371 (52%) pts presented cysts without signs of malignancy, 105/371 (28%) pts cysts with worrisome features and 75/371 (20%) pts cysts with high risk of malignancy. At multivariate analysis, the features significantly associated with a higher risk of progression at diagnosis included mass size, pancreatic duct dilation ($p < 0.001$), with an accuracy of 78% and a specificity of 88%. Whereas, the features with a significantly higher risk of progression at 2 year-follow up included the pancreatic dilation and the presence of mural nodules (OR 40.01) ($P < 0.001$), with an accuracy of 84% and a specificity of 93%.
CONCLUSION: Our results validated Sendai Criteria in clinical practice. Therefore, patients with no sign of malignancy and unchanged EUS imaging can be followed up with a lengthened interval. Due to a high progression rate, a strict follow up is recommended in pts with worrisome features. Patients with high risk stigmata need surgery at diagnosis.
Disclosure of Interest: None declared

P0216 AUTOMATIC DETECTION OF 'SUSPICIOUS' CAPSULE ENDOSCOPY VIDEO SEGMENTS

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INTRODUCTION: Manual review and annotation of capsule endoscopy (CE) videos requires a considerable amount of reviewing time. Furthermore, the diagnostic accuracy of this process – over lengthy reviewing sessions – may decrease due to reviewer's tiredness. Recent studies showed an average detection rate – for the clinically significant findings – as low as 40%.[1] We present a generic computational framework for automatic detection of abnormalities in CE videos.
AIMS & METHODS: A CE video (MiroCam®, InrtoMedic Co Ltd, Seoul, Korea), depicting inflammatory changes (aphthae, mucosal breaks, ulcers, erythema) was reviewed and manually annotated by experienced CE reader. A total of 1,984 frames, depicting any type of pathology, were thumbnailed. The proposed framework considers video frames as members of a vector space represented by their colour information. An unsupervised data reduction algorithm,[2] which does not require any prior knowledge about the data, was then applied on each segment. This algorithm clusters together frames that exhibit similar characteristics e.g. colour distributions. Its output is a subset of video frames extracted from each cluster by applying a threshold to the clustering result. The extracted frames are characteristic of the particular video segment and as a result representative of possible lesions.
RESULTS: The evaluation of the proposed framework aimed to determine its accuracy, in terms of the ratio of the neighbourhoods represented by at least one frame in the system's output and the neighbourhoods that were manually annotated as suspicious for containing lesions. The parameters considered include clustering from 2 to 6 clusters and thresholds[2] varying from 0.004 to 0.6. The obtained accuracy ranged between 76% and 98% depending on the desired sensitivity level of the algorithm, controlled by the threshold. Furthermore, the automatic selection of the representative CE video segments performed by the proposed approach, the number of video frames to be thoroughly examined can be reduced from 30% to 60% of the original video, depending on the clustering and threshold settings.
CONCLUSION: The application of the proposed framework to the evaluation of CE videos may reduce the rate of false negative evaluations by attracting the attention of the reviewer to automatically identified video segments (or single frames) of interest which are likely to contain lesions.
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P0217 WIRELESS CAPSULE ENDOSCOPE LOCALIZATION BASED ON VISUAL ODOMETRY

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INTRODUCTION: The localization of a wireless capsule endoscope (WCE) within the small-bowel is typically performed by wearable radiofrequency sensors triangulation. The accuracy of this approach is low.[1] Only a few approaches have been proposed for localisation of WCE based on visual features. These include methods addressing the estimation of the rotation angle of the capsule [2,3] & temporal video segmentation methods.[4] We present a WCE localization method, based only on visual information extracted from conventional WCE recording.
AIMS & METHODS: to check the accuracy of visual odometry in WCE with ex-vivo data.
Methods: Automatic detection of points of interest (POI) in WCE video frames, matching of the detected POI between consecutive frames, and determination of actual correspondences between subsets of these POI based on the random sample consensus (RANSAC) algorithm was performed. Instead of the speeded up feature extraction (SURF) algorithm, a maximally stable extremal regions (MSER) algorithm was used. Based on the scaling & the rotation of the content of the consecutive WCE frames, it is possible to estimate the displacement & the rotation of the capsule within the GI tract.
For the ex-vivo experiment a standard simulated intestinal environment was created. Markers were sewn onto the luminal surface of porcine small-bowel through which a capsule endoscope (MiroCam®, IntroMedic Co Ltd, Seoul, Korea) was propelled.
RESULTS: Comparative experiments using both SURF and MSER features, which indicated the superiority of the former over the latter, were conducted. We worked on a corpus of 1070 WCE frames (634 indicating forward motion, 436 indicating backward motion). The accuracy using SURF features was 81.5%

(87.2% on forward motion, 73.2% on backward motion), while using MSER was 67.2% (79.8% on forward motion, and 48.9% backward motion). Noteworthy, the proposed algorithm often fails when using MSER (6.7% of frames while <0.1% when using SURF) and a transform is not estimated due to the lack of adequate correspondences between POI.

CONCLUSION: Visual odometry is a promising technique and -potentially- a feasible alternative to other localization approaches in WCE.

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P0218 UTILITY OF THREE-DIMENSIONAL IMAGE RECONSTRUCTION IN THE DIAGNOSIS OF OESOPHAGEAL VARICES

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INTRODUCTION: Oesophagogastroduodenoscopy (OGD) remains the gold standard for the diagnosis of oesophageal varices (OVs). Oesophageal capsule endoscopy (OCE) is a non-invasive alternative. However, recent studies showed that OCE is lagging behind OGD in diagnostic accuracy [1]; it can be an acceptable alternative though in certain situations such as those who cannot tolerate OGD or are at risk of variant Creutzfeldt–Jakob disease (vCJD)[2]. Application of innovative 3D reconstruction software may improve OCE accuracy in the diagnosis of OVs [3].

AIMS & METHODS: 14 patients, intolerant or with contraindications for conventional OGD e.g. risk for vCJD (for public health purposes), underwent OCE with PillCam®ESO1/2. The OCE video recordings (from one of the 2 CE domes) from the entry in the oesophagus to exit in the stomach were deconstructed to individual frames. Following 3D reconstruction, the frames were stitched back to 3-D videos. Ten reviewers; 6 GI trainees (novice in CE review), 3 GI specialists with experience between 20 and 100 CE reviews and 3 expert CE reviewers read the OCE first in 2-D and then in a GUI (graphic user interface) offering (side-to-side) 2-D & 3-D. Furthermore, the consensus opinion of 3 senior hepatologists, with wide endoscopy experience in patients with liver disease, who reviewed the OCEs with the GUI was used as reference standard (RS). Interobserver agreement for each of the above groups was checked with kappa (κ) statistics.
When the RS for C2 (i.e. varices requiring treatment) was taken into account, the negative predictive value (NPV) of the entire group (10 reviewers) for C2 variceal diagnosis with2-D and 2D+3D was calculated.

RESULTS: The interobserver agreement for the entire group, novice, experienced and experts CE reviewers with 2-D was 0.145, 0.118, 0.125 and 0.025, respectively. The interobserver agreement for the entire group, novices, experienced and expert reviewers with 2-D & 3-D was 0.215, 0.104, 0.222 and 0.372, respectively. For C2 varices diagnosis (RS), the NPV of 2-D and 2-D & 3-D review was 66.6% and 80%, respectively.
Limitations: the use of subjective RS.

CONCLUSION: In oesophageal capsule endoscopy, the use of a GUI that incorporates 2-D and 3-D reconstructed videos leads to improved diagnostic agreement; furthermore, it improves significantly he NPV of OCE for C2 varices.

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P0219 LATERAL-VIEWING CAPSULE ENDOSCOPY EXPERIENCE FROM AN ACADEMIC CENTRE IN SCOTLAND

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INTRODUCTION: CapsoCamS®V1 represents a major departure from conventional 'wireless' capsule endoscopy (CE). This CE system utilises on-board data storage, which necessitates retrieval of the device for data collection. Four lenses in the middle of the device, offering panoramic views of the bowel lumen, have replaced a forward-facing lens. Battery life is also increased to ~15h by virtue of a variable image capture rate. Furthermore, the reviewing software provides 4 rectangular panels in a linear sequence, departing from conventional CE reading software.

AIMS & METHODS: Aim: To report our experience on the clinical use of CapsoCam®SV1 CE.

Setting: An academic hospital, tertiary referral-centre for CE for the South-East of Scotland.

Methods: Retrospective, single centre, observational study.

RESULTS: Since May 2012, 12 patients (4M/8F, mean age: 67.75 ±13.5 years; 8 inpatients) underwent CE with CapsoCam following the standard protocol of our unit. In 80% of patients, the examination was performed for obscure GI bleeding.
The mean time from capsule ingestion to data upload was 5.6 ±8.5 days. Two patients underwent successful endoscopic placement with the AdvanCE® delivery device. The gastric transit time (GTT), small-bowel transit time (SBTT) was 50.9 ±51.2 min and 5.46 ±3.15 h, respectively. The mean total working time for CapsoCam® was 14 ±3 h. Caecal entry was confirmed in 10/12 examinations. The ampulla of Vater (AoV) was visualised in 2/12 i.e. 20% of cases after correcting for quality of bowel prep (10 good). Diagnostic yield for findings was 33.3%.

CONCLUSION: A significant time interval between capsule ingestion and data upload is noted. However, capsule retrieval eliminates the need for radiologic confirmation of capsule excretion in cases of incomplete enteroscopy. The AdvancCE® delivery can be used for CapsoCam® endoscopic placement. The diagnostic yield and the rate of identification of the AoV is comparable to forward-viewing CE devices.

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P0220 OPTIMAL TIMING OF VIDEO CAPSULE ENDOSCOPY IN OVERT OBSCURE GI BLEEDING PATIENTS

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INTRODUCTION: Video capsule endoscopy (VCE) is crucial examination for diagnosis of small bowel bleeding. But diagnostic yield of VCE is 38% to 83% in overt obscure gastrointestinal bleeding (OGIB). For an accurate diagnosis of cause of overt OGIB, the timing to perform VCE is the valuable factor. This study is to investigate the diagnostic yield, rate of therapeutic intervention, and prognosis according to the timing of VCE in the overt OGIB patients.

AIMS & METHODS: We conducted a single center, retrospective study at Korea University Medical Center Anam Hospital from April 2008 to February 2014. Patients who presented overt OGIB with negative result of initial upper and lower endoscopy were enrolled. We compared the diagnostic yield, rate of therapeutic intervention, length of hospital stay, and rate of re-bleeding between patients with VCE performed in ≤48hrs and >48hrs after the occurrence of overt OGIB. We defined positive finding as active bleeding or any cause of small bowel bleeding.

RESULTS: In 111 patients, VCE were performed to evaluate overt OGIB during the period. Among them, 90 patients were included and 21 patients who lacked of medical records were excluded. Diagnostic yield was 65.51% in ≤48hrs group and 35.59% in >48hrs group ($p=0.037$). Therapeutic intervention was done in 45% of the ≤48hrs group and 14% of >48hrs group ($p=0.006$). The average day of hospital stay was 5.48 days in ≤48hrs group and 8.18 days in >48hrs group ($p=0.005$). Re-bleeding rate between the ≤48-hrs group and >48-hrs group was not significantly different.

CONCLUSION: Early VCE deployment within 48hrs of last overt OGIB may improved the diagnostic yield, rate of therapeutic intervention and decreased the length of hospital day.

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P0221 THROMBOCYTOSIS AND HIPOALBUMINEMIA: A PRIORITY PASS FOR CAPSULE ENDOSCOPY IN CROHN'S DISEASE?

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) may identify small bowel lesions in a large proportion of patients with Crohn's disease (CD).
AIMS & METHODS: To identify predictive factors of small bowel involvement in a cohort of patients with CD. Transversal multicenter study including consecutive patients with CD affecting the small bowel over a period of eight years. Small bowel inflammatory activity at SBCE was assessed with the Lewis Score (LS), and it was considered clinically relevant if LS≥135. Univariate analysis and multivariate regression of patients' baseline clinical, analytical and endoscopic (index ileocolonoscopy) variables were performed to identify pre-test predictors of relevant (LS≥135) lesions at SBCE in patients with known or suspected CD.
RESULTS: A total of 158 patients were included, 58% female, mainly with ileal (42%) or ileocolic (39%) location at ileocolonoscopy, non-stricturing non-penetrating behaviour in 74% of cases. SBCE lesions were non-significant (LS < 135) in 34 (22%) patients, mild (135≤LS < 790) in 68 (43%) and moderate to severe (LS > 790) in 55 (35%). Lesions were located in the first tertile of the small bowel in 38 (24.1%) patients, second tertile in 48 (30.4%) and third tertile in 113 (71.5%) patients. Multivariate regression identified thrombocytosis [OR 1,012 (95% CI: 1.002-1.022), p = 0.019] and low serum albumin [OR 0.803 (95% CI: 0.663-0.971), p = 0.023] as independent variables predictive of small bowel CD, [ROC = 0.846 (0.767-0.925)]. Clinical features, endoscopic distribution of the disease at ileocolonoscopy, and biomarkers such as anaemia or C-reactive protein were not predictive of SBCE lesions.
CONCLUSION: In patients with known or suspected CD, thrombocytosis and/or hipoalbuminemia are predictive of active small bowel inflammation at SBCE. Whether these biomarkers should play a role in the selection of patients for SBCE warrants further prospective evaluation.
Disclosure of Interest: None declared

P0222 DOES CAPSULE ENDOSCOPY WITH ALICE IMPROVE VISIBILITY OF SMALL BOWEL LESIONS?

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INTRODUCTION: ALICE (Augmented Live-body Image Color-spectrum Enhancement) refers to a spectral imaging technique for the MiroView (TM) system to perform medical tests through capsule endoscope (CE) system, where light of specific blue, green, and red wavelength is used to enhance the detail of certain aspects of the surface of the mucosa, but the data was limited.
AIMS & METHODS: This study is to evaluate the visibility of CE-ALICE depending on type of small bowel lesions.
A total of 50 patients who underwent CE at Soon Chun Hyang Bucheon Hospital from August 2008 to November 2011 were enrolled in this study. The lesions were classified as elevated (tumor and polyp, n = 5), flat (angiodysplasia and erosion, n = 18), depressed (ulcer, n = 27) lesions. Two experienced endoscopists analyzed CE-ALICE images obtained at setting 1-10 (setting 1: red 415 nm, green 415 nm, blue 540 nm; setting 2: red 415 nm, green 445 nm, blue 500 nm; setting 3: red 420 nm, green 470 nm, blue 500 nm; setting 4: red 400 nm, green 445 nm, blue 450 nm; setting 5: red 420 nm, green 480 nm, blue 540 nm; setting 6: red 420 nm, green 480 nm, blue 500 nm; setting 7: red 400 nm, green 500 nm, blue 450 nm; setting 8: red 455 nm, green 455 nm, blue 500 nm; setting 9: red 500 nm, green 455 nm, blue 455 nm; setting 10: red 455 nm, green 500 nm, blue 455 nm) compared with conventional images. Physicians rated the visibility of the lesions on ALICE images as follows: _2(improved visibility), _1 (somewhat improved visibility), 0 (visibility equivalent to that of conventional video CE visibility), _1 (somewhat decreased visibility), and _2 (decreased visibility). Scores for each lesion were totaled (per ALICE setting) and evaluated. Intraobserver agreement was also examined.
RESULTS: In elevated lesion (n = 5), with setting 2, 3, 4, 5, 6, 7, 9, 10, improvement was achieved but not significantly statistical (NS). In flat lesion (n = 18), with setting 3, 5, 10, improvement was achieved statistically for 100% (18/18), 100% (18/18), 100% (18/18) (p < 0.01). In depressed lesion (n = 27), with setting 2, 3, 6, 10, improvement was achieved statistically for 89% (24/27), 93% (25/27), 93% (25/27), 85% (23/27)
CONCLUSION: CE-ALICE improves visibility of flat and depressed lesion in small bowel.
Disclosure of Interest: None declared

P0223 UTILITY OF FECAL CALPROTECTIN IN THE EVALUATION OF PATIENTS WITH CROHN'S DISEASE CANDIDATES FOR CAPSULE ENDOSCOPY: PRELIMINARY RESULTS

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) is an expensive but useful imaging method in the diagnosis and extension of Crohn's disease (CD). Symptomatology and acute phase reactants (CRP and ESR) are not correlated with the presence of endoscopic activity in small Bowel. Fecal calprotectin (FC) is a biomarker that correlates well with small bowel inflammation.
AIMS & METHODS: The aim of our study is to assess if fecal calprotectin correlates with the presence of endoscopic activity in small Bowel, evaluated by capsule endoscopy (Lewis Score).
We included prospectively patients with suspected or diagnosed Crohn's disease referred for capsule endoscopy. All of them were submitted to SBCE and a measure of FC, ESR, and CRP. CDAI was also registered.
RESULTS: For this preliminary analysis, 30 patients were included (17 females and 13 males), mean age 38 +/- 13 years. The indication for capsule endoscopy was suspected CD (7 patients), extension study of the illness and/or lack of response to treatment (21 patients) and mucosal healing assessment (2 patients). One patient was excluded for the analysis because of the capsule was retained in stomach temporarily. Only 10% of patients had FC levels less than 100 mcg/g, two of them with no lesions in capsule endoscopy. FC levels higher than 100 mcg/g correlated more closely with the presence of lesions in capsule endoscopy (p = 0.006).
In our study, there is a slight but positive correlation between FC levels and Lewis Score (r = 0.4; p = 0.02). There is no correlation between clinical symptoms, CRP or ESR, and the presence of lesions in the capsule endoscopy.
CONCLUSION: Fecal Calprotectin seems to be useful in identifying patients with Crohn's Disease and small bowel involvement. It can be a good tool to select patients for performing capsule endoscopy
Disclosure of Interest: None declared

P0224 ABSENCE OF MUTUAL INTERFERENCE BETWEEN MIROCAM CAPSULE ENDOSCOPY, PACEMAKERS AND IMPLANTABLE CARDIAC DEFIBRILLATORS: A CLINICAL ELECTROPHYSIOLOGICAL STUDY

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INTRODUCTION: Capsule endoscopy (CE) has recently become one of the most important tools for small bowel investigation. Once swallowed by the patient, Mirocam capsule transmits images from the gut to an external recorder by the Human Body Communication (HBC) system. HBC uses the capsule itself to generate an electrical field and uses the human body as the conductor for data transmission. Because of the creation of an electric field, a potential electromagnetical interference with implantable cardiac devices has been postulated, so their presence is considered a relative contraindication for CE. Whereas some safety data are available about Given M2A capsule in patients with pacemakers (PM) and automatic implantable cardiac defibrillators (AICD), studies in this field regarding Mirocam capsule are lacking.
AIMS & METHODS: We report the use of Mirocam video capsule system (Intromedic Co Ltd, Seoul, Korea) in 6 patients with PM and in a patient with AICD over a 2-years period. Patients swallowed the capsule in the morning after a overnight fast; a bowel cleansing with 2 litres of polyethylene glycol (PEG) solution was administered in the afternoon before the procedure. All patients gave their written informed consent. Three different type of PM from 2 manufacturers (Altura and Insignia Ultra from Boston Scientific Corporation, Esprit from Sorin) and Atlas AICD from St. Jude Inc. were tested. A full technical control of the cardiac devices was performed by electrophysiologists before CE examination, using a manufacturer-specific programmer. This technical control included the evaluation of the following parameters: battery charge, shock impedance, leads impedance and sensing, leads pacing threshold, arhythmic events. After a cardiac visit and electrocardiogram (ECG), each patient was placed in Cardiac Care Unit. AICD electrical therapies were switched off just before capsule ingestion. During CE the patients were continuously monitored with cardiac telemetry, performed by Mortara X12 device (Mortara Instrument Inc., U. S. A.). At the end of the endoscopic procedure, before discharge, the patients repeated cardiac evaluation, ECG and a complete cardiac device check. The following characteristics were analyzed: changes in device parameters, inappropriate shocks, inappropriate anti-tachycardia therapy, inappropriate sensing or pacing, noise detection, device reset, programming changes, permanent electrical damages. CE records were reviewed by a skilled endoscopist.
RESULTS: For 6 patients indication for CE was obscure gastrointestinal bleeding (OGIB), in one was follow up of intestinal polyposis. Mean age was 74 years; all the patients were males. Capsule reached ileo-cecal valve in all except two cases. No complications related to capsule transit were observed. No technical problems related to imagine transmission were recorded. Causes of OGIB were found in 50% of cases. No polyps were found in patient with polyposis. No cardiac devices malfunctions nor interference in sensing or pacing were recorded; conversely, no malfunctions of CE caused by PM or AICD were registered.
CONCLUSION: Our results suggest that Mirocam capsule endoscopy can be safely performed in patients with different types of implantable cardiac devices.
Disclosure of Interest: None declared

P0225 SELF-EXPANDABLE METAL STENTS VERSUS PLASTIC STENTS FOR MALIGNANT BILIARY OBSTRUCTION: CLINICAL OUTCOME AND COST-EFFECTIVENESS IN POLISH ECONOMIC CIRCUMSTANCES

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INTRODUCTION: Most patients with malignant biliary obstruction are suited only for palliation of jaundice by endoscopic placement of a plastic stents (PS) or self-expandable metal stents (SEMS). The initial higher cost of the SEMS is considered to be balanced by a decreased need for repeated interventions.
AIMS & METHODS: To compare the clinical outcome and costs of biliary stenting with SEMS and PS in patients with malignant biliary strictures. A total of 114 pts (63F, 51M) who underwent 366 endoscopic retrograde biliary drainage (ERBD) for palliation of unresectable malignant biliary obstruction between 2009 and 2014 were retrospectively enrolled into the study.
RESULTS: ERBD with placement of PS was performed in 80 patients, with one-step SEMS insertion (direct placement without a prior plastic stent) in 20 patients and two-step SEMS insertion (placement of SEMS at second or consecutive endoscopic retrograde cholangiopancreatography following plastic stent placement, e.g. SEMS after PS) in 14 patients. Significantly less endoscopic procedures were performed in patients with one-step SEMS than PS alone and two-step SEMS technique (2.0±1.12, 3.1±1.7 and 5.7±2.1 respectively, $p<0.0001$). The median hospitalization time was similar for three groups of patient. The patients survival was longest in SEMS after PS group in comparison to SEMS group and PS group (596.2±270d, 276.1±141d and 207.5±219d, $p<0.001$). Overall median stent patency was 89.3±159 d for PS and 120.6±101 for SEMS ($p=0.01$). Stent dysfunction occurred more frequently in PS group than in SEMS groups (76.8% vs. 62.8%, $p=0.05$). No significant difference between the two stent types in terms of technical success and complications was observed. The mean total cost of hospitalization with drainage procedures was higher for SEMS group, then for SEMS after PS group and finally for PS group (1448±312€, 1152±135€ and 977±156€, $p<0.0001$). Estimated annual cost of subsequent ERBD due to recurrent biliary obstruction would be still higher for SEMS group than for PS group (4618€ vs. 3995€). Metal stents would be cost-effective if their patency exceed 202 days.
CONCLUSION: Biliary decompression by metal stents in patients with malignant jaundice is associated with longer patency and reduced number of additional biliary procedures, but repeated plastic stents' drainage is still more cost-effective strategy.
Disclosure of Interest: None declared

P0226 OUTCOMES OF PRIMARY AND REVISION EFFICACY OF COMBINED METALLIC STENTS IN MALIGNANT DUODENAL AND BILIARY OBSTRUCTIONS

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INTRODUCTION: Self-expandable metal stents (SEMSs) can be used for palliation of combined malignant biliary and duodenal obstructions. However, the results of the concomitant stent placement for the duration of the patients' lives, as well as the need for and efficacy of endoscopic revision, are unclear.
AIMS & METHODS: This study evaluated the clinical effectiveness of SEMS placement for combined biliary and duodenal obstructions throughout the patients' lives and the need for endoscopic revision. This study is a retrospective multicenter study of 50 consecutive patients who underwent simultaneous or sequential SEMS placement for malignant biliary and duodenal obstructions. The data were collected to analyze the sustained relief of obstructive symptoms until the patients' death and the efficacy of endoscopic revision, as well as stent patency, adverse events, survival and prognostic factors for stent patency.
RESULTS: Technical and immediate clinical success was achieved in all of the patients. Duodenal stricture occurred before the papilla in 35 patients (70%), involved the papilla in 11 patients (22%) and was observed distal to the papilla in 4 patients (8%). Initial biliary stenting was performed endoscopically in 42 patients (84%) and percutaneously in 8 patients. After combined stenting, 30 patients (60%) required no additional intervention until the time of their death. The remaining 20 patients were successfully treated using endoscopic stent reinsertion: 9 patients needed biliary revision, 3 patients needed duodenal restenting and 8 patients needed both biliary and duodenal reinsertion. The median duodenal stent patency and median biliary stent patency were 34 weeks and 27 weeks, respectively. The median survival after combined stent placement was 12 weeks. A Cox multivariate analysis showed that duodenal stent obstruction after combined stenting was a risk factor for biliary stent obstruction (Hazard ratio = 6.85; 95% CI = 1.43-198.98; $P=0.025$).
CONCLUSION: Endoscopic bilio-duodenal bypass is clinically effective, and the majority of the patients need no additional intervention until their death. Endoscopic revision is feasible and has a high success rate.
Disclosure of Interest: D. Carvalho: None declared, J. Canena Consultancy for: Boston Scientific, J. Coimbra: None declared, C. Rodrigues: None declared, M. Silva: None declared, M. Costa: None declared, D. Horta: None declared, A. Mateus-Dias: None declared, I. Seves: None declared, G. Ramos: None declared, L. Ricardo: None declared, A. Pereira Coutinho: None declared, C. Romão: None declared

P0227 TEMPORARY ENDOSCOPIC INSERTION OF UNILATERAL OR BILATERAL COVERED SELF-EXPANDABLE METAL STENTS (CSEMS) ABOVE THE HEPATIC DUCT CONFLUENCE FOR BENIGN BILE-DUCT DISEASE

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INTRODUCTION: cSEMS appear to enhance therapeutic efficacy for benign distal bile-duct strictures and leaks. Concerns over the use of cSEMS above the hepatic duct confluence remain since clinical data are very limited. Aim: To assess the feasibility and efficacy of cSEMS placement proximal to the hepatic duct confluence in benign disease.
AIMS & METHODS: Retrospective analysis of prospectively databased patients undergoing ERCP over a 10-month period at referral Unit. 34 Consecutive Patients (17 female; age 59 [32-87] years) underwent biliary cSEMS placement across the hilum for benign disease. Underlying diagnosis, number and type of cSEMS, presence of associated plastic stents, indication for cSEMS (primary vs. failed prior plastic stenting), duration of stenting, ease of removal, procedural & stent related complications, and final therapeutic outcome were determined.
RESULTS: Diagnoses: 28 biliary strictures (13 postcholecystectomy, 11 post-liver transplant, 4 undetermined) and 6 miscellaneous (2 high output fistulas, 2 with prior embedded uncovered SEMS, 1 sump syndrome, 1 primary sclerosing cholangitis). In 19.4%, 2 or 3 biliary cSEMS were placed. The contralateral hepatic duct was stented with a plastic stent in 80.6%. Transhilar biliary cSEMS were indicated primarily in 14 (41%) and as salvage of prior standard plastic stenting in the remainder 20. CSEMS used were all 10mm in diameter, Hanaro 23, Wallflex 8, Bonastent 2, Taewoong 1. There were 2 procedural complications related to cSEMS, one moderate cholangitis secondary to hepatic branch occlusion (requiring cSEMS removal), and one mild (pain requiring IV analgesia >24 hours). After a mean duration of stenting of 5.3 (1-15) months, removal was attempted in 64.3% and was technically successful in all 20 cases despite 4 partial migrations (3 proximal/ 1 distal; 2 with cholangitis, 2 asymptomatic). Strictures/leaks were successfully remodeled/controlled upon removal in 19/20 (1 persistent leak), pending long-term follow-up. 11 patients are still undergoing cSEMS replacement. Transient enlargement of the intrahepatic bile-duct was documented in 12/31, without any adverse clinical consequences. Overall complication & short-term success rates are 13% & 95%.
CONCLUSION: If the contralateral hepatic duct is stented and ipsilateral secondary radicals spared, transhilar cSEMS placement appears safe. Refractory benign disease can successfully be salvaged with this aggressive approach, with an acceptable safety profile. Transient intrahepatic duct enlargement was noted. This encouraging preliminary data warrant further study as the long-term efficacy and reproducibility of this approach remain in question.
Disclosure of Interest: None declared

P0229 PREOPERATIVE BILIARY DRAINAGE WITH A MODIFIED FULLY COVERED SELF-EXPANDABLE METALLIC STENT FOR POTENTIALLY RESECTABLE DISTAL MALIGNANT BILIARY OBSTRUCTION

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INTRODUCTION: Early biliary decompression is indicated for cholangitis in patients with malignant biliary obstruction (MBO). However, preoperative biliary drainage using plastic stents may increase the need of reintervention and perioperative complications. We evaluated the usefulness of a removable fully covered self-expandable metallic stent (FCSEMS) modified to minimize stent-induced complications in preoperative biliary drainage for potentially resectable distal MBO.
AIMS & METHODS: From January 2009 to Agust 2013, a total of 51 patients underwent biliary drainage using a modified FCSEMS (BONASTENT M-Intraductal, Standard Sci Tech Inc, Seoul, Korea) for suspicious distal MBO that was potentially resectable or on stage work-up. Further treatment was decided according to the final assessment; (1) curative intent surgery, (2) neoadjuvant chemoradiation, (3) palliative treatment with/without chemoradiation, or (4) removal of stent for finally proved benign biliary stricture.
RESULTS: The overall technical and clinical success rates of the biliary drainage using a modified FCSEMS were 100% (51/51). Complications related with stenting were developed in 5 patients (1 mild pancreatitis and 4 stent migrations). Final diagnosis was 46 MBS (24 pancreatic head cancers, 18 CBD cancers, 3 gallbladder cancers and 1 ampullay cancer) and 5 benign biliary strictures (3 chronic pancreatitis and 2 autoimmune pancreatitis). 19 patients had undergone curative intent pancreaticoduodenectomy. 3 patients had undergone surgical resection after neoadjuvant chemotherapy. No stent-induced postoperative complication occurred. The median stent patency in patients who had undergone palliative treatment was 148 days (range, 73-256). Removal of the stent was successful in all patients confirmed finally benign biliary strictures.
CONCLUSION: The modified FCSEMS may be effective for first line of biliary drainage in patients with potentially resectable distal MBO without interfere for further intervention.
Disclosure of Interest: None declared

P0230 DOES CHEMOTHERAPY PROLONG THE STENT PATENCY IN MALIGNANT DISTAL BILIARY STRICTURE?

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INTRODUCTION: Metallic stents for malignant distal biliary stricture have become one of the best palliative treatments in inoperative cases who were generally treated by chemotherapy; however its influence in stent patency has not been investigated and consensus is not established.
AIMS & METHODS: From 2002 to 2013, we have inserted metallic stents in totally 259 cases with malignant distal biliary stricture, and treated 164(63%) caes with chemotherapy and remaining 95(37%) cases with best supportive care (BSC). We investigated the efficacy of chemotherapy in its stent patency etc. retrospectively.
RESULTS: Subjects in this study were consisted of 206 (80%) pancreas cancers, 45(14%) biliary cancers, and 8(3%) papillary cancers. Metallic stents we used were 152(59%) partially covered Wallstents (P-WS), 54(21%) partially covered Wallflexs (P-WF), 34(13%) fully covered Wallflexs (F-WF), and 19(7%) fully covered Bonastents (F-BS). There was no significant difference on base line characteristics between chemotherapy group and BSC group except for age (68 vs 74 years olds). Chemotherapy we employed was Gemcitabine (GEM) alone, GEM +TS-1, and GEM+TS-1+CDDP etc. The median stent patency was 328 days in total, and the median stent patency of chemotherapy group was significantly longer (354 days vs188 days in BSC, $p = 0.001$). The median stent patency of biliary cancer in chemotherapy group was significantly longer (341 days vs 119 days in BSC, $p = < 0.001$), whereas the median stent patency of pancreas cancer in chemotherapy group was not significant.
CONCLUSION: We concluded that chemotherapy prolong the stent patency in malignant distal biliary stricture, especially biliary cancers.
Disclosure of Interest: None declared

P0231 ENDOSCOPIC DOUBLE SELF-EXPANDING METAL STENT PLACEMENT FOR THE TREATMENT OF MALIGNANT BILIARY AND GASTRODUODENAL OBSTRUCTION: A LARGE SERIES OF TREATED PATIENTS FROM A REFERRAL HOSPITAL FOR PALLIATIVE CARE

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INTRODUCTION: Patients with malignant gastroduodenal obstruction often have coexistent biliary obstruction and require simultaneous endoscopic treatment. The use of self-expandable metal stents (SEMS) is an effective palliative treatment in patients with unresectable malignant gastroduodenal and biliary obstructions.
AIMS & METHODS: The aims of this study are to evaluate the efficacy and safety of double SEMS placement in a large consecutive series of patients with malignant inoperable gastroduodenal and biliary obstruction. From March 2007 to March 2014 we collected data on all consecutive patients treated with double SEMS placement (Wallflex Enteral and Biliary by Boston Scientific, Niti-S Biliary by Taewoong). SEMS were placed under fluoroscopic and endoscopic guidance. First the scope was allowed to reach the duodenal stricture, then a guidewire equipped with an imaging catheter was passed through the stricture allowing the deployment of the duodenal SEMS. The duodenoscope was passed through the duodenal stent for accessing the papilla through the mesh of the SEMS. After common bile duct cannulation and cholangiography a guidewire was placed across the papilla. A balloon dilation to enlarge the spacing of the tight mesh of the duodenal stent was performed allowing the placement of the biliary SEMS. If possible balloon dilation of the duodenal stricture was performed allowing the deployment of the biliary SEMS before duodenal SEMS placement. Technical and clinical success, and adverse events were recorded.
RESULTS: 31 patients (20 male [65%]), with a mean age of 73.6±9.8 year, were treated: 27 had pancreatic head cancer (87%), 2 antro-bulbar cancer (7%), 1 cholangiocarcinoma (3%), 1 duodenal obstruction due to colon cancer (3%). The mean baseline bilirubin level and the median gastric outlet obstruction scoring system (GOOSS) score were 16.7±3.8 mg/dL and 1 (range 0-3) respectively. Technical success was achieved in all patients with significant reduction in bilirubin levels (8.4±3.2 mg/dL) and a satisfactory oral feeding at discharge (GOOSS score 3 [range 2-3]). No complications related to the SEMS placement were recorded. Biliary stent occlusion occurred in 2 patients (6%) after 3 and 10 months. In 1 patient (3%) migration of the biliary stent was recorded after 5 months. The median hospital stay was 4 days (range 3-8) with a median survival time of 6 months (range 3-8). All deaths were due to the natural course of underlying malignancy.
CONCLUSION: Endoscopic management of malignant gastroduodenal and biliary obstructions with double SEMS placement is the treatment of choice in advanced unresectable gastroduodenal tumors with biliary involvement too. It is a safe procedure and it enhances patients' quality of life. In advanced diseases or in frail patients palliative surgery should be considered only in case of endoscopic failure.
Disclosure of Interest: None declared

P0232 COMPARISON OF OUTCOMES BETWEEN INTERNAL STENT PLACEMENT AND PTBD IN PATIENTS WITH PLANNED CRT FOR PERIHILAR CHOLANGIOCARCINOMA

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INTRODUCTION: The optimal biliary decompression method in resectable perihilar-cholangiocarcinoma has been authorized as percutaneous transhepatic biliary drainage (PTBD). In case of locally advanced perihilar-cholangiocarcinoma, malignant biliary obstruction is judged to have palliation of jaundice by placement of an internal stents or PTBD. We aimed to investigate the efficacy of internal placement of biliary stent compared with PTBD for patients planned CRT in locally advanced perihilar-cholangiocarcinoma.
AIMS & METHODS: The patients who are histologically proven locally advanced perihilar-cholangiocarcinoma between Jan. 1995 and Dec. 2013 at single tertiary medical center in Korea, analyzed as prospective observational study. The perihilar cholangiocarcinoma was defined as disease occurring above the junction of the cystic duct up to the secondary branches of the hepatic duct.
RESULTS: Among one hundred seventy six locally advanced perihilar-cholangiocarcinoma patients, CRT was performed in 79 patients; endoscopic biliary decompression was forty six patients (26.14%), and PTBD was thirty three patients (18.75%). The mean period of internal stent indwelling is 152 days whereas 222 days in PTBD group ($p = 0.675$). The R0 operative rate after the CRT was 23.9% in endoscopic stenting group, and 12.1% in PTBD group ($p = 0.174$). The median overall survivals were 463 days at endoscopic stenting group and 439 days in PTBD group, respectively ($p = 0.874$). Repeated biliary decompression procedure was performed at endoscopic decompression group 26 patients (56.5%), 12 patients in PTBD group (36.4%) ($p = 0.077$).
In the subgroup analysis of endoscopic stenting group, there were 25 cases of SEMS, and 21 cases of biliary drainage using the plastic stent. The stent dysfunction was found in 20 patients (80.0%) with plastic stent and 6 patients (28.6%) in SEMS group ($p = 0.001$). Median stent patency time was 111 days and 402 days in the plastic stent and SEMS, respectively ($p = 0.002$). Post-operative major complications were not seen in both cases.
CONCLUSION: The endoscopic placement of internal stent might be useful method for biliary decompression in patients with planed CRT for locally advanced perihilar-cholangiocarcinoma, compared to PTBD. In case of biliary endoscopic drainage, the pre-CRT SEMS had lower rate for repeated endoscopic procedure than plastic stent in perihilar-cholangiocarcinoma.
Disclosure of Interest: None declared

P0233 ENDOSCOPIC OESOPHAGEAL STRICTUROTOMY AS PROMISING MODALITY IN THE TREATMENT OF BENIGN RESISTANT OESOPHAGEAL STRICTURES

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INTRODUCTION: The majority of benign oesophageal strictures result from long-standing gastroesophageal reflux disease. Treatment usually involves dilation combined with acid-suppressive therapy. Other causes of resistant strictures include post radiation, oesophageal sclerotherapy, caustic ingestions and surgical anastomosis. In the majority of patients, this can be accomplished with oesophageal dilation, though in cases of refractory strictures, additional therapy is required. There is little published data on the treatment of resistant esophageal strictures (ROS).
AIMS & METHODS: To describe our experience with Endoscopic Oesophageal Stricturotomy (EOS) for resistant oesophageal strictures. From January 2012 to July 2013 all patients with oesophageal strictures resistant to treatment with balloon dilatation +/- bougienage were selected for EOS. Data on Age, sex, co-morbidity, clinical presentation, procedural details, and outcome were retrospectively collected, anonymized, and analized. Endoscopic Oesophageal Stricturotomy procedures were exclusively done by an experienced endoscopist (M. B.). Patient with resistant strictures were assessed for suitability for Stricturotomy. Using Needle knife stricturotome (RX Needle Knife Boston scientific/ 5.5 F/1.8mm) Four quadrant incisions were made and tissue excised. Stricturotomy was followed by hydrostatic balloon dilatation if residual stenosis was present.
RESULTS: A total of five male dysphagic patients, median age 58, (range 29-81), with resistant oesophageal strictures were treated with EOS, during the study period. Two patients had strictures due to peptic fibrosis, two due to exposure to radiotherapy, and one had post surgery for oesophageal atresia. 80% (4/5) had multiple previous trials of unsuccessful balloon. One session of Stricturotomy was enough for 80% of patients, however, for one patient (20%) EOS were needed to be repeated 5 times. Only 40% (2 patients) needed balloon dilatation following the EOS. In all patients, successful response following initial EOS was obtained.
CONCLUSION: EOS is highly effective in treating selected patients with resistant benign oesophageal strictures. Initial response has been achieved to all five patients, refractory oesophageal stricture was noted in one patient, that has finally showed good response after the 5th Stricturotomy session. Short focal strictures may be more suitable for EOS. The risk of perforation following EOS is not yet known, and needs to be elucidated in longer studies. Stricturotomy is a valuable method in the treatment of patients with resistant oesophageal strictures.

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Disclosure of Interest: None declared

P0234 LONG-TERM COMPLICATIONS OF SELF-EXPANDABLE METALLIC STENT IN PATIENTS WITH ADVANCED ESOPHAGEAL CANCER

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INTRODUCTION: Self-expandable metallic stents (SEMS) are considered the best palliative treatment of dysphagia of patients with advanced esophageal cancer. Complications are a major concern, especially in patients with better prognosis and longer survival.
AIMS & METHODS: The aim of this study was to assess the prevalence of SEMS-related complications in the follow-up of patients with advanced esophageal cancer who survived longer than 6m. We performed a retrospective analysis of a prospective collected database of patients with advanced esophageal cancer submitted to SEMS palliation between February 2009 and December 2012 at the Cancer Institute of the University of São Paulo. Patients with follow-up longer than 180 days were included in this study.
RESULTS: Of the 145 patients from the database, 32 were selected. There was a predominance of male patients (78.1%), mean age of 60 years with squamous cell carcinoma (78.1%). The lesions were mainly located in the middle esophagus (53.1%). Twenty-nine stents were partially covered (90.6%) and three completely covered (9.4%). Twenty-two (68.7%) patients received chemo and/or radiotherapy before and 26 (81.2%) patients after SEMS insertion. Complications occurred in 20 patients (62.5%): migration (n = 9), overgrowth (n = 8), ingrowth (n = 4), fistula (n = 3), pulmonary infection (n = 2), food impaction (n = 2), GERD (n = 1), bleeding (n = 1) and intractable pain (n = 1). Most complications could be managed endoscopically. Fatal complications occurred in 2 (6.2%) patients: 1 bleeding and 1 pulmonary infection. The median survival after prosthesis was 305 days (range 182-630 days). A mean of 0.9 procedures per patient (range 0-10) were performed to maintain stent patency. At the end of the follow-up, 20 patients still had a functional stent, while 12 patients had either retrieved the stent or received a nasogastric tube.
CONCLUSION: The use of SEMS in patients with advanced esophageal cancer who live longer than 6m is associated with high complication rate. Most complications are usually nonfatal and are managed endoscopically.
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Disclosure of Interest: None declared

P0235 RISK FACTORS FOR METALLIC STENTS MIGRATION IN PATIENTS WITH ADVANCED ESOPHAGEAL CANCER

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INTRODUCTION: Migration is one of the most common complications after stent placement to palliate dysphagia in patients with inoperable esophageal neoplasia. It occurs in up to 36% of the cases, so it would be useful to recognize risk factors associated with this complication as preventive measures could be taken to prevent it.
AIMS & METHODS: The aim of this study was to identify risk factors for esophageal stents migration in patients with advanced esophageal cancer.
From 2009 to 2012, patients with advanced esophageal neoplasia who underwent SEMS placement were followed prospectively and data were collected to evaluated risk factors associated with stent migration. Patients with less than 1 month follow-up were excluded from the study.
RESULTS: A total of 145 patients with a median age of 63 years (SD±10) and male predominance (79.3%) were enrolled in the study. The most common histology was squamous cell carcinoma (109 cases, 75%) followed by adenocarcinoma (24 cases, 16.5%), and extra-esophageal cancer (12 cases, 8.5%). The lesion was located in the distal third of the esophagus in 54 (37.2%), in the mid-esophagus in 70 (48.3%) and in the proximal esophagus in 21 (14.5%) patients. Mean tumors length was 7.5cm (SD = ±2.8cm). Fifty-nine (40.7%) patients received chemoradiation prior and 13 (9.0%) after the stent implantation. Partially covered stents were placed in 135 (93%) pts and fully covered SEMS were placed in 10 (7%) pts. Evolution (n = 69, 47.5%), Hanaro (n = 44, 30.3%), Endoflex (n = 13, 9%), Wallflex (n = 12, 8.2%), Plastimed (n = 6, 4.2%) and Ultraflex (n = 1, 0.8%) stents were used. After a median follow-up of 156 days (range: 31– 630 days), the migration rate was 13.1% (19 patients, range: 1-323 days). The mean survival rate after the procedure was 146 days. Univariate analysis showed that fully covered stents (p = 0.049) and body stent diameter measuring less than 20mm (p = 0.004) were significantly associated with higher migration rate.
CONCLUSION: Fully covered stents and stents with body diameter measuring less than 20mm are associated with higher migration rate.
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Disclosure of Interest: None declared

P0236 ENDOSCOPIC ULTRASOUND (EUS) GUIDED SELF EXPANDING METAL STENTS (SEMS) PLACEMENT FOR GASTRIC OUTLET OBSTRUCTION

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INTRODUCTION: SEMS placement is an effective way of relieving gastric outlet obstruction, majority of them done endoscopically under fluroscopy guidance. This is known to be superior to surgical bypass with lower morbidity, mortality, and shorter hospital stay[1,2]. At times, despite direct vision through the endoscope and fluroscopy guidance, it can be difficult or unmanageable to position a SEMS
AIMS & METHODS: To evaluate use of EUS as an adjunct to safely and effectively delineate lumen through the obstructing lesion and place SEMS through EUS scope with / without fluroscopy guidance. All procedures were done using Olympus linear scope (GF-UCT240) and Evolution (Cook Medical) SEMS were used (22x 60-120mm).
RESULTS: Between February 2010 to November 2011, 15 patients had duodenal/enteral SEMS placement using EUS. All patients had prior CT scan and endoscopy. All had successful stent placement using EUS technique, when it was not possible to be done by endoscopic view supplemented with fluroscopy guidance in previous or done as tandem procedures in same sitting. One patient had 2 stents placed, one in afferent loop endoscopically and another one in efferent loop with help of EUS.
One patient had perforation, stent was placed successfully across a tight angulated stricture but caused tear as it expanded across the angulated obstruction, which was managed surgically.
Endoscopic implantation of SEMS in a malignant gastric outlet obstruction is a safe and effective method. However, any obstruction beyond direct access of scope, presence of food/liquid debris and some times contact bleeding obscuring views are impediments in successful implantation of a stent. Most of the time this is due to inability to visualise/delineate the lumen beyond direct vision even with help of fluroscopy. There is high risk of false passage formation/perforation if wire/catheter are advanced blindly. EUS has an added advantage of visualising lumen even in above circumstances, especially when endoscopic views are poor.
CONCLUSION: This is first ever case series reporting use of EUS in gastroduodenal SEMS placement. We believe this is useful adjunct to existing techniques. However, this needs to be evaluated further in larger comparative studies. As with any other complex intervention, this is highly dependent on experience of the operator in endoscopic stent placement as well as EUS modality.
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P0237 EFFICACY AND SAFETY OF A PARTIALLY COVERED DUODENAL STENT FOR MALIGNANT GASTRODUODENAL OBSTRUCTION

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INTRODUCTION: Duodenal stent placement has emerged as an effective and safe palliative treatment for patients with malignant gastroduodenal obstruction. The uncovered enteral stent is susceptible to re-stenosis due to tumor ingrowth. Although covering an enteral stent with a membrane almost solves the problem of tumor ingrowth, stent migration continues to be a major unresolved problem. Recently, a partially covered metallic stent was introduced for gastroduodenal obstruction.
AIMS & METHODS: Duodenal stent placement has emerged as an effective and safe palliative treatment for patients with malignant gastroduodenal obstruction. The uncovered enteral stent is susceptible to re-stenosis due to tumor ingrowth. Although covering an enteral stent with a membrane almost solves the problem

of tumor ingrowth, stent migration continues to be a major unresolved problem. Recently, partially covered metallic stent was introduced for gastroduodenal obstruction. Twenty patients with malignant gastroduodenal obstruction received palliative treatment with partially covered duodenal stents. Technical success was defined as the placement of the stent successfully. Clinical success was defined as the relief of obstructive symptoms and/or improvement of the Gastric Outlet Obstruction Scoring System score to ≥ 2 after the procedure.
RESULTS: A total of 20 patients (11 men and 9 women; median age 64.5 years, range 39-85 years) were enrolled in this study. Ten patients had pancreatic cancer, four patients had gallbladder cancer, two had cholangiocarcinoma, one had advanced gastric cancer, one had metastatic rectal cancer, one had liver sarcoma, and one had ampulla of Vater cancer. Stent placement was successful in 20 of 20 patients (technical success, 100%). Symptoms improved in 19 patients after stent placement (clinical success, 95%). The Gastric Outlet Obstruction Scoring System score improved significantly (P-value < 0.001). Tumor overgrowth developed in eight patients during patients' survival period (40%). Stent migration did not occur in any case. Median stent patency was 79.5 days (range 13-198 days). Adverse events occurred in 3 patients, comprising two cases of transient bacteremia, and one of asphyxia due to impaction of food material into the stent.
CONCLUSION: Partially covered duodenal stent was effective and safe for the malignant gastroduodenal obstruction and can prevent tumor ingrowth and stent migration.
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Disclosure of Interest: None declared

P0238 A NOVEL REINFORCEMENT METHOD FOR THE SURFACE OF GASTOINTESTINAL METAL STENT: GAS PLASMA TREATMENT

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INTRODUCTION: A gastrointestinal (GI) stent, which is made of Nickel-Titanium (NiTi) alloy coating with a silicone polymer, has been using for the relief of obstructive symptom in malignant stenosis of gastrointestinal tract. But the corrosion and fatigue failures of nitinol devices have been constant subjects of discussion. Recently, GI nitinol stent use is increasing abruptly, and fractures of GI stents have been reported. Although coating with the silicone polymer on the stent plays a key role in corroding, corrosion properties may differ along the surface of the NiTi alloy wire. The surface modification with plasma etching technology is a way to improve the physical properties of the target. We systematically investigated a reinforcement of nitinol alloy and surface modification to stick the silicone employing gas plasma treatment.
AIMS & METHODS: The fifteen NiTi alloy stents were treated in a few conditions of the plasma treatment, in which mixture rates of Ar and O_2 gas, applied voltages and duration of exposing time were varied. We prepared three kinds of stents; normal stent (product by normal process, sample 1), slightly etched normal stent (product by plasma treatment, sample 2) and natural oxide layer-eliminated normal stent (product that removed natural oxide regions by plasma treatment, sample 3). The stents were analyzed with a transmission electron microscope (TEM) and scanning electron microscope (SEM) to examine surface topographies of the stents and the interlocking state between wire and silicone polymer. We performed a potentiodynamic test to compare the corrosion state of each stent in GI state.
RESULTS: The surface profile of the samples showed that some content of the oxide layer for the normal stent was formed in thickness of about 100nm, while the others was 60~70nm by TEM analysis. Moreover, the oxide layer for normal product and slightly etched normal stent was likely to exhibit deposition of oxygen without interlocking that enhances cohesion, whereas natural oxide layer-eliminated normal stent showed behavior of strong interlocking between oxide and nickel. SEM image showed effective modification of nitinol wire to stick the silicone polymer by plasma etching technology. In a potentiodynamic test, the sample 3 removed natural oxide regions by plasma treatment, indicating the strongest corrosion resistance.
CONCLUSION: This result implies that an interlocking between nickel and oxide layer plays a significant role in corrosion resistance. Natural oxide layer by normal manufacture process induced micro-crack of nitinol GI, stent and removing the natural oxide layer by plasma treatment improved reinforcement and surface modification of nitinol GI stent. These results revealed that the plasma treatment could be employed to improve the surface property of GI stent for malignant outlet obstruction.
Disclosure of Interest: None declared

P0239 ENDOSCOPIC ELECTROCAUTERY DILATION OF POST-SURGICAL BENIGN ANASTOMOTIC COLONIC STRICTURES: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Benign anastomotic colonic stenosis sometimes occur after surgery and usually requires surgical or endoscopic dilation. Endoscopic dilation of anastomotic colonic strictures by using balloon or bougie-type dilators has been demonstrated to be safe and effective in multiple uncontrolled series. However, few data are available on safety and efficacy of endoscopic electrocautery dilation.
AIMS & METHODS: Aim of our study was to retrospectively investigate safety and efficacy of endoscopic electrocautery dilation of post-surgical benign anastomotic colonic strictures.
Patients with post-surgical benign anastomotic colonic strictures treated with endoscopic electrocautery dilation between June 2001 and February 2013 were considered. Anastomotic stricture was defined as a narrowed anastomosis through which a standard colonoscope could not be passed. Only annular anastomotic strictures were considered suitable for electrocautery dilation which consisted of radial incisions performed with a precut sphincterotome. Treatment was considered successful if the colonic anastomosis could be passed by a standard colonoscope immediately after dilation. Recurrence was defined as anastomotic stricture reappearance during follow-up.
RESULTS: Sixty-eight patients (43 women and 25 men, median age 63.6 yrs (22.6-81.7)) were included. Nine had undergone adiuvant radiotherapy and chemotherapy, 25 adiuvant chemotherapy only. Forty-four patients had a colorectal, 19 had a colo-colic and 5 an ileo-rectal anastomosis. Five patients had a colostomy and 12 an ileostomy. Two patients were referred for subocclusive symptoms, nine for stipsis and six for stool shape modification. The time-interval between colorectal surgery and the first endoscopic evaluation or symptoms development was 7.3 months (1.3-60.7). Electrocautery dilation was successful in all the patients. There were no procedure-related complications. Median follow-up was 35.5 months (2.0-144.0). Anastomotic stricture recurrence was observed in two patients who were successfully treated with electrocautery dilation and Savary dilation, respectively.
CONCLUSION: Endoscopic electrocautery dilation is a safe and effective treatment for annular benign anastomotic post-surgical colonic strictures.
Disclosure of Interest: None declared

P0240 BIODEGRADABLE STENTS IN PATIENTS WITH ACUTE LARGE BOWEL OBSTRUCTION SECONDARY TO A RECTAL TUMOR AND INDICATION FOR FURTHER NEOADJUVANT THERAPY: OUTCOMES AND SAFETY

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INTRODUCTION: Colorectal stenting is the first choice treatment in patients with acute large bowel obstruction due to the presence of a malignant tumor in the left colon. After colon decompresion, stenting allows accurate tumoral staging and patient preparation for further surgery. However, stenting is controversial in rectal tumors. The presence of a metallic stent in a patient undergoing neoadjuvant therapy increases disperse radiation and collateral inflammation in surrounding tissues, leading to a higher complication rate and poorer surgical results.
AIMS & METHODS: The aim of this study was to assess the outcomes of biodegradable stents in patients with obstructing rectal tumors undergoing neoadjuvant therapy. A prospective observational study was conducted including patients with acute large bowel obstruction due to a rectal cancer and candidates to neoadjuvant therapy. After large bowel obstruction was diagnosed, a CT scan was performed to confirm the etiology of the obstruction and, in patients with a rectal tumor, to characterize the lesion and to assess the indication of further neoadjuvancy. A biodegradable stent was inserted in these cases. Patients were followed until surgery or until death if surgical treatment was dismissed. Technical success at stent insertion, clinical success, stenting complications and surgical findings and outcomes (primary anastomosis and postoperative complications) were documented.
RESULTS: 8 patients [4 men/4 women; mean age: 62.6 yr (51-77)] were enrolled in the study. Once further neoadjuvant therapy was considered indicated, a polydioxanone monofilament biodegradable stent (Ella-CS. Czceh Rep) was successfully inserted in all patients (100%) [31/25/31 mm; 6 cm (n = 2), 8 cm (n = 6) length]. Initial colon decompression was achieved in every case (100%) but the stent migrated in one patient (12.5%) and a second stent was inserted. Patients underwent neoajuvant therapy [RT: 50.4 Gy in 28 sessions + capecitabine (825 mg/m2/12 h)] and were reevaluated with a CT scan at the end of treatment. 3 patients did not go for surgery after tumoral staging, received chemotherapy and did not present occlusive symptoms until death (mean follow-up: 220 days). 5 patients were operated 96 days after stent insertion (66-123 days). Primary anastomosis was performed in 3 (60%) whereas colostomy was performed in 2 (40%) due to severe local inflammation in one case and a silent perforation in the other. The only post surgical complication was a pneumonia in one patient (12.5%). No wound or anastomosis complications were registered
CONCLUSION: 1. Biodegradable stents are effective in patients with rectal tumors and secondary large bowel obstruction. 2. Association with neoadjuvant therapy causes local inflammation but allows primary anastomosis in 60% of cases and is not followed by an increased post surgery complication rate.
Disclosure of Interest: None declared

P0241 SELF-EXPANDABLE METAL STENTS FOR MALIGNANT COLONIC OBSTRUCTION

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INTRODUCTION: Tumoral obstructions in almost the entire gastrointestinal tract can be treated with interventional digestive endoscopy techniques. The use of self -expanding metal stents (SEMS) is a minimally invasive procedure providing a relatively simple and effective first- line treatment for the relief of obstructive symptoms.
AIMS & METHODS: To report data from a single center study on self-expandable metal stent (SEMS) placement for malignant colorectal obstruction. One hundred and six patients (64 males, mean age of 71±14 years), in a period of 96 months, were retrospectively evaluated and data on type and size of stent, complications, lesion location, and survival after the procedure were analyzed.
RESULTS: Most lesions were located in the rectum (50%, n = 53), 36% (n = 38) in the sigmoid colon, descending colon in 8.4% (n = 9) and 5.6%(n = 6) in the transverse colon. The mean length of the lesions was 65 ± 36mm. Most procedures were performed with palliative intent and in 4 patients two or more stents were placed. The stent was uncovered in 92% of cases and partially covered in 8% of the procedures. Complications were 4 neoplastic ingrowths, 3 stent migrations and 1 perforation. Seventy-five percent of patients were dead by the time of data collection, with a median interval between stenting and death of 105 days.
CONCLUSION: Colonic obstruction may be treated using endoscopic techniques. The placement of SEMS seems to be a safe and effective treatment.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00-17:00
SURGERY I - POSTER EXHIBITION - HALL XL

P0242 WHAT SWEDISH SURGEONS DO WHEN DETECTING COMMON BILE DUCT STONES DURING CHOLECYSTECTOMY

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INTRODUCTION: About 11,000 cholecystectomies are done annually in Sweden, most of which are completed laparoscopically (about 90%). Management strategies for common bile duct stones (CBDS) have been discussed in to an extreme extent and new options are rapidly emerging.
AIMS & METHODS: The aim of the study was to describe the current strategies applied in routine clinical practice in Sweden. A survey questionnaire was mailed to all hospitals (70) offering cholecystectomies and we obtained responses from all of them (100%). The questionnaire captured information on the details of clinical management strategies in a variety of different clinical manifestations of CBDS.
RESULTS: 35 (50%) of the hospitals reported a predefined policy regarding the management of CBDS. 65 (93%) hospitals used intra-operative cholangiography as a routine, 2 in selective cases and 2 did not. Management of a 3 mm large CBDS received that; 38 (54.3%) left it untreated, 23 (32.8%) performed some kind of intra-operative procedure, 3 (4.3%) preferred a post-operative ERCP; In case of a 6 mm large CBDS, the corresponding figures were; 3 (4.3%), 38 (52.2%), 17 (24.2%) respectively; In case of a 17 mm large CBDS: 23 (32.9%) preferred open CBD exploration and 4 (4.3%) a laparoscopic CBD-exploration, 6 (8.6%) post-operative ERCP. 40 (57.1%) of the hospitals used intra-operative ERCP with some kind of rendezvous cannulation technique.
CONCLUSION: Half of Sweden's surgical units do not follow a predefined policy regarding the intra-operative management of CBDS. Intra-operative ERCP with rendezvous cannulation technique is currently the strategy that is gaining popularity.
Disclosure of Interest: None declared

P0243 INDEPENDENT PROGNOSTIC FACTORS AFTER RESECTION OF PERIHILAR CHOLANGIOCARCINOMA: ANALYSIS OF 307 PATIENTS FROM TWO HPB CENTERS

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INTRODUCTION: The purpose of this study was to determine survival and independent prognostic factors after resection of perihilar cholangiocarcinoma (PHC).
AIMS & METHODS: Patients with PHC resected between 1991 and 2012 were identified from prospectively maintained databases from two institutions (in Europe and USA). Patients with final pathology other than PHC or in-hospital mortality were excluded. Prognostic factors were evaluated using univariate Kaplan-Meier survival analysis with log-rank test and multivariable cox-proportional hazards modelling using backward selection with likelihood ratio test.
RESULTS: 307 patients underwent resection for PHC. The median overall survival was 38 months, and 5-year survival 37%. In multivariable analysis four factors were independently associated with a poor prognosis: a positive resection margin, HR 1.69 [95% CI: 1.25-2.28], p = 0.001, one or more positive lymph nodes, HR 2.31 [1.66-3.23], p < 0.001, perineural invasion, HR 1.59 [1.13-2.23], p = 0.008, and moderate or poor differentiation, HR 1.64 [1.15-2.33], p = 0.006. Other traditional factors were associated with a poor prognosis only in univariate analysis, including lymphovascular invasion, non-papillary tumor, T-stage (7^{th} edition), and AJCC stage (7^{th} edition). Patients with at least 3 out of 4 poor prognostic factors (n = 90) had a median survival of 19 months [95% CI: 16-22] versus 52 months [95% CI: 40-64]. Analyzing R0 patients separately resulted in the same independent prognostic factors.
CONCLUSION: A positive resection margin, one or more positive lymph nodes, perineural invasion and moderate or poor differentiation are independent prognostic factors after resection of PHC. Based on these poor prognostic factors we will derive and validate a prognostic nomogram for resected perihilar cholangiocarcinoma.
Disclosure of Interest: None declared

P0244 SUCCESSFUL ENHANCED RECOVERY PROGRAMME IN MAJOR LIVER SURGERY

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INTRODUCTION: Enhanced recovery protocols after surgery accelerate patients' recovery and shorten hospital stay as a result of the optimization of perioperative care. In colorectal surgery these protocols show high-level evidence on reducing primary and total hospital stay without compromising the patient safety. This increased knowledge of perioperative pathophysiology and care has also been slowly implemented into liver surgery. However, in liver surgery the experience of optimized protocols is still limited.
AIMS & METHODS: Here we studied in a prospective way the implementation of multimodal rehabilitation protocol in a tertiary liver surgery unit within a one year period. This study involves the first 134 consecutive patients who were treated according to the enhanced recovery principles in open or laparoscopic liver surgery. An opioid-sparing pain treatment regimen was chosen for these patients together with early mobilization and oral feeding as well as avoidance or quick removal of drains and catheters shortly after surgery. Primary pain control was achieved either with epidural or locally inserted wound catheter analgesia. Peroral combination of pregabalin, ibuprofen and slow-release tramadol was also routinely administered shortly after the operation for pain relief.
RESULTS: All investigated liver resections were performed between April 1st, 2013 and March 31st, 2014. Most of the resections (72%) were major liver surgery involving 2 or more liver segments. Operations were done due to colorectal livers metastases (55% of cases), other liver metastases (9%), hepatocellular carcinoma (13%), gall bladder carcinoma (7%), peripheral cholangiocarcinoma (6%), and the rest 10% were done for benign liver tumors. Operations requiring hepatobiliary reconstructions were excluded from this study. 125 of the operations were open and 9 laparoscopic surgery.
56 of the operated patients were female, 78 male. Age median was 63 years (range 26-86 years). Only 2 patients were admitted to intensive care unit postoperatively; 1 planned admission, 1 due to perioperative pulmonary embolism. Median postoperative hospital stay was 4 days (range 2-11 days). 80% of all patients were discharged by the 5th postoperative day: 35% at the 3rd, 29% at the 4th and 15% at the 5th postoperative day. Two of the laparoscopically-operated patients were discharged at the 2nd, 6 at the 3rd and 1 patient at the 5th postoperative day. 5% of all patients were discharged via their own district hospitals.
Only 3 patients were readmitted back to the liver surgery ward; 1 patient (discharged at the 3rd day) because of pain problems and 2 patients (both discharged at the 5th day) because of elevated liver enzymes seen at the scheduled control visit few days after discharge.
CONCLUSION: Enhanced recovery protocol for perioperative care was introduced safely and effectively after major liver surgery. Routine discharge 2-3 days after laparoscopic resection and even 3-4 days after open resection is realistic and achievable.
Disclosure of Interest: None declared

P0245 HEPATOBILIARY SCINTIGRAPHY USING 99MTC-MEBROFENIN FOR THE ASSESSMENT OF LIVER FUNCTION AND BILIARY DECOMPRESSION IN PATIENTS WITH RESECTABLE HILAR CHOLANGIOCARCINOMA

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INTRODUCTION: Assessment of future remnant liver (FRL) function is crucial in resectable hilar cholangiocarcinoma (HCCA) while complete biliary drainage of the FRL is considered essential for postoperative function and regeneration in extended resections. ^{99m}Tc-mebrofenin-hepatobiliary-scintigraphy (HBS) provides segmental, quantitative information on parenchymal function in the uptake phase, while the excretion of ^{99m}Tc-mebrofenin depends on drainage of the biliary system.
AIMS & METHODS: The aim of this study was to evaluate the value of HBS in the preoperative work-up of patients undergoing resection for HCCA.
From 2008 to 2013, 67 patients suspected of HCCA underwent resection (7/67 (10.4%) hilar resection and 60/67 (89.6%) hilar resection in combination with liver resection). Preoperative HBS was used to generate time-activity curves from regions-of-interest (total liver and FRL). The excretion rate was calculated as decrease in mebrofenin activity in time (%/min) in the FRL.

RESULTS: HBS was performed in 51 of 67 patients. Preoperative biliary drainage had been performed in 44/51 patients. HBS showed sufficient function in 30/44 patients (group A), whereas 14/44 patients required additional procedures (group B), consisting of revision of biliary drainage (n = 8; 18.2%), portal vein embolization (n = 2; 4.5%) or a modified (parenchyma sparing) technique (n = 8; 18.2%). Overall excretion rate in group A was 2.17%/min (IQR25-IQR75 1.03-2.36) vs. 1.15%/min (IQR25-IQR75 0.81-1.50) in group B (p = 0.03).
Overall mortality in 67 patients was 7.5%. Morbidity was 50.0% and 42.9% in group A and B, respectively (p = 0.75). Two patients died due to postoperative liver failure: 1/30 (3.3%) in group A with sufficient FRL-function but low excretion rate and 1/14 (7.1%) in group B despite revision of biliary drainage (p = 0.54).
CONCLUSION: HBS provides combined quantitative assessment of parenchymal function (uptake phase) and biliary decompression (excretion phase) of the FRL enabling identification of patients who require additional or modified procedures prior to resection of HCCA.
Disclosure of Interest: None declared

P0246 IATROGENIC BILIARY INJURIES:MULTIDISCIPLINARY MANAGEMENT IN A MAJOR TERTIARY REFERRAL CENTER

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INTRODUCTION: Iatrogenic biliary injuries are considered as the most serious complications during cholecystectomy. Better outcomes have been shown in cases managed in a specialized center.
AIMS & METHODS: To evaluate the management and outcome of biliary injuries by multidisciplinary team in major referral hepatobiliary center. From January 2002 to January 2012,472 patients (302 females & 170 males) with post-cholecystectomy biliary injuries were managed with multidisciplinary team at National Liver Institute using endoscopy in 232 patients, in addition to percutaneous techniques in 42 patients and surgery in 198 patients.
RESULTS: Endoscopy was very successful initial treatment of 232 patients (49%) being less invasive in comparison to surgery in treatment of mild/moderate biliary leakage (68%) and biliary stricture (47%) with increased success by addition of percutaneous (Rendezvous technique) in 18 patients (3.8%). Surgery was needed in 198 (42%) for major duct transection, ligation, major leakage and massive stricture. Surgery was urgently in 62 patients and electively in 156 patients. Hepaticojejunostomy was done in most of cases (96) patients with transanastomatic stents. There was only one mortality after surgery due to biliary sepsis, and postoperative stricture was in 3 cases (1.5%) treated with percutaneous dilation and stenting.
CONCLUSION: Management outcome of biliary injuries becomes better with a multidisciplinary care team, with initial minimal invasive technique to major surgery in major complex injury encouraging for early referral to highly specialized hepatobiliary centers.
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Disclosure of Interest: None declared

P0247 IMPACT OF SARCOPENIA ON OUTCOMES FOLLOWING RESECTION OF PERIHILAR CHOLANGIOCARCINOMA

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INTRODUCTION: Loss of skeletal muscle mass, sarcopenia, reflects the frailty status of patients and has recently been associated with worse outcomes following surgery for malignancies of gastrointestinal origin. The aim of this study was to investigate the impact of sarcopenia on postoperative morbidity and survival following resection of perihilar cholangiocarcinoma (pHCCA).
AIMS & METHODS: Data were retrospectively collected from a prospectively maintained database including all patients in our institute undergoing major liver resections for suspected pHCCA between 1998 and 2013. Sarcopenia was assessed in patients in whom an adequate preoperative CT scan was available, by measuring total skeletal muscle mass at the level of the third lumbar vertebra. Sex-specific cut-off values for sarcopenia were determined by optimum stratification. Clinicopathological data, postoperative morbidity (Clavien-Dindo grade ≥3), mortality and long-term survival were analysed.
RESULTS: Sarcopenia was present in 41 (42%) of 97 patients with pHCCA and was correlated with lower body mass index. Sarcopenia was associated with 30-day/in-hospital mortality (24% vs. 9%, p = 0.037). Overall postoperative complication rate (Clavien-Dindo grade ≥3) was higher in sarcopenic patients (66% vs. 46%), though this was not statistically significant (p = 0.058). However, sarcopenia was predictive for sepsis (OR 6.77, 1.67 to 27.43, p = 0.007). Estimated five-year overall survival rate was lower for sarcopenic patients (18 vs. 36%, p = 0.024). After correction for lymph node status, resection margin status, tumour differentiation grade and postoperative complications in multivariable analysis, sarcopenia was revealed as an independent predictor for worse overall survival (HR 1.93, 1.08 to 3.43; p = 0.026).
CONCLUSION: Sarcopenia has a negative effect on postoperative outcome and overall survival following resection of pHCCA and should therefore be considered in preoperative risk assessment.
Disclosure of Interest: None declared

P0248 RESECTION AND RECONSTRUCTION OF THE HEPATIC ARTERY FOR ADVANCED CHOLANGIOCARCINOMA: COULD ARTERIOPORTAL SHUNTING ALTER MICROVASCULAR RECONSTRUCTION?

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INTRODUCTION: The anatomic features of the hepatic hilum facilitate invasion of the hepatic arteries by cholangiocarcinoma. To accomplish curative resection, hepatic artery resection and reconstruction is sometimes required for such advanced cases. One small study suggested that arterioportal shunting (APS) might be useful in these patients. Surgical results with more cases and the survival impact of APS for cholangiocarcinoma have not yet been investigated.
AIMS & METHODS: The aim of this case controlled study was to evaluate the safety of APS and whether APS could be an alternative to microvascular reconstruction.
Patients and Methods: Thirty nine patients with intra- or extra-hepatic cholangiocarcinoma who underwent hepatic arterial resection were evaluated. There were 18 patients with APS (APS group) and 21 patients with microvascular arterial reconstruction (MVR group).
RESULTS: Preoperative statuses of the patients from both groups were similar, except for a number of patients with preoperative portal embolization. There were no significant differences in incidences of postoperative complications (Clavien-Dindo ≤ IIIa) between the two groups. However, the incidence of liver abscess formation was significantly higher in the APS group (38.9% vs 4.8% p = 0.02). Treatments for these liver abscesses were complicated. Mortality (hospital death) was 6% in APS group, 0% in MVR group, respectively (p = 0.46). Cumulative 3- and 5-year survival rates were 53.1% and 22.1%, respectively, in the MVR group, and22.2% and 11.1%, respectively, in the APS group (p = 0.11).
CONCLUSION: Microvasucular arterial reconstruction should be used as the first-line strategy for patients with intra/extra-hepatic cholangiocarcinoma. APS is indicated when the artery cannot be microscopically anastomosed.
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Disclosure of Interest: None declared

P0249 SURGICAL OUTCOME OF "HILAR PLATE RESECTION": EXTENDED HILAR BILE DUCT RESECTION WITHOUT HEPATECTOMY

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INTRODUCTION: In the treatment of hilar cholangiocarcinoma, several studies have advocated en bloc major hepatectomy to achieve negative histologic margins and improved survival. However, we know that there are some patients with distal cholangiocarcinoma with longitudinal spread remaining in the hilar portion, without infiltration beyond the bile duct wall. We also know that there are a few patients with Bismuth type I hilar cholangiocarcinoma without infiltration beyond the bile duct wall. These tumors are likely to have superficial spreading, which would be difficult to accurately diagnose preoperatively. It remains unknown whether, for patients with such a non-invasive tumor, extended hepatectomy would be appropriate. We have done extended extrahepatic bile duct resection at the level of the hilar plate with curative or palliative intention for selected patients with or without hilar malignant tumors, calling this procedure "hilar plate resection" (HPR).
AIMS & METHODS: The results of a retrospective study evaluating the clinical benefits in patients who underwent HPR for biliary malignancies are reported.

Surgical procedure of HPR: Nodal clearance around the pancreatic head and skeletonization of the portal vein and the hepatic artery were performed first. The portal vein and the hepatic artery were then separated from the surrounding tissue upward to the hilar plate, where the duct cannot be further separated from the vasculature. This was considered "the limit of ductal transection without hepatectomy", which is at the right edge of the posterior portion of the right portal vein and the right edge of the umbilical portion of the left portal vein. Then, the gallbladder with the "cystic plate" was resected toward the hepatic hilum. Finally, the extrahepatic duct at the hilar plate was resected.
Patients: Fifty-two patients with cholangiocarcinoma underwent HPR. The procedure was performed in 28 patients with curative resection (cHPR group) and in 24 patients with palliative intention (pHPR group). In the same period, one hundred twenty-eight patients with cholangiocarcinoma underwent major hepatectomy with intrahepatic cholangiojejunostomy (Hx group). We compared with these groups in term of post operative complications and survival.
RESULTS: There were no significant differences in the number of patients with postoperative complications and in postoperative hospital stay. The overall cumulative survival rates of each procedure (Hx group, cHPR group, and pHPR group) were 40%, 38%, and 11% at 5 years, respectively. There was no significant difference between Hx and cHPR group in survival rates ($p = 0.87$). But the survival rate of the pHPR group was significantly lower than that of the Hx group ($p = 0.03$). The survival rate of the pHPR group was lower, but not significantly, than that of the cHPR group ($p = 0.08$).
CONCLUSION: HPR appears to be safe and feasible for selected patients with cholangiocarcinoma. However, the indications for HPR should be restricted.
Disclosure of Interest: None declared

P0250 LAPAROSCOPIC GASTRECTOMY FOR GASTRIC CANCER: RESULTS OF IMPLEMENTATION OF A NEW TECHNIQUE

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INTRODUCTION: Although different (neo)adjuvant strategies are being developed, surgical treatment remains the cornerstone of curative treatment for gastric cancer. Standard operative procedure has traditionally been an open (sub)total gastrectomy with a modified D2-lymphadenectomy. In an attempt to lower perioperative morbidity, we designed and standardized a laparoscopic technique to perform a (sub)total gastrectomy for the treatment of patients with potentially curable gastric cancer.
AIMS & METHODS: Aim of this study was to describe the short-term results of the first series of laparoscopic gastrectomies in patients with potentially curable gastric cancer.
In this prospective cohort trial we evaluated the first series of consecutive patients with potentially curable gastric cancer who underwent a laparoscopic (sub)total gastrectomy with a modified D2-lymphadenectomy the first year following introduction of the laparoscopic technique. Primary endpoint was perioperative morbidity and mortality. Secondary endpoints were hospital length of stay, number of harvested lymph nodes and radicality of surgery (R0 resection rate).
RESULTS: From February 2013 until April 2014 28 patients out of a total of 38 patients underwent a laparoscopic gastrectomy (73.7% of all gastrectomies). Eighteen patients (64.3%) underwent a total gastrectomy and 10 patients (35.7%) a subtotal gastrectomy. In 5 patients (17.9%) at least 6 cm of esophagus was co-resected. 18 patients (64.3%) received neo-adjuvant chemotherapy. There were 3 conversions (10.7%). Reasons for conversion were tumor involvement of the duodenum with a narrow relation to the pancreatic head in 2 cases and tumor ingrowth in the left hemidiafragm necessitating partial diaphragm resection in 1 case. The median operation time was 320 min (SD 66.8), median blood loss 200 cc (SD 269.6) and median hospital stay 8 days (SD 6.3). The overall complication rate was 21.4% (6 patients). There were 2 complications requiring re-intervention (7.1%). Both patients had an anastomotic dehiscence for which surgical drainage was performed. One of these patients eventually died of the septic consequences (total hospital mortality 3.6%). In 1 patient peri-operatively peritoneal metastases were detected and a palliative resection was performed. In 26 patients the tumor was radically removed (R0 resection rate 96.3%). Median lymph node count was 25 (SD 8.5).
CONCLUSION: Laparoscopic surgery for gastric cancer is feasible with good oncologic results and acceptable peri-operative morbidity and mortality. Implementation of this technique was evaluated as successful and therefore it is now standard surgical strategy at our center.
Disclosure of Interest: None declared

P0251 SUBMUCOSAL TUNNEL FOR PERITONEAL ACCESS ASSOCIATED WITH AN OVER-THE-SCOPE CLIPS (OTSC) CLOSURE: COMPARISON WITH TWO OTHER METHODS OF GASTROTOMY CLOSURE AFTER NOTES PROCEDURES

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INTRODUCTION: Safe transgastric NOTES procedures require a reliable closure of the gastrotomy. Recently a novel peritoneal access method via a submucosal tunnel has been described with encouraging preliminary results.
AIMS & METHODS: The aim was to compare a submucosal tunnel access plus over-the-scope clips (OTSC) for closure with two other closure modalities. It was a prospective ex-vivo study on forty-two specimens equally randomized in three groups and carried out in an Academic medical center. Fourteen procedures were performed in each group including: 1.) Tunnel (6 cm) + endoclips; 2.) Knife + balloon dilation access + OTSC; 3.) Tunnel + OTSC. The main outcome measurements were: pressurized air-leak test was realized to evaluate the strength of the closure. Stomach volumes, procedure times, number of clips, and incision sizes were also registered.
RESULTS: The mean air leak pressure was statistically higher in group 3 than in groups 1 and 2: 95.2 ± 19.3 mmHg vs. 72.5 ± 35.2 and 79 ± 24.5 mmHg ($p < 0.05$). The gastrotomy creation times for groups 1, 2 and 3 were 28.0 ± 10.1, 4.3 ± 1.4 and 20.1 ± 10.6 minutes, respectively, with significantly lower time in the group 2 ($p < 0.001$). The closure times were 16.1 ± 6.1, 6.5 ± 1.2 and 5.3 ± 3.0 minutes, respectively, and significantly longer in the endoclip group ($p < 0.001$). There was no difference in the volumes and the incision sizes between the three groups.
CONCLUSION: The combination of a submucosal tunnel access and OTSC offers a stronger closure than the other methods studied.
Disclosure of Interest: None declared

P0252 NEW MULTICOLORED MULTIMATERIAL BIOELASTIC ORGAN REPLICATION USING HYBRID MDCT AND 3D PRINTING TECHNOLOGY FOR TANGIBLE DIGESTIVE SURGERY SIMULATION

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INTRODUCTION: Our new technology of Bio-Texture Modeling by hybrid MDCT and 3D printing system enabled manufacturing patient-specific 3D organ replicas. We developed the latest generation of 3D printer by simultaneous jetting of different types of model materials.
AIMS & METHODS: The objective was to develop and evaluate patient-specific, anatomically accurate, bioelastic 3D replica for simulation, navigation and training of digestive surgery in 40 clinical cases. Based on DICOM data from MDCT, after generating its surface polygons using OsiriX application, the inkjet 3D printer created life-size copies of the 3D organs, blood vessels, and abdominal cavity. We programmed a printer to create clear models made from acrylic resins that allowed us to visualize and understand the gastrointestinal and hepatobiliary pancreatic complex internal structures and blood vessels or the exact tumor locations. We printed liver models compounding the polyvinyl alcohol (PVA) to make the model a realistic stand-in for ultrasonic diagnosis, hepatic intervention and surgical simulation.
RESULTS: The patient individual multicolored 3D printed models were useful for visible and tangible surgical simulation and navigation to plan and guide the successful gastrectomy, colectomy, hapatobiliary pancreatic surgeries in total of 40 patients including 20 laparoscopic surgeries. The 3D objects using a combination of transparent and soft materials allowed creation of translucent medical models that show visceral organs and other details that can be handled, overcoming the limitation of the conventional image-guided navigation. The gel-like support material, which is specially designed to support complicated geometries, is easily removed by hand. This provided realistic simulation of suturing and dissection to provide specific values of bio-texture in gastrointestinal hepatobiliary pancreatic organs for tensile strength and elongation to break. The PVA was available for wet tissue simulation in ultrasonography and intervention in hepatic surgery.
CONCLUSION: New 3D printing techniques delivered tangible and safe surgery training and could help younger, less experienced surgeons practice with accurate copies for digestive surgery. Its combines the advantages of conventional 3D modeling and precise virtual 3D planning and can be applied advantageously in personalized surgical simulation and navigation.
Disclosure of Interest: M. Sugimoto Financial support for research from: Fasotec Inc.

P0253 TRANSRECTAL NOTES VERSUS LAPAROSCOPIC AND OPEN CHOLECYSTECTOMY IN AN ANIMAL MODEL OF CALCULOSE CHOLECYSTITIS

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INTRODUCTION: Natural-orifice transluminal endoscopic surgery (NOTES) as an evolving concept has been studied in several experimental trials. However, randomized experimental study evaluating NOTES in the area of calculose cholecystitis is missing. Transrectal compared to more frequently used transvaginal access offers good manipulation in the upper abdomen and is not limited to the female population. Also the physiologic impact during NOTES may differ from laparoscopy and open procedures because of presumed longer operation and need of extensive body positioning.
AIMS & METHODS: The aim of the study was to compare transrectal NOTES, laparoscopic and open approach to cholecystectomy in animal with calculose cholecystitis.
Laparoscopy (3-ports) was performed, bile was aspirated from the bladder and 4 gallstones obtained by human cholecystectomy were inserted via cholecystotomy in all 42 animals four week prior planned intervention. Animals were than randomized into NOTES ($N = 14$), open ($N = 11$), laparoscopic ($N = 11$), and sham groups ($N = 6$). In NOTES cholecystectomy a double channel endoscope was used to enter the abdominal cavity via rectotomy performed by needle knife

and balloon dilatation. A standard laparoscopic grasper was advanced to grip the fundus. Cystic duct and cystic artery were clipped and the preparation finished with a hook knife. The access site incision was endosutured by OVESCO clip. Small (5-6cm) subcostal incision and 3-ports laparoscopy were performed in open and laparoscopic groups. For hemodynamic monitoring using LiDCO, central venous and arterial catheter were introduced. After a follow-up period of 30 days, the animals were euthanized and necropsies were performed.
RESULTS: The procedure time was significantly longer in NOTES than in open and laparoscopic groups 145 (90-240) vs. 40 (25-65) vs. 63 (40-90) minutes, $p < 0.001$. In 3 animals from NOTES group the bladder dissection was complicated by severe bleeding, which was not treatable endoscopically. NOTES technique was indicated as unfeasible and these animals could not be evaluated afterwards. Perforation of the gall bladder occurred in 9/11 in NOTES versus 1/11 (RR: 9.0; 1.36-59; $p = 0.02$) and 4/11 (RR: 2.3; 1.1-5.2; $p = 0.04$) in open and laparoscopy groups. All followed hemodynamic parameters including heart rate, mean arterial pressure, cardiac index, central venous pressure and systemic vascular resistance did not differ from sham animals in all groups. Gallstones with wall inflammation confirmed histologically were present in all extracted bladders. All rectotomies were healed, however intraabdominal infection occurred more frequently in NOTES (4/11) than in open (2/11) and laparoscopic (1/11) groups.
CONCLUSION: Despite the technical difficulties and longer operational times, NOTES did not affect hemodynamic parameters. However, the feasibility rate of NOTES in the area of calculose cholecystitis did not reach conventional approaches. There were more intraoperative and postoperative complications in NOTES group. Transrectal access can be used universally and closed safely but risk of intraabdominal contamination during the procedure remains an issue.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
IBD I – POSTER EXHIBITION – HALL XL

P0254 HCMV AND EBV VIRAL LOAD IN MUCOSA OF PATIENTS WITH CHRONIC INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Immunosuppressants and biologicals are considered the mainstay of therapy for inflammatory bowel disease (IBD) thanks to the possibility of inducing remission and preventing disease progression. However, the growing and earlier use of these medications predisposes the patients to an increased risk of opportunistic infections, which represent an important cause of morbidity and mortality. Human Cytomegalovirus (HCMV) and Epstein-Barr virus (EBV) play a prominent role in the development of acute colitis in immune-compromised patients. In a previous study, our group has defined the spectrum of conditions associated with infection by HCMV and EBV, associating their presence with the refractory to conventional therapies and identifying the main risk factors for reactivation, as well as to detect in quantitative real-time PCR (RT-PCR), performed on fresh intestinal biopsies, the most sensitive method for diagnosis.
AIMS & METHODS: We investigated the role of these viruses in IBD pathogenesis by evaluating the presence of viral DNA within the cells of the intestinal mucosa, in particular in enterocytes and lamina propria mononuclear cells (LPMCs). We enrolled 7 IBD patients (5/2 M/F, mean age 47), 1 patient with profound combined immunodeficiency (M, 28 years) and 8 healthy controls (HC). All patients underwent lower endoscopy with multiple biopsies. Enterocytes were separated on a Percoll density gradient and LPMCs obtained by enzymatic digestion. The viral load was assessed by quantitative RT-PCR on mucosal specimens, enterocytes and LPMCs. Wilcoxon and Mann-Whitney tests were applied for statistical analysis.
RESULTS: Viral DNA was found in the mucosa of all the patients and in 2 control subjects, with double positivity for HCMV and EBV DNA in 6 patients, while EBV DNA alone in the remaining 2 patients and HC. In different colonic locations, 6 patients showed peak values for EBV DNA above 10^3 copies/10^5 cells in at least one location, while only 2 patients had similarly high values for HCMV DNA. No HC showed peak values exceeding 10^2 copies/10^5 cells. Viral DNA was found within enterocytes in 5 patients and in none of the HC, while inside of LPMCs was evidenced in all patients and 3 HC. HCMV DNA was found in enterocytes of only 2 patients, while 6 patients had detectable DNA in LPMCs; instead 5 patients had EBV DNA in enterocytes and in all cases in LPMCs. EBV DNA median values in healthy and injured mucosa, both in the enterocytes (223.5 copies/10^5 cells) and in LPMCs (3348.5 copies/10^5 cells), were significantly higher when compared to the levels of HCMV DNA (0 copies/10^5 cells; 6.5 copies/10^5 cells in enterocytes and LPMCs respectively) of both patients and HC. Finally, in inflamed areas EBV DNA median values were higher than in healthy mucosa.
CONCLUSION: Our data demonstrated the presence of EBV DNA in colonic LPMCs and enterocytes of patients with IBD, with higher loads observed in the first population. We also observed high levels of EBV DNA in enterocytes and LPMCs in the presence of mucosal inflammation. This shows a preponderant role of EBV compared with HCMV, with further studies needed to improve the knowledge of the relationship between this virus and clinical manifestations.
Disclosure of Interest: None declared

P0255 AIEC-RECEPTOR CEACAM6 ABNORMAL EXPRESSION IN CROHN'S DISEASE DEPENDS ON HYPOXIA RESPONSIVE ELEMENTS METHYLATION STATUS AND CHROMATIN REMODELLING

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INTRODUCTION: Abnormal expression of CEACAM6 is observed at the apical surface of the ileal epithelium in Crohn's disease (CD) patients. This allows Adherent-Invasive *Escherichia coli* (AIEC) to colonize gut mucosa, leading to development of inflammation. Our aims were to understand the regulation of CEACAM6 expression in ileal mucosa of CD patients at the baseline and to investigate molecular mechanisms involved in AIEC infection-dependent CEACAM6 overexpression. Since changes in DNA methylation patterns were reported in CD patients, we analyzed whether epigenetic mechanisms are involved in the up-regulation of CEACAM6 expression in intestinal epithelial cells.
AIMS & METHODS: Protein expression and localization were analyzed before and after AIEC infection using immunofluorescence staining and Western-blot analysis. HIF-1α and histone H3 Serine 10 phosphorylation (H3S10p) levels were measured in CEACAM6 promoter region by chromatin immunoprecipitation (ChIP) in intestinal epithelial cells (IEC). Transgenic CEABAC10 mice expressing human CEACAM6 were orally challenged with 10^9 AIEC LF82 bacteria. At 3 days post-infection, ileum-associated AIEC were quantified, and mRNA levels were measured in isolated enterocytes.
RESULTS: Higher expression of CEACAM6 was observed in T84 cells compared to Caco-2 cells. This was associated to high binding of HIF-1 on the CEACAM6 gene promoter in an open chromatin state region characterized by increased in H3S10 phosphorylation level. In contrast, Caco-2 cells expressed low levels of CEACAM6 due to a compact chromatin state in CEACAM6 promoter (low level of H3S10p). AIEC infection led to increased CEACAM6 expression related to enhance HIF-1 binding to CEACAM6 promoter. Abnormal H3S10 phosphorylation in CEACAM6 promoter following AIEC infection in IEC enhanced HIF-1 binding, and subsequent CEACAM6 expression. In vivo, increased levels of CEACAM6 and HIF-1α proteins were measured in ileal enterocytes of AIEC-infected CEABAC10 mice, which could be due to high H3S10 phosphorylation enabling HIF-1α binding to CEACAM6 promoter.
CONCLUSION: AIEC bacteria increased CEACAM6 expression in ileal enterocytes of CEABAC10 mice by stabilizing HIF-1α transcription factor and by opening chromatin in CEACAM6 promoter. This allowed HIF-1α binding and subsequent gene transactivation, indicating that abnormal CEACAM6 expression in ileal mucosa of CD patients could be related to AIEC colonization-induced epigenetic regulation.
Disclosure of Interest: None declared

P0256 WESTERN DIET IN CEACAM6 EXPRESSING MICE: IMPACT ON SHORT-CHAIN FATTY ACIDS PRODUCTION AND HOST SUSCEPTIBILITY TO INTESTINAL INFLAMMATION

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INTRODUCTION: Recent advances have shown that abnormal inflammatory response observed in Crohn's disease (CD) involves interplay between intestinal microbiota, host genetic and environmental factors. The escalating consumption of fat and sugar in Western diets parallels an increased incidence of CD during the latter 20th century. Western lifestyle could explain the increasing prevalence of new diseases such as CD.
AIMS & METHODS: We aimed at understanding the multifactorial etiology of CD by evaluating the modulation of host physiology in response to nutrition. We analyzed the impact of a High-Fat/High-Sugar (HF/HS) diet in mice on gut micro-inflammation, selection of *E. coli* population, concentration of short-chain fatty acids (SCFA) and expression of their free fatty acid-receptors such as G-protein-coupled receptor 43 (GPR43). Mouse sensitivity to DSS-induced colitis was assessed to evaluate the impact of nutrition in the sensibility to chemically-induced colitis. Mice fed a conventional or a HF/HS diet during 18 week-period, fecal lipocalin-2 (Lcn-2) was measured by ELISA to detect low-grade inflammation during the course of treatment, *E. coli* populations associated to colonic and ileal mucosa were quantified, production of SCFA by microbiota were measured by gas chromatography in fecal samples. GPR43 receptor was visualized by confocal microscopy after immunostaining of colonic mucosa tissues. The severity of DSS-induced colitis (1% of DSS in drinking water, 10 days) was evaluated by disease activity index (DAI) measurement, histological score and cytokine release.
RESULTS: HF/HS diet increased Lcn-2 level in stools from 5 weeks until 18 weeks of treatment, showing that HF/HS diet creates a specific inflammatory environment in the gut. Interestingly, abnormal proportions of *E. coli* bacteria were recovered from colonic and ileal mucosa of mice under HF/HS diet, compared to mice under conventional diet. SCFA concentrations (acetate, propionate, butyrate) were significantly decreased in fecal samples from mice under HF/HS diet compared to mice fed a conventional diet. Combination of HF/HS diet led to dysbiosis with an overgrowth of pro-inflammatory *E. coli* bacteria and a decrease in protective SCFA producing bacteria. GPR43 receptor expression was reduced in mice treated with an HF/HS diet compared to mice under a conventional diet. In addition, HF/HS diet led to an exacerbation of gut inflammation

following DSS-induced colitis, with an increase of DAI, histological score and release of pro-inflammatory cytokines.
CONCLUSION: Western diet creates a low-grade inflammation in the gut with a decrease of protective SCFA producing bacteria, leading to overcolonization by *E. coli* opportunistic pathogen bacteria which could aggravate the inflammatory process resulting in chronic inflammation. Together, these findings support the multifactorial etiology of CD and highlight the importance of nutrition factors in CD pathogenesis.
Disclosure of Interest: None declared

P0257 VITAMIN D REGULATES THE TIGHT-JUNCTION PROTEINS EXPRESSION IN ACTIVE ULCERATIVE COLITIS

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INTRODUCTION: Epithelial barrier function is primarily regulated by the tight-junction proteins (TJ). Ulcerative colitis (UC) is characterized by Th2 immune response with inflammation and epithelial barrier dysfunction, including an elevation of claudin-2 protein function (1).
In UC, epithelial leaks appear early due to micro-erosions resulting from upregulated epithelial apoptosis and from a significant IL-13-dependent arrest in epithelial restitution (2).
Vitamin D is traditionally associated with bone metabolism. Importantly, recently studies support an important role of vitamin D in the pathogenesis as well as potential therapy of IBD. Vitamin D deficiency is in fact common in patients with IBD (3).
AIMS & METHODS: Our aim was to determine whether vitamin D could affect IL-13 and IL-6 levels, and regulate the activity of tight-junction proteins Claudin-1, -2, -4 and -7 in the inflamed and non-inflamed colonic mucosa of UC patients.
Methods: Biopsies from the colon (rectum, sigma) of patients with active UC were studied. Non-inflamed (NI) and inflamed (I) intestine tissues, obtained from the same patient, were cultured with 10 nM $1,25(OH)_2D_3$. After 24 h incubation the medium was removed and used for the determination of IL-13 and IL-6 levels by ELISA test. The lysates of biopsies were used to determine the levels of TJ protein by Western blot analysis.
RESULTS: Claudin-1 and Claudin-2 proteins were up-regulated in active UC. The treatment with $1,25(OH)_2D_3$ increases the Claudin-1 levels in the NI tract and decreases their level in the I tract, while the treatment with $1,25(OH)_2D_3$ remarkably decreases the Claudin-2 protein level in both I and NI tract. Claudin-4 and Claudin-7 proteins were down-regulated with Western Blot Analysis and their levels increase when both NI and I tract were cultured in the presence of the $1,25(OH)_2D_3$. IL-13 and IL-6 levels decrease incubating the biopsies with $1,25(OH)_2D_3$.
CONCLUSION: Our study reports a down-regulation of claudin-4 and claudin-7, and an up-regulation of claudin-2, that might lead to altered TJ structure and be related to the impaired epithelial function in active UC.
Our results, indicating the inhibition of cytokine levels and the regulation of Claudin-2, Claudin-4 and claudin-7 by $1,25(OH)_2D_3$, suggest that vitamin D may represent a potential target for the treatment of IBD.
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Disclosure of Interest: None declared

P0258 SMOKING IS ASSOCIATED WITH WATERY DIARRHEA AND DECREASED LIKELIHOOD TO ACHIEVE CLINICAL REMISSION IN COLLAGENOUS COLITIS

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INTRODUCTION: Smoking seems to be a risk factor for microscopic colitis and smokers develop the disease more than 10 years earlier than non-smokers. However, the impact of smoking on clinical activity and outcome has not been elucidated.
AIMS & METHODS: In a post-hoc analysis from pooled data of two randomized controlled trials (BUC-60/COC and BUC-63/COC) we assessed the association of demographical (gender, age, smoking habits, previous and/or concomitant medication, family history of inflammatory bowel disease) and clinical variables (duration of symptoms, mean number of stools/watery stools per day, abdominal pain, clinical remission). Moreover, we analyzed the predictive value of baseline parameters on clinical outcome in a logistic regression model.
RESULTS: Pooled data from 202 patients with active collagenous colitis (CC) were available thereof 36% current smokers, 29% former smokers and 35% non-smokers. Current smokers had an increased number of watery stools at baseline compared to non-smokers ($p = 0.05$). 20/137 (15%) patients treated with budesonide did not achieve clinical remission. The majority of these (85%) were either smokers or former smokers. An association was found between smoking status (current smokers vs. non smokers: OR 0.37, 95% CI: 0.14-0.96, $p = 0.041$; former smokers vs. non smokers: OR 0.21, 95% CI: 0.07-0.60, $p = 0.004$), mean number of watery stools per day (OR 0.77, 95% CI: 0.66-0.90, $p = 0.001$) and decreased likelihood to obtain clinical remission. All other variables showed no significant association.
CONCLUSION: Smoking is associated with increased number of watery stools and decreased likelihood to achieve clinical remission in collagenous colitis. Smoking seems to have an impact on disease activity and treatment outcome in patients with CC.
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P0259 REDUCED MUCOSAL EXPRESSION OF INSOLUBLE KERATINS 8, 18 AND 19 IN ACTIVE COLITIS RELATIVE TO PROXIMAL INACTIVE COLONIC MUCOSA: VALIDATION OF MASS SPECTROMETRY DATA

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INTRODUCTION: Intermediate filaments (IF) are one of the main components of the human cell cytoskeleton, which mainly consist of keratins (K). K8, K18 and K19 constitute the main keratins in the intestinal epithelial cells. Keratin alteration may play a role in the pathophysiology of ulcerative colitis (UC). K8 -/- mice develop chronic colitis (1). Heritable predispositions to UC were mapped to the K8/18 loci in human (2). K8 and K18 play a role in TNF-α induced-apoptosis (3). We have previously shown reduced expression of insoluble K8, K18 and K19 in active UC (ACT) relative to un-inflamed proximal colonic mucosa (INACT) using mass spectrometry (MS) analysis in the IF fraction of pooled patient samples from these two groups. The aim of this study was to use antibody-based relative quantification of K8, K18 and K19 in individual patient samples to validate MS results and describe variation in expression across the cohort.
AIMS & METHODS: IF proteins were extracted from rectal biopsies in patients with active colitis ($n = 9$) as well as endoscopically and histologically un-inflamed proximal colonic mucosa in each individual. IF proteins extracted from the sigmoid colon of a normal individual was used as an internal control. Each sample was dot-blotted on a membrane followed by immunoblotting for identification and quantification of keratins (8, 18 &19) sequentially. A control MCF-7 sample was included in all immunoblots to allow normalisation between sample groups. Relative keratins concentration for each dot- blotted sample was inferred by determining its signal intensity relative to the MCF-7 keratins signal intensity measured in turn by densitometry. Statistical analysis to compare the two groups was made separately for K8, K18 and K19 using Mann-Whitney U test.
RESULTS: Median relative IF protein levels from the active mucosa were 0.18, 0.28 and 1.48 for K8, K18 and K19, respectively were significantly lower than those from the un-inflamed inactive mucosa: 1.21, 1.16 and 3.59 for K8 ($p = 0.02$), K18 ($p = 0.03$) and K19 ($p = 0.02$), respectively. Median Baron's endoscopy score in ACT and INACT biopsy samples were 2 (range 2-3) and 0 (range 0-1), respectively. Median histological activity index in ACT and INACT were 2 (range 1-3) and 0 (range 0). Median disease duration was 5 years in the cohort.
CONCLUSION: This study confirms reduced expression of insoluble keratins in the active colonic epithelial cells relative to the un-inflamed proximal colonic mucosa and validates our previous MS observations. Insoluble keratin expression may be used as a tissue marker of disease activity.
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Disclosure of Interest: None declared

P0260 PANCREATIC EXOCRINE INSUFFICIENCY IS NOT A CLINICALLY SIGNIFICANT PROBLEM IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: It is not uncommon that patients with ulcerative colitis report symptoms such as diarrhea, bloating and abdominal discomfort despite a complete absence of biochemical and endoscopic signs of disease activity. One possible explanation to this phenomenon is that these patients may suffer from pancreatic exocrine insufficiency (PEI). One previous study has indicated that the prevalence of PEI may be as high as 17% in patients with inflammatory bowel disease (IBD) (1). However, most studies on PEI in IBD including the aforementioned have used fecal elastase (Fel-1) as the only method to investigate pancreatic exocrine function. Concerns have been raised about the diagnostic accuracy of Fel-1 to diagnose PEI in IBD due to dilution effects and increased degradation.

Hence, studies on the prevalence of PEI in IBD patients using more specific tests of exocrine pancreatic function are warranted. The 13C-mixed triglycerides (MTG) breath test is a non-invasive pancreatic function test that can be used to confirm the diagnosis of PEI with high sensitivity and specificity.
AIMS & METHODS: The aim of the present study was to investigate the prevalence of PEI and clinical factors associated with PEI in patients with ulcerative colitis. Cases with ulcerative colitis seen at the out patient clinic of Sahlgrenska University Hospital were included in the study. Ulcerative colitis disease activity was evaluated by the Mayo scoring system for assessment of ulcerative colitis activity, fecal calprotectin, and sigmoidoscopy. Patients were screened for PEI using the Fel-1 test. Subjects with low Fel-1 were further examined using the 13-CMTG breath test. Computed tomography (CT) was used to evaluate pancreatic morphology in cases where the 13C-MTG breath test could confirm the PEI diagnosis.
RESULTS: In total 192 patients with ulcerative colitis were included in the study (mean age 44 years, 110 (57%) male, 93 (48%) with active disease). Fel-1 below the lower limit of normal (200 μg/g stool) was observed in 15 (7.8%) patients. There was no difference in age, ulcerative colitis disease activity, stool frequency or azathioprine use between patients with low and normal Fel-1 (Table 1). Further examination of patients with low Fel-1 with the 13C-MTG breath test revealed normal pancreatic exocrine function in all but one patient. This patient had signs of atrophy of the pancreas on CT.
Table 1

	Fecal elastase <200 μg/g	Fecal elastase >200 μg/g	p-value
Age, median (inter quartile range)	43 (39-61)	43 (33-54)	0.21
UC, active disease (Mayo score >0)	8/15 (53%)	85/177 (48%)	0.79
Self-reported increased stool frequency	6/15 (40%)	59/177 (33%)	0.58
Calprotectin, median (inter quartile range)	120 (52 to 390)	64 (18 to 260)	0.30
Azathioprine use	1/15 (7%)	27/177 (15%)	0.70

CONCLUSION: Fel-1 values below normal can be found in a minority of patients with ulcerative colitis but the vast majority of these patients have no signs of PEI when further tested with the 13C-MTG breath test. Our diagnostic strategy using Fel-1 as a screening test followed by the 13C-MTG test as a confirmatory test indicated that clinically significant PEI is rare in patients with ulcerative colitis.
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P0261 ENTERIC GLIAL CELLS PRODUCE 15-HETE TO REGULATE INTESTINAL EPITHELIAL PROPERTIES: DYSREGULATION IN CROHN'S DISEASE

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INTRODUCTION: Accumulating data demonstrate that under physiological conditions, enteric glial cells (EGC) positively regulate the intestinal epithelial barrier (IEB). EGC are necessary for IEB homeostasis, increase IEB healing and decrease IEB permeability, identifying EGC as a source for soluble factors able to reinforce the IEB. The most recently discovered prostaglandin 15dPGJ2 is produced by EGC to regulate intestinal epithelial cell (IEC) proliferation and differentiation. However nothing is known considering other polyunsaturated fatty acid (PUFA) metabolites that could also be produced by EGC.
AIMS & METHODS: The PUFA signature of the JUG embryonic cell line as well as rat adult primary cultures of EGC were established using high sensitivity liquid chromatography tandem mass spectrometry. Immunohistochemistry was used to detect the 15-LOX producing enzyme of 15-HETE on rat and human EGC cultures and on human sub-mucosal plexus. Pharmacological approach was used to determine 15-HETE impact on Caco-2 monolayer cultivated or not in presence of EGC. Direct injection of 15-HETE into the colon wall was used to measure its impact on IEB permeability *in vivo*.
RESULTS: Among the 24 PUFA metabolite measured, rat EGC mostly produced 5- and 15-HETE. They also expressed the 15-lipoxygenase 2 (15-LOX2), whereas the 15-lipoxygenase 1 was undetectable. 15-HETE increased IEC spreading, IEB resistance and decreased IEB permeability without affecting IEC proliferation. In addition, 15-LOX2 was expressed in human EGC in culture but also *in situ* in EGC from submucosal ganglia. Interestingly, 15-HETE production by EGC from CD patients was significantly reduced compared to EGC from control patients. At the same time, CD EGC were unable to decrease IEB permeability, but addition of 15-HETE backed up the permeability to control conditions. *In vivo*, 15-HETE also reduced the IEB permeability, showing the potential of 15-HETE to reinforce IEB.
CONCLUSION: This study not only presents the first evidence for EGC functional abnormalities in CD, but also reveals that 15-HETE can reduce IEB permeability
Disclosure of Interest: None declared

P0262 INFLUENCE OF ANTI-TNF THERAPY ON THE BONE METABOLISM IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Several studies have concluded that patients with inflammatory bowel disease (IBD) are at increased risk of osteoporosis. The increase of proinflammatory cytokines, as TNF-α and interleukins (IL) appear to mediate, as a pathogenic mechanism, in the loss of bone mass density (BMD) in these patients. However, the influence of anti-TNF drugs on the bone metabolism of patients with IBD is not well known. Our aim is to evaluate the influence of anti-TNF drugs on bone mineral density and markers of bone remodeling in IBD patients.
AIMS & METHODS: Prospectively we have enrolled 8 patients (2 men and 6 women) with active IBD, 2 ulcerative colitis and 6 Crohn's disease, all with indication for treatment with anti-TNF drugs. Clinical data were collected on standardized data forms. BMD values were measured by dual-energy X-ray absortiometry (Hologic QDR 4500) at the lumbar spine (L1-L4) and femoral neck (FN) baseline visit and after a year of treatment. We determined serum 25-hydroxyvitamin D3 (25OHD ng/ml) and intact parathyroid hormone (PTH pg/ml). Bone turnover markers were measured by fully automated electrochemiliminescence system (Elecsys 2010, Roche Diagnostic, Germany): aminoterminal propeptide of type collagen (P1NP) and C-terminal telopeptide of type I collagen (CTX) at baseline visit, 8 week, 6 month and a year after treatment.
RESULTS: In our study, mean age was 42 years (age range 24-54). Two patients were treated with infliximab and 6 with adalidumab. All of them had been treated previously with 5-ASA, Azathioprine in 50% and corticoids in 20%. Mean basal weight (61 kg) did not change over treatment. The BMD in lumbar spine was 1.031 (0.112) g/cm^2 at baseline and 1.037 (0.127) g/cm^2 a year after. The BMD in FN was 0.755 (0.131) g/cm^2 and 0.774 (0.120) g/cm^2 respectively. The percentage of change in lumbar spine was 1% ($p=0.77$) and in FN 2.5% ($p=0.15$). Data table show biochemical parameters and different percentages over basal state.

	Baseline	8 week	6 month	Year
25OHD ng/ml	21 (9)	21 (9) [0%]	24 (12)[14%]	23 (12) [9%]
iPTH pg/ml	27 (11)	37 (13) [37%]*	30 (11) [11%]	38 (19) [40%]
P1NPmg/L	49 (26)	66 (26) [34%]*	61 (17) [24%]	43 (23) [-13%]
β-CTX ng/ml	0.421 (0.210)	0.380 (0.328) [-9%]	0.488(0.326) [15%]	0.419(0.332) [-2%]

CONCLUSION: 1. Bone mass in IBD patients with TNF- α inhibitors treatment were similar at baseline and after a year of treatment.
2. P1NP was increased 8 week after the beginning of treatment but P1NP returned to basal level after a year. Parathyroid hormone levels seem to increase early after the beginning of treatment and remains above basal levels over time. β-CTX and vitamin D, bone resorption markers, were stable during treatment.
3. Further studies are required to analyze the relationship between this therapeutic agents and bone metabolism in IBD.
Disclosure of Interest: None declared

P0263 EDUCATION OF PATIENTS WITH CROHN'S DISEASE ON THE RISKS OF SMOKING REMAINS CHALLENGING

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INTRODUCTION: The detrimental effect of smoking on development and progression of Crohn's disease (CD) is generally accepted. Although health care professionals undoubtedly spend a lot of time in education of patients, the actual awareness of smoking risks in CD patients is unclear.
AIMS & METHODS: We assessed several smoking behaviour parameters and patients' awareness on different consequences of smoking, through a simple questionnaire in a single referral centre. During the outpatient clinic of gastroenterology, 625 consecutive patients with CD, 238 patients with ulcerative colitis (UC) and 289 patients without an inflammatory bowel disease (non-IBD controls, NC) were requested to participate. Questionnaires included questions on former and actual smoking behaviour, cessation attempts, nicotine dependence (Fagerström score), and willingness to quit smoking. Patients were questioned on their awareness of smoking-related risks on several aspects of health, including detrimental effects on CD (Table 1).
RESULTS: Participation rates were 92% for CD ($n=575$, 46% male, 44 years, 44% never smoked), 93% for UC ($n=238$, 57% male, 45 years, 50% never smoked) and 76% for NC ($n=221$, 48% male, 48 years, 55% never smoked). At diagnosis, more CD patients were active smokers compared to UC patients (40% vs. 17%, $p<0.001$). Previous attempts to stop smoking and nicotine dependence were similar in all groups. Remarkably, smoking cessation rates after

diagnosis were not higher in CD compared to UC (both 56%, p = 0.997). In contrast, more CD than UC patients started smoking after diagnosis (12% vs. 6%, p = 0.050). As shown in Table 1, the majority of patients recognized dangers of smoking on general health (98-99%), lung cancer (95-97%), myocardial infarction (89-92%), and stroke (78-87%). Although CD patients more frequently acknowledged risks of smoking on their disease, only 37% were aware of the link with CD development, 30% of increased surgical rates, and 27% of increased postoperative recurrence rates. Of note, within the CD population, awareness was unrelated to actual smoking behaviour. Increased surgery rates were acknowledged by 30% of active, 32% of former and 29% of non-smokers (p = 0.783). Active smokers not willing to quit smoking, most often denied a potential bad influence of smoking on their disease. Previous surgery, level of education and employment did not influence awareness. Finally, UC patients were more frequently aware of an inverse relationship between smoking and UC development (39% UC, 16% CD, 4% NC, p < 0.001).

Smoking increases the risk of	Certainly not	I don't think so	I don't know	I think so	Certainly
bad general health					
CD	0%	0%	2%	13%	85%
UC	1%	0%	0%	12%	87%
NC	0%	0%	0%	6%	94%
lung cancer					
CD	0%	1%	4%	18%	77%
UC	0%	1%	4%	16%	79%
NC	0%	0%	3%	12%	85%
myocardial infarction					
CD	0%	1%	10%	28%	61%
UC	0%	1%	9%	31%	59%
NC	0%	0%	8%	25%	67%
stroke					
CD	0%	2%	17%	30%	51%
UC	0%	2%	20%	29%	49%
NC	0%	0%	12%	27%	61%
CD					
CD	4%	14%	45%	19%	18%
UC	2%	19%	61%	10%	8%
NC	0%	5%	71%	14%	10%
CD surgery					
CD	1%	10%	59%	20%	10%
UC	1%	10%	72%	12%	5%
NC	0%	4%	77%	11%	8%
postoperative CD recurrence					
CD	2%	9%	62%	18%	9%
UC	0%	12%	74%	10%	4%
NC	0%	3%	81%	9%	7%
UC					
CD	4%	12%	67%	13%	4%
UC	10%	29%	48%	8%	5%
NC	1%	3%	76%	13%	7%

CONCLUSION: Although CD patients were better informed on the detrimental effects of smoking, the awareness rate was still low. These data may also suggest more denial for the adverse consequences of smoking in active smokers. More efforts need to be done on informing and educating patients regarding the risks of smoking.

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P0264 HIF-1 MEDIATES THE HYPOXIC UP-REGULATION OF DLL4 AND JAG1 IN MACROPHAGES: RELEVANCE IN IBD

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INTRODUCTION: Mucosal healing, which has been established as a target goal in inflammatory bowel disease, involved the coordinated regulation of several signaling pathways, including Notch signaling which plays an essential role in differentiation. Macrophages constitute one of the central components of the inflamed mucosa, and have the ability to modulate epithelial cell function. We have previously reported[1] HIF-1α stabilization in macrophages from the mucosa of IBD patients and we aim to analyse here the expression of Notch ligands by macrophages and the role of HIF-1.

AIMS & METHODS: U937 cells were subjected to hypoxia (3% O_2) or normoxia (21% O_2) and protein levels of HIF-1α were analysed by Western blotting and the mRNA expression of *Dll4* and *Jag1* ligands by real time PCR (n = 5). In some cases, cells were subjected to transient transfection of HIF-1α with miRNA or with an empty vector (mock, n = 5). Analysis of the *Jag1* gene promoter was performed using a ChIP assay (n = 3). Colonic surgical resections from both damaged and non-damaged mucosa were obtained from IBD patients (n = 11). In both cases, macrophages were isolated from the mucosa and the expression of *Dll4* and *Jag1* ligands was determined by real time PCR. HIF1, CD68 and Jag1 immunofluorescence experiments were performed in the mucosa of IBD patients.

RESULTS: In mock U937 cells, hypoxia induced HIF-1α stabilization and a time-dependent increase in *Dll4* and *Jag1* mRNA expression, which starts to be significantly different from normoxia 5 h later (4.1 ± 0.4 and 18.5 ± 2.1 fold induction vs macrophages in normoxia, respectively). The increase induced by hypoxia was significantly decreased when macrophages had been treated with *miHIF-1α* (0.94 ± 0.34 and 4.3 ± 2.4 fold induction vs macrophages in normoxia, respectively). ChIP assay showed HIF-1α binding to the proximal promoter region of *Jag1* gene in hypoxia through the HREs sequences located between positions -106 and -638. Immunofluorescence experiments revealed that CD68-positive cells were co-localized with HIF-1α and Jag1 in the damaged mucosa of IBD patients. The mRNA expression of *Dll4* and *Jag1* was significantly higher in macrophages isolated from damaged mucosa than from non-damaged (1.5 ± 0.2 and 3.2 ± 0.7 fold induction vs macrophages from non-damaged mucosa, respectively).

CONCLUSION: HIF-1α mediates the increase in the expression of Dll4 and Jag1 induced by hypoxia in macrophages. Jag1 expression co-localizes with HIF1α in macrophages of the mucosa of CD patients and it is higher in macrophages from damaged than from non-damaged mucosa.

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P0265 THE MACROPHAGE PHENOTYPE DIFFERENTIALLY MODULATES NOTCH SIGNALING PATHWAY IN EPITHELIAL CELLS: RELEVANCE IN DISEASE CROHN'S

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INTRODUCTION: Crohn's disease (CD) is associated with impaired epithelial barrier function. Restoration of mucosal integrity involves proliferation and differentiation of intestinal epithelial cells and Notch signaling has been shown to be central in the regulation of these processes. Macrophages are present in the microenvironment surrounding the crypts in the intestine and may modulate the behavior of epithelial cells. We have previously reported presence of both M1 and M2 macrophage phenotypes in the mucosa of ulcerative colitis patients[1]. We aim to determine the role of different macrophage phenotypes on epithelial Notch signaling and the relevance of this pathway in CD.

AIMS & METHODS: U937 cells were polarized towards a M1 phenotype with IFNγ and LPS (24h) or M2 phenotype with IL-4 (72h) and these cells were co-cultured with HT29 cells for 24h. Next we determined in epithelial cells, the expression of HES1 by static cytometry and alkaline phosphatase activity. Damaged mucosa of patients with CD was obtained. Protein levels of HES1 and the expression of CD86 (M1 marker) or CD206 (M2 marker), were quantified in the mucosa.

RESULTS: Immunofluorescence experiments show that M1 macrophages co-cultured with HT29 cells did not significantly modify the expression of HES1 (87.4 ± 5.4% vs the basal expression in HT29 cells) but induce a significant (P < 0.05) increase in AP activity in epithelial cells (125.4 ± 3.0% vs the basal activity in HT29 cells). In contrast, M2-macrophages significantly (P < 0.05) reduced in HT29 cells both, HES1 expression (62.1 ± 11.1% vs the expression in HT29 cells) and AP activity (62.5 ± 4.1% vs the activity in HT29 cells). A quantitative analysis of the number of CD86-and CD206-positive cells in the damaged mucosa of CD patients as well as protein levels of HES1, reveal a negative and significant correlation between the ratio of M2/M1 macrophages and HES1 protein levels (Pearson r -0.6775, P value 0.031, n = 10).

CONCLUSION: M2 macrophages induced a profound reduction in epithelial Notch signaling and impair enterocyte differentiation while M1 macrophages failed to do that. In the damaged mucosa of CD patients, the prevalence of M2 macrophages, through diminution of both epithelial Notch signaling and enterocyte differentiation, may impair epithelial regeneration.

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Disclosure of Interest: None declared

P0266 A DIMINISHED NOTCH SIGNALLING AND IMPAIRED ENTEROCYTE DIFFERENTIATION IS OBSERVED IN EPITHELIAL CELLS FROM DAMAGED MUCOSA OF CROHN'S DISEASE PATIENTS

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INTRODUCTION: Mucosal healing has been established as a key treatment goal in Crohn's disease (CD) that predicts sustained clinical remission and resection-free survival of patients. This process depends on the proper reconstruction of the intestinal epithelium that depends on proliferation and differentiation of progenitor cells, a process that is tightly regulated by activation of the Notch signalling. We aim to determine the regulation of the Notch pathway and epithelial differentiation in the mucosa of CD patients.
AIMS & METHODS: Colonic surgical resections from both damaged and non-damaged mucosa were obtained from CD patients (n = 11). Human intestinal crypts were isolated from mucosa by using a non-enzymatic dissociation technique based on short-term EDTA treatment. Protein levels of IAP (marker of enterocyte differentiation) and HES1 (a specific Notch target gene) were analyzed by Western blotting and immunohistochemistry (HES1). The expression of MUC2 (a marker of goblet cell differentiation), CDX2 (a transcriptional activator of intestine specific genes involved in differentiation) and Math1 (a gene that is repressed by HES1) was analyzed in epithelial cells by real time PCR. The quantitative analysis of goblet cells was performed in the mucosa stained with PAS.
RESULTS: A comparative study (fold induction vs crypts from non-damaged mucosa) revealed a significant ($P < 0.05$) diminution in protein levels of HES1 (0.28 ± 0.07) and IAP (0.20 ± 0.10) and a significant increase in mRNA levels of MUC2 (11.8 ± 2.3), CDX2 (2.1 ± 0.8) and Math1 (3.4 ± 0.8) in crypts from damaged mucosa. Immunostaining for HES1 revealed lack of this protein in epithelial cells of the damaged mucosa. The percentage of goblet cells vs. total nuclei in the crypt was significantly ($P < 0.05$) higher in the damaged ($47.8 \pm 4.4\%$) than in the non-damaged mucosa ($29.2 \pm 2.4\%$).
CONCLUSION: The diminished Notch signaling and impaired enterocyte differentiation detected in epithelial cells from damaged mucosa of CD patients may mediate the weakened mucosal healing observed in these patients.
Disclosure of Interest: None declared

P0267 HUMAN INTESTINAL FIBROBLASTS ARE NOVEL TARGET CELLS FOR ALPHA-MELANOCYTE-STIMULATING HORMONE – POSSIBLE IMPLICATIONS FOR THE TREATMENT OF STRICTURING CROHN'S DISEASE WITH MELANOCORTIN PEPTIDES AND DERIVATIVES

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INTRODUCTION: Efficient treatment against fibrotic complications like intestinal strictures is still an unmet need in patients with Crohn's disease. In dermal fibroblasts, melanocortin peptides such as a-melanocyte-stimulating hormone (a-MSH) were shown to modulate collagen synthesis. Moreover, in the bleomycin scleroderma mouse model this peptide had anti-fibrotic effects. Thus, we wondered if human intestinal fibroblasts are also target cells for melanocortins in the context of extracellular matrix synthesis.
AIMS & METHODS: Human intestinal fibroblasts were isolated from macroscopically normal colonic specimens of patients undergoing scheduled colonic surgery (n = 5) and were characterized by immunohistochemistry with anti-desmin, anti-vimentin and anti-alpha-smooth muscle actin antibodies. Melanocortin receptor (MC) expression was determined by RT-PCR. Intracellular Ca2+ mobilization indicating functional coupling of the detected MC was assessed by FURA-2AM loading and fluorescence analysis. Collagen type I expression was determined by RT-PCR and secretion of procollagen type I C-terminal peptide by ELISA.
RESULTS: Immunocytochemistry with anti-desmin, anti-vimentin and anti-alpha-smooth muscle actin antibodies confirmed a myofibroblast phenotype of isolated cells. MC expression profiling proved that these cells exclusively express MC_1. Truncated transcripts for proopiomelanocortin (POMC), the precursor of a-MSH, were also detected but no functional full-length POMC mRNA. In accordance, cells lacked POMC protein expression ruling out an autocrine loop for alpha-MSH. No Ca^{2+} mobilization was detected by FURA-2AM loading, after stimulation with a-MSH and fluorescence analysis. However, a-MSH at doses between 10^{-6} and 10^{-10} M significantly suppressed procollagen type I C-terminal peptide secretion induced by TGF-b1. This effect was not paralleled by reduction in corresponding COL(I) mRNAs – indicating a posttranscriptional mechanism of the regulatory effect of a-MSH on collagen synthesis.
CONCLUSION: These findings demonstrate that human intestinal fibroblasts are novel targets for alpha-MSH. It will be intriguing to assess the effect of other melanocortins and derivatives in these cells on collagen synthesis as well as the impact of them in animal models of intestinal fibrosis.
Disclosure of Interest: None declared

P0268 HEARING LOSS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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INTRODUCTION: IBD has many characteristics of autoimmune diseases. Sensorineural hearing loss has been reported in many autoimmune diseases. Little is known about hearing loss in patients with IBD.
AIMS & METHODS: A prospective blinded comparative study was conducted over a 3 year period. IBD patients and controls underwent a complete otorhinolaryngeal examination and eudiometry test.
RESULTS: Altogether 105 participants (76 patients and 29 controls) took part in this study. 59(77%) had Crohn's disease (CD) and 17(23%) had ulcerative colitis (UC). Mean age was 36, 51% were males and 40% of the patients were presently hospitalized due to IBD exacerbation. 16/76(21%) of the IBD patients complained of hearing loss since first IBD diagnosis and 13% had current hearing disabilities. Audiometric examination revealed that any hearing loss (mild to severe) was found in 23(30%) of the IBD population, compared to 3 (10%) of the control group ($p < 0.05$). Sensironeural was the hearing deficiency type in 93% of them. Out of 46 patients, whose extraintestinal manifestation (EIM) status was clearly documented, 43% (n = 20) had EIMs. Hearing loss was present in 5/20 (25%) of these patients, compared to 0/23 who did not have EIMs ($p < 0.01$). IBD phenotype (inflammatory vs. obstructive/fistulary), current hospitalization and disease type (CD vs. UC) was not different between these groups.
CONCLUSION: Sensironeural hearing loss may be another EIM of IBD. It is found in 30% of IBD patients, and in up to 43% of patients with other EIMs. Early hearing evaluation should be recommended to IBD patients who have other EIMs
Disclosure of Interest: None declared

P0269 ANTI-TNF-A INDUCTION REGIMEN MODULATES GUT MICROBIOTA MOLECULAR COMPOSITION WHILE INDUCING CLINICAL REMISSIONS: RESULTS FROM A PRELIMINARY EVALUATION ON CROHN'S DISEASE PATIENTS

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INTRODUCTION: IBD, and in particular Crohn's disease, is chronic inflammatory condition characterized by an abnormal immune response towards self microbiota and by an abnormal gut microbiota composition, as determined by new molecular techniques. Anti-TNF-a is one of the strongest therapeutical options available, able to induce mucosal healing and restore mucosal immune homeostasis. Little information exists on the ability of antiTNF-a to modulate gut microbiota composition.
AIMS & METHODS: Aim of our study was to evaluate gut microbiota composition in Crohn's disease patients before and after 6 weeks after anti-TNF-a therapy.
Fecal samples were collected in 3 consecutive CD patients, the first day of the first dose of anti-TNF-a therapy (infliximab) and following 6 weeks: 2 patients displayed colonic CD and 1 ileo-ciecal CD (2 males of 23 and 33 years, and 1 female of 53 years), no-one took any antibiotic 2 weeks before starting anti-TNF-a therapy or during the active treatment. Harvey Bradshaw scores at baseline and after 6 weeks were respectively 4 and 3, 7 and 3 and 4 and 1.
Microbiota composition was assessed by Metagenomic, a technique assessing 16S rRNA (Roche 454 GS Junior), following DNA isolation from stool samples stored in –80°C. Data obtained were analyzed by suite Qiime.
RESULTS: Bacteria amplicons were detected in all samples. Prevalent classes of bacteria were: Bacteroidia (min 18% - max 95%), Firmicutes (min 2% - max 58%%) and Proteobacteria (min 2% - max 22%). Following anti-TNF-a therapy, bacteroidetes reduced in all patients (min from 3% – max from 67%). Firmicutes, on the contrary, increased in levels. In 2 patients also proteobacteria increased. Species Faecalibacterium was not present in 2 out of 3, but in one patient, Fecalibacterium increased from 17% before therapy to 23% after therapy.
CONCLUSION: Anti TNF-a treatment is associated with active modulation of intestinal microbiota, including decrease in bacteroidetes and increase in firmicutes. Metagenomics seems a promising technique whose real application in clinic is still under development.
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Disclosure of Interest: None declared

P0270 CHANGING TRENDS IN IBD HOSPITAL ADMISSIONS AND MANAGEMENT IN ENGLAND, 2001-02 TO 2010-11

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INTRODUCTION: Inflammatory bowel disease is a chronic disorder, affecting 240,000 people in the UK. The long-term impact of recent advances in IBD management on hospital admissions and surgery is uncertain.
AIMS & METHODS: Our aim was to investigate trends in hospital admission, fatality rates, surgery, endoscopy and cytokine inhibitor infusions for CD and UC in England between 2001-02 and 2010-11.
We used admissions data from Hospital Episode Statistics, a national administrative database of all National Health Service hospital admissions and population data from the Office for National Statistics, England.
RESULTS: From 2001-02 to 2010-11, age-sex standardised day-case admission rates increased by 460.4% ($p<0.001$) and 127.0% ($p<0.001$) for CD and UC respectively. There was no significant change in inpatient admission rates for CD and UC. Both inpatient and day-case rates of surgery and endoscopy fell for both CD and UC [inpatient: CD surgery -8.9% ($p<0.001$) CD endoscopy -14.4% ($p<0.001$) UC surgery -6.8% ($p<0.001$) UC endoscopy -10.5% ($p<0.01$); day-case: CD surgery -75.3% ($p<0.001$) CD endoscopy -55.9% ($p<0.001$) UC surgery -66.7% ($p<0.001$) UC endoscopy -17.2% ($p<0.001$)]. Day-case infusions, including cytokine inhibitor treatment, rose in both CD and UC, by 308.9% (14.8% to 60.6%, $p<0.001$) and 3475.0% (0.4% to 15.4%, $p<0.001$) respectively.
CONCLUSION: Over the past decade inpatient admission rates for IBD have remained static, but day-case admission rates have risen whilst the requirement for surgery and endoscopy has fallen. The reduction in surgical and endoscopic activity and the switch towards day-case activity may reflect recent advances in IBD management, notably, the substantial increase in anti-TNF therapy.
Disclosure of Interest: None declared

P0271 EPIDEMIOLOGY AND TEMPORAL TRENDS (2000-2012) OF INFLAMMATORY BOWEL DISEASE IN ADULT PATIENTS IN A CENTRAL REGION OF SPAIN

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INTRODUCTION: A growing incidence of IBD in southern Europe has been recently reported, with records of pediatric cases confirming these tendencies in Spain. Data on adult population however, has not been provided for over 10 years and needs to be updated.
AIMS & METHODS: This study has two main objectives: (1) to estimate the current prevalence of IBD in central Spain, and (2) to examine recent trends in disease prevalence. A further goal was to characterize changes in disease presentation over time.
A multicenter retrospective registry of all adult patients with a diagnosis of IBD, including both Crohn's disease (CD) and ulcerative colitis (UC), attended in 5 public hospitals covering a population of 514,368 inhabitants was carried out.
RESULTS: In 2012, the prevalence of CD and UC in adults was 137.17/100,000 inhabitants [95% confidence interval (CI): 114 – 160] and 99.84/100,000 inhabitants (95% CI: 79 –119), respectively. The mean incidence rate during 2000-1012 period of CD and UC was 8.9 and 5.6/100,000 inhabitants per year, respectively. Most of our patients (75.55%) were diagnosed during the last 13 years. CD affected equally both genders; a trend to progressive increase in the age at diagnosis, ileal location and inflammatory behavior was documented for CD patients. In contrast, UC affected with a higher frequency to male subjects (57.8%, $p=0.015$), specifically at an age over 40 years old. Age at UC onset trended to progressively increase from 2000 to 2012 ($p<0.001$), but the extension on the disease remained unchanged.
CONCLUSION: A significant increase in the prevalence of IBD, especially for CD, was documented in our region regarding previous estimation in Spain. CD incidence reached similar figures to those provided for Northern Europe, increasing the burden of IBD over the health system.
Disclosure of Interest: None declared

P0272 HEPATOBILIARY DISEASES IN A PROSPECTIVE POPULATION BASED COHORT WITH INFLAMMATORY BOWEL DISEASES (ICURE)

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INTRODUCTION: The relation between hepatobiliary diseases and IBD has been the focus for scientific research for many years. There are, however, few prospective population based cohort studies in this area. Between 2005 and 2009 all newly diagnosed cases of IBD in all age groups in the Uppsala Health Care Region were registered. The cohort consists of 790 individuals corresponding to an average incidence of 20.0 new cases of UC/100 000/year and 9.9 new cases of Crohn's disease/100 000/year (REFERENCES JCC. 2013 Oct 1;7(9):e351-7. and JCC. 2014 Mar 1;8(3):215-22.)
AIMS & METHODS: During the winter 2013/14 all medical records were scrutinized and the results were collected. Liver function tests and investigation of hepatobiliary diseases were collected. Liver function tests had been checked at least once in 97.1% of the cohort. The main method for the diagnosis of PSC was magnetic resonance cholangiopancreaticography (MRCP), or endoscopic retrograde cholangiopancreatography (ERCP) when the results were ambiguous. Parenchyma diseases were investigated with liver biopsy and biochemical tests. IBD was classified according to the Montreal classification.
RESULTS: Seventeen patients with PSC were diagnosed corresponding to an overall prevalence of 2.15% (for UC 1.90% and for Crohn's disease 2.65%). The average age of these was 25,0 years. Among the 92 paediatric patients (<17 years old) three patients had autoimmune hepatitis, but none PSC. Three patients have undergone liver transplantation and one has died of colonic carcinoma. Eleven patients have demonstrated persistent elevation of ALP but have had a normal MRCP or refused further investigation.
CONCLUSION: In this prospective population based cohort consisting of 526 patients with UC and 264 with Crohn's disease, 17 cases of PSC was found, among whom ¼ so far have been liver transplanted or have died because of carcinoma. The average age of those affected by PSC is considerably lower than usually is reported. Forthcoming study of ICURE will reveal if more patients will be affected by liver disease.
Disclosure of Interest: None declared

P0273 CELIAC DISEASE IN IBD. OBSERVATIONS FROM A POPULATION BASED COHORT OF IBD (ICURE)

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INTRODUCTION: IBD and celiac disease are diseases with worldwide distribution and an increased incidence of them have been reported from many areas. There is a shortage of studies investigating the possible concomitant appearance of these diseases in the same individual and whether those affected by both diseases demonstrate any particular phenotype. ICURE (IBD Cohort Uppsala health Region) is a population based cohort of individuals with ulcerative colitis ($n=526$, JCC. 2013 Oct 1;7(9):e351-7) Crohn's disease ($n=264$, JCC. 2014 Mar 1;8(3):215-22) and microscopic colitis ($n=272$). We have previously reported the occurrence of celiac disease among patients with microscopic colitis (Scand J Gast 2013;48:825-830) and we now aimed to study the patients with UC and Crohn's disease in the same respect.
AIMS & METHODS: In 790 individuals diagnosed with ulcerative colitis or Crohn's disease between 2005 and 2009, the possible concomitant occurrence of celiac disease was investigated. Medical notes were scrutinized and pathological specimens were re-examined.
RESULTS: Three hundred and ninety-nine of the 790 patients had been examined for the possibility of celiac disease, corresponding to an investigation of 49.4% of the total cohort. Sixteen patients with celiac disease were found, representing 2.05% of the cohort. Two patients with IBD and celiac disease developed collagenous colitis 5 and 7 years later and one PSC after 3 years. A young man with UC developed collagenous sprue. Compared with the non-celiacs the patients with both IBD and celiac disease were younger (22.5 vs. 34.5 years, $p=0.0015$) and those with colitis more often had an extensive disease (9/3 vs. 163/328, $p=0.0026$) and 76% were women.
CONCLUSION: Celiac disease is sufficiently common among patients with IBD to motivate screening for this condition in the regular workup of patients with ulcerative colitis and Crohn's disease. Those affected by both diseases are predominantly young women with extensive colitis.
Disclosure of Interest: None declared

P0274 WORK DISABILITY AND PRODUCTIVITY LOSS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES IN HUNGARY IN THE ERA OF BIOLOGICS

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INTRODUCTION: The IBD is a chronic and potentially debilitating disease course can represent a heavy burden for patients, impacting every aspect of the affected individual's life.
AIMS & METHODS: To assess work disability (WD) rates in an inflammatory bowel disease (IBD) cohort involving patients with Crohn's disease (CD) or ulcerative colitis (UC) cohort and to identify possible clinical or demographic factors associated with WD. Data from 443 (M/F: 202/241, CD/UC: 260/183, mean age: 35.5 (CD) and 40.5 (UC) years, biological drug exposure 31.2% / 11.5%) consecutive patients were included. WD data were collected by questionnaire and the Work Productivity and Activity Impairment (WPAI) instrument. Disability pension (DP) rates in the general population were retrieved from public databases.
RESULTS: The overall DP rate in this IBD population was 32.3%, with partial disability in 24.2%. Of all DP events, 88.8% were directly related to IBD. Overall, full DP was more prevalent in IBD (RR:1.51, $p<0.001$) and CD (RR:1.74, $p<0.001$) but not in UC compared to the general population and also in CD compared to UC (OR: 1.57, $p=0.03$). RR for full DP was increased only in young CD patients ($RR_{<35\ year\ olds}$: 9.4; $RR_{36\text{-}40\ year\ olds}$: 9.4 and 5.6, $p<0.01$ for both). In CD, age group, previous surgery, disease duration, frequent

relapses, and the presence of arthritis/arthralgia were associated with an increased risk for DP. Among employed patients, absenteeism and presenteeism was reported in of 25.9% and 60.3% patients, respectively, leading to a 28% loss of work productivity and a 32% activity loss, and was associated with disease activity and age group. Average cost of productivity loss due to disability and sick leave with human capital approach was 1450 and 430 €/patient/year, respectively (total productivity loss 1880 €/patient/year).

CONCLUSION: Risk of DP was highly increased in young CD patients (six to nine fold). Previous surgery and presence of arthritis/arthralgia was identified as risk factor for DP. Work productivity is significantly impaired in IBD and is associated with high productivity loss.

Disclosure of Interest: None declared

P0275 INCREASED INTESTINAL PERMEABILITY AMONG FIRST-DEGREE RELATIVES OF CROHN'S PATIENTS IS NOT ASSOCIATED WITH INCREASED MUCOSAL ULCERATIONS ON SMALL BOWEL VIDEO CAPSULE ENDOSCOPY

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INTRODUCTION: First-degree relatives (FDR) of Crohn's disease (CD) patients have the highest risk for developing CD. CD patients and a substantial portion of FDR have increased intestinal permeability. It is unclear whether FDR have abnormal permeability because of early, asymptomatic CD or whether this occurs without mucosal inflammation. Video capsule endoscopy (VCE) is the most sensitive means of imaging the small intestine and can identify mucosal lesions suggestive of subclinical CD. The purpose of our study was to determine if abnormal small intestinal permeability in healthy FDR is associated with small bowel mucosal abnormalities detected by VCE.

AIMS & METHODS: 342 CD patients consented to have their FDR between 10-45 years of age contacted regarding study participation. Eligible FDR underwent small bowel permeability testing as measured using the lactulose/mannitol (L/M) test that is based on the fractional urinary excretion of these sugars. FDR with abnormal permeability (defined as ≥ 0.030) were compared to FDR with normal small permeability (<0.025) by VCE to assess for small bowel inflammatory changes. The primary outcome was the number of mucosal ulcerations seen on VCE in each permeability group.

RESULTS: 223 FDR consented to participate and completed the intestinal permeability test. 40 (17.5%) had abnormally increased permeability. Subsequently, 59 subjects with normal and 29 subjects with abnormal permeability underwent VCE. On VCE, there was no difference in small bowel mucosal abnormalities with a mean of 2.27 (range 0-16) ulcers in the normal and 2.52 (range 0-15) ulcers in the abnormal permeability groups respectively (NS). Surprisingly, 23.5% of asymptomatic FDR had more than 3 small bowel lesions as shown by VCE, irrespective of their intestinal permeability. These lesions were significantly associated with fecal calprotectin of $>$ 50 mg/g stool.

CONCLUSION: There is no association between small bowel ulcerations seen on VCE between asymptomatic FDR of Crohn's patients with abnormally increased intestinal permeability and FDR with normal permeability. Thus, the increased small bowel permeability in FDR does not seem to be caused by subclinical CD, but is likely an intrinsic gut barrier defect. Surprisingly, over 23% of these FDR had 3 or more small bowel ulcers, associated with increased fecal calprotectin levels.

Disclosure of Interest: None declared

P0276 PRE-POUCH ILEITIS: A MORE TREATMENT REFRACTORY SUB-GROUP OF POUCHITIS

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INTRODUCTION: Following restorative proctocolectomy (RPC) with ileal pouch-anal anastomosis (IPAA) for ulcerative colitis, (UC) up to 50% of patients will develop pouchitis. Moreover, a subgroup will also develop inflammation in the pre-pouch ileum (pre-pouch ileitis, PI). Endoscopically, PI can mimic Crohn's disease (CD) but evidence suggests that PI may be a distinct disease entity. PI has been reported more frequently in UC patients with primary sclerosing cholangitis (PSC) undergoing IPAA. This group is also known to have higher rates of backwash ileitis and certain similarities have also been described between this and PI[1].

AIMS & METHODS: Our aim was to assess the incidence, predictive factors and response to treatment in a single centre cohort of pouch patients. We retrospectively collected data on 246 consecutive UC patients who underwent RPC and IPAA over the last 15 years. Endoscopic and histological records were used to identify individuals with PI, defined as ulceration seen in the afferent limb at endoscopy and evidence of active inflammation in biopsy samples.

RESULTS: Seventy-nine (32%) of the 246 patients were found to have had pouchitis. Twelve patients were found to have concurrent PI, representing 5% of the total cohort. No patients had PI in the absence of pouchitis. Of those with PI, 6 patients (50%) had antibiotic-refractory, chronic pouchitis (as previously defined[1]): four of whom required steroids/immunomodulators and two required treatment with anti-TNF agents. One had antibiotic-dependent pouchitis. The remaining 5 were antibiotic responsive and did not require long-term treatment for their symptoms. A higher proportion of patients in the PI group had PSC (2 of 12, 17%) compared to the non-PI group (11 of 234, 5%) though this difference did not reach statistical significance ($p = 0.07$).

Table 1: Showing demographic data for patients with and without pre-pouch ileitis (PI)

	PI (n = 12)	Non-PI (n = 234)
Gender (female:male)	4:8 (33%:66%)	109:125 (47%:53%)
Smoker	1 (8%)	26 (14%, n = 185)
Pouchitis	12 (100%)	67 (30%, n = 227)
PSC	2 (17%)	11 (5%, n = 234)
EIM	1 (8%)	21 (10%, n = 219)

CONCLUSION: Compared with pouchitis, PI is a rarer and less well-defined condition. Its recognition is relevant to clinicians as the inflammation involved is more extensive and can be more treatment refractory than isolated pouchitis. Our study demonstrates high rates of antibiotic-refractory, chronic pouchitis among those with concurrent PI when compared with published pouchitis cohorts[2]. An alternative possibility is that PI is a distinct clinical entity with different pathophysiology to isolated pouchitis. The diagnosis of PI should be considered in all patients with ulceration of the afferent limb rather than making the assumption that Crohn's disease is the underlying condition.

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P0277 UPTAKE OF INFLUENZA VACCINE IN ULCERATIVE COLITIS-A LONGITUDINAL, POPULATION BASED STUDY

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INTRODUCTION: The incidence of vaccine-preventable disease is increasing. Current practice guidelines recommend annual influenza vaccination for all inflammatory bowel disease (IBD) patients.

AIMS & METHODS: We aimed to determine the annual uptake of influenza vaccine in UC patients. Using the Business Objects database of Clalit Health Services in the Tel Aviv district we identified all patients over 18 years old with a diagnosis of Ulcerative colitis (UC) on 31.12.2005. This cohort was followed until 31.12.2012. Subjects over age 50 without IBD who are also targeted for influenza vaccination served as controls. The uptake of annual influenza vaccination was recorded.

RESULTS: 470 UC patients were included (241 (51.3%) males, age 50.4±18.4 years, disease duration 158.9±86.5 months), and 2960 controls. During the years 2006, 2007, 2008, 2009, 2010, 2011 and 2012 the uptake of influenza vaccination was 101 (21.5%), 122 (26.0%), 147 (31.3%), 181 (38.5%), 177 (37.7%), 170 (36.2%) and 178 (37.9%) amongst UC patients, and 993 (33.5%), 1360 (45.9%), 1524 (51.5%), 1611 (54.4%), 1446 (48.9%), 1576 (53.2%) and 1557 (52.6%) amongst controls ($p<0.0001$ for every year). Independent predictors of vaccination included age (OR, 1.05; 95% CI, 1.03-1.06; $p<0.001$) and cardiovascular risk (OR, 1.81; 95% CI, 1.31-2.49; $p<0.01$).

CONCLUSION: Although uptake influenza vaccination is consistently lower in UC compared to controls, an upward trend was observed over the study period. Public health initiatives should target this high-risk population to promote immunization.

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P0278 UK IBD TWIN AND MULTIPLEX REGISTRY: CONCORDANCE AND ENVIRONMENTAL RISK FACTORS OF TWINS WITH IBD

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INTRODUCTION: Twins offer insight into the relative importance of genetic and environmental factors in disease development. Twin studies to date show concordance in monozygotic twins with CD and UC to be 20-55% and 6.3-17% respectively. Dizygotic concordance rates are 0-3.6% (CD) and 0-6.3% (UC) (1). The UK IBD Twin and Mutliplex Registry is a research database established in October 2013; this study reviews disease patterns and environmental risk factors of twin pairs recruited.
AIMS & METHODS: Data subjects were recruited via clinician referral, IBD charities and retracing members of a database dormant since 1996. Adult twin pairs discordant and concordant for IBD were recruited. Data subjects completed a questionnaire regarding demographics, disease history and environmental exposure. Medical records were reviewed when available.
RESULTS: Demographics, Concordance and Zygosity: 100 twin pairs were recruited. Mean age 57 years 5 months, range 21-83 years. 31 monozygotic:69 dizygotic. Ratio CD:UC = 48:52. Concordance of twin pairs classified by zygosity and disease type is as follows:

	Crohn's Disease	Ulcerative Colitis
Monozygotic	**53.3%**	**25%**
Dizygotic	**10%**	**19.4%**

Early Environment: Higher rates of exclusive breastfeeding were reported in concordant compared with discordant pairs (27.3% n = 22 pairs vs 16.7% n = 78 pairs). Self reports of perceived childhood illness did not show any difference between IBD and healthy twins of discordant pairs (16.7%, 13/78 vs 19.2%, 15/78). However, the IBD twin more often recalled frequent gastrointestinal infection prior to IBD onset in comparison with their healthy twin (10.3%, 8/78 vs 3.8%, 3/78).
Diet: IBD twins from discordant pairs reported higher rates of consuming "ready made" meals at least weekly before disease incidence (12.8%, 10/78 vs 5.1%, 4/78).
Smoking: On review of discordant twin pairs (n = 72), there was no significant difference in numbers of current, ex and non smokers between subjects with UC (n = 41), CD (n = 32) and their healthy twin at time of symptom onset.
Medication and Stress: On review of all IBD sufferers, 7.1% (8/112) and 13.4% (15/112) used NSAIDS and antibiotics within 3 months preceding onset. 48.2% (54/112) reported significant stress within the year preceding onset.
Time of onset in concordant pairs: The mean lag between diagnosis of concordant pairs was 7 years 5 months.
CONCLUSION: Concordance of twin pairs with CD is in keeping with previous studies. However UC concordance is greater than expected; in particular 19.4% dizygotic twin pairs with UC are concordant. This is 4 fold expected rates of non-twin sibling concordance(2), suggesting early environment to be important in pathogenesis. This study supports an associaton between diet, stress and gastrointestinal infection with IBD onset. The lack of associatoin with smoking at incidence may reflect sample size.
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Disclosure of Interest: None declared

P0279 TEMPORAL TRENDS IN NON-STRICTURING, NON-PENETRATING BEHAVIOUR AT DIAGNOSIS OF CROHN'S DISEASE IN ÖREBRO, SWEDEN: A POPULATION-BASED RETROSPECTIVE STUDY UPDATED FOR 1988-2010

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INTRODUCTION: The incidence of Crohn's disease is continuing to rise in several countries and in others it appears to have already levelled off. We updated our previous population based study[1] by retrieval of additional information on patients diagnosed with Crohn's disease between 1963 and 1987, and included patients diagnosed with Crohn's disease up to 2010.
AIMS & METHOD: The aim was to assess temporal trends in incidence, prevalence and disease phenotype at diagnosis. Patients of all ages with a potential diagnosis of Crohn's disease were identified retrospectively by evaluation of medical notes of all current and previous patients at the Colitis clinic, Örebro University Hospital amended by computerised search in the inpatient, outpatients, primary care and histopatological records. The medical notes were reviewed and patients were included if they lived within the catchment area at any time during their disease course, were diagnosed between 1963-2010 and fulfilled the Lennard-Jones criteria for Crohn's disease. Disease phenotype was defined according to the Montreal classification.
RESULTS: The mean incidence for the period 1988-2010 was $7.6/10^5$ (95% CI: $6.7\text{-}8.4/10^5$). A comparison with the earlier period 1963-1987 showed increased age and sex standardised incidence rates of Crohn's disease, with an incidence rate ratio of 1.32 (1.11-1.57). The median (range) age at diagnosis increased from 28 (3–79) years to 37 (5–87) years (p = 0.0002). Similarly, the point prevalence increased from $178/10^5$ (157-199) on 31 December 1987 to $267/10^5$ (244 – 291) on 31 December 2010. Non-stricturing, non-penetrating disease at diagnosis increased from 12.2% in 1963-1987 to 32.3% in 2005-2010.
CONCLUSION: The incidence of Crohn's disease during the last two decades increased. A striking increase in non-stricturing, non-penetrating disease at diagnosis was observed, suggesting earlier diagnosis or phenotypic change. The observed point prevalence in 2010 is among the highest reported.
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Disclosure of Interest: None declared

P0280 INTERLEUKIN 6 GEN POLYMORPHISM IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Interleukin 6 (Il-6) plays an important role in the development of inflammatory process in IBD patients. The 174 G/C IL-6 promoter polymorphism affects IL-6 transcription. The GG genotype seems to induce higher IL-6 levels while the C allele (GC or CC) seems to be associated with decreased transcription and secretion of IL-6.
AIMS & METHODS: Our study aimed to evaluate the effect of single nucleotide polymorphism of IL-6 (174 G/C) on the disease course in patients with UC and CD.
Material and methods: 105 patients (aged 18-75 years) with diagnosed IBD: 50 with CD and 55 with UC were involved in the study. The controls consisted of 124 healthy individuals. In all patients were evaluated following parameters: disease duration, disease location, presence of complications, present pharmacotherapy, past surgical procedures, BMI, cigarette smoking. In all subjects morphology, biochemical parameters, CRP, fibrinogen, IL-6 level and IL-6 polymorphism were assessed.
RESULTS: No statistically significant differences in IL-6 polymorphism were observed between patients with UC, CD and controls. Patients with GG genotype were significantly younger at the disease onset. In IBD patients with GG genotype higher mean IL-6 level was noticed as compared to other genotypes (4.685 +/- 5.9 vs 2.715 +/- 5.1 in GC and 3.186 +/- 3.6 in CC). In both UC and CD patients with GG and GC genotype a positive correlation between IL-6 and fibrinogen level as well CRP was found. In IBD patients with CC genotype no correlation between IL-6 and fibrinogen was found (p = 0.48).
CONCLUSION: The risk of developing IBD is not connected with IL-6 polymorphism. However, IL-6 variation might have an influence on the course of the disease in IBD patients.
Disclosure of Interest: None declared

P0281 THE TPMT AND ABCB1 POLYMORPHISMS IN IBD PATIENTS IN CRETE: IMPACT ON DISEASE AND RESPONSE TO TREATMENT

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INTRODUCTION: It is well known that polymorphisms of the TPMT gene (coding for thiopourine methyl-transferase), influence response to treatment with azathioprine. Polymorphisms of the ABCB1 gene (coding for p-glycoprotein 170) has been associated with IBD and resistance to treatment but results are conflicting.
AIMS & METHODS: The aim of this study was to determine the frequencies of TPMT and ABCB1 gene polymorphisms in IBD patients from Crete, a population genetically homogeneous, and how these polymorphisms might influence response to treatment and disease behaviour. A total of 222 IBD patients, records were reviewed for intake of azathioprine, possible adverse reactions, response to treatment and need for colectomy. All patients were genotyped for TPMT gene polymorphisms, that have been related to intolerance to azathioprine (G238C, G460A and A719C) as well as ABCB1 gene polymorphisms (G2677T/A and C3435T), using a PCR-RFLP method. The same polymorphisms were also determined in 119 age and sex healthy controls.
RESULTS: Allele frequencies of TPMT gene in our study population were found to be in concordance with those reported in other Caucasian populations. 76 IBD patients were identified receiving azathioprine, of whom 16 were discontinued (10 CD, 6 UC) due to adverse reaction. 2 of them were found to carry the G460A and A719G alleles (TPMT 3A genotype) (12.5%). For the ABCB1 gene, G2677T/A allele frequencies were found to be similar to those reported in the literature. There was no association of G2677T/A or C3435T with clinical phenotype, or resistance to treatment. However, 77.3% of 22/222 patients who did not respond to therapy and required surgery, were found to carry both the C3434T and the G2677T mutation
CONCLUSION: Our study was conducted in a genetically homogenous population in the island of Crete. No correlation of any single SNP was found with

either clinical activity or response to treatment. However, most patients who carried both the G2677T and C3435T mutations were refractory to treatment, a finding which implies that resistance to treatment in IBD patients is a more complex issue, which requires the presence of a genetic locus rather than a single SNP.
Disclosure of Interest: None declared

P0282 FCΓ RECEPTOR TYPE IIIA POLYMORPHISMS AND THEIR CORRELATION WITH CLINICAL OUTCOME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE DURING A LONG TERM FOLLOW UP

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INTRODUCTION: A total of 20-30% of patients with active Crohn's disease (CD) do not respond to anti-TNF-α treatments and up to 40% of patients in chronic therapy experience a loss of response. Furthermore about 50% of patients with ulcerative colitis (UC) experience a loss of response to anti-TNFα therapy after one year. The cause of this limited efficacy is unclear, but past studies hypothesized that the individual variation of drug metabolism may play an important role. Thus, given the limited data available, the role of Fcγ IIIa receptor (i.e. one of the four receptors involved in the catabolic pathway of anti-TNF-α drugs) polymorphisms should be further explored.
AIMS & METHODS: The aim of this prospective, long-term follow up study was to evaluate the correlation between Fcγ IIIa receptor polymorphisms and clinical outcome in IBD patients undergoing biologic therapy.
We enrolled consecutive IBD patients who achieved clinical remission by anti-TNF-α therapy. Blood samples were collected at the beginning of biological therapy. The assessment of IBD activity was based on the Harvey-Bradshaw Index score (HBI, remission <5, mild disease 5-7, moderate disease 8-16, severe disease >16) for CD patients and on the Mayo score (Mayo <2 remission, mild disease 2-5, moderate/severe disease 6-12) for UC patients. Biochemical evaluation and clinical score were assessed every 8 weeks. For the genotyping analysis we used a Light Snips (Tib-Molbiol, Genova, Italy) and the Real-Time PCR Technique developed by Light Cycler 480 Instrument (Roche, Mannheim, Germany).
RESULTS: We prospectively included 39 patients (12UC/27 CD, 16F/23M) with a median follow-up of 66.8 weeks (10-112). A total of 25 (64.1%) (10UC/15CD) patients kept in remission during the whole follow up period, while 14 (35.9%) (2UC/12CD) experienced disease relapse. As shown in the Table, four out of 14 (28.6%) (1UC/3CD) patients who experienced disease relapse, had FcγIIIa-158 V/V receptor polymorphism, while the remaining 10 (71.4%) (9CD/1UC) had FcγIIIa-158 F/V or F/F receptor polymorphisms. Out of 25 patients who kept in remission, 3 (12%) (1CD/2UC) had FcγIIIa-158 V/V receptor polymorphism, whereas the remaining 22 (88%) (14CD/8UC) showed FcγIIIa-158 F/V or F/F receptor polymorphisms. Patients in remission tended to have more often FcγIIIa-158 V/V receptor polymorphism compared to patients who relapsed, but statistical significance was not reached.

	Patients in Remission (n = 25)	**Relapsers (n = 14)**	*p value*
Polymorphism **V/V**	3 (12%)	4 (28.6%)	0.2251
Polymorphism **V/F +F/F**	22 (88%)	10 (71.4%)	

CONCLUSION: The evaluation of Fcγ IIIa-158 V/V receptor polymorphism does not seem useful in identifying patients who are more likely to lose anti TNF-α response during long term period. However, further larger studies are necessary to investigate the role of Fcγ IIIa receptor polymorphisms.
Disclosure of Interest: None declared

P0283 GENOME-WIDE STUDY OF ANTI-TNF RESPONSE IN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Biomarkers predictive of treatment response will help select the optimal treatment for the individual patients. Genome-wide association studies (GWAS) on anti-TNF response in patients with Crohns Disease (CD) and ulcerative colitis (UC) are limited.
AIMS & METHODS: We performed a GWAS using ImmunoChip on a clinically-based cohort of anti-TNF treated patients with CD and UC. Data on the first treatment of anti-TNF was sampled retrospective from 18 medical departments in Denmark by young medical doctors from the patient records. Efficacy was evaluated using a simple 3-step scale (full/partial/non-responds) based on the information in the patient records. Efficacy reflected the maximum response within 26 weeks after anti-TNF treatment initiation. In total, 130061 autosomal single nucleotide polymorphisms (SNPs) pass quality control QC) (62341 failed QC) in 592 unrelated individuals (+ 34 failing QC). SNPs were assessed for full versus non-responders (partial responders were omitted).
RESULTS: In total, 364 cases had CD (270 full, 41 partial, and 53 non-responders) and 197 cases had UC (124 full, 23 partial, and 50 non-responders) and 31 cases had undetermined disease and/or response. Loci previously published to be risk factors for CD or UC could be shown to be significantly associated with differences in anti-TNF response in CD (full vs. non-response) and UC (full vs. non-response), respectively.
CONCLUSION: This is the first GWAS of anti-TNF treatment response in IBD. Power for detecting associated markers was limited. Collaboration between owners of anti-TNF treated cohorts e.g. in the regi of the International Inflammatory Bowel Disease Genetic Consortium (IIBDGC) may increase the power for identifying SNPs associated with treatment response.
Disclosure of Interest: M. Hübenthal: None declared, A. Franke: None declared, V. Andersen Consultancy for: MSD & Janssen

P0284 RARE VARIANTS IN XIAP IN MALE PEDIATRIC-ONSET CROHN'S DISEASE

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INTRODUCTION: The genetic basis of inflammatory bowel disease (IBD) is incompletely understood and it has been suggested that rare genetic variants contribute to the heritability of IBD.
AIMS & METHODS: Here, we aimed to study rare variants involved in the pathogenesis of IBD. We performed exome sequencing and detailed immunological profiling in a patient with early onset Crohn's disease (CD). The coding region of the gene encoding X-linked inhibitor of apoptosis protein (XIAP) was sequenced in samples of 275 paediatric IBD patients and 1047 adult-onset CD patients. XIAP genotyping was performed in samples of 2680 IBD patients and 2864 healthy controls. Functional effects of the identified variants were investigated in primary peripheral blood mononuclear cells (PBMCs) and cultured cell lines.
RESULTS: A novel, de novo, nonsense mutation in the gene encoding XIAP, a gene previously linked to primary immunodeficiency, was identified in a male patient with early-onset CD. Sanger sequencing of XIAP in large cohorts of paediatric IBD and adult-onset CD revealed several additional XIAP variants. XIAP variants were detected in four percent of male patients with paediatric-onset CD and were confined to this subset of IBD patients without detection of XIAP variants in either UC or adult-onset CD. CD in patients harbouring XIAP variants was characterized by small and large intestinal involvement, perianal disease, and stricturing behaviour. Functional studies in primary PBMCs and cultured cell lines revealed that the majority of identified XIAP variants were associated with selective defects in NOD1 and NOD2 signalling. NOD1/2 defects occurred as a consequence of impaired association of mutant XIAP with RIPK2 and/or altered XIAP-dependent ubiquitylation of RIPK2 thus uncoupling NOD1/2 from its downstream mediator NF-κB.
CONCLUSION: Our studies reveal the frequent occurrence of XIAP variants in male, pediatric onset CD. Moreover, our data provide a mechanistic basis to the previously unexplained observation of functional NOD2 defects in the absence of genetic variants in NOD2. Finally, given the known association of XIAP mutations with primary immunodeficiency and the observed defect in NOD1/2 signaling, our data lend further support to the concept of primary immunodeficiency in a subset of CD patients.
Disclosure of Interest: None declared

P0285 MALNUTRITION SCREENING IN INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: According to current guidelines, all IBD patients should be screened regularly for malnutrition with a validated tool (focusing on BMI, weight loss and food intake). In a previous screening study conducted in hospitalized patients (n = 1252) malnutrition was as observed up to 20% using the body mass index (BMI) calculation, while it was high as 40% according to the validated malnutrition universal screening tool (MUST). We hypothesized that even MUST is not the sufficient method to evaluate the risk of malnutrition of an IBD patient.
AIMS & METHODS: 173 consecutive IBD (126 with Crohn's disease – CD and 47 with ulcerative colitis – UC) patients were enrolled into the study. Body composition was measured by InBody 720 body analyser device, using the bioelectrical impedance method. BMI and MUST were also calculated and compared to main results of BIA (skeletal muscle mass – SMM, body fat mass – BFM fat free mass-FFM).
RESULTS: Rate of malnutrition in IBD patients was detected in 16%, 32% and 44% in patients using BMI, MUST and BIA, respectively. Almost half of the CD patients have a high risk of malnutrition based on the BIA parameters (48%), while it was lower using the MUST criteria (34%) or the simple BMI calculation (17%).
We compared patients' body composition regarding their ranking on MUST scale. We found that UC patients' SMM and FFM altered significantly in the

MUST cathegories (SMM p = 0.032, FMM p = 0.034 S, BFM p = 0.083 NS), while we found no significant changes among CD patients. (SMM p = 0.823, FMM p = 0.815, BFM p = 0.660 NS).
Although the differences weren't significant, highest risk of malnutrition was detected in stenosing CD patients (57%, 43% and 29% with BIA, MUST and BMI, respectively). High portion of CD and UC patients was underweighted (48% vs. 34%). Fat tissue deficiency was more pronounced in CD than in UC (52% vs. 23%), even in patients with stenosing disease phenotype (57%).
CONCLUSION: BMI calculation is not the appropriate method to estimate the risk of malnutrition in IBD patients. MUST score calculation is able to detect a higher portion of endangered subjects. Although the availability is not as wide as it should be, the BIA method is the most accurate test to evaluate the risk of malnutrition. According to our findings it is a useful tool to plan the dietary therapy of the patients, and it can be a recommended method especially in UC patient care.
Disclosure of Interest: None declared

P0286 CORRELATION BETWEEN THE CLINICAL, ENDOSCOPIC AND HISTOLOGICAL ACTIVITIES OF ULCERATIVE COLITIS

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INTRODUCTION: The assessment of ulcerative colitis (UC) activity is based on a combination of symptoms, clinical examination and endoscopic finding. The most important goals of the recent therapies of UC are to induce and maintain clinical remission and to achieve mucosal healing. Mucosal healing is defined as Mayo endoscopy subscore of 0 or 1 in the majority of the studies. Interestingly, rate of endoscopic remission has been shown to be higher than that of clinical remission in some trials.
AIMS & METHODS: The **aim** of our study was to evaluate the correlation between clinical and endoscopic disease activities of UC defined by activity scores. Clinical activities were defined by two activity indices: the Rachmilewitz Activity Index (CAI) and the partial Mayo score. Every patient underwent colonoscopy performed by 3 experienced gastroenterologists and endoscopists. They graded the findings both according to the endoscopic part of the Rachmilewitz Activity Index (EI) and the Mayo endoscopic subscore. Mucosal healing was defined as Mayo endoscopic subscore and EI of 0. Histological activity was scored by Riley score.
RESULTS: 100 UC patients were enrolled in the study (49 males, 51 females; mean age at diagnosis: 32.5 years). They were diagnosed on the basis of standard clinical, endoscopic and histologic criteria. Clinical and endoscopic activities showed strong correlations using both scoring systems (p = 0.0029 and p = 0.0001). Endoscopic disease activity also correlated with the histological activity (p≥0.001). Significant correlation was shown between the clinical activity and mucosal healing (p = 0.0012 and p≥0.001). No association was showed with the extension of the disease and clinical or endoscopic activity.
CONCLUSION: Assessment of mucosal healing is very important for guiding therapy and for evaluation of remission in patients with UC. Our result showed that the correlation between the clinical, endoscopic and histological activities is very good in UC. Mucosal healing highly associated with clinical remission.
Disclosure of Interest: None declared

P0287 DIAGNOSTIC DELAY IN PEDIATRIC CROHN'S DISEASE PATIENTS IS LONGER THAN IN PEDIATRIC ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: We have recently shown that the median diagnostic delay (time from first IBD symptoms until IBD diagnosis is established) was 9 months in adult Crohn's disease (CD) patients and 4 months in adult ulcerative colitis (UC) patients in Switzerland. Of note, 25% of CD patients had a diagnostic delay >24 months. We also showed that the length of diagnostic delay in CD patients represents a risk factor for complicated disease course and intestinal surgery. There is a lack of data regarding diagnostic delay in pediatric IBD patients.
AIMS & METHODS: We aimed to assess the diagnostic delay in pediatric CD and UC patients and to identify risk factors for long diagnostic delay. Data from the Swiss IBD cohort study were analyzed. Patients were recruited from university centers (80%), regional hospitals (19%), and private practices (1%). Data on diagnostic delay was provided by parents and physician questionnaires. Diagnostic delay was further divided into the time interval from first symptoms to the first consultation with the physician (patient-related interval) and the interval from first physician consultation until IBD diagnosis was established (physician-related interval). Long diagnostic delay was defined as delay lying avove the 75th percentile. Non-normal data are presented as median, interquartile range [IQR] and range.
RESULTS: A total of 100 pediatric CD (37% females) patients and 75 pediatric UC patients (56% females) were included. Age at disease onset was 12 [10-14] years in CD and 11 [7-13] years in UC patients. Diagnostic delay in CD was 4 [2-8] (range 0-82) months with the interval form first symptoms to physician visit of 1 [0-3] (range 0-24) months and from physician visit to diagnosis of 3 [1-9] (range 0-82) months. In UC patients the median diagnostic delay was 2 [1-7] (range 0-52) months with an interval from first symptom onset to physician visit of 0 [0-3] (range 0-36 months) and from physician visit to diagnosis of 2 [1-4] (range 0-20) months. Diagnostic delay in CD patients was significantly longer than in UC patients (median 4 vs. 2 months, p = 0.011). Long diagnostic delay was defined as period of >8 months in CD and >7 months in UC patients. Neither gender, age at diagnosis, disease location, positive IBD family history, nor provenience (rural vs. non-rural) were associated with long diagnostic delay.
CONCLUSION: the median diagnostic delay in pediatric CD and UC patients in Switzerland is 4 and 2 months, respectively. However, one fourth of pediatric CD patients needs >8 monhts and one fourth of pediatric UC patients needs >7 months from first symptom onset to IBD diagnosis.
Disclosure of Interest: None declared

P0288 BEHAVIOR OF P-GLYCOPROTEIN 170 (P-GP) FUNCTIONAL ACTIVITY IN PERIPHERAL BLOOD LYMPHOCYTES (PBL) OF IBD PATIENTS DURING TREATMENT WITH ANTI-TNFS

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INTRODUCTION: Pgp, encoded by the MDR1 gene is a transmembrane, ATP-dependent, efflux pump, expressed in cells with barrier function and PBL, removing drugs, toxins, xenobiotics. IBD share drugs Pgp influenced with other diseases (as steroids, 6-MP in leukemia cells). Pgp overexpression was implicated in highly active resistant RA (Tsujimura, *Ann Rheum Dis* 2008) induced by IL2 and TNF, influencing steroid efflux from lymphocytes, reporting that a single infliximab (IFX) infusion overcame refractoriness with elimination of Pgp high expressing CD4+lymph and recovery of dexametasone in PBL with Ppg marked decrease. Pgp measure in PBL could be an early marker of AntiTNFs efficacy and Pgp activity could modify the efflux of concurrent Pgp substrates drugs.
AIMS & METHODS: We aimed to study Pgp activity in PBL of IBD pts. treated with antiTNFs, investigating a potential role in IBD management. Pgp functionality was evaluated in PBL of IBD and healthy controls (HC: n30), studied in 5 groups of IBD pts. (n123 recruited) with at least 10 CD/10 UC each: - Before and after 20 days of AntiTNF (IFX or ADA) in steroid refractory (group 1) or thiopurine refractory (group 2), - Before and after 3 mo of 6-MP in steroid refractory (group 3), - In Thiopurine sensitive (group 4) and Steroid sensitive (group 5). Response criteria: at 45 days of AntiTNFs or 3 mo. of 6-MP (CDAI: a 70 points drop, Mayo score 3 points+30% drop) categorized in: remission (CDAI≤150, Mayo Sc.≤2) and partial response. Rhodamine123 (fluorescent Pgp substrate) efflux was studied by flow cytometry, expressed by the behaviour of 2 markers defined by % of cells with different fluoresc. levels: M1 (high fluoresc./low Pgp pump activity), M2 (low fluoresc./Pgp high activity, used for the results).
RESULTS: Basal Pgp values (mean±SD) in total PBL (M2) were: Group 1: 41.4 ±18.5, Group 2: 32.1 ±13.6, Group 3: 44.1±19.8, Group 4: 36.1±16.9, Group 5: 37.5±16.4 and HC 39.0±12.3. Major finding was a significant decrease of Pgp after AntiTNFs in IBD in most of responder pts. (Δ -difference- in refractory vs remission p: 0.030018, and 0.0023 for groups 1 and 2, and vs. partial response p = 0.014 in group 2, Mann Whitney). Initial Pgp values of pts. with available Pgp post AntiTNFs measures according response were: Group 1 (n 20) 38.0±17.7, 44.6±8.4, 38.6±21.0, Group 2 (n 23) 35.9±16.0, 34.8±9.9, 23.1±7.1 for remission, partial response and refractory. Post AntiTNFs: 26.2±16.0, 29.0±12.1, 47.0±19.3 (Group 1) and 21.0±11.6, 22.3±11.5, 36.0±11.7 (Group 2). Pts. with 6-MP monotherapy (n23) did not show signif. changes in Pgp. A signif. decrease of Pgp in CD3 lymph. (only group 2 p < 0.003) after AntiTNFs was observed in remission vs refractory pts. In B lymph. lower values post AntiTNFs (group 1) were shown in responders as a trend. Values of post-treat. IBD were lower than HC (p < 0.04).
CONCLUSION: 1) We found that AntiTNFs decreased Pgp activity in PBL of IBD pts., significantly associated with treatment response; 2) AntiTNFs could modify the transport of concurrent Pgp substrates. MDR1 polymorphism typing is ongoing. Longer follow-up and larger size sample are needed to verify the value of Pgp activity measurement in IBD management.
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P0289 PREDICTIVE FACTORS FOR CHRONIC INFLAMMATORY BOWEL DISEASES IN PATIENTS PRESENTING WITH NEW ONSET DIARRHEA

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INTRODUCTION: The diagnosis of chronic inflammatory bowel diseases (IBD) requires chronic changes over time (colonoscopic inflammatory changes lasting at least 6 months and chronic histological inflammation). The onset of chronic IBD may mimic acute diarrhea (defined as having sudden onset and lasting less than four weeks); on the other hand, acute diarrhea may be mistaken with a new case of chronic IBD. Our aim was to find clinical or biological predictive factors for the diagnosis of chronic IBD.
AIMS & METHODS: A prospective study was conducted on all cases of new onset diarrhea which presented in our Gastroenterology Unit during 2012. Their

initial evaluation included clinical exam, complete biological picture and colonoscopy. All cases of new onset diarrhea with uncertain etiology were followed and the final diagnosis was established at least 6 months after the onset, by repeating colonoscopy with biopsy. The final diagnosis was correlated with clinical and biological parameters evaluated at the first presentation.
RESULTS: A total of 120 patients with new onset diarrhea presented to our unit in 2012. After the initial work-up, 82 patients had a positive diagnosis (infectious colitis, colorectal cancer, radiation colitis, ischemic colitis). The remaining 38 patients, including both patients with inflammatory changes at colonoscopy and patients with normal colonoscopy were reevaluated by colonoscopy and biopsies after 6 months. For 11 patients, results were conclusive for chronic IBD, 5 patients had collagenous or lymphocytic colitis, and 22 patients were diagnosed with acute self-limiting colitis or irritable bowel syndrome (IBS). Among the parameters we analysed, anemia and hypoalbuminemia in the onset of the symptomatology were significantly correlated with the subsequent diagnosis of chronic IBD; elevated levels of inflammatory parameters like C-reactive protein and erythrocyte sedimentation were present in similar proportions in the different types of final diagnosis except IBS; other biological parameters were not contributive; non-significant correlation was found with respect to age, weight loss and clinical history or associated symptoms.
CONCLUSION: Anemia and hypoalbuminemia are predictive factors for chronic inflammatory bowel diseases in patients presenting with new onset diarrhea; a more extensive initial work-up applied in these patients could bring an early diagnosis for IBD.
Disclosure of Interest: None declared

P0290 INCIDENCE AND RISK FACTORS OF C. DIFFICILE INFECTION IN ULCERATIVE COLITIS

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INTRODUCTION: Recent epidemiologic studies have shown that patients with inflammatory bowel disease (IBD), in particular those with ulcerative colitis (UC) are at increased susceptibility for *Clostridium difficile* infection (CDI) compared with the general population.
AIMS & METHODS: The objectives of this study were to assess the incidence and risk factors for CDI in UC patients in a tertiary center from North-Eastern Romania.
Data of all UC patients admitted at the Institute of Gastroenterology and Hepathology, Iasi, Romania, between January 2012 and October 2013 were analyzed. In patients with concomitant CDI, risk factors for CDI were identified.
RESULTS: A total of 70 UC patients were included in this prospective study, amongst which eight (11.5%) were identified as having a concomitant CDI. On univariate analysis, age $>$ 65 years (OR = 1.53, CI = 0.93-16.27; p = 0.048), male gender (OR = 1.38, CI = 0.30-14.91; p = 0.032), hemoglobin $<$9 g/dL (OR = 1.93, CI = 0.19-18.52; p = 0.043), severe UC disease (OR = 1.22, CI = 0.14-10.5; p = 0.037), and serum albumin $<$3 g/dL (OR = 1.86, CI = 1.12-10.14; p = 0.012) were associated with CDI. However, on multivariate analysis, only severe disease and serum albumin retained statistical significance.
CONCLUSION: CDI was detected in one of eight patients admitted with a UC flare; severe UC disease and low serum albumin were independent risk factors for CDI.
Disclosure of Interest: None declared

P0291 ASSESSMENT OF WALL INFLAMMATION AND FIBROSIS IN CROHN'S DISEASE AND ITS CORRELATION WITH BOWEL SONOGRAPHY AND MRI-ENTEROGRAPHY

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INTRODUCTION: Crohn's disease (CD) is a chronic inflammatory bowel disorder which is relapsing and remitting in nature and is characterised by transmural inflammation. About the therapeutical management of CD, it is believed to be particularly important to differentiate between active inflammation and fibrotic lesions in CD patients. Bowel sonography (BS) and MRI-enterography (MRI) are procedures widely used for diagnosing CD and its complications.
AIMS & METHODS: to define the features of the CD strictures, also correlating BS and MRI with histopathology.
We performed an observational prospective study including all CD patients undergoing surgery for strictures. Pre-operative assessment was performed by BS and MRI. BS investigated for: bowel wall thickness (BWT), bowel wall stratification, power-Doppler vascular pattern of the bowel wall, mesentery hypertrophy and enlarged lymphnodes. MRI study included: BWT, T1-weighted gadolinium-based contrast uptake, enhancement pattern, mural and lymph node/cerebrospinal fluid (CSF) signal intensity ratios on T2-weighted fat-saturated images, mesenteric signal intensity on T2-weighted fat-saturated images. Histopathological inflammation was graded by the acute inflammatory score (AIS); the semi-quantitative degree of fibrosis was performed according to the literature. Statistical analysis was performed using chi-square, Mann–Whitney U test and Cohen's k measure.
RESULTS: The study included 20 CD patients. The indications to surgery were: obstructive symptoms in 13 patients, penetrating complications in 7 patients. All but 3 strictures (87%) showed acute inflammation coexisting with fibrosis while only 3 strictures were predominantly fibrotic On BS, the presence of a layered bowel wall stratification was the only variable associated with the presence of fibrosis (k = 0.72; p $<$ 0.03). About MRI, AIS correlated with mural thickness and mural/CSF signal intensity ratio on T2 sequences (p = 0.04, p = 0.02) but not with mural enhancement on T1 images (p = 0.62).
CONCLUSION: The majority of strictures in CD patients treated by surgery are consistent with a mixed type inflammation (acute inflammation plus fibrosis). The presence of stratified BS pattern shows a significantly higher degree of fibrosis while the evidence of high mural signal intensity on T2-weighted fat-saturated images on MRI reflects histological features of acute inflammation. Even if the ideal definition of the type of the strictures in CD still remains significantly out of reach, the combined use of BS and MRI can offer useful information in a sub-group of patients needing surgery for complicating CD.
Disclosure of Interest: None declared

P0292 "NEUTROPHIL VOLUME DISTRIBUTION WIDTH" AS A NEW MARKER IN MONITORING INFLAMMATORY BOWEL DISEASE ACTIVITY

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INTRODUCTION: Inflammatory bowel diseases (IBD) are immune-mediated disorders resulting in chronic, relapsing inflammation of the gastrointestinal tract. A prominent feature of inflammation in IBD is the involvement of effector cells such as neutrophils, eosinophils and mast cells. Neutrophil volume distribution width (NVDW) generated by VCS technology is a new marker which reflects neutrophil activation.
AIMS & METHODS: We sought to investigate the value of NVDW parameter in monitoring disease activation in IBD patients. Neutrophil VCS parameters were measured in IBD patients admitted to our outpatient clinic. Age and sex matched healthy subjects were taken as the control group. Patients with acute or chronic infection and accompanying inflammatory disease were excluded. Pediatric Crohn Disease Activity Index (PCDAI) and Pediatric Ulcerative Colitis Activity Index (PUCAI) were used to define disease activation. Complete blood count, albumin, eritrocyte sedimentation rate, C-reactive protein ve fecal calprotectin were studied routinely at each visit.
RESULTS: A total of 34 pediatric patients with IBD and 29 controls were enrolled in the study. NVDW was significantly higher in patients with IBD compared to healthy controls (p $<$ 0.001). An increased NVDW level was observed in IBD patients with activation (22.42±2.13) compared to those in remission (19.22±1.63) (p $<$ 0.001). There was no statistically significant difference between IBD patients in remission and healthy controls (p = 0.115). A significantly increased NVDW was observed in CD patients with activation compared to CD patients in remission (22.87±2.19 vs 19.68±1.85, p = 0.002). NVDW was significantly higher UC patients with activation compared to UC patients in remission (22.07±2.08 vs 18.53±0.93, p $<$ 0.001). NVDW was correlated with WBC count (r:0.712), platelet count (r:0.347), ESR (r:0.471), CRP (r:0.699), fecal calprotectin (r:0.812), PUCAI (r:0.852) ve PCDAI (r:0.670). The best cut-off of NVDW for prediction of disease activation in CD and UC in this series was 20.39 with a sensitivity of % 90.9 and a specificity of %75 (AUC:0.852 CI 0.698-1.000 p = 0.002) and 19.74 with a sensitivity of % 92.9 and a specificity of % 90.9 (AUC:0.961, CI:0.889-1.000, p $<$ 0.001) respectively.
CONCLUSION: As a quantitative, objective, and sensitive parameter, NVDW has a potential to be an additional predictor for disease activation in IBD.
Disclosure of Interest: None declared

P0293 IBS-LIKE SYMPTOMS ARE COMMON IN PATIENTS WITH ULCERATIVE COLITIS IN DEEP REMISSION BUT THEY DO NOT SEEM TO BE CAUSED BY LOW GRADE INFLAMMATORY ACTIVITY

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INTRODUCTION: Gastrointestinal (GI) symptoms compatible with Irritable Bowel Syndrome (IBS) are common in patients with ulcerative colitis (UC). It has been suggested that these symptoms are a reflection of occult inflammation rather than coexisting IBS.
AIMS & METHODS: The aim was to investigate possible factors correlating with IBS-like symptoms in UC patients in deep remission by assessing inflammatory markers, other GI symptoms, psychological symptoms and quality of life (QOL). In total, 297 patients with UC were included at a regular outpatient clinic visit. The patients completed self-administrated questionnaires to assess diagnostic criteria for IBS (Rome III), severity of GI symptoms (Gastrointestinal Symptom Rating Scale (GSRS)), QOL (IBDQ), psychological symptoms (Hospital Anxiety and Depression scale (HAD)), stress (QPS Nordic) and non-GI somatic symptoms (PHQ-12). Fecal calprotectin was used as inflammatory marker. Patients with a normal rigid sigmoidoscopy and calprotectin $>$200 μg/g were further investigated with flexible sigmoidoscopy. Deep remission was defined as a total Mayo-score $\leq$2 (endoscopic findings, rectal bleeding and physician global assesment subscores = 0), with no relapse during the three-month period prior to visit. Comparisons where made between patients in deep remission with (UCR+IBS) and without (UCR-IBS) IBS-like symptoms and patients

with active disease (UCA). Comparisons between the three groups were performed with Kruskal-Wallis test and thereafter post-hoc tests with Mann–Whitney U test and Bonferroni correction, with p-value <0.017 considered significant.

RESULTS: Among the patients, 46% (n = 138) met the criteria for deep remission and 18% (n = 25) of these patients experienced IBS-like symptoms. There was no difference in fecal calprotectin levels between the UCR+IBS and the UCR-IBS patients. The UCR+IBS patients reported significantly more severe GI symptoms in general, lower QOL scores, higher levels of anxiety, stress and non-GI somatic symptoms than the UCR-IBS patients (see table). The level of somatic and psychological symptoms did not differ between the UCR+IBS patients and the UC patients with active disease (see table).

Median (IQR) Level of sign p < 0.017	UCR+ IBS (n = 25)	UCR- IBS (n = 113)	UCA (n = 159)	UCR+ IBS vs UCR-IBS	UCR+ IBS vs UCA	UCA vs UCR-IBS
Calprotectin (μg/g)	18 (7-30)	32 (13-64)	280 (80-715)	p = 0.044	**p < 0.001**	**p < 0.001**
GSRS Total	2.5 (2.1-3.1)	1.5 (1.2-1.9)	2.5 (1.8-3.1)	**p < 0.001**	p = 0.701	**p < 0.001**
Anxiety (HAD)	5.0 (3.5-8.0)	2.0 (1.0-5.0)	4.5 (2.0-8.0)	**p = 0.001**	p = 0.291	**p < 0.001**
Depression (HAD)	2.0 (1.0-7.5)	1.0 (0.0-3.0)	3.0 (1.0-6.0)	p = 0.048	p = 0.941	**p < 0.001**
Stress (QPS Nordic)	2.0 (1.0-3.0)	1.0 (0.0-2.0)	2.0 (1.0-3.0)	**p = 0.003**	p = 0.281	**p = 0.001**
Non-GI Sympt (PHQ)	6.0 (3.5-8.5)	3.0 (1.0-5.0)	4.0 (2.0-7.0)	**p < 0.001**	p = 0.132	**p < 0.001**
QOL (IBDQ)	183 (163-198)	205 (192-213)	167 (144-195)	**p < 0.001**	p = 0.142	**p < 0.001**

CONCLUSION: IBS-like symptoms in UC patients in deep remission are common. Psychological factors rather than low grade inflammatory activity seem to be of importance for symptom generation. Interestingly, UC patients in deep remission with IBS-like symptoms experience GI symptoms, reduced psychological well-being and QOL compatible with UC patients with active disease.

Disclosure of Interest: None declared

P0294 THE SEVERITY OF ABDOMINAL PAIN AT ONSET OF ULCERATIVE COLITIS IS ASSOCIATED WITH IBS-LIKE SYMPTOMS DURING CLINICAL REMISSION

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INTRODUCTION: Symptoms compatible with Irritable Bowel Syndrome (IBS) are common in patients with ulcerative colitis (UC) in clinical remission. It has been suggested that these symptoms might arise due to postinflammatory changes comparable with postinfectious IBS. Factors that increase the risk for developing IBS-like symptoms in patients with new onset of ulcerative colitis are not known.

AIMS & METHODS: The aim was to study factors in patients with new onset of UC that predicts development of IBS-like symptoms during clinical remission. In total, 98 patients with new onset of UC were followed prospectively during three years with yearly follow up visits. The patients completed self-administrated questionnaires at each visit to assess diagnostic criteria for IBS (Rome II), severity of gastrointestinal (GI) symptoms (GI Symptom Rating Scale (GSRS)) and psychological symptoms (Hospital Anxiety and Depression scale (HAD)). Fecal calprotectin, ESR and CRP were used as inflammatory markers. The Mayo score was used to evaluate clinical disease activity. Remission was defined as a total Mayo score ≤ 2 and an endoscopic subscore ≤ 1, with no relapse during the three-month period prior to visit. Data from the first visit at the onset of UC were compared between the group of patients that fulfilled the criteria for IBS while in remission (UCR+IBS) during follow-up and the group that did not (UCR).

RESULTS: Among the UC patients, 87 met the criteria for clinical remission, and 25 (29%) of these reported IBS-like symptoms in remission, on at least at one of the three follow-up visits. The UCR+IBS patients suffered from more severe GI symptoms including abdominal pain (see table) during their primary flare than the UCR patients. The patients that experienced mild to severe abdominal pain had an increased risk for developing IBS-like symptoms during follow-up (OR = 3.1 (95% CI 1.1-8.4) p = 0.03), this occurred in 39% (n = 17) of these patients compared to 20% (n = 8) of the patients that reported none or minor abdominal pain. Female gender (p = 0.10), being unmarried/single (p = 0.05) and higher depression scores (HAD p = 0.09) tended to be more common among UCR+IBS patients. There was no difference in clinical disease activity (Mayoscore p = 0.42), inflammatory markers (Calprotectin p = 0.29, CRP p = 0.36, ESR p = 0.58) or disease extension (p = 0.57) between the two groups.

Table to abstract P0294

GSRS - Median (IQR)	**UCR+IBS**	**UCR**	**p - value**
Total	3.5 (2.2-4.0)	2.7 (2.1-3.3)	**<0.05**
Diarrhea	5.0 (3.3-6.3)	5.3 (3.8-6.7)	0.56
Constipation	2.3 (1.7-2.8)	2.0 (1.7-2.7)	0.30
Abdominal Pain	2.7 (1.8-2.8)	2.0 (1.7-3.0)	**<0.05**
Indigestion	3.8 (2.8-4.6)	3.3 (2.4-4.1)	0.09
Reflux	1.0 (1.0-2.0)	1.0 (1.0-1.5)	0.07

CONCLUSION: Patients with ulcerative colitis that develop IBS-like symptoms during follow-up experience more severe GI symptoms, including abdominal pain, at disease onset, despite no difference in inflammatory disease activity. This might indicate a more sensitive GI tract in this category of patients.

Disclosure of Interest: None declared

P0295 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A POTENTIAL BIOMARKER FOR AXIAL INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Axial arthropathy associated with inflammatory bowel diseases (IBD) includes isolated sacroiliitis, inflammatory back pain and ankylosing spondylitis. There is no reliable laboratory test that can be used as a diagnostic tool in the management or diagnosis of axial arthropathy in IBD. Neutrophil gelatinase associated lipocalin (NGAL) is a recently identified molecule, which has tissue destructive effects by protecting matrix metalloproteinase-9 from autodegradation. This represents an important mechanism by which NGAL may contribute to the degradation and remodelling of the extracellular matrix, leading to rheumatologic manifestations of IBD. Previously, we showed that serum NGAL levels in IBD patients were significantly higher than healthy controls.

AIMS & METHODS: To investigate serum NGAL levels in IBD patients with or without axial arthropathy. A total of 83 patients (64 with IBD, 19 with IBD and axial arthropathy), and 40 age- and sex-matched healthy controls (HC) were included in this study. Patients with peripheral joint involvement were excluded. Serum NGAL levels were measured using ELISA.

RESULTS: The patients were aged between 16 and 74 years, and their mean age was 39.1 ± 11.5 years. Age, gender, and disease-year distributions were not statistically significantly different among the groups. Serum NGAL levels were elevated significantly in IBD patients with axial artropathy [median 234 U/L, range (122-312) ng/ml] compared to IBD patients without axial involvement [168 U/L (57-310 ng/ml] (p:0.001) and HC group [122 (45-234) ng/ml] (p:0.004). NGAL levels of the IBD group were significantly higher than those of the control group (p:0.001). There was no significant difference between the IBD group and IBD with axial involvement group in Hgb, WBC, CRP, and ESR values.

CONCLUSION: Serum NGAL levels were found to be elevated in IBD patients with axial involvement when compared to IBD patients without involvement, suggesting a partial pathophysiologic role in this particular extraintestinal manifestation. NGAL seems to be a promising biomarker for the diagnosis and management of axial arthropathy in IBD.

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P0296 ANORECTAL STRICTURE IN CROHN'S DISEASE: NATURAL FATE OR CHALLENGING TARGET TO TREAT?

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INTRODUCTION: The natural history of non-fistulising perianal Crohn's disease (PCD) remains unknown.

AIMS & METHODS: This study aimed to assess the long-term outcome of anorectal strictures. Between January 2005 and October 2013, a tertiary referral centre prospectively recorded each clinic of patients with PCD with detailed data about the phenotype and disease activity of luminal and anal CD, medical treatment and surgery. At each visit, CD and PCD were assessed using the Harvey-Bradshaw Score, the Cardiff-Hughes classification and with the Perianal Disease Activity Index. Follow-up was determined by the duration between the diagnosis of anorectal stricture and the last visit. Cumulative incidence of stricture healing (disappearance of the anal stricture) was estimated using a Kaplan-Meier method

and factor associated with an unfavourable course (persistent stricture S2, persistent stoma or proctectomy) with non-parametric test.
RESULTS: A total of 102 patients (M/F: 37/65) were included. The duration of CD at diagnosis was 8.9 years. After a median follow-up period of 2.8 years, 52 of the 88 followed patients (59%) achieved anorectal stricture healing. Two patients (2%) developed anal adenocarcinoma. Female gender (HR 2.05 [1.1-4.03], p = 0.0221), disease duration of CD of less than 10 years (HR 1.94 [1.01-3.63], p = 0.0271), and anal fistula at stricture diagnosis (HR 2.36 [1.21-5.05], p = 0.0106) were significantly associated with anorectal stricture healing in a multivariate analysis model. Twenty-eight patients (32%) had an unfavourable course at the end of follow-up. Gender and introduction or optimisation of TNFα antagonist treatment decreased the risk of unfavourable course in multivariate analysis. Conversely, the Luminal B2 phenotype at CD diagnosis was the only factor associated with unfavourable course.
CONCLUSION: Anorectal stricture does not imply a non-reversible and complicated condition related to severe perianal Crohn's disease. However, both diagnosis of cancer and sepsis drainage remain challenging in this situation.
Disclosure of Interest: None declared

P0297 REDUCING UNNECESSARY COLONOSCOPY – A COST MINIMIZATION ANALYSIS OF NEW DIAGNOSTIC STRATEGIES FOR EXCLUDING ORGANIC BOWEL DISEASE IN PRIMARY CARE PATIENTS

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INTRODUCTION: In general practice, complaints of the lower digestive tract are frequently presented. Of those affected, only an estimated 7% suffers from organic bowel disease (OBD), such as inflammatory bowel disease, diverticulitis and cancer. [1] These patients should be referred for colonoscopy without delay. Unfortunately, OBD is found in only one third of referred patients, indicating a considerable number of unnecessary referrals in primary care.[2] Our research group developed several diagnostic strategies to optimize colonoscopy referral policy.
AIMS & METHODS: We aim to assess the benefits and costs of the diagnostic strategies developed to reduce unnecessary colonoscopy referrals in primary care. The diagnostic strategies combine patient history and physical examination with two point of care tests (POCT); calprotectine and/or iFOBT. We evaluated the benefits and costs of three diagnostic strategies, each at three cut-off points. Strategies are: 1. iFOBT added to history and physical examination (iFOBT), 2. calprotectine added (Calpro), and 3. both POCT added (CiF). The three different cut-off points are based on OBD risk for referral. Benefits are prevented costs and prevented unnecessary referrals for colonoscopy. Costs are additional costs and missed diagnoses.
RESULTS: A reduction of 0.5% (iFOBT), 5.4% (Calpro) and 5.9% (CiF) in the number of colonoscopies cover the additional testing costs. The largest cost-savings are achieved by iFOBT and CiF. At the 2.5% cut-off, these strategies provide a modest cost reduction (1.3 and 0.2mln Euros, respectively) with 84 (2%) and 0 (0%) patients incorrectly not referred for colonoscopy annually in the Netherlands. At a referral threshold of 5% OBD probability, a cost reduction of €5.8 (iFOBT), €2.3 million (Calpro) and €4.7(CiF), Euros would be achieved at an annual cost of 720 (4%), 720 (4%) and 306 (3%) incorrectly averted referrals in the Netherlands, respectively. Cost reduction for all strategies even increased at 7.5% OBD risk, but this threshold yielded much higher incorrectly referred patients for all three strategies, above 1000 patients annually in the Netherlands.
CONCLUSION: Implementation of the diagnostic strategies as developed in the CEDAR study are likely to reduce the colonoscopy related costs at a burden of incorrectly averted referrals for colonoscopy. Implementation of the CiF and iFOBT strategies at the lowest threshold value for referral, is likely to be safe and modestly cost-saving. The CiF and iFOBT strategy at the 5% OBD probability threshold, might also be a valuable alternative in current practice given the substantial costs savings and relative safety. The most appropriate threshold and the resulting cost savings needs to be determined for the health care setting in which it will be used.
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Disclosure of Interest: None declared

P0298 DIFFERENTIATING CROHN'S DISEASE FROM INTESTINAL TUBERCULOSIS IN A TUBERCULOSIS ENDEMIC AREA

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INTRODUCTION: Crohn's disease (CD) and Ileocolonic Tuberculosis (ITB) mimic each other in clinical, endoscopic and histologic features. In an ITB endemic country like India differentiating one from the other remains a challenge.
AIMS & METHODS: The aim of our study was to revalidate the existing clinical, laboratory and histological parameters that aid in differentiating Ileocolonic Tuberculosis from Crohn's disease.
Methods: We prospectively included patients with Ileocolonic ulcers. Patients were diagnosed as either ITB or CD based on established criteria. All patients were evaluated for Extra Intestinal Tuberculosis. Patients were followed up and a repeat colonoscopy was performed at 3 months and at of 6 months of treatment; diagnosis was revised if the patient did not demonstrate mucosal healing when compared to the previous colonoscopy. Patients who completed follow up were included in final analysis.
RESULTS: Sixty patients were included in the study of which fifty-five patients completed follow up and were included in the analysis. A final diagnosis of CD was made in 37 patients (67%), ITB in 18 patients (33%). Differentiating features of ITB and Crohn's are summarised in table -1. Quantiferon TB Gold in Tube test was positive in 94.4% of ITB patients versus 19.3% of Crohn's disease patients (P- <0.001). The Sensitivity, Specificity, Positive predictive value, Negative predictive value for Quantiferon TB Gold in tube test was 94.44%, 83.78%, 73.91% and 96.88% respectively.

Variables	CD (n = 37)	TB (n = 18)	P value
Mean Age (in years)	32.5	45	0.1
Male/ Female	20/17	8/10	0.7
Mean Duration of illness (Months)	13.6	8	***0.026***
Bleeding PR	7 (18.9%)	0 (0)	***0.04***
Fever	4 (10.8%)	8 (44.4%)	***0.004***
TB QuantiferonGold in Tube			***<0.001***
Positive	6	17	
Negative	31	1	
Granuloma Characteristics			
Caseation	0 (0)	5 (28%)	
Large	5(13%)	12 (66.6%)	
Confluent	7 (19%)	13(72.2%)	
More than 5 granulomas/hpf	8 (21%)	10 (55.5)	
Band of epitheloid Histiocytes	71(19%)	8 (44.4%)	
Lymphoid cuff	19 (51%)	11 (61%)	
Pericryptal	21(56.7%)	3 (16.7%)	
Microgranulomas	30 (81.1%)	3 (16.7%)	
Focally enhanced colitis	15 (40.5%)	2 (11.1%)	
Histology abnormal in endoscopically normal sites	23 (60.5%)	1(5%)	

CONCLUSION: Longer duration of illness, bleeding per rectum, pericryptal granuloma's, microgranuloma's, focally enhanced Colitis, histological changes in antrum and histological abnormality in endoscopically normal sites favored Crohn's disease. Presence of fever, large granulomas, caseating granulomas, confluent granulomas, favored ITB. Quantiferon TB Gold in Tube test had good sensitivity but poor specificity in differentiating ITB from Crohn's disease.
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Disclosure of Interest: None declared

P0299 REPRODUCIBILITY OF SEROLOGIC ANTIBODY ACTIVITY AT DIAGNOSIS AND AFTER TREATMENT IN PEDIATRIC ULCERATIVE COLITIS AND CROHN'S DISEASE

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INTRODUCTION: Serologic nuclear and anti microbial antibodies have been recognized as predictive markers of disease course and complications in ulcerative colitis (UC) and Crohńs disease (CD). The stability of serologic titers over time of these markers has been questioned.
AIMS & METHODS: The aim of the present study was to compare antibody titers before and after treatment in newly diagnosed treatment naive pediatric patients with inflammatory bowel disease (IBD). Patients aged <18 years, (N = 57) diagnosed with IBD were included between 2005-2007 and followed prospectively. Blood specimens were analyzed for antibodies (Prometheus labs, San Diego) at diagnosis, and repeatedly after 1-2 years of treatment.
RESULTS: Among the 19 UC patients 68% were ANCA-positive versus 32% of the 38 CD patients (p = 0.02). In CD and UC patients respectively, the median titers in EU/ml at baseline against I2, 249 and 257, Anti-Omp C, 3.1 and 3.6, ASCA IgA, 8.4 and 3.1, ASCA IgG, 11.9 and 3.1 and CBir, 27 and 16, were not significantly different at follow- up. The titers against ASCA IgA and IgG were significantly higher in the CD patients versus UC patients both at diagnosis and at follow-up (p = 0.01 and p < 0.01, respectively) with post-treatment ASCA IgA 7.5 and ASCA IgG 12.8 in CD versus 3.1 and 6 in UC respectively (p < 0.01 and 0.03). There were no statistically significant differences for gender, or between the different treatments of CD patients, in whom 18 of 38 patients had received infliximab.
CONCLUSION: UC patients were significantly more frequently ANCA positive, whereas the CD patients had significantly higher titers against ASCA IgA and IgG both at diagnosis and at follow-up. The present study demonstrates a general reproducibility of the presence and titers of serologic antibodies from the

time of diagnosis until 1-2 years of follow- up for IBD, indicating that serologic markers measured at diagnosis may be applied as prognostic markers even after years of treatment.
Disclosure of Interest: None declared

P0300 ULTRASOUND BASED REAL TIME ELASTOGRAPHY RELIABLY IDENTIFIES FIBROTIC GUT TISSUE IN PATIENTS WITH STRICTURING CROHN'S DISEASE (GUT-RTE)

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INTRODUCTION: Crohn's disease (CD) is a relapsing inflammatory disease. Many patients experience intestinal strictures that require surgery if non amenable to medical therapy. Moreover, there is an unmet need to objectively assess new treatment endpoints such as disease modification, structural damage and restitution. Real time ultrasound elasticity imaging has not been systematically developed yet to evaluate the viscoelastic properties of the human gut in vivo.
AIMS & METHODS: In this prospective, controlled and partially blinded study unaffected and affected gut segments of 10 CD patients (male = 6, median age = 49, median Harvey Bradshaw index = 6) were examined pre-, intra- and postoperatively with ultrasound including real time elastography (RTE) to assess strain. Following surgical resection strain of full gut wall segments was analyzed by direct tensiometry. Histopathological scoring of fibrosis with two independent, specific stains, molecular quantification of collagen content as well as morphometrics were performed. Data were aggregated at patient level and non-aggregated at segment level prior to statistical analysis including a non-linear model where appropriate.
RESULTS: RTE strain was significantly different between unaffected and affected segments (mean ± SD 169.0 ± 27.9 vs. 43.0 ± 25.9; $p<0.001$). Moreover, mean RTE strain per patient was completely different in unaffected (all > 132) compared with affected (all < 87) segments. An RTE strain cut point of 110 reliably distinguished segments. Tensiometry strain in segments with an RTE strain of >110 was significantly greater than in those with < 110 (mean ± SD 77.1 ± 21.4 vs. 12.9 ± 9.5; $p<0.001$). These findings were further corroborated by morphometrics, collagen content and fibrosis score.
CONCLUSION: RTE allows bedside assessment of gut tissue mechanical properties in CD.
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P0301 CORRELATION BETWEEN MAGNETIC RESONANCE ENTEROGRAPHY, CAPSULE ENDOSCOPY, FECAL CALPROTECTIN AND CRP IN PATIENTS IN CLINICAL REMISSION WITH KNOWN SMALL BOWEL CROHN'S DISEASE PRELIMINARY RESULTS FROM THE PROSPECTIVE ISRAELI IBD RESEARCH NETWORK (IIRN) STUDY

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INTRODUCTION: The correlation between clinical activity and intestinal inflammation in Crohn's Disease (CD) is modest. Biomarkers and imaging techniques are objective tools able to assess the biological activity.
AIMS & METHODS: Our aim was to objectively evaluate disease activity in patients in clinical remission (CR) with small bowel CD (SBCD) by using capsule endoscopy (CE), magnetic resonance enterography (MRE) and correlate the findings with laboratory parameters of inflammation.
Thirty-five consecutive patients with known SBCD in CR were prospectively recruited and underwent MRE, followed by Agile patency capsule (PC), and if patency was proven, a video capsule. The Lewis score was calculated for each tertile. C-reactive protein (CRP) and fecal calprotectin (FC) were evaluated for their association with clinical activity, MRE and CE findings.
RESULTS: Eight of 35 cases with abnormal passage of PC were excluded, all of which were predicted by MRE (NPV 100%). All video capsules reached the cecum, including 9 additional cases predicted to be retained by MRE which proved to be false positives (53%) by the PC. CE detected active disease in the proximal-mid SB in 44% of the patients and in the distal SB in 48%. MRE detected proximal-mid SB disease in only 18% and distal disease in 67% of patients. Most (81%) of patients with SB lesions detected by CE had elevated FC (cutoff, 30μg/g) while CRP (cutoff, 5mg/l) was increased in 19% of these patients. FC modestly correlated with Lewis score ($r=0.4$). There was no correlation between CRP and Lewis score. Similarly, 78% of patients with active disease on MRE had increased FC, while CRP was elevated in 22% of the patients.
CONCLUSION: 1. A PC prior to the CE procedure diminished the likelihood of CE retention, and was superior to MRE in prediction of capsule retention. 2. Despite CR active inflammation was detected in > 50% of patients by CE. 3. Proximal SB disease was better detected by CE than MRE. 4. FC associated better than CRP with disease activity found by CE or MRE. 5. When used properly, CE is a safe procedure in patients with SBCD.
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Disclosure of Interest: None declared

P0302 SYSTEMATIC ANALYSIS OF FACTORS ASSOCIATED WITH PROGRESSION AND REGRESSION OF ULCERATIVE COLITIS IN THE SWISS IBD COHORT STUDY

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INTRODUCTION: There is a lack of studies having systematically assessed in a large cohort of patients with ulcerative colitis (UC) the disease location over time as well as risk factors associated with progression or regression of disease extent.
AIMS & METHODS: We aimed to assess disease location over time and to evaluate associated risk factors. Data from the Swiss IBD cohort study were analyzed. Patients were recruited from university centers (68%), regional hospitals (14%), and private practices (18%). Disease locations over time were analyzed and risk factor analysis for a change in disease location was performed using logistic regression modeling. Non parametric data are illustrated as median and interquartile range [IQR].
RESULTS: A total of 1,016 UC patients (45.6% females, median age at diagnosis 31 [23.3-40.5] years) were included. At diagnosis, UC patients presented with the following disease locations: 199 (19.6%) proctitis, 338 (33.3%) left sided colitis, 381 (37.5%) extensive colitis/pancolitis, and 98 (9.6%) unknown. During a median of 9 [5-16] years disease duration, a disease progression was documented in 145/1016 (14.3%) of patients, a regression in 176/1016 (17.3%) of patients, whereas 624/1016 (61.4%) of patients had a stable disease location (7% of patients with unknown evolution of disease location over time). Logistic regression modeling identified the following factors associated with disease progression in UC patients presenting with proctitis or left-sided UC at diagnosis: treatment with systemic steroids (OR 2.077, 95% > CI 1.359-3.174, $p=0.001$), treatment with immunomodulators (azathioprine, 6-MP, methotrexate) (OR 1.647, 95% > CI 1.119-2.424, $p=0.011$), treatment with TNF-antagonist(s) (OR 1.668, 95% > CI 1.077-2.581, $p=0.022$), and treatment with calcineurin-inhibitors (OR 3.159, 95% > CI 1.679-5.943, $p < 0.001$). Neither gender, age at UC diagnosis, body mass index, presence of extraintestinal manifestations, smoking status at diagnosis, positive UC family history, nor 5-ASA treatment were associated with disease progression. No specific factors were found to be associated with regression in UC patients with extensive colitis/pancolitis or left-sided colitis at diagnosis.
CONCLUSION: Over a median of 9 years disease duration about two-thirds of UC patients maintained the initial disease location whereas one-third either had a progression or a regression of the initial disease location. Treatment with systemic steroids, immunomodulators, TNF-antagonists, or calcineurin-inhibitors was significantly associated with disease progression.
Disclosure of Interest: None declared

P0303 PSORIASIS PHENOTYPE IN INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL PROSPECTIVE STUDY

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INTRODUCTION: Psoriasis has been associated with Inflammatory Bowel Disease (IBD). However, whether IBD is associated with specific phenotypes of psoriasis is unknown.
AIMS & METHODS: In a case-control prospective study, we aimed to assess psoriasis phenotype in IBD patients (pts), when using a non-IBD patients population as controls (non-IBD C). From January 2011 to November 2013, dermatological assessment was performed in 251 IBD pts under follow up. Dermatological assessment was focused in detecting the presence of psoriasis (present/absent) and in defining its characteristics (localization, phenotype), including severity (mild/moderate/severe). In order to define psoriasis phenotype in IBD, each IBD pt with psoriasis was matched for gender, ethnicity and age (±5 years) with one non-IBD pt with psoriasis, referring to the same centre. Data were expressed as median (range) and differences between groups assessed by the T test or the chi-squared test, as appropriate.
RESULTS: Dermatological assessment was performed in 251 IBD pts (115 F, age 46 yrs, range 16-85; IBD duration 9 yrs, range 1-46): 93 UC (42 M, age 50, range 22-85; UC duration 7 yrs, range 1-41; UC extent: proctitis 33, left 13, extensive 42, ileal pouch 3, ileostomy 1, ileo-rectal anastomosis 1) and 158 CD (91 M, age 43, range 16-80; CD duration 10 yrs, range 1-46; CD colitis 13, ileocolitis 32, ileitis 51, neo-terminal ileum 56, ileostomy 2, distal ileum + jejunum 4). Non-IBD C included 62 pts (35 M, age 47, range 18-75). Among the 251 IBD pts, psoriasis was detected in 62 (25%; 36 CD, 26 UC). In the IBD group, the median age and IBD duration were comparable in pts with or without psoriasis (years:

age 50 range 23-72 *vs* 47 range 16-85; IBD duration 9.5, range 1-46 *vs* 9, range 1-41; p = ns for both). Mild plaque type psoriasis was detected in a higher proportion of IBD pts (52/62; 84%) than non-IBD C (33/62; 53%; p < 0.001). Scalp psoriasis and sebopsoriasis were the more common psoriasis phenotype in IBD (21/62; 84%), followed by palmo-plantar psoriasis (9/62; 14%) and by inverse psoriasis (8/62; 13%). Psoriatic arthritis was detected in 10/62 (16%) non-IBD-C and in 6/62(10%) IBD patients (p = n.s.). Among the 62 IBD pts with psoriasis, psoriasis developed after anti-TNFs in 6 (10%), including palmo-plantar (n = 4), sebopsoriasis (n = 1), inverse psoriasis (n = 1).
CONCLUSION: Results from a cohort of IBD patients matched with non-IBD control patients suggest that specific phenotypes of psoriasis may be associated with IBD.
Disclosure of Interest: None declared

P0304 CONTRAST ENHANCED ULTRASOUND AS A POINT-OF-CARE TECHNIQUE IN COMPLICATED CROHN'S DISEASE PATIENTS

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INTRODUCTION: Crohn's disease (CD) is associated with penetrating complications such as phlegmons and intra-abdominal abscesses. As the management of the patients is influenced by the presence of such complications, a readily available tool for the diagnosis of extramural complications in CD is needed. Preliminary findings suggest that the assessment of vascularity within intra-abdominal masses may distinguish between phlegmons and abscesses.
AIMS & METHODS: Aim of our study was to evaluate the use of contrast enhanced ultrasound (CEUS) to distinguish between phlegmons and intra-abdominal abscesses in CD patients as a point-of-care technique. From November 2011, consecutive patients with complicated CD were enrolled. Indications of patient assessments by CEUS were symptoms, signs and biochemical exams indicating penetrating behavior (abdominal pain, mass, fever, elevated CRP and leukocytosis). A total of 22 CD pts (14 M; median age 27 yrs, range 18-75; disease duration: median 54 mos, range 1-564; CD site: ileal in 13 pts, ileocolonic in 9 pts; CD behavior: penetrating in 20 pts, stricturing in 2 pts; previous ileocolonic resection in 9 pts) were included. Clinical evaluation by an IBD expert and other cross sectional imaging techniques (MR and CT) were considered as the standard.
RESULTS: CEUS detected abscesses in 9 and phlegmons in 12 pts. One patient had an unspecified lesion that was diagnosed as metastasis by PET. Six out of 9 abscesses were confirmed by CT-Enteroclysis and these pts underwent surgery during the follow up. The remaining 3 pts with abscesses were treated with antibiotics and are still in follow up (17.5 mos). In the phlegmon group, 4 out of 12 patients were evaluated by CT or MRI that confirmed CEUS findings in 3 cases but in one patient a deep abscess was identified and surgery was scheduled. Eight out of 12 pts were clinically followed up (median: 16 mos). Two of these patients developed an abscess after one week from CEUS despite medical treatment. Overall CEUS correctly identified 19 out of 22 lesions (86%) on the basis of cross sectional imaging modalities and clinical follow up used as final diagnosis.
CONCLUSION: CEUS is a non-invasive, radiation-free and point-of-care technique able to differentiate phlegmons from abscesses driving a prompt clinical management in complicated CD patients.
Disclosure of Interest: None declared

P0305 ACCURACY OF SMALL INTESTINE CONTRAST ULTRASONOGRAPHY COMPARED TO MAGNETIC RESONANCE ENTEROGRAPHY IN CHARACTERIZING LESIONS IN PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: Small intestine contrast ultrasonography (SICUS) can detect intestinal damage in patients with Crohn's disease (CD).
AIMS & METHODS: We evaluated the diagnostic accuracy of SICUS in determining the site, extent, and complications of CD, compared with magnetic resonance (MR)-enterography as the standard. We performed a retrospective analysis of 59 patients with CD [(M = 34; median age: 46, CD site: ileal 36 (61%), ileocolonic 18 (30%), jejuno-ileal, 3 (5%), colonic 1 (2%); behaviour: non-stricturing non-penetrating 10 (17%), structuring 31 (53%), penetrating 18 (30%); previous surgery 25 (42%)] evaluated by SICUS and MR-enterography 3 months apart, between January 2011 and March 2014. We evaluated disease site (based on bowel wall thickness), extent of lesions, presence of complications (stenosis, prestenotic dilation, abscess, or fistulas) using MR-Enterography as the standard. Sensitivity, specificity, and diagnostic accuracy were calculated. We determined the correlations in maximum wall thickness and disease extent in the small bowel between results from SICUS and MR-Enterography.
RESULTS: SICUS identified the site of small bowel CD with 96% sensitivity, 71% specificity, and 93% diagnostic accuracy; it identified the site of colon CD with 73% sensitivity, 93% specificity, and 88% diagnostic accuracy. Results from SICUS and MR-enterography correlated in determination of bowel wall thickness (rho = 0.51) and disease extent (rho = 0.75; P < .0001 for both). SICUS detected ileal stenosis with 90% sensitivity, 94% specificity, and 91.5% diagnostic accuracy, and pre-stenotic dilation with 66% sensitivity, 83% specificity, and 73% diagnostic accuracy. SICUS detected abscesses with 75% sensitivity, 100% specificity, 98% diagnostic accuracy, and fistulas with 82% sensitivity, 81% specificity, and 81% diagnostic accuracy.
CONCLUSION: SICUS identified lesions and complications in CD patients with high levels of sensitivity, specificity, and accuracy compared to MR-enterography. SICUS might be used as an imaging tool as part of a focused diagnostic and follow up examination of patients with CD.
Disclosure of Interest: None declared

P0306 ASSOCIATION BETWEEN HIGH ADALIMUMAB DRUG LEVEL AND MUCOSAL HEALING IN PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: The current approach to managing loss of response to anti-TNF agents is based on clinical symptoms and empirically increasing the dose or shortening the treatment interval as opposed to tailoring the drug concentrations in individual patients. The primary objective of this study was to evaluate adalimumab drug levels (ADL) and antibodies to adalimumab (ATA) in relation to disease activity.
AIMS & METHODS: A cohort of 61 patients with Crohn's disease (CD) treated with adalimumab between 2005-2013 were recruited to the study. Demographic and clinical information was obtained from chart reviews and patient interview. Disease activity was determined by Harvey-Bradshaw Index (HBI), ileocolonoscopy reports, and CRP levels. Clinical remission was defined by HBI≤4. Mucosal healing was defined by the disappearance of all ulceration in all ileocolonic segments. ADL and ATA were tested using a liquid phase assay. ATA ≤ 1 U/mL were considered low titer.
RESULTS: 61 CD patients were included in the analysis. 39 of the patients were previously on infliximab. 37 were on doses of adalimumab greater than 40mg every other week. 18 of the patients were on concomitant immunosuppressant therapy (methotrexate or azathioprine). 40 of the patients were in clinical remission. 11 (18%) subjects exhibited elevated ATA titers (>1 U/mL). 14 had any detectable ATA (> 0 U/mL). ADL levels were significantly higher in patients with low ATA compared to those with elevated ATA titers (p = 0.001). ADL levels were not associated with CRP levels or with clinical remission (p = 0.07 and p = 0.93, respectively. However, high median ADL drug level (≥5.8 μg/mL) was associated with complete mucosal healing (p = 0.017).
CONCLUSION: Adalimumab levels are not significantly associated with clinical remission or CRP levels in Crohn's disease patients. However, high adalimumab drug levels were associated with complete mucosal healing. Further evaluation with larger, prospective studies is required to further assess the important of drug level monitoring in this setting, however, this study suggests that achieving adequate adalimumab levels may be important toward realizing the goal of mucosal healing. Our results also demonstrate the importance of using endoscopic assessment rather than clinical or laboratory assessments to assess therapy response.
Disclosure of Interest: None declared

P0307 USEFULNESS OF A FAECAL CALPROTECTIN RAPID SEMIQUANTITATIVE TEST IN PREDICTING RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS IN REMISSION

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INTRODUCTION: Faecal calprotectin (CALf) is fairly correlated with clinical and endoscopic activity in ulcerative colitis (UC), and it has also been demonstrated to be a good predictor of relapse. However, the routine use of CALf measurement is constrained by the need for the patient to carry stool samples, as well as handling and processing them in the laboratory. The availability of hand held, single-use devices for CALf measurement that could be performed by the patient himself, might spread the use of CALf in clinical practice.
AIMS & METHODS: Aim: To evaluate the usefulness of a rapid semi-quantitative test of CALf in predicting relapse in patients with UC in remission.
Patients and Methods: A prospective, multicentre study that included patients with left-sided or extensive UC in clinical remission for ≥6 months on maintenance treatment with mesalazine. At baseline and every 3 months, patients were evaluated clinically and semi-quantitative CALf was measured using a monoclonal immunochromatography rapid test (*PreventID Caldetect*™, Immunodiagnostic AG, Germany) without manipulation of stools or laboratory analysis, until relapse or 12 months of follow-up.
RESULTS: At least one determination of CALf with clinical follow-up was available in 192 out 206 patients initially included in the study. 55% with extensive UC, 62% required corticosteroids in the past, and 88% were non-smokers. From a total of 695 measurements of CALf, 81 (12%) were above the upper

threshold of normality of the test (>60 μg/g) and 57 (8%) had limiting values (15-60 μg/g). During follow-up, 32 relapses (17% of patients) occurred. Having a CALf >60 μg/g was significantly associated with relapse at follow-up (35% *vs.* 12%, p<0.0001), with a PPV of 35% and a NPV of 88%. 644 CALf determinations with a three-month follow-up were available; undetectable CALf was significantly associated with absence of recurrence, with a PPV of 100% and a NPV of 93% (0% *vs.* 6%, p=0.002).

CONCLUSION: Rapid semi-quantitative measurement of CALf, with no need for laboratory analysis and faecal samples handling, may be useful for monitoring patients with UC in remission.

Disclosure of Interest: None declared

P0308 MICRORNA-320 AS A BIOMARKER TO MONITOR THE COURSE OF DISEASE ACTIVITY IN EXPERIMENTAL COLITIS AS WELL AS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The pathogenesis of inflammatory bowel disease (IBD) is still incompletely understood and patient-tailored therapy is an unmet need. Thus, biomarkers are needed to follow the course of disease; however, sensitive non-invasive markers to monitor the disease activity are still missing. Previously, we could demonstrate a significant increase of microRNA-320 (miR-320) expression in murine DSS-induced colitis. Aim of this study was to evaluate the potential of miR-320 to monitor the course of inflammation in immunological and bacterial driven experimental colitis as well as in IBD patients.

AIMS & METHODS: MiR-320 expression was assessed by qRT-PCR in murine colonic tissue after induction of T cell transfer colitis as well as *Salmonella* and *Citrobacter (C.) rodentium*-induced colitis. Additionally, miR-320 level was measured in human blood and stool samples from patients with Crohn's disease (CD; n=8) or Ulcerative colitis (UC, n=4) in remission or during acute flare and in healthy controls (n=11). Disease activity was assessed by Crohn's disease activity index (CDAI; active disease: CDAI>220; inactive disease: CDAI<150) in CD patients and the clinical activity index (CAI; active disease: CAI>4; inactive disease: CAI<3) in UC patients.

RESULTS: MiR-320 level in tissue samples from the transfercolitis was significantly increased in animals with severe colitis (>10% loss of body weight) as compared to controls (0.18±0.01 (colitis) vs. 0.11±0.03 (control);$P=0.05$) whereas there was no significant increase of miR-320 in samples from *C. rodentium*-induced colitis (0.6±0.3 (control) vs. 1.1±0.7 (colitis);$P=0.2$) and *Salmonella*-induced colitis (0.6±0.4 (control) vs. 0.06±0.02 (colitis);$P=0.3$). MiR-320 expression in blood of CD patients was significantly increased in acute flare (mean CDAI=231±7.2) as compared to remission (mean CDAI=97±33.9) and healthy controls (x-fold increase:435.4±152.7 (flare) vs. 70.1±28.7 (remission);$P=0.05$; vs. 24.6±8.8 (control);$P<0.001$). Moreover, miR-320 level of controls was significantly lower as compared to CD patients in remission ($P=0.01$). Furthermore, miR-320 expression in blood as well as stool from CD patients revealed a strong correlation with the CDAI ($r^2=0.78$ (blood);$r^2=0.81$ (stool)). In UC patients, miR-320 expression in blood obtained during acute flare (mean CAI=6) or quiescent disease (mean CAI=1.5) also revealed a significant increase of miR-320 expression as compared to healthy controls (182.15±111.4 vs. 24.6±8.8;$P=0.03$). As opposed to CD, miR-320 level in blood from UC patients was not significantly increased in acute flare as compared to quiescent disease. However, miR-320 expression in stool from UC patients was significantly enhanced in acute flare as compared to quiescent disease (225.35±35.4 (flare) vs. 68.5±40.6 (remission);$P=0.02$) showing a strong correlation with the CAI ($r^2=0.68$).

CONCLUSION: Our preliminary results indicate that miR-320 expression is increased in classical IBD models but not significantly altered in bacterial-induced colitis. Furthermore, miR-320 expression in human blood and stool samples follows the course of disease activity in IBD patients. Future studies are needed to elucidate the potential of miR-320 to predict relapse and disabling courses of disease.

Disclosure of Interest: None declared

P0309 THE APPROPRIATENESS OF TESTING AND INTERPRETATION OF ANTI-TNF DRUG AND ANTIBODY CONCENTRATIONS: WHEN SHOULD THEY BE ORDERED, AND WHAT TO DO WITH THE RESULTS?

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INTRODUCTION: The availability of drug concentration and antibody testing for anti-TNF therapy promises optimized drug dosing and informed decision-making for patients with inflammatory bowel disease (IBD) treated with these agents. However, there is no consensus on when to test and how to interpret the results for various clinical scenarios. We applied the RAND/UCLA Appropriateness Method toward establishing the appropriateness of when these tests should be obtained, and how to act upon their results.

AIMS & METHODS: A comprehensive literature review was conducted on the topic of drug concentration and anti-drug antibodies in patients with IBD for all approved anti-TNF therapies. This review was presented to an expert panel including clinician and pharmacokinetic experts who have published on the topic, and the Building Research in Inflammatory Bowel Disease Globally group, a globally diverse panel of 13 gastroenterologists clinically experienced in IBD treatment and therapeutic drug monitoring. A total of 35 scenarios assessed the appropriateness of obtaining these tests, and 143 additional scenarios addressed the appropriateness of various clinical strategies in response to test results. Panelists used a modified Delphi method to rate each scenario through a web-based survey, and then met in-person to discuss and anonymously re-rate appropriateness on a 1-9 scale (1-3 inappropriate, 4-6 uncertain, 7-9 appropriate). Disagreement was assessed using a validated index.

RESULTS: Assessment of anti-TNF drug and antibody concentrations was rated appropriate at the end of induction therapy in primary nonresponders, in secondary nonresponders, at least once during the first year of therapy, in patients experiencing immune-related side effects, and when restarting a drug following a drug holiday (before 2nd infusion). Routine assessment in responders at the end of induction was rated uncertain. Panelists rated the appropriateness of various clinical management options including changing therapy within-class, switching out of class, adjusting drug dose/interval, adding/adjusting concomitant immunomodulators, and "doing nothing" for each of 6 permutations of high/low drug concentration and high/low/undetectable antibody concentrations. These ratings were highly dependent on the specific clinical scenario for which the test was obtained. For example, switching out of class when drug and high antibody concentrations were detected was "appropriate" at the end of induction in nonresponders, "uncertain" at the end of induction in responders, and "inappropriate" during maintenance in responders.

CONCLUSION: The appropriate timing and how to respond to anti-TNF drug and antibody testing for IBD was determined through a modified Delphi panel based on expert interpretation of the literature. The time to test and clinical action on the results is dependent on the specific clinical scenario. These recommendations can help guide clinicians to best optimize anti-TNF therapy.

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P0310 IBD RECURRENCE AFTER STOPPING ANTI-TNF-ALPHA THERAPY: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY COMPARING MESALAMINE AND AZATHIOPRINE – AD INTERIM RESULTS

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INTRODUCTION: The advent of tumor necrosis factor (TNF) antagonists has dramatically changed the management of patients with inflammatory bowel diseases (IBD). However, despite more than a decade of clinical experience, there is still debate about the optimal exit strategies from biologic therapies. Indeed, an important issue concerns how to manage patients with long-standing remission after stopping anti-TNF-α drugs. Data on different maintenance strategies are lacking.

AIMS & METHODS: We aimed to assess the efficacy of mesalamine (MESA) vs. azathioprine (AZA) as maintenance therapy in IBD patients who withdrew biological therapy after obtaining deep remission (i.e. clinical remission, biomarker remission and mucosal healing). Consecutive IBD patients who achieved deep remission due to anti-TNF-α therapies withdrew them and were prospectively randomized to two different maintenance treatments: MESA 2.4 gr/die in ulcerative colitis (UC) and 3 gr/die in Crohn's Disease (CD) patients or AZA 2.5 mg/kg/die. Then, patients were followed up every two months or before in case of relapse, by means of routine biochemistry, clinical examination and endoscopy at 1-year or before in case of relapse. The Harvey-Bradshaw Index (HBI; remission <5) and Mayo score (remission <3) was used to evaluate clinical activity for CD and UC, respectively, whereas endoscopy activity was assessed by means of Mayo endoscopic score (endoscopic remission <2) or CD endoscopic index (CDEIS; endoscopic remission <3).

RESULTS: We prospectively enrolled 16 patients with IBD [6UC/10CD; 8F/8M; median age 44 (25-57)] who were followed-up for a median period of 48 (20-78) weeks after achieving deep remission due to anti-TNF-α therapy. Ten patients [2UC/8CD; 5F/5M; median age 37.5 (25-53)] were randomized to MESA 2.4 gr/die or 3gr/die and 6 patients [1UC/5CD; 3F/3M; median age 41.2 (21-47)] to

AZA 2.5 mg/kg/die. All AZA-treated patients (100%) kept in remission during the entire follow up period [median period of 55.5 weeks (20-76)], whereas 3/10 (30%) MESA-treated patients [1UC/2CD; 0F/3M; median age 42 (29-52)] experienced clinical relapse after a median period of 14 weeks (8-26). The latter three patients were shifted to AZA and clinical remission was restored.
CONCLUSION: Our preliminary data showed that AZA is more effective than MESA in maintaining clinical remission in IBD patients who stopped biological therapy after obtaining deep remission. Moreover, we observed that disease recurrence due to mesalamine failure occurs a few weeks after biologic withdrawal and can be successfully treated with AZA.
Disclosure of Interest: None declared

P0311 MRI AND CLINICAL ASSESSMENTS FOR PERIANAL CROHN'S DISEASE: GAIN AND LIMITS

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INTRODUCTION: Assessment of perianal Crohn's disease (PCD) remains challenging. ECCO guidelines recommended Magnetic resonance imaging (MRI) as a gold standard but both accuracy and advantage of MRI remain scarce as compared to systematic clinical assessment. The aim of the study was to define diagnosis values of both assessments.
AIMS & METHODS: Between January 2006 and April 2012, consecutive patients with PCD assessed by MRI and clinical exam were prospectively recorded. At each visit, perianal activity (Perianal Disease Activity Index) and perianal phenotype (Cardiff-Hughes classification) were notified. MRI analyses were independently reviewed and interpreted according to Cardiff-Hughes and Van Assche classifications.
RESULTS: Overall, 122 combined evaluations were assessed in 70 different patients. MRI failed to show superficial ulcerations in 20 of 21 patients as well as severe ulcerations in 13 of 15 patients. MRI constantly failed to diagnose anal stenosis (n = 21). According to fistulizing lesions, the global agreement between clinic and MRI was 60% to assess complex fistula. Clinical assessment underestimated 52% of multiple or ramified fistula tracts. Clinical exam (including induration) failed to diagnose half abscesses described on MRI.
Table. Overall value of clinical or MRI assessment for each items

Items		test	G-S	Se	Sp	Youden Index**	Pos LR	Neg LR	C
Ulceration		MRI	Clinic	0.08	0.94	0.02	1.33	0.98	0.68
Stenosis				0	1	0	-	1	0.83
Fistula	Cardiff*	Clinic	MRI	0.94	0.15	0.09	1.12	0.40	0.58
	Induration			0.4	0.86	0.26	2.86	0.70	0.28
	Abscess			0.14	1	0.14	-	0.86	0.70

CONCLUSION: ECCO guidelines for assessment of PCD should be applied with some caution because of the low sensitivity of MRI for the diagnosis of non-fistulizing PCD. Concomitant clinical and MRI assessments should be recommended.
Disclosure of Interest: None declared

P0312 STEM CELL THERAPY IN EXPERIMENTAL ULCERATIVE COLITIS: LOCAL VERSUS SYSTEMIC APPROACH

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INTRODUCTION: Ulcerative colitis (UC) is a chronic inflammatory bowel disease of unknown etiology(1), affecting patient's quality of life, and increases cancer colon. Its incidence and prevalence are growing all over the world (2). Its conventional therapy commonly fails to give satisfactory results and may cause serious side effects(3). So, new treatment is needed**.** In UC, both damaged intestinal tissue and the immune system need to be repaired. Only stem cells (SCs) can do this(4). Among adult SCs, adipose derived SCs can be easily obtained with less heterogeneity in their immunophenotype and multilineage differentiation ability than do bone marrow derived MSCs(5). Several papers had reported the efficacy of systemically infused MSCs in treating experimental UC, but some trapped in liver and lung, decreasing their effect in local injury site (colon) and increasing required dose(4). Meanwhile, some papers reported the use of MSCs on experimental external wounds and reported some efficacy(6).
AIMS & METHODS: Evaluate effectiveness of stem cell therapy through local enema & intravenous approaches. Induction of UC in sprague dawley (SD) rats by 5% dextran sulphate sodium (DSS). Isolation of MSCs from adipose tissue was done under sterile conditions. Cells were characterized using cell surface markers by fluorescence-activated cell sorting analyses. First group was control healthy group. Second group received 5% DSS for 7 days with no therapy. Third group received local $1x10^6$ ADMSCs enema. Fourth group received systemic iv $1x10^6$ ADMSCs. Disease activity index (DAI) was assessed daily. On day 7 colon was examined macroscopically & microscopically.
RESULTS: All groups received DSS had DAI higher than healthy control group with statistically significant difference ($p < 0.05$). Both groups receiving stem cells showed less DAI, macroscopic & microscopic score than control diseased group ($p < 0.05$). Local enema group and systemic iv groups had no statistically significant difference in DAI, macroscopic nor microscopic scores.
CONCLUSION: Stem cell therapy via enema is a potential future therapy with expected low side effects than systemic route for treating UC.
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P0313 SUSTAINED CLINICAL BENEFIT AND IMPROVED QUALITY OF LIFE FROM MAINTENANCE INFLIXIMAB TREATMENT IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Infliximab is effective in inducing remission in inflammatory bowel disease and many patients are treated for several years with sustained clinical remission.
AIMS & METHODS: To evaluate the long-term outcome of maintenance infliximab (IFX) treatment in inflammatory bowel disease (IBD), regarding inflammatory activity, concomitant medication, quality of life (QoL) and whether reduced intestinal surgery could be observed after initiation of treatment. Patients with Crohn's disease or ulcerative colitis, responding to IFX treatment during one year and thereafter on continuous maintenance treatment, were eligible. Two hundred patients with Crohn's disease (CD; n: 164), or ulcerative colitis (UC; n: 36), were involved. Median age at diagnoses was 22 (3-64) years. Five mg /kg body weight IFX was usually administered every eight week. Inflammatory activity was assessed by Harvey Bradshaw index (HBI) in Crohn's disease. Concomitant medications were followed during the study period, and Short Health Scale (SHS), a validated short questionnaire, was used for measuring QoL. Hb, LPK, Albumin, CRP and calprotectin were monitored. Side effects and reasons for discontinuation were recorded. In this retrospective study the observation period ended in March 2014. Parameters and treatment duration were estimated by last observation carried forward.
RESULTS: Median disease duration at start of treatment was 5.0 (0.2 - 44) years. Median duration of IFX treatment was 3.4 (1.0-13.9) years. Table 1: Parameters of inflammatory activity before and after start of IFX treatment

	HBI (n:164)	CRP (n: 196)	Alb (n:199)	WBC (n:198)	Calprotectin (n:50)
Before	8.04	29.23	34.98	8.70	3135 (1872-6200)
After	2.76	8.45	37.28	7.54	158 (30-1503)
P-value	<0.0001	<0.0001	<0.0001	<0.0291	<0.0012

SHS (n:60) was significantly improved in all QoL dimensions. Steroid treatment and immunosuppression at start of IFX treatment were 51% and 62%, respectively. Corresponding figures at latest infusion were 10% and 43%. No opportunistic infection has been diagnosed. Ten infusion related moderate to severe side effects were observed, leading to treatment discontinuation. Loss of response occurred in 42 patients. Of those, 20 needed intestinal surgery. Twelve changed anti-TNF therapy, one patient received alternative biological treatment and 9 continued without biological treatment. Surgery before initiation of IFX therapy was necessary in 27% compared to 11% after treatment. Sixteen patients in remission decided to stop treatment and 13 of those are still in remission with only 4 on immunosuppression. One patient died several years after stopping treatment from lung cancer and the remaining 2 were restarted on anti-TNF. Twenty-four patients moved, while on therapy. Three patients were lost to follow up and two stopped treatment because of malignancies.
CONCLUSION: Almost three-quarters of the patients demonstrated clinical benefit from IFX treatment. Use of steroids was dramatically reduced with less influence on the use of immunosuppression. SHS showed significant improvement of QoL. During the studied time period, surgery was less frequent after initiation IFX treatment.
Disclosure of Interest: None declared

P0314 MEAN PLATELET VOLUME AND NEUTROPHIL-TO-LYMPHOCYTE RATIO AS NEW BIOMARKERS OF SUSTAINED RESPONSE TO INFLIXIMAB THERAPY IN CROHN'S DISEASE PATIENTS

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INTRODUCTION: The loss of response to infliximab (IFX) in Crohn's disease (CD) patients is currently an important clinical problem. Therefore, searching for predictors of maintenance or loss of response to anti-tumor necrosis factor-α (anti-TNF-α) agents has become the aim of current studies in the field. Recently, the neutrophil-lymphocyte ratio (NLR) and mean platelet volume (MPV) have been proposed as new biomarkers of subclinical inflammatory process. Here we hypothesized that NLR or MPV may be used as cost-effective biomarkers of subclinical inflammation during 52-week IFX therapy in CD patients responding to induction treatment.
AIMS & METHODS: The study aimed at establishing whether NLR or MPV at baseline and pre-infusion at week 14 are good predictors of sustained response after week 14 in CD patients undergoing 52-week IFX therapy. 30 adult patients with CD (11 women and 19 men; mean age±SD 32.0±8.6 years), who underwent a 52-week course of treatment with IFX and achieved response to induction treatment evaluated at week 14 were enrolled to the study. The control group consisted of 12 healthy subjects. The association between NLR or MPV, baseline disease parameters and maintained clinical response or remission during IFX therapy was assessed.
RESULTS: Fifteen of CD patients (50%) have not reached full one year maintenance IFX treatment without loss of response. The analysis showed a statistically significant higher NLR (4.62±2.43 vs. 1.49±0.76; $p<.001$) and lower MPV (10.25±0.99 vs. 11.29±1.08 fL; $p=.003$) in CD patients compared to controls. Higher NLR at baseline (5.85±2.71 vs. 3.39±1.28; $p=.003$) and at week 14 (4.79±2.61 vs. 2.58±1.23; $p=.006$) were observed in CD patients with loss of response to IFX maintenance treatment than in those with sustained response. NLR lower than 4.068 at baseline predicts sustained response with 80% sensitivity and 87% specificity. NLR lower than 3.667 at week 14 predicts sustained response with 67% sensitivity and 80% specificity. MPV at week 14 in CD patients with loss of response was significantly higher (11.31±1.16 fL vs. 10.19±0.52 fL; $p=.001$) than in CD patients with sustained response. In patients with sustained response to maintenance IFX treatment higher ΔMPV between baseline and week 14 was calculated (0.78±0.34 fL vs. 0.23±0.39 fL; $p<.001$). MPV higher than 10.3 fL at week 14 predicts sustained response with 67% sensitivity and 80% specificity. ΔMPV between baseline and week 14 higher than 0.4 fL predicts sustained response with 87% sensitivity and 93% specificity.
CONCLUSION: In CD patients with loss of response to IFX therapy higher NLR and lower MPV were observed. It can be suggested that NLR and MPV may serve as good predictors of sustained response to IFX maintenance treatment in CD patients as well as may allow selection of the most appropriate therapy based on the individual approach. Further studies are warranted to confirm our observations and to establish the cut-off points in a larger cohort.
Disclosure of Interest: None declared

P0315 ANTI-DRUG ANTIBODIES INHIBIT NEUTRALIZATION OF TNF-ALPHA IN INFLIXIMAB TREATED PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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INTRODUCTION: Infliximab (IFX) trough levels (TL) as well as c-max levels have been positively associated with its efficacy and negatively with IFX immunogenicity in patients with IBD. Clearance of IFX is increased in the presence of anti-drug antibodies (ADA). However, to what extent ADAs impact the binding and neutralization of soluble TNF-alpha *in vivo* remains largely unknown. In this study we assessed the relationship between IFX-, ADA- and TNF-alpha levels at a mid-infusion visit and at trough in patients with IBD on maintenance therapy.
AIMS & METHODS: Serum samples from 90 consecutive patients with IBD (Crohn's disease: $n=66$, ulcerative colitis: $n=24$) on IFX maintenance therapy were obtained at mid-infusion visits and at trough. IFX and ADA were measured by a homogeneous mobility shift assay from Prometheus, which allows detection of ADA in the presence of IFX. Serum TNF-α was measured by a Collaborative Enzyme Enhanced immuno-Reactive (CEER) Assay.
RESULTS: Patients had received a median number of 11 IFX infusions (range 3 - 71) with a median dose of 5.5 mg/kg (4.1- 10.9 mg/kg) before study entry. ADAs were detected in 18 pts at mid-infusion and in 21 pts at trough. In ADA positive pts median serum concentration of IFX was significantly lower than in ADA negative pts both at mid-infusion and at trough. Inversely, significantly higher serum concentrations of TNF-α were detectable in ADA positive pts at both visits (see Table). At trough the TNF-α/IFX ratio was significantly higher in ADA positive patients than in those without ADA ($p<0.0001$). No difference was seen in TNF-α levels when segregated by IFX serum levels alone.

	Mid-infusion			Trough		
	ADA neg. n = 69	ADA pos. n = 21	p-value	ADA neg. n = 69	ADA pos. n = 21	p-value
IFX (μg/ml) median (range)	13.59 (3.2-35.2)	0.75 (0.08-16.37)	<0.0001	6.36 (range)	0.42 (range)	<0.0001
TNF-α (pg/ml) median (range)	5.5 (range)	10.2 (range)	0.04	7.5 (range)	25.6 (range)	<0.0001

Interestingly, 3/10 (30%) ADA negative pts at mid-infusion with an IFX concentration below 8 μg/ml turned ADA positive at trough versus 1/36(3%) pts with an IFX concentration ≥8 μg/ml.
CONCLUSION: ADA detected in patients with IBD on IFX maintenance therapy impairs neutralization of soluble TNF-α and is associated with lower serum concentrations of IFX and higher levels of TNF-α both at mid-infusion and at trough. Our finding favours a strategy of a pre-emptive dose optimization in ADA positive patients due to insufficient control of inflammation.
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P0316 INFORMATION NECESSARY TO PREDICT INDIVIDUAL INFLIXIMAB (IFX) PHARMACOKINETICS (PK) IN PATIENTS WITH IBD

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INTRODUCTION: The increasing interest in monitoring serum IFX concentrations for purposes of therapeutic dose adjustment (TDA) has led to the availability of various assays whose validity remains to be determined. Only population-based approaches to determine individual IFX PK are used so far.
AIMS & METHODS: Objectives: 1) Evaluate the performance of 3 different IFX assays and 2) Determine how many samples are needed in order to estimate individual PK accurately and precisely.
Serum samples were collected after the 3rd IFX infusion for measurement of IFX and anti-drug antibodies (ADA) in 117 patients with IBD (87 = CD, 30 = UC). The mean IFX dose was 5.84 mg/kg for patients with a mean weight of 68.37 kg (ADA positive $n=19$, ADA negative $n=98$). For each patient, at least 2 samples from within the same infusion interval were available. 41 patients had >2 IFX concentrations. IFX serum concentrations were measured with ELISA assays provided by Theradiag (France) (TD) and Immundiagnostik (ID, Bensheim, Germany). IFX and ADA were also determined by a homogeneous mobility shift assay from Prometheus. Assay performance was evaluated by running a population PK model using Nonmem (version 7.2 Icon Dublin Ireland). Estimated clearance, between subject variability (BSV) and residual error were compared with literature values. Bayesian updating and forecasting was conducted using individual patient data and forecasting with different subsets of information for each subject. Initially, only subject demographics (age, weight, gender, albumin, ADA status and planned dose) were used. Forecast concentrations based only on this information were compared with the first observed concentration value. Subsequent evaluations included progressively more PK observations. Agreement between observed and forecast concentrations was evaluated graphically and via root mean square error (RMSE) and concordance.
RESULTS: Ability of assays to estimate clearance was variable with Prometheus and ID performing better than TD, but all provided reasonable estimates. The number of observations needed to accurately and precisely estimate individual PK was similar for all 3 assays. If no serum concentrations are available the precision of the prediction of subsequent IFX concentrations is poor (RMSE = 0.46, concordance = 0.43) which is reflective of high BSV in IFX PK. With more serum IFX concentration per patient, precision of forecast concentrations increased. With 3 observations (RMSE = 0.15, concordance = 0.86), PK estimates were markedly improved. With 4 observations the predicted concentration was within the assay error (RMSE and concordance). Two vs. one observation within a dose interval does not substantially impact precision, but does impact time required to collect enough observations to obtain precise estimates of future IFX PK.
CONCLUSION: Assay quality is important for precisely estimated IFX clearance in IBD patients. TDA according to patient demographics and patient factors is imprecise. At best 3 to 4 measurements of IFX would be taken early on. Based on this information it becomes feasible to dose to a target concentration and to determine the dose necessary. It further provides tools to prospectively determine which concentrations are leading to most favourable responses.
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P0317 PROSPECTIVE, RANDOMIZED CLINICAL TRIAL COMPARING THE EFFICACY OF TWO VACCINES AGAINST HEPATITIS B VIRUS (HBV) IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS

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INTRODUCTION: Around 50% of IBD patients do not respond to the HBV vaccine. To increase the success rate, different vaccination protocols have been proposed although no study has been able to establish the optimal strategy for IBD patients.
AIMS & METHODS: Aims: To compare the success rate between two HBV vaccines in IBD patients: traditional (Engerix®) and a new vaccine with adjuvant (Fendrix®). Secondary aim was to identify predictor factors of response to the vaccine.
Methods: IBD patients with negative HBV serology and without previous vaccination against HBV were randomized to receive Fendrix® or double doses of Engerix® at months 0, 1, 2 and 6. Anti-HBs concentration was measured 2 months after the 3rd and 4th doses (EUDRA CT number:2010-023947-14).
RESULTS: 170 patients had been included: 55% male, 52% with Crohn's disease, 30% under immunosuppressants and 37% under anti-TNF treatment. 54% of patients received Engerix® and 46% Fendrix®; the main characteristics of patients (age, gender, type of IBD and treatment) were similar between the 2 groups. Overall, 44% of patients had response (anti-HBs^3 100 IU/l) after the first 3 doses (161 patients have already received 3 doses), and 71% after the completion of the vaccination (134 have completed the vaccination). The response rate after the 4 doses was 67% with Engerix® vs. 76% with Fendrix® ($p = 0.2$); considering anti-HBs^{3}10 IU/l (the standard threshold), the response rate was higher with Fendrix® than with Engerix® (87 vs. 73.6%, $p = 0.04$). In patients under immunosuppressants or anti-TNF drugs, the response (anti-HBs^{3}100 IU/l) after the 4 doses was 55% with Engerix® vs. 69% with Fendrix® ($p = 0.12$). In the multivariate analysis, older age (odds ratio [OR] = 0.9, $p < 0.0001$) and immunosuppressants or anti-TNF concomitant treatment (OR = 0.04, $p < 0.0001$), but not the type of vaccine (OR = 1.9, $p = 0.1$), were associated with the response rate to the vaccination. 7.7% of patients flared up during the study period, and 13% suffered adverse events (only 41% related with the vaccine, and all of them mild). The frequencies of flaring up and adverse events were similar between the 2 groups.
CONCLUSION: A statistically significant different response rate to Fendrix® (single dose) or Engerix® (double dose) has not been demonstrated in IBD patients yet (although the trial is still ongoing). A 4-dose schedule increases the response rate around 30% compared with a 3-dose regimen. The older age and the immunosuppressive and anti-TNF treatment decrease the success rate of the vaccine. Both vaccines seem to be safe in IBD patients.
Disclosure of Interest: M. Chaparro Other: Dra. M Chaparro has served as a speaker and has received research funding from MSD and Abbvie, J. Gordillo: None declared, E. Domènech: None declared, M. Esteve: None declared, M. Barreiro de-Acosta: None declared, A. Villoria: None declared, E. Iglesias-Flores: None declared, E. Alvarado: None declared, J. Naves: None declared, O. Benítez: None declared, L. Nieto: None declared, X. Calvet: None declared, V. García-Sánchez: None declared, J. R. Villagrasa: None declared, A. Marín: None declared, M. Ramas: None declared, I. Moreno: None declared, J. Maté: None declared, J. P. Gisbert Other: Dr. P. Gisbert has served as a speaker, a consultant and advisory member for, and has received research funding from MSD and Abbvie.

P0318 EFFICACY OF A SECOND ANTI-TNF IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE WHOSE PREVIOUS ANTI-TNF TREATMENT HAS FAILED: A META-ANALYSIS

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INTRODUCTION: One-third of patients with Crohn's disease (CD) or ulcerative colitis (UC) receiving anti-TNF therapy do not respond to treatment (primary failure), and a relevant proportion experience a loss of response (secondary failure) or intolerance.
AIMS & METHODS: To investigate the efficacy of a second anti-TNF agent after failure or intolerance to a first drug.
METHODS: *Inclusion criteria:* Studies evaluating the efficacy of infliximab (IFX), adalimumab (ADA), and certolizumab pegol (CZP) as the second anti-TNF drug in CD or UC. *Search strategy:* Bibliographical searches in PubMed. *Data synthesis:* Percentage of response/remission; the meta-analysis was performed using the inverse variance method.
RESULTS: We included 42 studies (35 CD, 6 UC, 1 pouchitis). The CD studies comprised 30 switching IFX→ADA, 4 IFX→CZP, and 1 ADA→IFX. Overall, the second anti-TNF in CD induced remission in 43% (95%CI = 38-48%; $I^2 = 75\%$; 27 studies; 2,345 patients) and a response in 65% (95%CI = 57-73%; $I^2 = 92\%$; 26 studies; 1,922 patients) of patients. The remission rate was higher when the reason to withdraw the first anti-TNF was intolerance (61%; 95%CI = 40-82%; $I^2 = 89\%$) than after secondary (45%; 95%CI = 34-57%; $I^2 = 79\%$) or primary failure (30%; 95%CI = 22-37%; $I^2 = 8\%$); response rates were, respectively, 72%, 66%, and 60%. Six UC studies were identified, all of them switching IFX→ADA, and only 4 of them reporting remission rates (151 patients), with figures ranging from 0% to 50%
CONCLUSION: The efficacy of a second anti-TNF in CD patients largely depends on the cause for switching. The remission rate was higher when the reason to withdraw the first anti-TNF was intolerance (61%), compared with secondary failure (45%) and primary failure (30%).
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P0319 THE ONE-YEAR EFFICACY OF INFLIXIMAB DOES NOT DEPEND ON THE TIMING OF BIOLOGICAL THERAPY IN ULCERATIVE COLITIS

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INTRODUCTION: Infliximab is an effective therapeutic option in patients with refractory ulcerative colitis (UC). The optimal timing of infliximab therapy is still one of the outstanding questions in the therapy of UC.
AIMS & METHODS: The aim of our study was to assess whether there is an association between the one-year remission rates and the elapsed time between the diagnosis and the start of infliximab therapy. 116 UC patients treated with infliximab were enrolled in this retrospective study. The time elapsed between the diagnosis and the first biological therapy was assessed in every patient, who was then categorized to groups according to the elapsed time (>5 years and <5 years; 0-2 years, 2-5 years, 5-10 years etc).
RESULTS: The mean elapsed time between the diagnosis and the start of biological therapy was 7 years (0-38 years). 50.4% of patients started infliximab therapy within 5 years after diagnosis. After induction with infliximab 65.6% of the enrolled patients achieved remission and 34.4% achieved response. After one-year treatment period, the remission and response rates remained 67.7% and 21.8%. 10.6% of patients showed loss of efficacy at one year infliximab therapy. Complete mucosal healing was detected in 31.2% and deep remission in 13.9% of the patients at week 52. Response rates to infliximab therapy at one year were significantly lower compared to rates at week 14 ($p = 0.029$). The rate of remission and loss of efficacy did not depend on the elapsed time between the diagnosis and the start of biological therapy. However, response rates were higher in longer elapsed time ($p = 0.036$).
CONCLUSION: Infliximab is effective for drug-refractory UC to induce and maintain clinical remission. Our results did not reveal an association between the remission rates and the elapsed time between the diagnosis and the first biological therapy in UC.
Disclosure of Interest: None declared

P0320 HEAD-TO-HEAD COMPARISON OF 5 FECAL MARKERS TO PREDICT RESPONSE TO INDUCTION AND MAINTENANCE THERAPY WITH INFLIXIMAB IN ULCERATIVE COLITIS PATIENTS; A PROSPECTIVE STUDY

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INTRODUCTION: The role of faecal markers in monitoring anti TNF alpha therapies has been insufficiently explored. This study aimed to determine the usefulness of five faecal proteins in the prediction of clinical response to Infliximab (IFX) in Ulcerative Colitis (UC): calprotectin (fCal), Lactoferrin (fLac), M2PK (fM2PK), neopterin (fNeo), and zonulin (fZo).
AIMS & METHODS: Thirty-one consecutive patients with an active UC, requiring IFX [5 mg/kg at week 0 (W0), 2, 6 and every 8 W] were prospectively studied. At W0, W2, W6 and W14, clinical activity was recorded and a stool sample collected. Clinical response to induction therapy was defined at W14 as a reduction of at least 3 points and 30% of the Mayo score. In 25 patients, endoscopies were performed at W0 and W12; an endoscopic Mayo subscore of 0 or 1 defined endoscopic remission. Clinical response to maintenance therapy was evaluated at W52 and optimization or discontinuation of IFX were considered as a failure.
RESULTS: At W0 the median partial Mayo Score, the endoscopic Mayo and the UCEIS scores were 7/9 (2-9), 3/3 (2-3) and 8/11 (6-11) respectively. At W14, 19 patients (61%) were clinical responders and 13 (52%) experienced an endoscopic response. The median levels of fCal drop dramatically from W0 to W14 in responders [from 4260 µg/g (96-25051) to 128 µg/g (11-3782); $p = 0.0001$]. In contrast, it did not differ significantly in non-responders [from 9077 µg/g (215-50000) to 2781 µg/g (203-14149); $p = 0.287$]. Same trends were observed for fLac

and fM2PK levels. At W2, fLac and fM2PK predicted accurately clinical response to IFX induction (area under the curve (AUC) = 0.82, 0.84 and 0.88 respectively): cuts-offs of 800 µg/g for fCal, 20000 ng/g for fLac and 50 UI/mL for fM2PK determined by ROC curves allowed to discriminate clinical responders from non responders to induction therapy, with good sensitivities (Se) (82%, 81% and 88%, respectively), and specificities (Sp) (69%, 70% and 80%, respectively). FLac measured at W2 were the more valuable marker to predict endoscopic remission at W12 [(AUC = 0.80, Se and Sp = 72% with a cut-off of 32891 ng/g). At W14, the three previous markers were also reliable to predict clinical response at W52 (AUC = 0.82, 0.86 and 0.75 respectively) with best cut-offs of 146 µg/g for fCal, 3457 ng/g for fLac and 2.25 UI/mL for fM2-PK. FCal, fLac and fM2PK were well correlated with both the endoscopic Mayo subscore and the UCEIS. FNeo and fZo did not show any relevant result.

CONCLUSION: FCal, flac and fM2-PK predicted with a good accuracy the clinical response to induction and maintenance IFX therapy in UC. The measurement of one of these markers at W0 and at the end of induction might distinguish responders from non responders to IFX maintenance therapy within one year.

Disclosure of Interest: None declared

P0321 ALTERATIONS OF FECAL MICROBIOTA AND METABOLIC LANDSCAPE IN RESPONSE TO ORAL OR INTRAVENOUS IRON REPLACEMENT THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Iron deficiency is a common complication in patients with inflammatory bowel diseases (IBD) and oral iron replacement therapy is suggested to exacerbate IBD symptoms. We hypothesized that oral iron may impact the composition of the gut microbiota and thereby affect the disease status.

AIMS & METHODS: An open-labelled clinical trial including patients with Crohn's disease (CD; N = 29) or ulcerative colitis (UC; N = 19) as well as control patients with iron deficiency (iron saturation < 16% and ferritin < 100) (N = 20) was performed to compare the effects of oral (PO; ferrous sulfate) vs. intravenous (IV; iron sucrose) iron replacement therapy over a period of three months. The health status was assed via quality of life (EQ 5D and SIBDQ) and disease activity (HBI and PMS) questionnaires. Stool and sigmoid mucosal biopsies were collected before and after treatment. Gut bacterial diversity and composition were assessed by high-throughput sequencing of 16S rRNA genes (V4 region). Fecal metabolites were analyzed by ESI-FT-ICR-MS.

RESULTS: PO and IV treatments were comparable regarding amelioration of iron deficiency, with superior but not significant levels of ferritin and iron saturation in the IV group. Worsening or improvement of disease activity and quality of life were independent of iron treatments (no difference between PO and IV). Fecal bacterial diversity was significantly different between control, UC and CD patients before and after iron treatment. Samples from IBD patients were characterized by marked inter-individual differences as well as lower phylotype richness and proportions of unknown *Clostridiales*. We identified the presence of 18 CD-specific molecular species (OTUs), many of which matched sequences of facultative anaerobic bacteria. Major shifts in bacterial diversity occurred in approximately half of the participants after treatment, independently of disease. In those samples where bacterial profiles shifted, changes in diversity were significantly higher in IBD patients. However, no consistent changes in the occurrence of specific OTUs relative to iron treatment could be identified, suggesting individual-specific responses to treatment. Metabolite analysis using OSC-PLC classification showed a clear separation of both UC and CD from control patients before the iron treatment. After therapy, metabolite profiles were only different in UC patients indicating a possible convergence of CD patients with control subjects in response to the iron treatment. Separation into IV- and PO-specific metabolite profiles appeared in the control and CD group but not in the UC group.

CONCLUSION: Shifts in bacterial diversity associated with iron treatment are independent of the route of administration and are more pronounced in IBD patients. Efficiency and clinical outcome of both iron therapies are comparable in both IBD patient cohorts.

Disclosure of Interest: None declared

P0322 DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING PARAMETERS AS PREDICTORS OF REMISSION IN CROHN'S DISEASE PATIENTS TREATED WITH ANTI-TNF THERAPY

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INTRODUCTION: Anti-TNFα agents are the most effective therapy in Crohn's disease (CD). However, almost one-third of the patients experience primary failure to anti-TNF therapy. Diffusion-Weighted Magnetic Resonance Entero-Colonography (DW-MREC) has shown good accuracy to detect and assess inflammatory activity in CD[1,2].

AIMS & METHODS: We aimed to study the DW-MREC parameters as predictors of advanced remission (clinical remission defined as CDAI <150 AND CRP <5 mg/L), surgery, clinical remission (CDAI <150) or clinical response (ΔCDAI≥70) after induction regimen of anti-TNFα (week 12).

Overall, 28 consecutive CD patients were prospectively included during 1 year. All the patients underwent a DW-MREC[1,2] within 4 weeks before starting anti-TNFα. Adalimumab (ADA) was administered as 160mg at W0, 80mg at W2 and 40mg e.o.w. Infliximab (IFX) was administered as 5mg/kg at W0, W2 and W6. The collected MRI parameters were: Clermont score[1,2], apparent diffusion coefficient (ADC), Magnetic Resonance Index of Activity (MaRIA), presence of stenosis, fistula, abscess, sclerolipomatosis or mesenteric lymph nodes.

RESULTS: Median age and disease duration at inclusion were 37 years (17-71) and 34 months (0-456) respectively. Overall, 14 (50%) were smokers, 7 (25%) underwent previous intestinal resection and 7 (25%) had ano-perineal lesions. 13 patients (46.4%) had ileal CD (L1), 3 (10.7%) colonic CD (L2), 12 (42.8%) ileocolonic CD (L3). CD phenotypes were non-stricturing non-fistulizing (B1), stricturing (B2) and fistulizing (B3) in 9 (32.1%),12 (42.9%), and 7 (25.0%) patients, respectively. While 13 patients were treated with IFX (44.4%), 15 were treated with ADA (55.6%). Among them, 10 (35.7%) patients received concomitant thiopurines. At inclusion, median CDAI was 225 (170-393) and median C-reactive protein value was 17.1 mg/L (2.9-148). 13 patients (46.4%) experienced advanced remission at W12.

Mean ADC seemed lower (1.912 vs 2.162, p = 0.07) and mean MaRIA seemed higher (47.0 vs 41.9, p = 0.13) in the patients treated with anti-TNFα therapy which experienced advanced remission at W12.

Presence of mesenteric lymph nodes was predictive of no need for surgery at W12 in the patients treated with anti-TNFα therapy (p = 0.01). Sclerolipomatosis seemed also predictive of no requirement for surgery at W12 in the patients treated with anti-TNFα therapy (p = 0.13). Presence of mesenteric lymph nodes was predictive of response to anti-TNFα therapy at W12 (p = 0.05).

CONCLUSION: MRI parameters reflecting inflammatory activity (presence of mesenteric lymph nodes, sclerolipomatosis, low ADC) seemed predictors of advanced remission or response to anti-TNFα agents in CD. Despite the lack of power due to small sample size, the intermediary results of our study show that DW-MREC could be a useful and promising tool to predict effectiveness of anti-TNFα therapy in CD.

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P0323 PREDICTIVE FACTORS OF EARLY INFLIXIMAB INFUSION REACTIONS IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Anti-TNF agents including infliximab (IFX), a chimeric antibody, are the most effective therapies in inflammatory bowel diseases (IBD). Early IFX Infusion Reaction (EIIR) is rare, but is a serious complication in IBD patients, and could lead to drug withdrawal and consequently impact the therapeutic strategy. The role of premedication remains uncertain.

AIMS & METHODS: We aimed to establish predictors of EIIR in IBD patients and to assess the impact of premedication.

Patients, disease and infusions characteristics, collected for all IFX infusions performed in our IBD Unit, were retrieved from electronic charts from 2008 to 2013. The EIIR were defined as events related to IFX infusions occurring within two hours of the infusion. Univariate and multivariate analysis were performed taking into account the inter-patients and intra-patients variability and interaction test.

RESULTS: Among the 80 included IBD patients, 51 (63.8%) had Crohn's disease (CD). The mean age and disease duration were 38.8 years (±14.1) and 7.4 years (±7.0) respectively.

Overall, 23 IBD patients (28.8%) experienced EIIR. Age, prior history of intestinal resection, atopy or allergy, familial history of IBD, type of IBD, disease location, disease extent or disease duration were not predictive of EIIR. In univariate analysis, non-stricturing non fistulising CD was predictive of EIIR (26.4% vs 52.2%, p = 0.03). This result was confirmed by multivariate analysis. Of 1107 infusions, we observed 38 EIIR (3.4%). In univariate analysis, the first four infusions (26.4% vs 52.6%, p = 0.002) and the resumption of IFX after drug holiday (17.2% vs 29.0%, p = 0.001) were predictive of EIIR. Multivariate analysis confirmed that the resumption of IFX after drug holiday was a major risk factor of EIIR (OR = 24, p < 0.001) but not the first four infusions. Surprisingly, a premedication (anti-histaminic or hydrocortisone) seemed to be a risk factor for EIIR in univariate and multivariate analysis while concomitant therapies did not prevent EIIR. As resumption of IFX after drug holiday was a major risk factor for EIIR, interaction test was performed and showed that the increased risk induced by the premedication was related to resumption of IFX after drug holiday.

The patients who experienced EIIR and those who did not experience EIIR have had to discontinue IFX therapy in 69.6% (16/23) and 50.9% (29/57) of cases, respectively (NS).

CONCLUSION: EIIR is a major event in the history of IBD patients treated by IFX as it leads to drug discontinuation and thus limits considerably the available therapeutic armamentarium. **The resumption of IFX after drug holiday is the major risk of EIIR** and could be predicted in part by the measurement of anti-drug antibodies. Non stricturing non penetrating CD could be also a risk factor.

The efficacy of premedication remains questionable and could be limited to the high risk patients.
Disclosure of Interest: C. Duron: None declared, A. Buisson Lecture fee(s) from: Abbvie, MSD, M. Goutte: None declared, B. Pereira: None declared, G. Bommelaer: None declared

P0324 COMPARISON BETWEEN INFLIXIMAB AND ADALIMUMAB FOR THE TREATMENT OF PERIANAL FISTULISING CROHN'S DISEASE

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INTRODUCTION: Infliximab (IFX) and Adalimumab (ADA) have improved the management of perianal Crohn's disease (CD). However, comparative studies have not been reported previously.
AIMS & METHODS: Our aim was to compare the outcomes of CD patients with perianal fistulising disease treated with IFX or ADA.
A retrospective medical record review of CD patients, who received IFX or ADA for perianal fistulising disease, was conducted. Fistulas were assessed using Magnetic Resonance Imaging (MRI), and seton placement was performed when appropriate. A 36-month follow-up was performed.
RESULTS: Twenty CD patients (9 males and 11 females; median age 31.5 years, range 18-39) were treated (9 with IFX and 11 with ADA). Seton placement was performed in 18 patients (8 in IFX and 10 in ADA group).
The baseline Harvey-Bradshaw index (HBI) and perianal disease activity index (PDAI) significantly decreased after 6 weeks and remained at similar levels for the entire follow-up in both groups.
The complete response rate of fistulas was 75% of patients at 36 months (78% in IFX and 73% in ADA group), with no significant difference between the two study groups.
Setons were withdrawn from twelve patients (5 in IFX and 7 in ADA group), who experienced complete response and showed no radiological evidence of disease at 12-month follow-up.
Two patients with complex fistulas failed to obtain fistula closure under anti-TNFα (one in each groups). Changing the anti-TNFα was useless and both patients underwent to permanent colostomy.
CONCLUSION: Efficacy of IFX and ADA was similar in treating perianal fistulising CD patients.
Disclosure of Interest: None declared

P0325 EFFICACY AND SAFETY OF GRANULOCYTE, MONOCYTE/MACROPHAGE ADSORPTIVE APHERESIS IN STEROID-DEPENDENT ACTIVE UC WITH INSUFFICIENT RESPONSE OR INTOLERANCE TO IMMUNOSUPPRESSANTS AND/OR BIOLOGICAL THERAPIES (THE ART TRIAL): SAFETY RESULTS AT 12 WEEKS

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INTRODUCTION: Current medical treatment options for patients with steroid-dependent, active ulcerative colitis (UC) with insufficient response or intolerance to immunosuppressants (IS) and/or biologicals are limited and not evidence-based. In addition, the recognised related safety profiles are considerable. The clinical use of Granulocyte, Monocyte/Macrophage Adsorptive (GMA) apheresis with Adacolumn® has previously demonstrated a safe and efficacious use in this subgroup of UC patients.
AIMS & METHODS: This study was an uncontrolled, open-label, multicenter trial conducted in the UK, France and Germany (ART, NCT01481142). Consecutive eligible patients (18-75 years, steroid-dependent active UC with a Rachmilewitz (CAI) index $\geq$6 and an Endoscopic Activity Index (EAI) $\geq$4, and insufficient response or intolerance to IS and/or biologicals) were included. Patients received at least 5 weekly GMA apheresis. Evaluation visits were planned at Week 12, 24 and 48. The primary endpoint was the remission rate (CAI $\leq$4) at Week 12 in the Intention-to-treat (ITT) population. We report safety results observed along with the earlier communicated 12 weeks interim efficacy results of 55.9% response and 39.3% remission.
RESULTS: The safety population comprised 85 subjects having received at least one apheresis treatment. 14 out of 85 patients (16.5%) discontinued up to Week 12. 61/85 patients (71.8%) experienced any AE; in 54 patients (63.5%) these were of mild or moderate intensity, all transient, mainly consisting of headaches and problems related to venous access difficulties. Six (7.1%) patients experienced serious adverse events (SAEs), all unrelated to the study treatment. SAEs or AEs that led to discontinuation or withdrawal from the study were either related to the indication being studied (ulcerative colitis), or to poor venous access/ vascular access. There were no clinically significant changes in vital signs. There were few shifts from baseline to week 12 among clinically significant values in safety-relevant laboratory parameters.
CONCLUSION: GMA apheresis with Adacolumn® has shown benefit in more than 50% of patients with moderate to severe, active, steroid-dependent UC and insufficient response or intolerance to IS and/or biological agents. No new safety signals were observed, confirming the safety profile of GMA apheresis even in a difficult-to-treat UC patients group.
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P0326 MID-AND LONG-TERM OUTCOMES AND REMISSION MAINTENANCE RATE BY PROLONGED TREATMENT WITH TACROLIMUS FOR REFRACTORY ULCERATIVE COLITIS

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INTRODUCTION: Efficacy of tacrolimus (TAC) as remission induction therapy for refractory ulcerative colitis (UC) has been reported. However, hitherto mid- and long-term outcomes and remission maintenance rates following a prolonged treatment with TAC have not been evaluated.
AIMS & METHODS: In this study, we were interested to evaluate the clinical remission maintenance rate for TAC in patients with UC. For this study, we included 29 patients (15 male and 14 female) who had received a TAC-based induction therapy between April 2009 and December 2013 (mean observation period 728 $\pm$ 311 days). In 10 patients, TAC was administered for 90 days including the period of remission induction, followed by switch to an immunomodulator (azathioprine) to maintain remission (group 1). In 19 patients, TAC was continued beyond the period of remission induction to maintain remission (group 2). The patients in groups 1 and 2 were matched with respect to gender, disease duration, pre-TAC haemoglobin (Hb), C-reactive protein (CRP), clinical activity index (CAI, according to Lichtiger), and endoscopic index (EI) at one month after TAC administration. The total dose of prednisolone administered up to the time when clinical remission was achieved, duration of hospital stay, and the time to recurrence between the two groups were factored into analyses. Remission was defined as a CAI score of 4 or less at week 4 or later after TAC administration. Likewise, recurrence was defined as a case in whom the blood trough level was increased (10 ng/dl or above) by means of intense intravenous regimen of prednisolone, switch to a biological preparation, repeat or dose-escalating TAC administration required to induce remission.
RESULTS: There was no significant difference in gender, disease duration, pre-TAC Hb, CRP, CAI, total dose of prednisolone administered until remission, duration of hospital stay, and the time to recurrence between the two groups. The mean TAC administration period in group 2 was 235 $\pm$ 122 days vs 86 $\pm$ 13 days for group 1. Further, the EI scores at one month after TAC administration were 5.8 $\pm$ 1.6 and 7.8 $\pm$ 2.1 for group 1 and group 2, respectively; the difference was significant ($P < 0.012$). Regarding the treatment safety, finger tremor was observed in 2 patients in group 1 and 5 patients in group 2, renal dysfunction was observed in none of the group 1 patients, but in 3 of group 2 patients.
CONCLUSION: In this study, although no significant difference was found in the time to recurrence, the EI score at one month after TAC treatment was significantly higher in group 2 compared with group 1. This finding suggests that a maintenance dose of TAC is likely to maintain remission even in patients with delayed mucosal healing. However, longer TAC therapy may carry higher risk of adverse side effects.
Disclosure of Interest: None declared

P0327 STRESS AND NONSTEROIDAL-ANTIINFLAMMATORY DRUGS (NSAID)-INDUCED EXACERBATION OF EXPERIMENTAL COLITIS IS ATTENUATED BY ANTIBIOTIC RIFAXIMIN AND PROBIOTIC SACCHAROMYCES BOULARDII

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INTRODUCTION: Clinical and experimental studies have indicated that stress plays an important role in the initiation and perpetuation of inflammatory bowel disease (IBD), however, the mechanism of stress-induced alterations in the severity of the inflammatory process of colonic mucosa remains unclear. Colonic microbiota is important component of IBD pathogenesis but its influence on the colonic mucosal barrier under stress conditions as well as the efficacy of treatment with antibiotics or probiotics on experimental colitis have not been fully explained.
AIMS & METHODS: We studied the effect of cold stress on healing of experimental colitis induced in rats by intrarectal administration of 2,4,6- trinitrobenzenosulfonic acid (TNBS) and we assessed the involvement of colonic microflora in healing of TNBS colitis in rats exposed to stress and stress combined with aspirin (ASA) treatment. The efficacy of antimicrobial therapy by antibiotic rifaximin or probiotic *Saccharomyces boulardii* on stress-induced impairment of the healing of experimental colitis in the absence or presence of ASA treatment was investigated. Animals with TNBS-induced colitis and exposed to cold stress for 20 min every second day were treated i.g. daily with 1) vehicle (saline), 2) *Saccharomyces boulardii* (10^8CFU/rat), 3) rifaximin (100 mg/kg), 4) ASA (20mg/

kg) alone or 5) ASA (20 mg/kg) combined with *Saccharomyces boulardii* (10^8CF/rat) or rifaximin (100 mg/kg). At day 10 upon colitis induction, the colonic blood flow (CBF) was determined by H_2-gas clearance technique, the blood was withdrawn for measurement of plasma MPO, IL-1β and TNF-α levels and the expression of proinflammatory markers IL-1β, TNF-α, iNOS, COX-2 and HIF-α were analyzed in colonic mucosa of stressed rats.

RESULTS: Exposure to stress significantly increased the area of TNBS damage and the concomitant administration of ASA further augmented the area of these lesions. This delay in mucosal healing caused by cold stress was accompanied by a significant fall in the CBF, the significant rise in tissue weight, a 4-fold increase in MPO activity and the mucosal overexpression of IL-1β, TNF-α, iNOS, COX-2 and HIF1α. In stressed animals, the significant increase of *E. coli* counts in feces and the spleen were observed and this effect was significantly attenuated by both rifaximin and *Saccharomyces boulardii*. Treatment with rifaximin and to lesser extent with probiotic *Saccharomyces boulardii* significantly decreased the area of colonic lesions while increasing CBF and significantly reducing the plasma IL-1β and TNF-α levels and the colonic expression of proinflammatory markers.

CONCLUSION: 1/ Stress exacerbates experimental colitis due to increase of intestinal pathogenic *E. coli* and this pathogenic bacteria translocation to the extra-intestinal organs such as spleen, and 2/ Modifying of the intestinal microbiota through probiotics or selected antibiotics could be of clinical importance in the limitation of the consequences of environmental factors such as stress and adverse effects of NSAID therapy in patients with lower GI-tract disorders.

Disclosure of Interest: None declared

P0328 TNF-ALPHA AS INDUCTION AND MAINTENANCE THERAPY FOR CROHN'S DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY IN GERMANY

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INTRODUCTION: The nationwide BioCrohn Registry (*Bio*logical Registry with *Crohn*s Disease Patients in Germany) of the German Competence-Network IBD is a five-year prospective registry of about 1,500 patients with Crohn's disease (CD) in Germany. This is a sub-study of the BioCrohn Registry reporting the anti TNF-alpha antibody (TNF) steroid-free remission rates of induction and maintenance therapy in 391 anti-TNF-naïve CD-patients with adalimumab (ADA) or infliximab (IFX) up to 12-months follow-up.

AIMS & METHODS: Within the framework of this non-interventional prospective online documentation, data in respect to the course of disease, psychosocial burden of disease, health economics and the genetic profile were examined. End of 2012 the recruitment was stopped having 1,525 CD-patients included by 59 different gastroenterology practices and hospitals with IBD experience. All patients have a 5 year follow-up period. The databank for baseline and 12-months data has been closed in 03/2013 and after databank cleansing now we have the finalized data including the 6- and 12-months visits.

RESULTS: 391 TNF-naive CD-patients (ADA: n = 264; IFX: n = 127) have been analysed (average age: 36 years; female: 52%; smokers 34%; disease duration: 9.3 years; bowel resection: 33%; prior immunosuppressive therapy: 75%). Baseline characteristics were similar in the two groups. The IBD-therapy followed an accelerated step-up management. Immunosuppressants were used in 19% at 6 and in 21% after 12 months. Accordingly to the TNF therapy, the use of systemic glucocorticoids dropped over time (baseline until 6 and 12 months) from 22.0% to 6.3% and 8.3%, respectively ($p < 0.001$). The remission rate (PGA) at 6 months was 70.9% and 72.1% after 12 months. In spite of the TNF-induced clinical remission (> 70%) the psychosocial impairments with anxiety/depression (EQ-5D) showed only minor improvement and remained on a relatively high level (baseline: 37%, 6 months: 31%, 12 months: 28%). In the induction therapy with TNF we found a steroid-free remission (HBI < 5) in 67.1% at 6 months and in 68.9% at 12 months in the maintenance therapy. Evaluating the efficacy of ADA vs. IFX we did not find any difference in steroid-free remission rates as an induction therapy at month 6 (ADA: 68.2%; IFX: 64.6%; p = n.s.) or as a maintenance therapy at month 12 (ADA: 68.1%; IFX: 70.6%; p = n.s.). In the per protocol TNF-group with regular visits at 6 and 12 months (n = 264) 91.7% of these patients were still on TNF after 12 months. Additionally 5.7% of the ADA-patients switched to IFX and 9.2% of the IFX-patients switched to ADA. This means that 76.8% of the patients starting with TNF were on the same TNF therapy after 12 months.

CONCLUSION: In this real life setting anti-TNF therapy could induce steroid-free remission in about 70% with the relatively early escalation of therapy in IBD-experienced centres. In comparison there is no difference in steroid-free remission rates between ADA vs. IFX.

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P0329 PREDICTORS OF HOSPITALIZATION IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS FROM ULTRA 1 AND ULTRA 2

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INTRODUCTION: Patients with moderately to severely active ulcerative colitis (UC) are frequently hospitalized due to disease deterioration. The factors associated with hospitalization risk in patients treated with non-biologic therapy for UC are analyzed in patients randomized to placebo (PBO) in ULTRA 1[1] and ULTRA 2[2].

AIMS & METHODS: ULTRA 1 had an 8 to 12 week double-blind (DB) phase followed by an open-label (OL) all adalimumab (ADA) phase to week 52. ULTRA 2 was a 52-week DB trial in which patients with inadequate response could receive OL ADA 40 mg beginning at week 12. Patients with loss of response or intolerance to prior anti-TNF use could enrol in ULTRA 2. Logistic regression was used to determine predictors of all-cause and UC-related hospitalization in PBO randomized patients from ULTRA 1 and ULTRA 2. Baseline variables assessed were age, sex, disease duration, pancolitis, prior anti-TNF use, CRP, albumin, Mayo score, aminosalicylate use, immunomodulator use, corticosteroid use, alcohol use, smoking status, and weight. Model 1 also included baseline endoscopy subscore (2 vs 3) and Model 2 also included stool frequency (SFS, 0-1 vs 2-3), rectal bleeding (RBS, 0-1 vs 2-3), and PGA (0-2 vs 3) subscores. Patients were censored 70 days after moving to OL ADA.

RESULTS: Selected odds ratios for the association of baseline variables with hospitalization for PBO randomized patients from ULTRA 1 and 2 are shown in the table. In both regression models, male sex was a significant predictor for lower risk of all-cause and UC-related hospitalization, whereas lower baseline albumin and higher baseline CRP concentration were significant predictors for higher risk of all-cause and UC-related hospitalization. Alcohol use was associated with UC-related hospitalization in both models. Disease activity at baseline, as measured by Mayo score or individual subscores, disease duration, prior anti-TNF use, pancolitis, or use of aminosalicylates, immunomodulators, or corticosteroids were not associated with hospitalization risk in either model.

Table. Logistic regression odds ratios for hospitalization in PBO-randomized patients from ULTRA 1 and 2

	Model 1		Model 2	
	All-cause	UC-related	All-cause	UC-related
Sex (male)	0.37**	0.41*	0.35**	0.38*
Baseline CRP (mg/L)	1.01*	1.02**	1.01*	1.02**
Albumin (<40 g/L)	2.39*	2.82**	2.50*	3.00**
Current alcohol use	1.82	2.11*	1.82	2.12*

CONCLUSION: In this analysis, factors associated with hospitalization in patients receiving non-biologic therapy for UC were sex, increased inflammation (as measured by CRP) and low baseline albumin. These factors may be useful when evaluating future therapeutic interventions in patients with UC failing conventional therapy.

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P0330 DEEP REMISSION IMPROVES CLINICAL OUTCOMES AFTER INFLIXIMAB DISCONTINUATION IN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Recent studies underlined the importance to treat inflammatory bowel diseases (IBD) looking beyond symptoms and considering also tangible indicators of disease remission, such as mucosal healing and normalization of biomarkers. A clear definition of deep remission has not been validated yet. However, the achievement of clinical remission associated to mucosal healing has been demonstrated to improve clinical outcomes during biological treatments. Some studies also showed that high C-reactive protein (CRP) levels at the time of infliximab (IFX) discontinuation may represent a risk factor for clinical relapse. No data are available so far about clinical outcomes of IBD patients who discontinue IFX being in deep remission defined as the combination of clinical remission, mucosal healing and normal CRP.
AIMS & METHODS: This single-centre study included IBD patients who discontinued maintenance treatment with IFX because of sustained steroid-free clinical remission (HBI$\leq$4 for Crohn's disease -CD- and partial Mayo score$\leq$2 for ulcerative colitis –UC-, with no intake of systemic steroids during the last 12 months before discontinuation). Deep remission was defined as sustained steroid-free clinical remission associated to normal CRP ($\leq$5 mg/l) and mucosal healing (defined as absence of ulcers in CD, or endoscopic Mayo score of 0-1 in UC). Primary endpoint was the comparison of clinical relapse between two groups of patients who were in deep remission (group 1) or not (group 2) at the time of IFX discontinuation. Secondary endpoints were endoscopic recurrence, hospitalizations, surgeries and retreatment with anti-TNFα between the two groups.
RESULTS: Sixty-one patients (40 CD, 21 UC) were included in the study (group 1 n = 34, group 2 n = 27). Median follow-up after IFX discontinuation was 36 months (IQR 23-60). No significant differences were found among baseline characteristics. The rate of clinical relapse resulted significantly different between groups: 14/34 (41%) in group 1 relapsed in comparison with 21/27 (78%) in group 2 ($p = 0.009$). Mucosal healing was the only other variable associated to a lower incidence of clinical relapse ($p = 0.03$). Median values of CRP at the time of IFX discontinuation were not associated to a different clinical outcome. Time to clinical relapse was significantly shorter in group 2: patients not in deep remission at the time of IFX discontinuation relapsed after a median of 12 months (IQR 8,25-19.5) in comparison with 36 months (IQR 23-57) of group 1 ($p < 0.001$). No differences were found considering rates of endoscopic recurrence, hospitalization, surgery and need for anti-TNFα retreatment. However, patients in group 2 required hospitalization and retreatment with anti-TNFα significantly earlier in comparison with group 1 ($p = 0.02$ and $p = 0.03$, respectively).
CONCLUSION: IBD patients who discontinue IFX because of sustained steroid-free clinical remission may relapse over time. However, the presence of deep remission (clinical remission associated to mucosal healing and normal CRP) at the time of IFX discontinuation seems to guarantee better clinical outcomes.
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P0331 PHARMACOLOGY OF ETROLIZUMAB IN A PHASE 2 STUDY IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

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INTRODUCTION: Etrolizumab, a humanized antibody to the integrin $\beta7$, blocks $\alpha4\beta7$:MAdCAM-1 and $\alpha E\beta7$:E-cadherin interactions, and has been shown in a Phase 2 study to be effective at inducing clinical remission in patients with moderate-to-severely active ulcerative colitis (UC).[1] Maximal occupancy of $\beta7$ receptors was observed on lymphocyte subsets in peripheral blood and colonic tissue in both dose cohorts (monthly subcutaneous doses of 100mg [low] or 300mg+loading dose [high]), with a corresponding increase in B and T intestinal homing lymphocytes in peripheral blood.[2] Here we present the pharmacodynamic (PD) effects of etrolizumab in colonic tissue and the serum pharmacokinetics (PK) from the Phase 2 study.
AIMS & METHODS: Changes from baseline were assessed in colonic tissue gene expression at weeks 6 and 10 (qPCR, n = 96) and in αE cells at week 10 (immunohistochemistry [IHC], n = 55 & 73 in epithelium and lamina propria, respectively). Serum drug levels were measured at multiple time points following etrolizumab administration.
RESULTS: Etrolizumab displayed linear kinetics, with ~4.4 fold exposure separation between the two dose cohorts. The average serum concentration of etrolizumab at week 10 was 8.5μg/mL and 37.8μg/mL for the low and high dose cohorts, respectively. There were no differences in $\beta7$ gene expression in colonic tissue between the etrolizumab and placebo treated groups. αE^+ cells were decreased in the intestinal crypt epithelium, but not in the lamina propria, in etrolizumab-treated patients compared with placebo. Reduction in multiple markers associated with proinflammatory infiltration and active disease was observed in etrolizumab-treated patients who achieved clinical remission compared to those who did not, including decreases in expression of proinflammatory cytokines, lymphocyte subset markers (CD3, CD19), MAdCAM-1, and epithelial cell-associated αE^+ cells. Although maximal occupancy of $\beta7$ receptors was observed in both low and high dose groups, there were no apparent differences in PD effects between the two etrolizumab-treated cohorts. Furthermore, within the etrolizumab-treated cohorts, there were no observed drug exposure/clinical remission relationships.
CONCLUSION: In this Phase 2 study, we confirmed etrolizumab target engagement and subsequent biological effects, both in peripheral blood and at the site of disease pathobiology. PD effects were consistent with decreased inflammation in the colonic mucosa, particularly in patients who attained clinical remission. These findings contribute to the understanding of the mechanism of action of etrolizumab: blockade of leukocyte homing to, and decreased inflammation in, the colon.
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P0332 CLINICAL OUTCOME OF PERIANAL CROHN'S DIESEASE AND IMPACT OF TREATMENT STRATEGIES OVER THE TIME

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INTRODUCTION: Perianal Crohn's disease (pCD) is associated with complications leading to recurrent surgery and tissue damage. Immunosuppressive drugs (IS) including anti-TNF have changed the management of pCD.
AIMS & METHODS: Our aim was to describe the management and the natural history of a cohort of patients with active pCD and to identify predictive factors of poor evolution.
Methods: A retrospective study of pCD patients registred in the database of the university hospital of Liège, Belgium. Perianal lesions included abscess, fistulae, anal fissure, anal strictures. pCD treatments included antibiotics, surgical drainage (with or without seton), stoma. Medical treatments including IS and anti-TNF were recorded at pCD diagnosis and over follow-up. pCD relapse was defined as antibiotherapy for recurrent abscess, the need for surgical drainage or stoma. The subroups of patients followed before (old cohort) and after (young cohort) the year 2000 were compared in a subanalysis.
RESULTS: 181 patients with pCD were included. Mean follow-up was 7.9 years Mean time between CD and pCD diagnosis was 6.3 years. Lesions at pCD diagnosis were abscess in 93/181 (51%), fistula in 91/181 (50%; 77/93 of complex fistulae), anal fissure in 28/181 (15%), anal stricture in 18/181 (10%). At diagnosis abscess drainage was performed in 31/181 (17%), drainage + seton in 44/181 (24%), stoma in 18/181 (10%). 132/181 (74%) and 83/181 (47%) had IS and anti-TNF respectively at pCD diagnosis. Relapse rate was 51% within a mean time of 33 months. During follow-up 15% required a stoma. Predictive factors of relapse were perianal abscess ($p<0.0001$, $HR=4.4$), fistula ($p<0.0001$, $HR=4.5$) or surgical drainage at diagnosis ($p<0.0001$, $HR=4.5$), young age at pCD diagnosis (28 versus 31 yo, $p=0.02$), short time between CD and pCD diagnosis (5.7 versus 7 years, $p=0.01$), IS ($p=0.04$, $HR=1.8$) and anti-TNF ($p=0.01$, $HR=1.5$) at pCD diagnosis. Anti-TNF during follow-up, time to introduce them and duration of anti-TNF treatment were not predictive of relapse. The young and old cohort had the same characteristics at pCD diagnosis except a higher use of IS (87% vs 48%, $p<0.0001$) and anti-TNF (3% vs 68%, $p<0.0001$) in the young cohort. Clinical outcome including the time to relapse, type of relapse, need for surgery and stoma was similar in both cohorts.
CONCLUSION: In our cohort of pCD patients half of them had a perianal relapse over the time requiring surgery in more than 2/3 of them. At pCD diagnosis perianal abscess, fistula, surgical drainage, young age, treatment with IS or anti-TNF were associated with a higher risk of relapse. Although higher prescription of anti-TNF and IS in the last years new treatment strategies have not impacted the outcome of pCD.
Disclosure of Interest: None declared

P0333 BIOMARKER ANALYSES FROM A PHASE 2 STUDY EVALUATING THE ANTI-INTERLEUKIN-13 ANTIBODY TRALOKINUMAB IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Interleukin-13 (IL-13) is a central cytokine effector in the T-helper 2 immune response that has been proposed to be a key driver of ulcerative colitis (UC) pathogenesis. Tralokinumab (CAT-354) is a human immunoglobulin G4 antibody that inhibits binding of IL-13 both to IL-13 receptor (IL-13R) alpha 1 and IL-13R alpha 2.
AIMS & METHODS: The aim of these analyses was to gain insight into the mechanistic action of tralokinumab in a phase 2 study in patients with UC. Overall, 111 patients with moderate-to-severe UC were randomised in a 1:1 ratio to receive tralokinumab 300 mg or placebo subcutaneously every 2 weeks during a 12-week treatment phase. Serum samples were obtained at baseline and at 2-week intervals throughout the treatment phase. Biopsies were taken during colonoscopy at baseline and after 8 weeks of treatment from mucosal areas judged by the endoscopist to represent inflamed and normal colonic mucosa. IL-13 levels were assessed in serum and biopsy homogenates at baseline and following treatment. Changes from baseline to week 8 in colonic mRNA expression were assessed by *in situ* hybridisation for the tight junction protein claudin-2 and by quantitative PCR for selected IL-13-regulated genes. Data were analysed by treatment and treatment response, with clinical response defined as a decrease in total Mayo score of ≥ 3 points and $\geq 30\%$, and a decrease in rectal bleeding subscore of ≥ 1 point or an absolute subscore of 0 or 1.
RESULTS: A time-dependent increase in total IL-13 serum levels was observed with tralokinumab but not with placebo. Free IL-13 was detectable in homogenates of inflamed colonic mucosa; however, there was no consistent trend regarding changes from baseline after 8 weeks' treatment with tralokinumab. At baseline, *in situ* claudin-2 mRNA expression was higher in inflamed versus normal colonic mucosa. Claudin-2 mRNA expression decreased from baseline in clinical responders. There were numerical increases from baseline in colonic mucosal mRNA levels for IL-6, IL-8 and S100 calcium binding protein A8 (a subunit of calprotectin) in clinical responders in the tralokinumab group compared with clinical responders in the placebo group. A numerical decrease from baseline in mRNA for tumour necrosis factor receptor superfamily member 12A was seen in the tralokinumab group compared with placebo. However, gene expression changes were small and would not remain significant after correcting for multiple statistical comparisons.
CONCLUSION: Claudin-2 may be a useful prognostic biomarker for UC. Total IL-13 in serum increased with tralokinumab treatment, supporting systemic target engagement. In colonic mucosa, small expression changes in IL-13-regulated genes were associated with tralokinumab treatment, though measurement of free IL-13 could not confirm target engagement by tralokinumab in colonic mucosa.
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P0334 THREE-YEAR STEROID FREE REMISSION AND SAFETY OF AZATHIOPRINE TREATMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Purine analogue azathioprine (AZA) is widely used for induction and maintenance of remission in steroid dependent patients with inflammatory bowel disease (IBD).
AIMS & METHODS: We investigated its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients three years after the institution of treatment. Data from consecutive IBD outpatients referred in our Institution, between 1985-2012, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2–2.5 mg/kg. Blood chemistry was analysed before administration of the drug, every 10-15 days for the first 3 months and then every 1-2 months following the institution of treatment.
RESULTS: Out of 2472 consecutive IBD outpatients visited in the index period, AZA was prescribed to 360 patients, 189 (52.5%) were affected by Crohn's disease (CD) and 171 (47.5%) by ulcerative colitis (UC). Seventy-eight patients with a follow-up <36 months were excluded from the study. Two hundred and eighty-two patients were evaluated, 152 (53.9%) with CD and 130 (46.1%) with UC. One hundred and fifty-four (54.6%) were male and 128 (45.4%) female (average age of 33.75 ± 13.82 SD years, range 14-76 y.). Three years after the institution of treatment, 170 (60.3%) patients still were in steroid-free remission (101 CD vs 69 UC, 66.4% and 53.1%, respectively, $p=0.0279$), 62 (22%) had a relapse requiring retreatment with steroids (38 UC vs 24 CD, 29.2% and 15.8%, respectively, $p=0.0091$), 50 (17.7%) discontinued the treatment due to side effects (27 CD vs 23 UC, 17.8% and 17.7%, respectively). Loss of response from 1st to 3rd year of follow-up was low, about 12%.
CONCLUSION: Three years after the onset of treatment 60% of patients did not require further steroid courses. After the first year loss of response was low in two subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.
Disclosure of Interest: None declared

P0335 EFFICACY OF AN MMP9-SPECIFIC MONOCLONAL ANTIBODY IN A DSS-INDUCED COLITIS MODEL OF ULCERATIVE COLITIS

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INTRODUCTION: Ulcerative colitis (UC) remains a high unmet medical need with no current curative therapies; the majority of patients with UC require life-long treatment to prevent disease progression. UC is characterized by disease-specific upregulation of matrix metalloproteinase 9 (MMP9). MMP9 can exert pathogenic effects both by degrading extracellular matrix (ECM) proteins and participating in tissue destruction and by activating or releasing growth factors and cytokines from the ECM or cell surface. Previous attempts to target MMPs with broad-spectrum or semi-selective inhibitors in oncology and inflammatory diseases have been unsuccessful, partly due to their lack of specificity.
AIMS & METHODS: Here we used immunohistochemistry to confirm MMP9 induction at colitic foci in both human and DSS-exposed mice and evaluated efficacy of a therapeutically-dosed MMP9-specific monoclonal antibody (AB0046) in a DSS-induced colitis model of UC.
RESULTS: MMP9 immunoreactivity was limited in the healthy colon, but was strongly induced and had a similar pattern of expression at active disease sites in human UC and mouse DSS-colitis tissue. In disease, MMP9 was expressed in abscessed and necrotic crypts and regions of cryptitis containing neutrophilic infiltrates as well as by macrophages within the lamina propria. Extracellular MMP9 staining colocalized with regions of destruction in the epithelial crypt basement membrane. Inhibiting MMP9 in established DSS-induced colitis with AB0046 resulted in a significant protection (50%) against body weight loss and endoscopically assessed disease, and a 45% reduction in the incidence of diarrhea. Colons from AB0046-treated animals exhibited less crypt destruction, less inflammatory cell infiltration, and a reduction in MMP9 expression. In concordance with the IHC analysis, AB0046 treatment resulted in a decrease in histopathologic disease scores. Interestingly, AB0046 treatment resulted in reduction of serum markers of inflammation including IL-6, CXCL2, KC/GRO, MPO, LIF, MCP-1/2/5, MIP-3β, and TIMP-1.
CONCLUSION: MMP9 is highly expressed in human UC and in mouse DSS-exposed colons. The ability of MMP9 to degrade basement membrane and to activate or release pro-inflammatory factors from the ECM make this protein a compelling therapeutic target in colitis. Treatment of established DSS-induced colitis with an MMP9-specific monoclonal antibody resulted in improvement in clinical measures of disease, histopathology, as well as in systemic markers of inflammation. These data suggest that an MMP9 specific monoclonal antibody is a promising therapeutic strategy for treatment of UC. Gilead Sciences has developed a humanized MMP9-specific monoclonal antibody that is currently in a Phase 1b clinical trial in UC.
Disclosure of Interest: D. Marshall Other: Is an employee of Gilead Sciences, Inc., R. Spangler Other: Is an employee of Gilead Sciences, Inc., C. O'Sullivan Other: Is an employee of Gilead Sciences, Inc., J. Adamkewicz Other: Is an employee of Gilead Sciences, Inc., V. Smith Other: Is an employee of Gilead Sciences, Inc.

P0336 INFLIXIMAB ONE HOUR INFUSIONS – A GOOD CHOICE FOR IBD PATIENTS?

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INTRODUCTION: The use of anti-TNF agents as maintenance therapy in IBD patients is well documented. However, administration of Infliximab (IFX) implies long hours at the hospital, with significant costs and inconvenience. A shorter infusion protocol would minimize such drawbacks, maintaining the same safety and efficacy.
AIMS & METHODS: To evaluate the safety and efficacy profile of one hour IFX infusion.
Between November 2012 and December 2013, the occurrence of acute adverse reactions to IFX was prospectively documented. Patients under maintenance therapy, with at least 4 infusions with no history of reactions, received one hour infusions. This was followed by 1-hour surveillance in the next 5 infusions, and 30 minutes from then on.
RESULTS: From a total of 95 patients under IFX therapy (Average age: 38.8 ± 14.2 years old; Female - 58%; Crohn's Disease – 66, Ulcerative Colitis – 25, Unclassified IBD – 4), about 68% (65/95) started receiving one hour infusions (average of 6 per patient, total of 390 infusions), while 31.6% (30/95) were kept under the usual two hour protocol, with two hour infusions followed by one or two hours of surveillance.
In the one hour infusion group, 38.4% were under combined therapy with immunosuppressive agents and 23% received hydrocortisone and/or clemastine as prophylactic medication. There was no adverse reaction noted in this group. In 92.3% of the patients, the therapeutic regimen remained the same, but in the remaining 7.7%, an increase in dosage or interval shortening was needed. One patient had to change to Adalimumab (ADA) due to poor response to IFX.
In the 2-hour infusion group, 56.7% were under combined therapy with immunosuppressants and 43.3% received prophylactic medication. A total of 5 reactions were described (2.46%), 2 of which were severe (0.98%), leading to IFX definitive suspension. Initial regimen was maintained in 93.3% (28/30) of these patients, while 6.7% (2/30) had to increase IFX dosage or shorter intervals between infusions.
CONCLUSION: During maintenance therapy, 1 hour infusions are safe and effective, minimizing costs associated with IFX therapy, and allowing shorter hospital stays and better quality of life to IBD patients.
Disclosure of Interest: None declared

P0337 BODY MASS INDEX VARIATION IN INFLIXIMAB-TREATED IBD PATIENTS

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INTRODUCTION: A significant number of patients with IBD present with nutritional deficiencies and malnutrition is relatively common. There are several ways of describing response to Infliximab (IFX). However, nutritional status is rarely used as a tool to evaluate the efficacy of this anti-TNF agent.
AIMS & METHODS: To establish a relation between BMI changes and clinical response in patients treated with IFX.
Patients with IBD treated with IFX for at least a year were included. Their BMI was measured before starting IFX, after remission induction therapy, and then after 1 and 3 years of maintenance therapy. Response to IFX was evaluated through clinical and laboratorial data.
RESULTS: A total of 62 patients were included (average age 37.3 ± 13.8 years old; 71% females; Crohn's Disease – 45, Ulcerative Colitis – 19). Their initial average BMI was 21.4±3.07 (10 patients with BMI < 18.5 – 16.1%; 8 patients with BMI > 25 – 12.9%). After induction, no significant change was noted in BMI, but one year later, a meaningful increase was noted (21.4 to 22.7; $p = 0.049$). After three years of therapy, this tendency was more evident (21.4 to 22.8; $p = 0.026$), as only 2 patients still had BMI < 18,5, whilst 16 had weight excess (26%).
There was a significant increase in BMI in patients who responded to therapy, in contrast to those who maintained clinical activity. The average BMI actually decreased in the latter group (+1,81 *vs.* -0,96; $p = 0.012$). This increase was noted particularly in patients who had initial BMI < 18.5 ($p = 0.032$), as well as in male patients and with small bowel involvement. Factors such as age, disease duration, smoking or other medication did not show significant association with BMI.
CONCLUSION: Nutritional deficits are common clinical issues in IBD patients. Therapy with Infliximab is clearly associated with improved nutritional status in patients who are responders, unlike those who mantained disease activity. This association is more clearly noted in the group with lower initial BMI.
Disclosure of Interest: None declared

P0338 MONITORING VITAL SIGNS DURING INFLIXIMAB INFUSION – IS IT REALLY USEFUL?

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INTRODUCTION: Monitoring vital signs is part of the surveillance protocol during Infliximab infusions in most IBD reference centers. Despite being innocuous, it is a time consuming task, representing another burden to already strained healthcare professionals. In this era of increasing medical care costs, and with the growing number of IBD patients treated with biological agents, it becomes essential to analyze if this practice is able to predict or identify adverse reactions to Infliximab.
AIMS & METHODS: To evalute the usefulness of monitoring vital signs during Infliximab infusions.
From January 2013 to December 2013, each patient's pulse (HR), systolic blood pressure (SBP), temperature (Temp) and pulse oximetry (SpO2) were registered during Infliximab infusions. Acute adverse reactions were also recorded.
RESULTS: A total of 593 Infliximab infusions were administered to 95 patients (average of 6.2 ± 1.3 infusions per patient; median age: 38.8 ± 14.2 years old; 59% females; Crohn's Disease – 66, Ulcerative Colitis – 29). The overall incidence of acute infusion reaction was 2.2% (13 of 593 infusions), affecting 6 patients (6.3%). Two of them were serious, with bronchospasm and angioedema. Comparing baseline vital signs between groups with and without acute reactions, no relevant differences were noted (HR: 78 *vs.* 81/min, $p = 0.23$; SBP: 106 *vs.* 109 mmHg, $p = 0.12$; Temp: 35.9 *vs.* 36.1°C, $p = 0.68$; SpO2: 98% *vs.* 99%, $p = 0.42$). Vital signs measured immediately before and during acute reactions were also compared. No significant change was noted in most cases, except during the two serious reactions, in which there was an increase in heart rate (67 to 110 beats/min and 86 to 112/min) and a fall in one of the patients' SpO2 (97 to 85%), maintaining stable blood pressure and temperature.
CONCLUSION: Scheduled monitoring of vital signs during Infliximab infusions was unable to predict acute reactions or to identify patients with increased risk of such reactions, though it can help to assess its severity. Such conclusions do not suggest a more distant surveillance, but emphasize that clinical symptoms should be the main focus.
Disclosure of Interest: None declared

P0339 HISTOLOGICAL AND ENDOSCOPIC REMISSION INDUCED BY INFLIXIMAB IN MODERATE TO SEVERELY ACTIVE ULCERATIVE COLITIS PATIENTS – HERICA STUDY

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INTRODUCTION: Correlation between histological activity, endoscopic findings, levels of calprotectin and lactoferrin in ulcerative colitis (UC) are not well established. Infliximab can induce remission. Residual microscopic active inflammation may predict relapse. Non-invasive methods such as calprotectin may be appropriate for this purpose.
AIMS & METHODS: The primary aim was to evaluate the histological remission induced by infliximab at week 8 (Geboes <3.0); secondary aims were to evaluate the association between histological remission, mucosal healing, faecal calprotectin and faecal lactoferrin. 20 patients with moderate to severe UC (Mayo score 6-12) with inadequate response to corticosteroids or corticosteroid dependence, all of them anti-TNF naïve, started infliximab in a prospective, open-label, multi-centre study, with 1 year of follow-up, 4 visits assessments (baseline, week 8, week 30, and week 52). Topical treatment was not allowed. In each visit, Mayo score, faecal calprotectin and lactoferrin were evaluated, and sigmoidoscopy with biopsies was performed. The worst sample was used for histological score (Geboes index – GI) and the patients were considered in deep remission when in clinical remission (Mayo score <2) and GI ≤ 3 and calprotectin levels <100mg/L and lactoferrin ≤ 7.25mg/L and mucosal healing at endoscopy (0 or 1).
RESULTS: Out of the 20 patients, 13 had left-sided colitis (E2) and 7 had pancolitis (E3). At weeks 8, 30 and 52, 15%, 30% and 35% of the patients, respectively, were on histological remission. At the same intervals, 10%, 20% and 10% of the patients, respectively, were in deep remission. Sixty-six percent of those on histological remission at week 8 had persistent remission at week 30 and 52, and 100% of those on histological remission at 30 week persisted thereafter. Calprotectin >100mg/L at week 8 predicted histological activity (sensitivity: 76%; specificity: 100%), with a positive predictive value (PPV) of 100% and a negative predictive value (NPV) of 42%. Lactoferrin levels higher than 7.25 mg/L at week 8 predicted histological activity (sensitivity: 94%; specificity: 66%), with a PPV of 94% and a NPV of 66%. The probability of being in histological remission once achieving mucosal healing (PPV) was 55% (weeks 30 and 52) and the probability of endoscopic mucosal healing with calprotectin ≤ 100mg/L was 100% and 75%, respectively, at weeks 30 and 52.
CONCLUSION: Infliximab is able to induce and maintain histological remission in ulcerative colitis patients. High levels of calprotectin and lactoferrin predict persistent histological activity.
Disclosure of Interest: None declared

P0340 ANTI-TNF HAS A FAVORABLE EFFECT ON INSULIN SENSITIVITY IN NON-DIABETIC, NON-OBESE PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Insulin resistance is very common in autoimmune systemic diseases and recently it was also found in children and adults with inflammatory bowel disease (IBD). Inflammation and insulin resistance are closely linked, and inflammatory cytokines such as tumor necrosis factor alpha (TNFa) may inhibit insulin signaling and promote insulin resistance. The aim of this study was to investigate the effect of anti-TNF therapy on glucose and lipid metabolism in non-diabetic, non-obese patients with IBD.
AIMS & METHODS: We studied 41 patients with IBD (25M/16F, 36.4 ± 11 (19-64) years old, 28 with Crohn's disease and 13 with ulcerative colitis), without known history of diabetes. Eighteen patients (9M/9F, 33.6 ± 8.8 years) were on anti-TNF therapy for more than 1 year, while the other 23 patients (16M/7F, 38.7 ± 12.5 years) were treated with azathioprine and mesalazine (Aza/Mes). Nine of the patients from the second group were then treated with anti-TNF and studied again 6 months after. Fasting glucose, insulin, c-peptide, HbA1c, lipids, and CRP levels were determined and HOMA-IR index was calculated, in all patients. Statistical analysis of the data was performed using SPSS 16.00.
RESULTS: Three of the patients were diagnosed with overt diabetes and were excluded from the analysis. Patients from the two therapy groups were matched for age (anti-TNF: 33.6 ± 8.8 years vs Aza/Mes: 38.7 ± 12.5 years, $p>0.05$) and BMI (anti-TNF: 23.3 ± 3.4 vs Aza/Mes: 23.1 ± 1.7, $p>0.05$), and were not obese. We did not find any statistical differences between the patients from the two therapy groups in the levels of fasting glucose (anti-TNF: 88 ± 10.7 vs Aza/Mes: 93.4 ± 14.9 mg/dl, $p>0.05$), insulin (anti-TNF: 10.9 ± 7.9 vs Aza/Mes: 12.1 ± 6.6 mIU/ml, $p>0.05$), c-peptide (anti-TNF: 1.9 ± 0.9 vs Aza/Mes: 2.2 ± 1.4 ng/ml, $p>0.05$), HbA1c (anti-TNF: 5.2 ± 0.3 vs Aza/Mes: $5.3 \pm 0.4\%$, $p>0.05$), total cholesterol (anti-TNF: 168.6 ± 32.7 vs Aza/Mes: 162.8 ± 34.3 mg/dl, $p>0.05$), HDL (anti-TNF: 57.5 ± 15.7 vs Aza/Mes: 53.8 ± 20.3 mg/dl, $p>0.05$), LDL (anti-TNF: 95.8 ± 28.7 vs Aza/Mes: 90.7 ± 24.4 mg/dl, $p>0.05$), triglycerides (anti-TNF: 75.8 ± 37.6 vs Aza/Mes: 90.8 ± 61.3 mg/dl, $p>0.05$), CRP (anti-TNF: 3 ± 5.4 vs Aza/Mes: 4.9 ± 6.1, $p>0.05$) and in the HOMA-IR index (anti-TNF: 2.77 ± 2 vs Aza/Mes: 3.1 ± 1.9, $p>0.05$). In patients who were treated for 6 months with anti-TNF, a statistically significant decrease in insulin (before: 15.4 ± 5.8 vs after: 10.2 ± 2.7 mIU/ml, $p=0.049$) and c-peptide (before: 2.4 ± 1.2 vs after: 1.4 ± 0.4 ng/ml, $p=0.038$) levels as well as the HOMA-IR index (before: 4.1 ± 2.1 vs after: 2.3 ± 0.7, $p=0.047$) was observed, without any statistically significant changes in weight, BMI, glucose, HbA1c, lipids and CRP levels (in all comparisons $p>0.05$).
CONCLUSION: These preliminary data indicate that anti-TNF therapy may have a favorable effect on insulin sensitivity in non-diabetic, non-obese patients with inflammatory bowel disease.
Disclosure of Interest: None declared

P0341 HUMAN SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF THE GPR84 ANTAGONIST GLPG1205, A POTENTIAL NEW APPROACH TO TREAT IBD

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INTRODUCTION: Free fatty acids (FFAs) are nutritional components and metabolic intermediates that play important roles in a wide range of cellular functions (energy source, membrane structure, signalling). Recently, FFAs have been reported to activate a family of G protein-coupled receptors, which are involved in the pathophysiology of a variety of diseases, including metabolic and inflammatory disorders. GPR84 is activated by medium chain FFA (carbon length C9-C14). The receptor is primarily expressed on white blood cells (PMN, monocyte/macrophage) consistent with a reported role for GPR84 in inflammation.
We identified GLPG1205 as a potent and selective antagonist of GPR84, inhibiting GPR84 activation in HEK cells, as well as GPR84-induced neutrophil migration. In a mouse IBD model (DSS), GLPG1205 dose-dependently decreased the disease activity index, to a similar level as sulphasalazine and cyclosporine. The histological score for colon lesions, neutrophil influx as well as colonic MPO content was substantially reduced.
AIMS & METHODS: To evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of GLPG1205 in healthy volunteers, and identify a dose for subsequent Proof of Concept studies in inflammatory bowel disease.
GLPG1205 was administered as a liquid suspension, providing maximal dose flexibility, as single doses (10 up to 800 mg) or multiple doses (50, 100 and 200 mg once daily (QD) for 14 days). Each dose level was evaluated in panels of 8 male healthy volunteers, with 6 receiving GLPG1205 and 2 placebo. In order to evaluate target engagement, PD was assessed by a competitive radiolabeled binding assay in whole blood, using a tritiated GPR84 antagonist chemically closely related to GLPG1205.
RESULTS: In healthy volunteers, GLPG1205 was generally safe and well tolerated up to 100 mg QD for 14 days, with no adverse effects on ECG, vital signs or laboratory parameters. The most relevant adverse event was headache. The PK of the compound showed a good oral bioavailability with a long half-life ($>$ one day) and a dose-proportional increase in exposure. Steady state was reached after 8 to 10 days. GLPG1205 showed concentration-dependent target engagement in whole blood (*ex vivo*), showing similar potency as in *in vitro* assays. The single-dose PK/PD data demonstrated a clear relationship between drug exposure and PD effect. Complete target occupancy for 24 hours after once daily dosing in volunteers was observed at doses of 100 and 200 mg QD.
CONCLUSION: GLPG1205, a potent and selective inhibitor of GPR84, is safe and generally well tolerated in healthy volunteers. It shows a favorable PK/PD profile, clearly demonstrating the ability of the compound to antagonize GPR84, a target which might be implicated in several neutrophil- and macrophage-driven inflammatory conditions. At 100 mg once-daily, full 24-hour inhibition was obtained. This dose will be studied in Proof of Concept studies to evaluate the efficacy and safety of GLPG1205 in patients with Crohn's disease and ulcerative colitis.
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P0342 EFFECTS OF A FODMAP- RESTRICTED DIET ON IRRITABLE BOWEL SYMPTOMS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The FODMAP (fermentable oligo- di- and monosaccharides, and polyols) -restricted diet has previously been proven effective to improve symptoms in patients with irritable bowel syndrome (IBS). FODMAPs are small osmotic active and poorly absorbed short-chain carbohydrates, and include fructose (found in fruit), lactose (found in milk products), fructans (found in grain and vegetables), galacto-oligosaccharides (found in legumes) and polyols (found

in sweetened products). FODMAPs are rapidly fermented by bacteria in the colon and can cause bloating, increased gas production, abdominal pain and altered bowel movements. FODMAPs do not cause IBS, but a FODMAP-restricted diet may improve the symptoms. Patients with inflammatory bowel disease (IBD) often suffer from persistent symptoms even though the inflammatory activity is in remission. This study aimed to investigate the FODMAP-restricted diet in patients with IBD in remission with persistent symptoms consistent with IBS.

AIMS & METHODS: A 6 week intervention was undertaken in 12 IBD-patients (10 ulcerative colitis and 2 Crohns disease, 3M/9W, age 23-57 years) in remission with CRP < 5mg/L and faecal calprotectin < 100mg/kg, and fulfilling the ROME-III criteria for IBS. FODMAP intake was determined by 4 days prospective dietary registrations at 0 and 6 weeks. Instructions and follow-up were given by a clinical dietician. IBS-symptoms and quality of life (QoL) were assessed with questionnaires (IBS-SSS and SF-36). Compliance was assessed by VAS-scales. Colonic fermentation was measured by breath tests with sampling for 180min after intake of 10g lactulose. Statistics: T-tests and ANOVA ($p < 0.05$).

RESULTS: FODMAP intake was significantly reduced from median 6.3g/d to 1.5g/d ($p = 0.0005$). IBS symptoms were significantly reduced from median IBS-SSS score 265.0 to 67.6 ($p < 0.0001$), and resolved in 58% of patients (remission classified as score < 75). Symptoms were reduced in the first 3 weeks and remained stable from 3 to 6 weeks. Mental-related QoL significantly improved from median score 43.8 to 53.3 ($p = 0.039$). There was a positive trend for physical-related QoL with mean score 41.0 vs. 47.1 ($p = 0.05$). QoL improved over the whole 6 weeks of the intervention. The scores for the SF-36 health domains "bodily pain" (53.3) and "vitality" (52.1) improved most, with p-values 0.004 and 0.017, respectively. Gas production did not change (AUC 3488 vs. 3390 ppm x min, $p = 0.8$). Mean compliance with the diet was 93%, and 73% continued the diet one month after the intervention.

CONCLUSION: The FODMAP-restricted diet resolved or improved IBS symptoms and QoL, and should be considered an effective treatment for patients experiencing symptoms in spite of remission from IBD.

Disclosure of Interest: None declared

P0343 INCREASED EXPRESSION OF T-CELL-ASSOCIATED GENES IN BASELINE BIOPSIES FROM TNF ANTAGONIST NAIVE PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS WHO UNDERGO REMISSION IN RESPONSE TO ETROLIZUMAB IN A PHASE II TRIAL

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INTRODUCTION: Etrolizumab is a humanized antibody to the integrin $\beta7$ subunit that blocks $\alpha4\beta7$ and $\alpha E\beta7$ binding to MAdCAM-1 and E-cadherin, respectively. In a recent phase II randomized double-blind placebo-controlled trial (EUCALYPTUS), induction therapy with etrolizumab showed clinically meaningful efficacy compared to placebo at week 10 in patients with moderate to severely active ulcerative colitis.

AIMS & METHODS: RNA sequencing of inflamed colonic biopsies from TNF antagonist naïve etrolizumab-treated patients who took part in EUCALYPTUS was used as a hypothesis-free approach to identify gene expression patterns associated with clinical remission in response to etrolizumab. Gene set enrichment analysis of pre-defined immune cell gene sets was performed. Following this, differentially expressed genes of interest were evaluated in sorted CD4+ or CD8+ $\alpha E\beta7$-positive and -negative T cells from colonic biopsies of non-EUCALYPTUS UC patients and control subjects.

RESULTS: TNF antagonist naïve patients that underwent remission in response to etrolizumab had higher baseline expression of T cell-associated genes in mucosal biopsies, while high baseline expression of neutrophil-associated genes was associated with etrolizumab non-response. Patients with higher than median gene expression levels of the T cell associated genes ITGAE (αE integrin), granzyme A and TMEM200A were enriched for remission in response to etrolizumab. As increased αE gene expression was associated with remission, sort purified $\alpha E\beta7$-positive T cells from biopsies of UC patients were used to test for increased expression of other remission-associated T cell genes. Gene expression of granzyme A in CD4+ and CD8+ T cells ($p < 0.01$) and TMEM200A in CD8+ T cells ($p < 0.05$), along with other effector molecules such as granzyme B and perforin in CD4+ T cells ($p < 0.05$), were found to be increased in $\alpha E\beta7$-positive T cells relative to $\alpha E\beta7$-negative T cells from UC patients but not healthy subjects. Finally, gene expression of the effector molecules granzyme A and B were decreased following etrolizumab treatment in patients achieving remission.

CONCLUSION: Enrichment of T cell associated genes, including αE and granzyme A, was observed in baseline colonic biopsies from TNF antagonist naïve patients that achieved clinical remission in response to etrolizumab. These candidate biomarkers may identify patients whose disease pathobiology is predominantly T cell-mediated and may benefit from etrolizumab treatment.

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P0344 QAX576, AN ANTI–INTERLEUKIN (IL)-13 MONOCLONAL ANTIBODY, FOR THE TREATMENT OF PATIENTS WITH FISTULISING CROHN'S DISEASE (CD): RESULTS OF A PROOF-OF-CONCEPT STUDY

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INTRODUCTION: Recent studies have identified IL-13 as a key cytokine driving the tissue remodelling that accompanies fistula formation in CD. This study assessed the effect of QAX576, an anti–IL-13 monoclonal antibody on fistula healing in patients with fistulising CD.

AIMS & METHODS: In this 52 weeks (6 weeks treatment, 46 weeks observation), multi-centre, parallel group, double-blind, active controlled study, 23 patients (≥18 years) were planned to be included. Enrolment was stopped after 10 patients due to slow recruitment. Eligible patients (CD ≥ 6 months, ≥ 1 perianal fistula, ≥ 1 ineffective fistula treatment but no previous anti-TNF α treatment failure) were randomized to receive intravenously either QAX576 10 mg/kg (at baseline, Weeks 3 and 6; placebo at Week 2; $n = 6$) or infliximab (IFX) 5 mg/kg (at baseline, Weeks 2 and 6; placebo at Week 3; $n = 4$). The primary variable was the number of patients (responders) achieving complete closure of all perianal fistulas for ≥ 4 weeks (compared to historical placebo rate of ~13%). Secondary variables included clinical assessments of the fistulas and MRI-based activity scores of the fistula tracts.

RESULTS: Nine patients were included in the pharmacodynamic analysis set (QAX576 = 6; IFX = 3 [one patient excluded due to protocol deviation]). The primary endpoint was achieved by two patients (33.3%; 90% CI: 0.114, 0.656) in the QAX576 group. One patient stopped treatment due to abscess formation (Week 3), one due to lack of efficacy (Week 14). In the QAX576 group, patients had 1-4 secreting fistulas at baseline. Both responders had complete closure with absence of any secretion within 3 weeks, although the MRI activity score remained stable or even increased in these two patients. Fistula secretion remained stable in three patients and fluctuated in one. All patients in the IFX group were responders.

Immunohistochemistry of fistula tissue at baseline confirmed epithelial expression of IL-13Rα2 (but not IL-13Rα1) and de-differentiation of distorted, entrapped crypts; SNAIL expression as marker of invasiveness was not found.

Overall, 35 AEs were reported in four patients (66.7%) in the QAX576 group; 24 AEs were reported in four patients (100%) in the IFX group. Majority of AEs were mild or moderate in severity. No death was reported in this study. One SAE (procedural pain) was reported in the IFX group.
CONCLUSION: In this study, QAX576 was well tolerated. As expected IFX was a powerful agent to induce fistula closure. Blockade of IL-13 may be effective, too, as compared to historical placebo rates, although the very low patient number does not allow a formal assessment.
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P0345 THE INFLUENCE OF ANTI-ADALIMUMAB ANTIBODIES ON ADALIMUMAB TROUGH LEVELS, TNF-A LEVELS AND CLINICAL OUTCOME

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INTRODUCTION: There is increasing evidence on the role of low trough levels and the development of anti-TNF-α antibodies for the occurrence of lack/loss of response to Infliximab (IFX) therapy in patients with Crohn's Disease (CD). Therefore, several recent papers and guidelines suggested the need for dosing IFX concentrations and anti-IFX antibodies in order to treat better CD patients. To date, there are limited data on the role of Adalimumab (ADA) trough levels and anti-ADA antibodies (AAA) for the management of CD patients.
AIMS & METHODS: We assessed the role of AAA on ADA trough levels, TNF-α concentrations, clinical biomarker (i.e. C-reactive protein) and clinical outcome. In this prospective observational cohort study, performed at a single tertiary referral center, 23 [14M/9F; mean age 41 (range 21-66)] infliximab-naïve patients with CD achieving disease remission and in maintenance treatment with ADA were included and followed-up. Blood samples were drawn at standardized time points (i.e. every 6 months or in case of CD relapse) just before ADA injection. Trough ADA serum concentration and AAA were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Blood samples were considered positive for AAA presence if AAA were $\geq$ 1.7 U/mL and for ADA trough levels if ADA levels were $\geq$ 5 µg/ml. Disease activity was assessed at the same points by means of routine biochemistry and the Harvey-Bradshaw Index (HBI, remission <5, mild disease 5-7, moderate disease 8-16, severe disease >16).
RESULTS: We have data from 189 blood samples. AAA were observed in 42/189 (22.2%) samples, out of whom 16/42 (38.1%) had levels of AAA $\geq$1.7 U/mL. ADA trough levels were found in 183/189 (96.8%) samples, out of whom 168/183 (91.8%) had a value of drug levels $\geq$5 µg/ml. Overall, 5/23 (21.7%) patients had AAA and 22/23 (95.6%) were positive for ADA levels. Blood samples with AAA had lower ADA trough levels [7.54 (0-26.49) vs. 9.45 (0.14-23.62); $p=0.002$] and higher TNF-α concentrations [5.9 (4.1-11.5) vs. 3.6 (0-27.2); $p=0.0007$] than blood samples without evidence of AAA. Moreover, patients with blood samples positive for AAA reported HBI values higher compared to patients without evidence of AAA [10 (3-17) vs. 5 (2-17); $p<0.0001$]. Finally, no difference was found in terms of mean PCR values between patients with AAA and those without [8.1 (3-76.4) vs. 5.2 (2.6-56); $p=0.39$].
CONCLUSION: Development and presence of AAA decreases ADA trough levels and increases TNF-α concentrations in blood samples from CD patients on maintenance treatment with ADA, thus favoring clinical relapse in them as demonstrated by the increased values of HBI scores recorded at the time of blood sampling.
Disclosure of Interest: None declared

P0346 TNF-A LEVELS STRONGLY CORRELATED WITH DISEASE ACTIVITY BASED ON HBI AND CDEIS IN PATIENTS WITH CROHN'S DISEASE IN MAINTENANCE TREATMENT WITH ADALIMUMAB

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INTRODUCTION: In the last two decades the therapeutic paradigm of Crohn's disease (CD) has changed dramatically thanks to the use of biological drugs. In this scenario, we must consider the pivotal role of tumor necrosis factor-alpha (TNF-α), a pro-inflammatory cytokine, in the pathogenesis and relapse of CD. High levels of TNF-α have been associated with the development of intestinal inflammation in CD and blocking this cytokine with anti-TNF-α molecules may result in mucosal healing. In addition several studies have shown increased TNF-α levels in the serum and in the intestinal mucosa of patients with CD. However, little is known about the course of TNF-α levels and their relationship with disease recurrence in CD patients during maintenance treatment with Adalimumab.
AIMS & METHODS: We assessed TNF-α levels in patients with CD who were in maintenance treatment with ADA and correlated them with clinical and endoscopic disease activity. In this prospective observational cohort study, performed at a single tertiary referral center, 23 [14M/9F; mean age 41 (range 21-66) infliximab-naïve patients with CD in maintenance treatment with ADA were included and followed-up. Blood samples were drawn at standardized time points (i.e. every 6 months and in case of CD relapse) just before ADA injection. Antibodies against ADA (AAA) were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Blood samples were considered positive for AAA presence if $\geq$1.7 U/mL. Disease activity was assessed at the same points by means of the Harvey-Bradshaw Index (HBI, remission <5). Moreover, endoscopic activity was assessed at baseline and at the time of relapse by means of CD endoscopic index (CDEIS; endoscopic remission <9).
RESULTS: We have data from 133 blood samples. AAA were observed in 26/1339 (19.5%) samples, and 10/26 (38.5%) had a value of AAA $\geq$1.7 U/mL. TNF-α levels were present in all samples assessed [mean 4.4, range (0-27.2)]. Patients in clinical remission based on HBI had lower TNF-α levels compared to patients who relapsed [3.7 (0.2-20.2) vs. 5.6 (1.3-27.2); $p=0.0002$]. Similarly, patients in endoscopic remission based on CDEIS had lower TNF-α levels compared to patients who relapsed [3.1 (0.2-20.2) vs. 4.3 (1.3-27.2); $p=0.0034$]. Per-patient median TNF-α levels were strongly correlated with median HBI scores ($r^2=0.702$, $p<0.0001$). Moreover, TNF levels were also correlated with CDEIS ($r^2=0.350$, $p=0.001$).
CONCLUSION: TNF-α levels strongly correlated with disease activity based on HBI and CDEIS indices in patients with CD in maintenance treatment with ADA. Indeed, moderate to severe patients often have high sustained TNF-α levels.
Disclosure of Interest: None declared

P0347 LONG-TERM OUTCOMES OF PATIENTS WITH ULCERATIVE COLITIS TREATED WITH INFLIXIMAB

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INTRODUCTION: Data on the long-term efficacy of infliximab for the treatment of ulcerative colitis are scarce. Sustained remission, recurrence and outcomes after infliximab withdrawal beyond one year as well as predictors of long-term outcomes are unknown.
AIMS & METHODS: The medical records of all patients with ulcerative colitis and treated with infliximab in a referral center between 2001 and 2012 were reviewed through September 2013. The cumulative incidence of surgery, remission and recurrence with or without infliximab withdrawal were estimated using the Kaplan-Meier method. Independent predictors of all outcomes were identified using a Cox proportional hazards model.
RESULTS: A total of 100 patients (63 males) with ulcerative colitis and treated with at least one infliximab infusion were included. At infliximab initiation, 17% of patients had severe acute colitis defined by the absence of response following intravenous steroid and 56% of patients had pancolitis. Concomitant treatment at infliximab initiation included steroids and immunosuppressants for 62% and 52% of patients, respectively. After a median follow-up of 55.1 months, the cumulative probabilities of surgery were 27%, 33% and 36% at 1, 3 and 5 years, respectively. A CRP $>$ 6mg/L at week 6 was associated with colectomy (HR = 3.43, 95% CI, 1.17-10.9; $p=.023$). Clinical remission was obtained in 64% of patients but almost half of the patients relapsed (28/64; 44%). Overall the cumulative probabilities for sustained clinical remission were 19%, 31% and 38% at 1, 3 and 5 years, respectively. The absence of infliximab withdrawal was the only factor independently associated with sustained clinical remission (HR = 4.6, 95% IC, 1.66-13.85; $p=0.0029$). Infliximab was withdrawn in 38 of the 64 patients in clinical remission. After a median follow up of 54 months following infliximab withdrawal, 10% (4/38) underwent colectomy, 63.2% (24/38) patients relapsed, and 36.8% (14/38) remained in clinical remission. The cumulative probabilities of relapse after IFX withdrawal at 1, 3 and 5 years were 24%, 61% and 81%, respectively. A young age $<$ 21 years at UC diagnosis (HR = 12, 95% IC, 2.77-58.24; $p=0.001$) and platelets rate $>$ 400000/mm3 at IFX withdrawal (HR = 6.68, 95% IC 1.55-30.82; $p=0.011$) were associated with relapse.
CONCLUSION: After a follow-up of almost 5 years, about one-third of patients experienced sustained clinical remission and one-third of patients underwent surgery. Most of the patients relapsed after infliximab withdrawal. These results suggest early optimization of infliximab treatment to avoid dreaded outcomes and to continue infliximab among responders to sustain remission.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00

PAEDIATRIC: LOWER GI – POSTER EXHIBITION – HALL XL

P0348 CORRELATION OF PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY FINDINGS IN THE DUODENUM AND TERMINAL ILEUM OF PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS, A PILOT STUDY

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INTRODUCTION: Studies over the past two decades have convincingly demonstrated the role of barrier dysfunction in the pathogenesis of inflammatory bowel disease (IBD). We have previously found that optical biopsy with probe-based confocal laser endomicroscopy (pCLE) could be used to assess mucosal barrier function and predict disease relapse in pediatric IBD patients. The purpose of this pilot study is to evaluate the correlation of pCLE findings between duodenal and terminal ileum in pediatric IBD patients.
AIMS & METHODS: This is a prospective study of pediatric IBD (Crohn's disease - CD and ulcerative colitis-UC) patients undergoing pCLE during both EGD and colonoscopy in a tertiary referral center. The barrier function was assessed with the density of epithelial gaps on pCLE of the duodenum and terminal ileum. Adequate imaging of the duodenum and terminal ileum were defined as at least 3 normal, non-diseased areas sampled; a minimum of 3 villi with the highest number of epithelial gaps were analyzed. The epithelial gap density was calculated based on the total number of epithelial gaps observed normalized per 1000 epithelial cells counted on adequately imaged villi.
RESULTS: A total of 13 IBD patients (9 CD, 4 UC) underwent EGD and colonoscopy with adequate pCLE imaging of the duodenum and terminal ileum in the study. There were 8 F (62%) and 5 M (38%) with a median age of 15 yr (range 10 to 20). The median duration of disease at the time of pCLE was 3 yr (range 0 to 9); for therapy, 4 patients (31%) were on anti-TNF agents, 6 (46%) were on 5-ASA and/or immunomodulators, 1 (7%) were on steroids, 2 (15%) were on no therapy. The disease distributions for CD were: ileo-colitis in 7 patients (78%), ileitis in 1 (11%) and colitis 1 patients (11%). For UC: 1 patients (25%) had pan-colitis, distal colitis in 2 (50%) and proximal colitis in 1 (25%). The gap density (mean ± SE) in the terminal ileum was 5.6 ± 1.7 gaps/1000 cells, while in the duodenum was 1.7 ± 0.5 gaps/1000 cells. There were modest correlation between the gap density in the terminal ileum and duodenum with a spearman correlation coefficient of 0.42 ($p = 0.15$)
CONCLUSION: In this pilot study of pediatric IBD patients, we found pCLE findings of barrier function as measured by epithelial gap density in the terminal ileum and duodenum had modest correlation. Future larger studies are warranted to further investigate the correlation of barrier function in the proximal and distal intestine.
Disclosure of Interest: None declared

P0349 INCIDENCE OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN MINHO-PORTUGAL IS INCREASING

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INTRODUCTION: INTRODUCTION: Inflammatory bowel disease (IBD) includes Crohn's disease (CD), ulcerative colitis (UC) and indeterminate IBD (IIBD). Although it primarily affects adults, the diagnosis in patients under 18 is about 25% to 30%, being CD the most frequent. Studies report an increase in the incidence of CD, but a stable incidence of UC. A 2010 study in Minho reports an incidence of 6.4/100000 (CD:66%; UC:34%).
AIMS & METHODS: Our aim was to characterize patients diagnosed with IBD from 2002 to 2013, between the ages of 0 to 17 years and 365 days, residents in Minho (districts of Braga and Viana do Castelo), calculate the incidence and evaluate the health-related quality of life. We conducted a retrospective study, by collecting information from the patient's personal clinical chart. Also performed was a cross-sectional study applying the IMPACT-III© questionnaire that assesses the quality of life of pediatric patients with IBD above 9 years old.
RESULTS: 137 subjects were found. The incidence in 2002-2013 was 5.0/100000 children-years (CD:66%, UC:32%, IIBD:2%), increasing from 2.4/100000 (CD:65%, UC:35%) in the first three years to 8.8/100000 (CD:75%, UC:23%, IIBD:2%) in the last three ($p < 0.0001$). Abdominal pain was the most frequent symptom in CD and hematochezia in UC. In the IMPACT-III©, the average score was 136.5 ± 19.2 ($n = 32$), with a Cronbach's alpha = 0.91.
CONCLUSION: There was a significant increase in the incidence of IBD, mainly due to CD. The symptoms usually indicate the type of IBD, and again in pediatric cases, abdominal pain is more prevalent than diarrhea in the presentation of CD. The quality of life seems to be similar to that found in other studies, still showing good internal consistency of the IMPACT-III©.
Disclosure of Interest: None declared

P0350 CUMULATIVE INCIDENCE AND ASSOCIATED FACTORS OF MUCO-CUTANEOUS MANIFESTATIONS IN PAEDIATRIC-ONSET CROHN'S DISEASE: A POPULATION-BASED STUDY

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INTRODUCTION: Muco-cutaneous manifestations (MCM) are common in adult patients with Crohn's disease (CD), but their frequency in paediatric-onset CD is unknown.
AIMS & METHODS: **The aims of our study** were in a population-based paediatric-onset CD cohort: i) to determine the cumulative incidence of MCM, including aphtous stomatis (AS), erythema nodosum (EN) and pyoderma gangrenosum (PG); and ii) to identify the socio demographic and clinical factors at CD diagnosis associated with a higher risk of developing MCM during the CD course.
Patients and Methods: Clinical data at diagnosis and at maximal follow-up were recorded in a population-based paediatric-onset CD cohort ($n = 537$, < 17 years at CD diagnosis) diagnosed from 1988 to 2004. Data on MCM were reviewed by a dermatologist. Risks of developing MCM were estimated by survival analysis and Cox models.
RESULTS: Median age at CD diagnosis was 14.6 years ($Q1 = 12.2$; $Q3 = 16.1$) and 53.6% of patients were males. At CD diagnosis, 87 patients (16.2%) had MCM including 26 of them (30%) with at least 2 MCM. After a median follow-up of 11 years ($Q1 = 7$; $Q3 = 15$), 148 patients (28%) developed a total of 175 MCM, including 110 (63%) AS, 59 (34%) EN, and 6 (3%) PG. Cumulative incidence of developing MCM was 21% [17.7 -24.6], 25% [21.6-29.0], 27% [23.5-31.2] and 28% [24.3-32.3] at 1, 5, 10 and 15 years, respectively. In multivariate analysis, female gender (HR = 2.6 [1.4-4.6]; $p = 0.002$), patients < 15 years at diagnosis (HR = 2.2 [1.3-3.8]; $p = 0.003$) and L4 location at diagnosis (HR = 2.2 [1.3-3.6]; $p = 0.002$) were significantly associated with a higher risk of developing MCM during the CD course.
CONCLUSION: In this population-based paediatric-onset CD cohort, MCM are frequent both at diagnosis and during CD course, and are associated to female gender, young age and L4 location at CD diagnosis. These results reinforce the need of a close collaboration between dermatologists, paediatric gastroenterologists and gastroenterologists in paediatric-onset CD in order to optimize the therapeutic management of these patients.
Disclosure of Interest: C. Templier: None declared, H. Sarter: None declared, D. Turck: None declared, M. Fumery: None declared, G. Savoye: None declared, B. Catteau: None declared, C. Spyckerelle: None declared, E. Laberenne: None declared, O. Mouterde: None declared, D. Djeddi: None declared, S. Buche: None declared, L. Peyrin-Biroulet: None declared, E. Delaporte: None declared, C. Gower-Rousseau Lecture fee(s) from: Ferring, MSD

P0351 LONG-TERM EFFICACY OF ADALIMUMAB IN PAEDIATRIC PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: The efficacy of adalimumab (ADA) in children with moderately to severely active Crohn's disease enrolled in the IMAgINE 1 trial has been reported up to week (wk) 52[1]. Long-term efficacy of ADA in patients (pts) enrolled in the on-going open-label (OL) extension, IMAgINE 2, is presented.
AIMS & METHODS: Pts who completed IMAgINE 1 through wk 52 were allowed to enroll in IMAgINE 2. Pts entering from blinded therapy received OL ADA according to body weight (≥40 kg: 40 mg ADA every other wk [EOW]; <40 kg, 20 mg ADA EOW). At or after wk 8, pts experiencing flares (increase in PCDAI ≥15 points compared to PCDAI at previous visit) could move to wkly (EW) dosing. Pts entering IMAgINE 2 from OL ADA (40 mg ADA or 20 mg ADA EW) continued to receive the same dose. Remission (PCDAI≤10) and response (PCDAI decrease ≥15 points from IMAgINE 1 baseline) over time were assessed in pts who entered IMAgINE 2. Missing data were handled using non-responder imputation (NRI) and last observation carried forward (LOCF). Endpoints are also reported as observed. A data cut-off of Jun 30, 2013 was used for this analysis.
RESULTS: Of the 188 randomized pts in IMAgINE 1, a total of 100 pts enrolled in IMAgINE 2. As of Jun 30, 2013, a total of 54 pts are ongoing in the study. Approximately 2/3 of pts entered IMAgINE 2 in remission and almost all entered with response (67% and 95%, respectively). Observed remission and response

rates remained stable over time during IMAgINE 2 (Table). Mean PCDAI scores decreased from 40.1 at IMAgINE 1 baseline to 8.6 at wk 192 of IMAgINE 2 (Table). Adverse event rates from IMAgINE 1 baseline up to wk 260 have been previously reported and no new safety signals were observed with prolonged ADA use.[2]

Table. Rates of remission and response and observed mean PCDAI scores during IMAgINE 2

Week	0	24	48	72	96	120	144	168	192
Remission (%)									
NRI	67.0	59.0	55.0	50.0	54.0	51.0	51.0	42.0	26.0
LOCF	67.0	62.2	61.2	57.1	61.2	62.2	63.3	62.2	61.2
Observed	67.0	62.8	66.3	64.1	70.1	73.9	79.7	79.2	81.3
Response (%)									
NRI	95.0	88.0	75.0	74.0	72.0	66.0	64.0	48.0	29.0
LOCF	95.0	91.8	85.7	87.8	85.7	85.7	87.8	82.7	81.6
Observed	95.0	93.6	90.4	94.9	93.5	95.7	100	90.6	90.6
Mean PCDAI	10.2	10.3	9.2	8.9	9.4	7.9	6.1	7.5	8.6

The number of pts declined over time due to discontinuations and not all pts had reached later time points. Results after wk 192 are not shown as few pts had reached longer study durations.

CONCLUSION: Results of the on-going OL study support clinically meaningful efficacy with long-term ADA therapy beyond four years of exposure in children with moderately to severely active CD.

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Disclosure of Interest: W. Faubion Consultancy for: Genentech, Connecticut Children's Medical Center - Safety officer on subcontracted award through NIH for clinical trial, Other: Board membership (no personal compensation): Shire Development, Inc - Pediatric UC Advisory Board, Janssen Services LLC - DEVELOP Registry Scientific Advisory Committee, UCB Biosciences Advisory board, M. Dubinsky Financial support for research from: Janssen, Consultancy for: AbbVie, Janssen, Takeda, Pfizer, Prometheus labs, Santarus, UCB, F. Ruemmele Lecture fee(s) from: Shering-Plough, Nestlé, MeadJohnson, Ferring, MSD, Johnson & Johnson, Centocor, Other: Board membership: SAC:DEVELOP (Johnson & Johnson), invited to MSD France, Nestlé Nutrition Institute, invited to Nestlé Health Science, invited to Danone, invited to MeadJohnson, Biocodex, J. Escher Financial support for research from: MSD, Lecture fee(s) from: MSD, Consultancy for: Janssen Biologics, Other: Board membership: scientific advisory committee of DEVELOP study (Janssen Biologics), J. Rosh Financial support for research from: AstraZeneca, AbbVie, Janssen, UCB, Lecture fee(s) from: Abbott Nutrition, Prometheus, Consultancy for: AbbVie, Janssen, Soligenex, Other: Board membership: GI Health Foundation, A. Lazar Shareholder of: AbbVie, Other: Employee: AbbVie, S. Eichner Shareholder of: AbbVie, Other: Employee: AbbVie, Y. Li Shareholder of: AbbVie, Other: Employee: AbbVie, N. Reilly Shareholder of: AbbVie, Other: Employee: AbbVie, R. Thakkar Shareholder of: AbbVie, Other: Employee: AbbVie

P0352 LONG-TERM SUSTAINED RESPONSE AND DURABILITY OF INFLIXIMAB FOR THE PEDIATRIC INFLAMMATORY BOWEL DISEASE IN KOREA

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INTRODUCTION: Inflammatory bowel disease (IBD) is increasing in Korea, especially in the pediatric population. Along with the classical treatment of 5-ASA, steroid, and immunomodulators, biologic agents such as infliximab (IFX), adalimumab are used increasingly. However, the safety and efficacy of IFX has not been evaluated much for long-term follow-up.

AIMS & METHODS: This is a single-center retrospective cohort study of 100 pediatric IBD (Crohn disease 90, Ulcerative colitis 10) who used infliximab from 2004 to 2014. The total duration of IFX administration, the dose intensification (DI), the sustainability and efficacy of DI, and immunomodulator use with or without IFX were analyzed. We also analyzed 3 groups to assess the efficacy and durability of IFX into sustained remission, recaptured response, and treatment failure group. Recaptured response meant the patients who recaptured remission by dose intensification.

RESULTS: The total duration of follow-up for patients was 61.7±46.6 months. The mean duration of IFX administration was 31.0±28.0 months. Average age of IFX initiation was 14.1±3.3 years. The interval between IFX initiation and dose intensification was 23.4±23.3 months. Dose intensification was in 53 patients out of 100 for the study period. Sustained remission was in 44 patients out of total and recaptured response was in 42, respectively. Treatment failure was 16 out of 100, who discontinued IFX eventually. We checked for sustained remission rate annually and the rate was declining over time with 46% at 12-24 months, 41% at 24-36 months, and 40% at 36-48 months, respectively.

CONCLUSION: This study shows that almost half of the patients with IFX maintained sustained remission until 2-year follow-up. And recapture rate was 75% for DI, which means high response of treatment efficacy for IFX dose-up. Further study about DI will be needed for the risk factors, for optimal timing of application in clinical course, and for any possible adverse events in long-term follow-up.

Disclosure of Interest: None declared

P0353 FOCUSED EDUCATION AND VACCINE ACCESS IN CLINIC IMPROVE INFLUENZA VACCINATION RATES IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Patients with inflammatory bowel disease (IBD) are at increased risk of experiencing complications of influenza infection, thus international guidelines recommend annual influenza vaccination for this population. The vaccine is available at no cost in primary care physician offices, walk-in clinics and pharmacies in Ontario, Canada, yet vaccine uptake remains low.

AIMS & METHODS: We sought to understand barriers to obtaining influenza vaccination in a pediatric IBD cohort, and to determine the impact of educational intervention and vaccine provision in IBD clinic on vaccine uptake. The study was completed over two successive influenza seasons. During the 2012-2013 season (Year 1), we surveyed parents and IBD patients aged ≥14 years regarding influenza vaccination attitudes and practices. The following year (Year 2), an educational module was developed to address concerns about vaccination identified in Year 1. Parents and patients presenting to IBD clinic in the ten weeks prior to the 2013-2014 influenza season were provided with the educational module (Phase 1). When the trivalent inactivated influenza vaccine (TIIV) became available, patients were offered both the educational module and the opportunity for vaccination during their IBD clinic visits (Phase 2). Chi-squared analysis was used to identify significant differences in vaccination rates in each intervention group. Demographic factors were associated with survey responses and vaccination status.

RESULTS: During Year 1, 180 of 183 parents (98%) completed the survey along with all 108 adolescents. Median patient age at time of study was 11 years, 63% were males, and 67% had Crohn's disease. Most patients (74%) were on immunomodulator or biologic medications. In Year 1, 47% of patients obtained the TIIV, and 34% of patients reported obtaining the vaccine annually. Reasons for non-vaccination included a perceived lack of benefit (29%) and concerns about adverse events (20%). Most families (91%) reported they would obtain influenza vaccination if their physician provided evidence of its benefit. Year 2 patients ($n = 228$) did not differ significantly in age, IBD subtype, disease severity or medications from Year 1 patients. 95% of patients and parents who reviewed the educational module reported that it was useful. 71% reported that the module informed their decision to obtain the TIIV, including 19% who had not planned to obtain the TIIV prior to reviewing the module. In Year 2, the vaccination rate in Phase 1 patients who received the educational module alone was 75%, compared to 89% of Phase 2 patients who received both the educational module and the option of obtaining the TIIV in IBD clinic ($p = 0.0043$). Amongst the patients who took part in both Year 1 and Year 2 ($n = 129$), serial determinations of influenza vaccination rates demonstrated an increase from 45% to 82% ($P < 0.0001$).

CONCLUSION: Despite widespread access to the TIIV at no cost, traditional methods of promoting vaccination have yielded low uptake in IBD patients. Providing a focused educational module on efficacy and safety addressed barriers faced by vaccine-hesitant families and improved influenza vaccination rates. Additional vaccine uptake can be achieved by combining educational intervention with provision of influenza vaccination during IBD clinic visits.

Disclosure of Interest: None declared

P0354 ACCUMULATION OF INTRA-ABDOMINAL ADIPOSE TISSUE IN PEDIATRIC CROHN'S DISEASE

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INTRODUCTION: Increased visceral adipose tissue (VAT) inflammation is a characteristic hallmark of surgical resections from Crohn's disease (CD) patients. Recent evidence points towards an active immunological role of VAT in CD pathogenesis in addition of VAT being a defense mechanism for bacterial translocation during intestinal inflammation. Magnetic resonance imaging (MRI) studies showed accumulation of intra-abdominal VAT in adults, especially in patients with fistulas and strictures.

AIMS & METHODS: We aimed to quantify the abdominal adipose tissue compartments using MRI (Achieva, Philips Healthcare, Hamburg, Germany) in 29 pediatric CD patients compared with 14 control children (CC) undergoing MRI examination of abdomen for other reason. Total abdominal (TA) adipose tissue, consisting of subcutaneous (SC) and intra-abdominal (IA) adipose tissues were retrospectively measured by a radiologist blinded to the clinical data in transverse slices centered on the umbilicus and expressed as mean ± standard deviation in cm^2. IA/TA and IA/height ratios were assessed and analyzed for association markers. We recorded the mathematically weighted Pediatric Crohn's Disease Activity Index (wPCDAI), disease phenotype, laboratory and anthropometric data at the time of MRI. Mann-Whitney test was applied to analyze differences

between patients and CC. The correlation significance was determined by means of Spearman correlation analysis. $P<0.05$ was considered statistically significant.
RESULTS: CD patients included 20 males and 9 females (mean age 14.8 ± 3.6 years, range 7.7-18.3) with a mean BMI of 18.3 ± 2.7, range 14.0-23.2. Median disease duration from diagnosis to MRI was 21 months (range 0-136). Non-complicated disease behavior (B1) was present in 25/29, 4/29 had stricturing (B2) and 6/29 perianal disease. CC included 4 males and 10 females (mean age 12.8 ± 4.5 years, range 3.0-18.0), BMI (mean 17.6 ± 3.2, range 13.4-23.6). CD patients had higher IA adipose tissue (41.7±20.3 vs. 28.7±11.6, $p<0.05$) but similar SC and TA adipose tissues compared to CC (104.4 ± 70.9 vs. 96.54 ± 50.8 and 146.1 ± 84.7 vs. 125.3 ± 61.5, NS). The IA/TA and IA/height ratios were significantly higher in CD patients compared to CC, respectively (0.31±0.10 vs. 0.24±0.04 and 25.9±12.7 vs. 18.4±7.8, $p<0.05$). Patients with disease duration under 2 years ($n=14$) had lower IA/TA ratio (0.28±0.08 vs. 0.35±0.10, $p<0.05$) compared to longer disease. The IA/TA ratio correlated with disease duration ($p<0.05$, $r=0.425$). No association was found between IA/TA and IA/height ratios and disease phenotype or therapy.
CONCLUSION: Intra-abdominal adipose tissue is increased and accumulates with disease duration in pediatric-onset CD.
Disclosure of Interest: None declared

P0355 PHARMACOKINETICS AND SAFETY OF MULTIMATRIX MESALAZINE IN CHILDREN AND ADOLESCENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Oral formulations of mesalazine (5-aminosalicylic acid; 5-ASA) are recommended first-line therapy for adults with active mild-to-moderate ulcerative colitis (UC). However, little data are available on the use of mesalazine in paediatric UC. This phase 1, multicenter, randomized, open-label study (NCT01130844) evaluated the pharmacokinetic and safety characteristics of 5-ASA and its associated metabolite, acetyl-5-ASA (Ac-5-ASA), after once-daily administration of multimatrix mesalazine to children and adolescents with UC.
AIMS & METHODS: Patients aged 5-17 years with a UC diagnosis of ≥3 months were eligible to enrol. Study participants (stratified by body weight) were administered 30, 60, or 100 mg/kg/day multimatrix mesalazine once-daily for 7 days. In order to attain these doses in children, smaller-sized 300 mg and 600 mg multimatrix mesalazine tablets were developed to supplement the existing approved 1200 mg tablet. Mesalazine was administered to patients at home on Days 1-4 and on-site on Days 5-7, during which pharmacokinetic blood and urine samples were collected and safety evaluations performed. Plasma and urine concentrations of 5-ASA and Ac-5-ASA were determined using a validated LC/MS/MS assay. Derived pharmacokinetic parameters for assessment included maximum concentration ($C_{max,\ ss}$), time of $C_{max,\ ss}$ (t_{max}), area under the curve for one dose interval (AUC_{ss}), renal clearance (CL_R), and percent of dose absorbed.
RESULTS: A total of 52 patients (21 at 30 mg/kg; 22 at 60 mg/kg; and 9 at 100 mg/kg) were treated. Mean (standard deviation) age was 13.3 (3.06) years, and median (range) time since UC diagnosis was of 1.83 (0.2- 9.6) years. By Day 5, steady state plasma concentrations for 5-ASA and Ac-5-ASA were attained for all dose groups. On Day 7, dose-proportional increases in mean AUC_{ss} and $C_{max,\ ss}$ for both 5-ASA and Ac-5-ASA were observed between 30 and 60 mg/kg/day cohorts. For 30, 60, and 100 mg/kg/day doses, the mean percentages of 5-ASA absorbed from multimatrix mesalazine were 29.4%, 27.0%, and 22.1%, respectively. The mean CL_R ranges for 5-ASA and Ac-5-ASA, respectively, were 5.0-6.5 L/h and 10.0-16.2 L/h. Treatment-emergent adverse events were reported by 19.2% of all patients; events were similar among different dose and age groups and no new safety signals were identified.
CONCLUSION: Across all dose groups, children/adolescents with UC receiving multimatrix mesalazine demonstrated pharmacokinetic profiles for 5-ASA and Ac-5-ASA similar to those observed in historical adult data. Multimatrix mesalazine was well tolerated across all dose and age groups, and no novel safety signals were reported.
Disclosure of Interest: C. Cuffari Consultancy for: Shire, Prometheus and Abbott Nutritionals, D. Pierce Shareholder of: Shire, Other: Former employee of Shire, B. Korczowski: None declared, K. Fyderek Financial support for research from: Received a grant from Shire for the study research conducted, H. Van Heusen Shareholder of: Shire, Other: Employee of Shire, S. Hossack Other: Employee of Covance, which received funding from Shire for assistance with the pharmacokinetic analysis, P. Martin Shareholder of: Shire, Other: Employee of Shire

P0356 DEVELOPMENT OF THE DAILY ULCERATIVE COLITIS SCALE FOR CHILDREN AND CAREGIVERS: FINDINGS FROM COGNITIVE DEBRIEFING INTERVIEWS

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INTRODUCTION: To test and refine the Daily Ulcerative Colitis Scale (DUCS), an electronic daily sign and symptom diary with a patient-reported outcomes (PRO) version for children 8-17 years and an observer-reported outcomes (ObsRO) version for caregivers of children aged 5-10 years.
AIMS & METHODS: This was a two–visit cognitive debriefing interview study involving children with mild to moderate ulcerative colitis (UC) aged 8-17 years and caregivers of children aged 5-10 years. ''Mild'' to ''Moderate'' UC was defined based on the Pediatric Ulcerative Colitis Activity Index (PUCAI) score at the time of the interview. The interviews involved an initial set of open-ended questions on the signs, symptoms and impacts of UC to confirm findings from a previous concept elicitation study, followed by cognitive debriefing of the DUCS along with items to assess global health, and items to examine device usability and characteristics of the sample. The visit 1 interview was held in person and lasted approximately 1 hour. Visit 2 took place by telephone 3 days after visit 1 and lasted about 25 minutes and was used to explore feasibility. Sample characteristics were analysed using descriptive statistics (mean, SD, median, range for continuous variables and N, % for categorical variables). Interview transcripts were analysed using qualitative analysis software, MAXqda, in which codes were applied to allow focussed review of responses across the sample. Findings were used to refine the DUCS to ensure clarity, relevance and comprehensiveness.
RESULTS: The PRO sample consisted of 38 participants (22 females and 16 males), with 2 participants completing interviews for 2 different diary versions for a total of 40 completed interviews. Age at study enrollment ranged from 8 to 17 years (mean of 12.8; SD 2.4; median of 13). The average PUCAI score, administered at visit 1, was 12.3 (SD 14.2), range 0 to 45. The caregivers of 7 children participated in the cognitive debriefing interviews of the ObsRO version. One caregiver tested two different versions of the eDiary for a total of 8 completed ObsRO interviews. The average age of the 7 caregiver participants was 41.5 years (SD 6.4; median of 42). The caregivers' children were an average age of 8.5 years (SD 1.7; median of 9). Findings from the visit 1 concept elicitation questions were consistent with those of the initial concept elicitation study. Four rounds of revisions were made to the PRO and ObsRO DUCS based on patient/caregiver interview feedback, as well as feedback from the FDA. The FDA suggested changes such as changing response scales, as well as the addition of questions to capture certain symptoms overnight. Patient input influenced changes such as clarification of text and graphics, and the selection of the optimal pain scale. The eDiary's usability was also assessed. Both child and adult participants found the device easy to use and navigate.
CONCLUSION: The DUCS eDiaries are content valid instruments capturing signs and symptoms of pediatric UC and are appropriate for measuring treatment benefit in pediatric UC clinical trials.
Disclosure of Interest: E. Flood Other: Employee of ICON, which was contracted by Shire to perform the research for the creation of the DUCS, D. Silberg Shareholder of: Shire, Other: Employee of Shire, B. Romero Other: Employee of ICON, which was contracted by Shire to perform the research for the creation of the DUCS, K. Beusterien Other: Performed this work when she worked at Oxford Outcomes, which provides consulting services to Shire, M. H. Erder Shareholder of: Shire, Other: Employee of Shire

P0357 AORTIC INTIMA-MEDIA THICKNESS AS AN EARLY MARKER OF ATHEROSCLEROSIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Aims of this study were to determine the presence of endothelial dysfunction by measuring aortic intima-media thickness (aIMT) and carotid intima-media thickness (cIMT) and to evaluate the role of traditional risk factors for premature atherosclerosis in children with inflammatory bowel disease (IBD).
AIMS & METHODS: Thirty-four children with IBD [25 Crohn's disease (CD) and 9 ulcerative colitis (UC); mean age 11.1 years] and 27 healthy subjects matched for sex and age were enrolled. In all patients, demographic characteristics and risk factors for atherosclerosis (age, sex, body mass index, blood pressure, dyslipidemia, active and passive smoking, family history for cardiovascular diseases), CD and UC clinical activity scores and inflammatory markers, were evaluated. Aortic IMT and cIMT were measured by high resolution B-mode ultrasound.
RESULTS: Aortic IMT was significantly higher in patients than controls ($p<0.001$). No significant differences were found for cIMT, although the carotid thickness was higher in IBD patients than healthy subjects. At a univariate analysis, inflammatory markers levels and tobacco smoking exposure were significantly related to higher aIMT values, while at a multivariate analysis the inflammatory status was the only independent variable correlated with high aIMT.
CONCLUSION: Aortic IMT is an earlier marker of preclinical atherosclerosis in young children with active IBD, than cIMT. The inflammatory status and the smoking exposure are significantly correlated with the premature endothelial dysfunction. These data emphasize the importance of controlling the chronic intestinal inflammation and endorsing smoke-free environments for children and adolescents with IBD
Disclosure of Interest: None declared

P0358 GROWTH IMPROVEMENT IN ADALIMUMAB-TREATED PAEDIATRIC PATIENTS WITH CROHN'S DISEASE: DATA FROM IMAGINE 1

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INTRODUCTION: Children with Crohn's disease (CD) often have impaired growth. The IMAgINE 1 trial demonstrated the safety and effectiveness of adalimumab (ADA) on inducing and maintaining remission in children with moderately to severely active CD[1]. The impact of ADA therapy on growth in patients with delayed growth at trial entry is analyzed.
AIMS & METHODS: In IMAGINE 1, patients aged 6-17 years with baseline (BL) PCDAI >30 received open-label induction of ADA at weeks 0/2 according to body weight (≥40kg, 160/80mg; <40kg, 80/40mg). At week 4, patients were randomized to double-blind higher-dose (HD) ADA (≥40kg, 40mg every other week [EOW]; <40kg, 20mg EOW) or lower-dose (LD) ADA (≥40kg, 20mg EOW; <40kg, 10mg EOW) to week 52. Patients were allowed to escalate to blinded weekly therapy for flare or non-response, followed by open-label HD ADA weekly for continued flare or non-response. Change from BL in height velocity z-score was measured at weeks 26 and 52 in patients with and without growth delay at BL (defined as height velocity z-score ≤ -1.0) in all ADA patients regardless of treatment group. Subgroup analyses by BL corticosteroid use, disease severity (based on median BL PCDAI of study population (PCDAI < 40, moderate CD; PCDAI ≥ 40, severe CD), and prior infliximab (IFX) use were performed.
RESULTS: Overall, statistically significant improvement in growth was observed at weeks 26 and 52 with ADA maintenance therapy in patients with growth delay (median height velocity z-score at BL -2.9 and median change from BL at weeks 26 and 52; 2.4 and 3.3, respectively, each $p<0.001$), but not in patients with normal growth (BL median 0.2; median change from BL = 0 at weeks 26 and 52). No statistically significant differences between LD and HD ADA were observed. Growth improvement trended to be larger in patients with BL corticosteroid use, with severe CD, and in IFX naïve patients (Table).
Table. Median BL height velocity z-score values and change from BL at weeks 26 and 52 in patients with growth delay (height velocity z-score ≤ -1.0 at BL)

	BL	ΔWeek 26	ΔWeek 52
LD	-3.0 (N = 47)	2.5* (N = 47)	3.4* (N = 30)
HD	-2.8 (N = 42)	2.3* (N = 42)	3.3* (N = 29)
IFX naïve	-3.1 (N = 54)	2.7* (N = 54)	3.8* (N = 41)
IFX experienced	-2.3 (N = 35)	1.7* (N = 35)	1.4* (N = 18)
Corticosteroid use at BL	-2.8 (N = 38)	2.5* (N = 38)	4.3* (N = 23)
No corticosteroid use at BL	-2.9 (N = 51)	2.3* (N = 51)	2.3* (N = 36)
Moderate CD	-3.2 (N = 26)	2.7* (N = 26)	3.0* (N = 22)
Severe CD	-2.7 (N = 63)	2.3* (N = 63)	3.8* (N = 37)

CONCLUSION: ADA treatment significantly improved growth in children with moderately to severely active CD and growth delay. The pronounced effect of ADA on growth in children with concomitant corticosteroid use or severe disease by PCDAI requires confirmatory studies.
REFERENCES
1. Hyams et al. *Gastroenterol* 2012; 143: 365-374.
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P0359 TREATMENT OF CORTICOSTEROID NAÏVE PAEDIATRIC AND ADOLESCENT PATIENTS WITH ULCERATIVE COLITIS BY THERAPEUTIC DEPLETION OF MYELOID LINEAGE LEUCOCYTES AS MONOTHERAPY OR IN COMBINATION WITH LOW DOSE PREDNISOLONE AFTER FAILURE OF FIRST-LINE MEDICATIONS

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INTRODUCTION: Given that patients with active ulcerative colitis (UC) have elevated and activated myeloid lineage leucocytes including the CD14+CD16+ monocyte phenotype known to be a major source of tumour necrosis factor-α, selective depletion of these leucocytes by granulocyte and monocyte adsorption (GMA) should be an effective intervention in UC patients. This thinking is most relevant in paediatric and adolescent patients in whom long-term drug therapy may adversely affect their growth and development.
AIMS & METHODS: This study was to evaluate the efficacy of GMA as a remission induction therapy in children and adolescents with UC in whom first-line medications had failed. In a single centre setting, a total of 27 consecutive children and adolescents, age 11-19 years, bodyweight 31.5-56.5kg were given mesalazine or sulphasalazine as a first-line medication. Twenty patients relapsed while under first-line medication or did not respond to first-line medication and received GMA with the Adacolumn, 2 sessions in the first week, and then weekly, up to 11 sessions. Patients who achieved a decrease of ≥5 in the clinical activity index (CAI) were to continue with GMA, while non-responders were to receive 0.5 to 1.0 mg/kg bodyweight/day prednisolone (PSL) plus additional GMA sessions. However, PSL was to be tapered immediately after CAI started to fall. At entry and week 12, patients' UC severity was clinically and endoscopically evaluated, allowing each patient to serve as her/his own control.
RESULTS: At entry, all 27 patients were corticosteroid naïve and none had extensive loss of the mucosal tissue at the affected sites. Seven patients achieved sustained remission with the first-line medications and did not receive GMA. Eight patients did not respond well to the first 5 GMA sessions and received PSL plus GMA, and in 2 of these with severe UC, the PSL dose was temporarily increased to 2mg/kg bodyweight while 12 patients responded to the first 5 GMA sessions and received additional sessions. At entry, the average CAI was 13.0±2.4, range 8-17, and the average endoscopic index was 8.8±1.6, range 7-11. The corresponding values at week 12 were 2.1±0.2, range 1-4 ($P<0.001$) and 2.4±0.2, range 1-4 ($P<0.001$). PSL was tapered to 0mg within 3 months in the 8 PSL treated patients. Therefore, at week 12, all 27 patients had achieved clinical remission, majority with mucosal healing (complete remission). Except difficulties in achieving blood access causing needle pain in a few cases, no serious GMA related adverse event was observed, and compliance was good, no refusal to receive GMA and no withdrawal from the GMA treatment.
CONCLUSION: In this study, GMA in paediatric and adolescent corticosteroid naïve patients with active UC refractory to first-line medication was associated with clinical remission and mucosal healing, while in non-responders to GMA monotherapy, addition of PSL enhanced the efficacy of GMA and tapering of the PSL dose immediately after the fall in CAI score was not associated with UC relapse. Therefore, with its favourable safety profile, the majority of young steroid naïve patients with active UC refractory to first-line medication should respond well to GMA and be spared from pharmacological interventions.
Disclosure of Interest: None declared

P0360 PAEDIATRIC IBS IS ASSOCIATED WITH INCREASED SERUM LEVELS OF PROINFLAMMATORY CYTOKINES

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INTRODUCTION: The pathogenesis of irritable bowel syndrome (IBS) in children is not completely understood, but in adults IBS has been associated with low-grade inflammation. The aim of this study was therefore to evaluate the serum levels of cytokines to determine whether paediatric IBS is associated with increased immune activity.
AIMS & METHODS: In the population based birth cohort BAMSE (n = 4089) adolescents were invited to participate in the 16-year follow up, of which 2547 (62%) agreed to undergo blood testing and clinical examination. Serum samples were obtained from 41 IBS patients (33 (80%) females) and 97 controls with no gastrointestinal (GI) symptoms (63 (65%) females). IBS patients fullfilled the Rome III criteria and were symptomatic at the time of blood sampling. MesoScale Discovery (MSD) multiplex immunoassay analysis was used for the measurement of the following serum cytokines; IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-13, IL-17A, IFN-γ, IL-1β, and TNF. Data shown as median (pg/ml), range 25-75 percentile.
RESULTS: IBS patients had increased serum levels of IL-6 as compared to controls with no GI symptoms (0.39 pg/ml (0.3-0.7) vs. 0.30 pg/ml (0.2-0.4); $p=0.006$). Also levels of TNF (1.65 pg/ml (1.2-2.0) vs. 1.3 pg/ml (1.0-1.8); $p=0.06$) and IL-8 (4.51 pg/ml (3.5-5.6) vs. 3.77 pg/ml (2.9-5.3); $p=0.1$) tended to be increased in serum of IBS patients relative to controls. The levels of IL-6, TNF or IL-8 did not differ between patients with or without constipation or atopic symptoms (asthma, eczema and/or rhinitis). The levels of IL-1β were under the detection limit in more than 80% of the samples and were therefore

not statistically analysed. Remaining serum cytokines, IL-2, IL-4, IL-5, IL-10, IL-12p70, IL-13, IL-17A and INF-γ were similarly expressed in IBS patients and controls.
CONCLUSION: Children with IBS have increased serum levels of proinflammatory cytokines, which mimics previously presented data from adults with IBS. Thus, paediatric IBS, similar to IBS in adults, is associated with increased immune activity.
Disclosure of Interest: None declared

P0361 3D HIGH-DEFINITION ANORECTAL MANOMETRY IN CHILDREN WITH FUNCTIONAL ANORECTAL DISORDERS

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INTRODUCTION: 3D high-definition anorectal manometry (3D HDARM) is the most precise tool to assess function and 3D topographic picture of pressures along the anal canal. Until now, it has been used only in adult population. The feasibility in paediatric population has not been evaluated so far.
AIMS & METHODS: The aim of the study was 3D manometric evaluation of anorectal function in children with functional anorectal disorders.
Children with functional anorectal disorders diagnosed according to III Rome Criteria were prospectively enrolled in the study. Manometry procedures were performed with ManoScan A300 (Given Imaging Ltd) without premedication. Pressures within the anal canal and 3D picture of sphincters were obtained. If possible, defecation dynamics and thresholds of sensation were evaluated.
RESULTS: 40 children (24 male; age: 9 weeks-15 years, median: 80 months) were studied. All children suffered from functional constipation. 13 out of 40 children presented with fecal incontinence and constipation. Mean resting and squeeze sphincter pressures were 78.98 mmHg and 190.27 mmHg, respectively. The length of the anal canal was 0.9-4.3 cm. Dyssynergic defecation type I was the most common type of abnormal defecation dynamics (9 out of 24 children). Sensation of urge was absent in 6 out of 18 children with the maximum volume of balloon equalled 140 cc. Recto-anal inhibitory reflex was present in all children. There were no lesions of sphincters according to 3D topographic picture of the anal canal.
CONCLUSION: 3D HDARM is a feasible method that can be used in paediatric population.
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P0362 RECURRENT ABDOMINAL PAIN IN ADOLESCENTS: COMORBIDITY WITH RECURRENT HEADACHE, BACK PAIN, DIZZINESS, PRESYNCOPE/SYNCOPE, CHRONIC FATIGUE AND ASSOCIATION WITH FERRITIN, SOLUBLE TRANSFERRIN RECEPTOR AND C-REACTIVE PROTEIN LEVELS

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INTRODUCTION: Many of common complains in routine adolescents medicine practice such as recurrent abdominal pain (RAP) and other recurrent pain syndromes, dizziness, presyncope/syncope and chronic fatigue are significantly associated with anxiety disorders and depression. Data about association of these conditions are limited. Some cases of RAP may be associated with iron deficiency and inflammatory diseases, but association iron deficiency and inflammatory markers with RAP frequency is not studied well.
AIMS & METHODS: 459 adolescents aged 12-18 were screened for RAP (criteria were as follow: (1) More than two episodes of RAP per month in the last 2 months OR (2) Abdominal pain intensity according 7-items Likert-type pain scale $\geq$ 4). Criteria for recurrent headache were as follow: (1) Headache episodes in the last year $>$ 10 OR (2) Headache episodes $>$ 1 per month in the last three months OR (3) Headache intensity according 7-items Likert-type pain scale $\geq$ 4. Criteria for recurrent back pain and dizziness were as follow: (1) More than two episodes per month in the last 2 months OR (2) Intensity according 7-items Likert-type scale $\geq$ 4. Adolescents were asked about history of presence of symptoms presyncope/syncope. Chronic fatigue was estimated with original 10-items questionnaire with assessment of as difficulty or inability initiating activity; reduced capacity maintaining activity; and difficulty with concentration, memory, and emotional stability. Plasma concentrations of ferritin, soluble transferrin receptor (sTfR) and C-reactive Protein (CRP) were estimated with ELISA kits.
RESULTS: We have found positive association between RAP and recurrent headache ($p = 0.002$), recurrent back pain ($p = 0.002$), recurrent dizziness ($p = 0.002$), and chronic fatigue ($p = 0.002$). Results are shown in Table 1.
Table to abstract P0362

Comorbidity symptoms positive adolescents	RAP absence (n = 384)	RAP presence (n = 75)	P (two-tailed exact Fisher test)
Recurrent headache (n = 193)	38.8%	58.7%	0.002
Recurrent back pain (n = 80)	15.1%	29.3%	0.005
Recurrent dizness (n = 42)	6.8%	21.3%	0.003
Presyncope/syncope (n = 88)	17.1%	26.7%	0.079
Chronic fatigue (n = 28)	3.9%	17.3%	<0.001

We have found lower ferritin level ($p = 0.024$), higher sTfR level ($p = 0.043$), and higher sTfR/log ferritin index ($p = 0.037$) in adolescents subgroup with frequent episodes of RAP ($>$ 2 times per month). No differences have been found in CRP levels according assigned RAP criteria and RAP frequency. We have also found no distinctions in ferritin, sTfR, and CPR levels in accordance of presence/absence of headache, back pain, dizziness, presyncope/syncope, and chronic fatigue.
CONCLUSION: RAP in adolescents has comorbidity with broad spectrum of other symptoms (recurrent headache, back pain, dizziness and chronic fatigue). Because of most of these conditions have psychosomatic pathogenic components, we suggest that RAP diagnostics and treatment in adolescents should require estimation and correction their mental health status. We also suggest that adolescents with frequent episodes of RAP should be tested for iron deficiency.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
OTHER LOWER GI DISORDERS I – POSTER EXHIBITION – HALL XL

P0363 PSYCHOLOGICAL EFFECTS OF COLORECTAL CANCER SCREENING INVITATIONS: A RANDOMIZED TRIAL

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INTRODUCTION: A cancer screening programme with the ability to reduce mortality might be seen as a health service for many with objective benefit for only a few. Screening might cause worries, and has a potential negative influence on the mental health of the population that could outweigh the benefits. The present study therefore aimed to investigate the psychological reactions towards invitations to screening for colorectal cancer, as part of an evaluation of a pilot for a national screening programme in Norway.
AIMS & METHODS: In a prospective, randomized trial participants were invited to either flexible sigmoidoscopy (FS) screening, Faecal Immunochemical test (FIT), or no screening (the control arm). With the invitation, the participants received a Health-related Quality of Life (HRQoL) questionnaire (The ShortForm-12) and an anxiety and depression questionnaire (Hospital Anxiety and Depression Scale), which they were asked to complete and return. Number of invited individuals and questionnaire response rates in the randomization arms were 3804 and 47% in the FS arm, 6780 and 51% in the FIT arm, and 6433 and 33% in the control arm, respectively. Among the responders, mean ages in the trial arms were 63.5, 62.4 and 62.9 years, and 55%, 56% and 57% were women, respectively.
RESULTS: A one-way Analysis of Variance revealed no significant difference between the three arms in four out of the eight HRQoL dimensions (table 1). However, contrast analysis revealed that the FIT arm showed significantly lower physical functioning compared to the control arm. The FS arm showed significantly better social functioning and mental health, compared to both the FIT arm and the control arm, and better role of emotions compared to the control arm. Further, there was a significant difference between the three arms in the anxiety subscale of HADS (table 1). The FS arm had lower anxiety levels compared to the control arm and to the FIT arm. The minimal important difference was operationalized as a difference of at least half a s.d. Thus none of the statistical differences were considered clinically relevant, indicating little effect of being invited for screening on HRQoL and anxiety.
Mean

	FS	FIT	Control	p*	p FS vs control	p FIT vs control	p FS vs FIT
Physical functioning	85.5	84.1	86.3	**.02**	.37	**.01**	.10
Role physical	82.5	80.0	80.6	.11			
Bodily pain	82.4	81.1	81.8	.26			
General health	67.0	67.3	67.9	.63			
Vitality	60.3	58.7	59.3	.19			
Social functioning	89.5	87.3	87.0	**<.01**	**<.01**	.64	**<.01**
Role emotional	87.6	85.6	84.2	**.02**	**.01**	.19	.06
Mental health	81.5	79.7	80.1	**.03**	**.03**	.97	**.01**
Anxiety	3.4	3.8	3.9	**<.01**	**<.01**	.81	**<.01**

Table 1. *One-way ANOVA of differences between the three arms, $p < .05$. Higher scores indicate better HRQoL, and higher levels of anxiety.
CONCLUSION: Our findings indicate no negative psychological reactions to receiving an invitation for colorectal cancer screening with either of the two screening modalities FS or FIT. Thus the burden of participating in a screening programme seems limited at invitation.
Disclosure of Interest: None declared

P0364 THE COST-EFFECTIVENESS OF "FULL SPECTRUM ENDOSCOPY (FUSE)" COLONOSCOPY FOR COLORECTAL CANCER SCREENING

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INTRODUCTION: As compared with Standard Forward Viewing (SFV) colonoscopy, Full Spectrum Endoscopy (Fuse) colonoscopy increases the adenoma detection rate and thereby impacts the recommended post-polypectomy surveillance intervals per current US and European guidelines [1].
AIMS & METHODS: As compared to SFV colonoscopy, we aimed to assess the cost effectiveness of FUSE colonoscopy in a CRC screening and surveillance program. We constructed a Markov model to simulate the occurrence of colorectal neoplasia in a cohort of 100,000 subjects ages 50 to 100 years of age. The cost-effectiveness of FUSE was compared with that of SFV colonoscopy, with each test being assumed to be repeated every 10 years for those 50 to 80 years of age. Sensitivity for adenomatous and hyperplastic polyps $\leq$5 mm, 6-9 mm, and high-risk polyps ($\geq$10 mm; $<$10 mm with unfavourable histology or multiplicity) were derived from the recent RCT tandem Fuse colonoscopy study [1]. Post-polypectomy surveillance was modeled according to polyp histology. Medicare costs were adopted and used in the analysis.
RESULTS: For the modeled cohort, the significantly higher sensitivity of FUSE colonoscopy in detecting additional colonic adenomas resulted in an increase in CRC prevention from 58% to 74%, corresponding to a gain of 9 days per person (2,413 life-years for the entire cohort). This 16% increase led to an absolute reduction in the cost of CRC care from $90 million to $57 million. This $33 million cost savings was only minimally impacted by the higher cost of more frequent post-polypectomy colonoscopy surveillance rates, so that FUSE was associated with a savings of $146 per person. Thus, SFV colonoscopy appeared to be "dominated" by the FUSE colonoscopy strategy, with FUSE colonoscopy being both more effective and less costly. By assuming 68 million of American subjects between 50 and 80 years of age and an annual incidence of 107,483 CRC cases without screening for a discounted annual CRC care cost of $3.7 billion, the additional efficacy of FUSE over SFV would result into the annual prevention of 10,318 CRC and the annual saving of $0.3 billion for CRC related costs.
CONCLUSION: As compared to SFV colonoscopy, FUSE colonoscopy appears to be more cost-effective for CRC screening and surveillance. In particular, the higher associated costs of more frequent post-polypectomy colonoscopy surveillance were compensated by the significant overall reduction in CRC treatment costs.
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Disclosure of Interest: None declared

P0365 SESSILE SERRATED VERSUS CONVENTIONAL ADENOMAS. DIFFERENT POLYPS IN DIFFERENT POPULATIONS

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INTRODUCTION: There are emerging data indicating that Sessile Serrated Adenomas may have different epidemiological characteristics than conventional adenomas.
AIMS & METHODS: This prospective study was aimed to identify any differences in the characteristics of patients with Sessile Serrated Adenomas with and without dysplasia (SSA/Ds) in comparison to patients with conventional Adenomatous Polyps (APs). 85 patients with APs and SSA/Ds were included and data regarding age, sex, smoking, BMI, waist-hip-ratio and medical history (arterial hypertension and diabetes mellitus) were collected. A univariate and a multivariate regression analysis were performed using z test.
RESULTS: 156 APs and 53 SSA/Ds of 85 patients (mean age 66.1±9.8 and 63.1±9.4 years, respectively) with their characteristics and the results from univariate and multivariate regression analysis are presented in the following table.

SSA/D vs AP (univariate)	OR	P-value	95% C. I.
Sex (women/men)	2	0.034	1.05-3.84
BMI	0.92	0.031	0.85-0.99
Waist-hip-ratio	0.01	0.06	0.0002- 1.30
Diabetes Mellitus	0.09	$<$0.001	0.02-0.33
Hypertension	0.24	$<$0.001	0.12- 0.47
SSA/D vs AP (multivariate)	**OR**	**P-value**	**95% C. I.**
Diabetes mellitus	0.1	$<$0.001	0.03-0.36
Hypertension	0.3	0.001	0.14-0.63

There was no statistical significant difference regarding sex, BMI and waist-hip-ratio ($p>0.05$) in the multivariate regression analysis. A peak incidence of SSA/Ds was observed in the ages of 51-60 years compared to a peak incidence in the ages of 61-70 years of APs ($p=0.001$). No significant difference between groups regarding smoking was observed ($p>0.05$).

CONCLUSION: SSA/Ds compared to APs are more common in women, they have a peak incidence 10 years earlier and tend to occur in patients with lower BMI. Waist-hip-ratio, although not statistically significant, had a trend for lower values in patients with SSA/D. The results from both analyses show that SSA/Ds are less common in patients with diabetes mellitus and hypertension in comparison to APs.
Disclosure of Interest: None declared

P0366 SESSILE SERRATED ADENOMAS, ARE THERE ANY RISK FACTORS?

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INTRODUCTION: Evidence is conflicting regarding the risk factors for development of Sessile Serrated Adenomas.
AIMS & METHODS: This prospective study was performed in order to identify differences in the characteristics of patients with Sessile Serrated Adenomas with and without dysplasia (SSA/D) in comparison to patients with normal colonoscopies. Data from127 patients (100 with normal colonoscopies and 27 with SSA/Ds) regarding age, sex, smoking habits, BMI, waist-hip ratio and medical history (arterial hypertension, diabetes mellitus, past history of polyps) was collected and analyzed by multivariate logistic regression analysis. Four age subgroups: 41-50, 51-60, 61-70 and 71-80 were analyzed with univariate logistic regression analysis. Analyses was performed using Stata 9.0
RESULTS:

SSA/D vs Normal (multivariate)	OR	P-value	95% C. I.
Age	1.04	0.008	1.01-1.08
Current smokers	4.35	0.003	1.63-11.59
Personal medical history of polyps	3.34	0.004	1.48-7.58
Age SSA/Ds vs Normal (univariate)	**OR**	**P-Value**	**95% CI**
41-50	1.33	0.84	0.07-23.5
51-60	9.88	0.032	1.21-80.07
61-70	8.72	0.047	1.02-74.11
71-80	26.18	0.003	3.03-225.9

No statistical significant difference was observed regarding diabetes mellitus, hypertension, BMI and waist-hip-ratio.
CONCLUSION: Smoking and personal past history of polyps increase the risk for SSA/Ds in comparison to normal population. Increasing age also increases the risk for SSA/Ds, especially after the age of 50.
Disclosure of Interest: None declared

P0367 DRUG ALLERGY AND RISK OF LYMPH NODE METASTASIS IN RECTAL CANCER

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INTRODUCTION: Previous epidemiologic studies have reported that a history of allergy is associated with reduced risk of colorectal cancer and other malignancies. However, no information is available for the association between allergy and risk of lymph node metastasis.
AIMS & METHODS: Our study was designed to determine this association in rectal cancer.
Patients who were treated at our hospital in the period from January 2003 to June 2011, and with a pathological hospital discharge diagnosis of rectal adencarcinoma, were included. The clinical, laboratory and pathologic parameters were analyzed. Multivariate logistic regression model was used to determine the association. Moreover, for type of allergic drug, sub-group analysis was performed.
RESULTS: 469 patients were included, including 231 with pathological lymph node metastasis (pLNM) (49.3%) and 238 without pLNM. Univariate analysis showed, compared with patients without pLNM, patients with pLNM had a younger age (60.6±12.8 yr *vs.* 63.6±12.2 yr, $p=0.012$), a lower percentage of drug allergy (8.7% *vs.* 16.0%, $p=0.016$), an increased CEA (median/interquartile-range 5.40/2.40-13.95 *vs.* 3.50/2.08-8.67, $p=0.009$), and a lower serum sodium (141±3.1mmol/L vs. 142±2.9 mmol/L, $p=0.028$). Multivariate analysis showed that drug allergy was associated with a reduced risk of pLNM (OR = 0.553; 95% CI, 0.308-0.994; $p=0.048$). In addition, our results showed that: (1) for tumor classification, patients with drug allergy had a higher percentage of group patients with pT1/ pT2; and (2) for type of allergic drug, this inverse association was found for penicillins, not for other allergic drugs.
CONCLUSION: Drug allergy is associated with a reduced risk of pLNM in rectal cancer.
Disclosure of Interest: None declared

P0368 PROGNOSTIC VALUE OF HUMAN PAPILLOMAVIRUS IN ANAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Anal cancer is an uncommon malignancy but its incidence is increasing worldwide. Chemoradiation is the standard primary treatment for patients with loco-regional limited disease. However, once patients develop metastatic spread, the prognosis is very poor. Human papillomavirus (HPV) is present in around 80% of anal cancers but its prognostic/predictive value is essentially unknown.
AIMS & METHODS: We retrospectively evaluated 50 patients with anal squamous cell carcinoma treated at our Institution with chemoradiotherapy for loco-regional disease. HPV status was evaluated from paraffin-embedded tumor tissues collected at the time of diagnosis by a polymerase chain reaction analysis.
RESULTS: Among 50 patients 42 (84%) were HPV-positive. Thirty-two (64%) patients were positive to genotype 16, two (4%) to genotype 18 and three (6%) to both 16 and 18. Lymph nodal involvement and clinical stage at diagnosis were more advanced for HPV-positive patients. After a median follow-up of 4 years (range 0.4-13.8) 46 (92%) patients were alive. Overall, 8 patients relapsed: 1 loco-regional, 1 regional and 6 distant recurrences were observed. Four patients died from metastatic disease. Five-year disease-free survival (DFS) in HPV-positive and HPV-negative patients was 92.5% and 50.0%, respectively ($p < 0.01$). In multivariate analysis, HPV-positivity was associated with a statistically significant better 5-year DFS. Five-year overall survival in HPV-positive and HPV-negative patients was 93.3% and 66.7%, respectively ($p = 0.12$).
CONCLUSION: In our study HPV-positive anal cancers had a statistically significant improved DFS compared to HPV-negative group.
Disclosure of Interest: None declared

P0369 ASSOCIATION BETWEEN COLORECTAL NEOPLASMS AND METABOLIC SYNDROME IN A PORTUGUESE POPULATION

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INTRODUCTION: There has been a growing recognition of metabolic syndrome (MS) as an important risk factor for cardiovascular disease and malignancies. Several investigators from Eastern countries have considered MS as a possible risk factor for colorectal neoplasms.
AIMS & METHODS: The aim of this study was to evaluate the association of MS and colorectal cancer and adenomas in a Western country, where the incidence of MS is over 27%.
Methods: Prospective study between March 2013 and March 2014. MS was diagnosed according to National Cholesterol Education Program-ATP III. Demographic characteristics, anthropometric measurements, metabolic risk factors and colonoscopy pathologic findings were assessed in patients with MS (group 1) who underwent routine colonoscopy at our department. This data was compared with consecutive patients without metabolic syndrome (group 2), with no differences regarding sex and age. Informed consent was obtained and the ethics committee approved this study. Statistical analysis was performed with T-student and χ^2 tests; p-value≤0,05 was considered statistically significant.
RESULTS: We evaluated a total of 258 patients, 129 with MS; 50% males; mean-age 67,1 years (50-87). Among the MS group, 94% had high blood pressure, 91% had increased waist circumference, 60% had diabetes, 55% had low HDL cholesterol level, 50% had increased triglyceride level and 54% had obesity ($BMI \geq 30 kg/m^2$). 51% presented 4 criteria of MS. MS was associated with increased presence of adenomas (43% vs 25%, $p = 0.004$) and colorectal cancer (13% vs 5%; $p = 0.027$), compared with patients without MS. MS was also positively associated with multiple (≥3) adenomas (35% vs 9%, $p = 0.024$) and sessile adenomas (69% vs 53%; $p = 0.05$). No differences existed between location ($p = 0.086$), grade of dysplasia ($p = 0.196$) or size of adenomas ($p = 0.841$). Increased waist circumference was an independent risk factor for the presence of adenomas (85% vs 15%, $p = 0.05$).
CONCLUSION: In our population, MS was associated with colorectal cancer and adenomas. Central obesity was also associated with an increased risk. Recommendations for colorectal cancer screening in patients with MS may need to be different from the average risk population. To our knowledge, no previous study evaluated this association in Portuguese patients.
Disclosure of Interest: None declared

P0370 THIRD ROUND OF TWO-SAMPLE IMMUNOCHEMICAL FECAL OCCULT BLOOD TEST SCREENING IN THE NETHERLANDS

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INTRODUCTION: Screening for colorectal cancer (CRC) by means of immunochemical fecal occult blood test (abbr. iFOBT or FIT) requires successive rounds for an optimal preventative effect. The diagnostic yield of advanced neoplasia may increase with the use of two FITs per round. Therefore, in this study we assessed the diagnostic yield and participation rate of two-sample FIT screening during three successive rounds in a population-based screening pilot in the Netherlands.
AIMS & METHODS: A representative sample of the Dutch population (n = 3197) aged 50-75 years was randomly selected and invited by mail for three rounds of two-sample FIT screening with a 2-year interval. Participants received two identical FIT tests per round to sample on two consecutive bowel movements. Tests were analyzed using the OC Sensor Micro (Eiken Japan) with a positivity cut-off level of 50ng Hb/ml (≥ 10 μg Hb/g feces). Participants with at least one positive test were offered colonoscopy. For each round, we excluded individuals who met exclusion criteria (history of CRC, IBD, colon imaging ≤ 3 years, life expectancy < 5 years, inability to give informed consent) died, moved away or were positive at previous rounds.
RESULTS: The participation rate was 64.4% (95% Confidence Interval (CI) 62.5–66.4%) at the third round, compared to 62.1% (1647/2652; 95% CI: 60.2-63.9%) in the second and 61.3% (1875/3061; 95% CI: 59.6–63.1%) in the first round. One test was positive in 145 (9.8%; 95% CI 8.4–11.4) individuals and in 41 (2.8%; 95% CI 2.0–3.7) both FITs tested positive. Of the 134 (92%) patients who proceeded to colonoscopy, 5 had CRC and 13 had an advanced adenoma (defined as an adenoma ≥10mm, with ≥25% villous component or high-grade dysplasia). The positive predictive value (PPV) for advanced neoplasia was 13.4% (95% CI 8.6-20.3) for at least one positive test and 18.4% (95% CI 9.0-33.9) when both tests were positive. The two-sample methodology detected 61.1% additional participants with advanced neoplasia ($p = 0.28$) who would have been missed with a single FIT test per round; 4 (80%) participants who had CRC and 7 (53.9%) who had an advanced adenoma had only 1 positive test.
Table, 2-sample FIT screening (≥1positive) in multiple rounds

	Eligible invitees	Participation	PR	DR Advanced neoplasia	DR CRC	PPV Advanced neoplasia %
	n	n (%)	n (%)	n (%)	n (%)	(95% CI)
Round 1	3061	1876 (61.3)	239 (12.8)	76 (4.1)	12 (0.6)	34% (28.3 – 40.7)
Round 2	2654	1647 (61.2)	141 (8.6)	26 (1.6)	4 (0.2)	19.0% (13.3 - 26.4)
Round 3	2297	1480 (64.4)	145 (9.8)	18 (0.8)	5 (0.2)	13.4% (8.6 - 20.3)

CONCLUSION: Two-sample FIT screening is associated with a stable and high participation rate of more than 60% after three rounds. Positivity rates and detection rates with two-sample FIT screening, are higher compared to historical data of screening with one-sample FIT per round (van Roon Gut 2012). This implies that FIT screening with two samples has an added benefit to detect a maximum number of individuals with advanced neoplasia.
Disclosure of Interest: None declared

P0371 LIFESTYLE, ENVIRONMENT OR GENDER – WHAT HAS BIGGER IMPACT ON THE INCIDENCE OF COLORECTAL NEOPLASIA?

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INTRODUCTION: Recommendations for colorectal cancer (CRC) screening are based on patients' age and family history of cancer, although men are at higher risk for adenomas and CRC and develop the lesions earlier than women. Several risk factors such as BMI, gamma GT levels, presence of diabetes and physical activity are known to increase the incidence of adenomas and CRC but less is known about the impact of those risk factors on prevalence of colorectal neoplasia in men and women.
AIMS & METHODS: To investigate the impact of risk factors on sex specific adenoma detection rates (ADR) and advanced adenoma detection rates (AADR). We included patients who attended preventive health check up examinations and screening colonoscopy at the same time point (within six months) in Austria between November 2007 and December 2012.
RESULTS: The investigated risk factors had greater impact on male patients than on female patients. High BMI influenced ADR ($p < 0.0001$) and AADR ($p < 0.0001$) in male patients and ADR ($p = 0.0229$), but not AADR ($p = 0.2720$) in female patients. High gamma GT levels also increased ADR ($p < 0.0001$, OR = 1.11, CI = 1.05-1.16) and AADR ($p = 0.0045$, OR = 1.12, CI = 1.04-1.21) in male, but not in in female patients ($p = 0.5237$, OR = 1.02, CI 0.96-1.09 for ADR and $p = 0.3804$, OR = 0.95, CI 0.85-1.07 for AADR). Presence of diabetes has an impact on ADR ($p = 0.0049$, OR = 1.2) and AADR ($p < 0.0001$, OR = 1.6) in male, but not in female patients ($p = 0.276$, OR = 1.1 and $p = 0.234$, OR = 1.3). Physical activity impacts ADR ($p = 0.0018$, OR = 0.8) and AADR ($p < 0.001$, OR = 0.6) in male as well as AADR in female patients ($p = 0.0150$, OR = 0.7) but not the ADR in female patients (0.0792, OR = 0.8).
CONCLUSION: Our results show that acknowledged risk factors for colorectal neoplasias seem to affect particularly male patients which raises the need of implementation of gender specific prevention recommendations for CRC, especially for men with risk factors.
Disclosure of Interest: None declared

P0372 ANTI-HER2/NEU PEPTIDE WAS LABELED WITH TC-99M TO DETECT HER2-POSITIVE TUMORS IN COLORECTAL HCT-15 DERIVED XENOGRAFTS

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INTRODUCTION: HER2/*neu* is reported as an overexpressed target on the cell surface in variety of solid cancers such as gastric cancer and breast cancer. Here, we (1) validated that HER2 is a tumor-treated target in colorectal cancer, and (2) designed an anti-HER2/neu peptide (AHNP)-labeled Tc-99m to detect the expression of HER2 in HER2-postive HCT-15-induced tumors.
AIMS & METHODS: The aim of this study was to create a HER2-binding peptide, AHNP, labeled with Tc-99m to detect HER2-positive tumors. First, the colorectal cancer cells, HCT-15, were used to investigate the binding specificity of AHNP. The AHNP was conjugated with HYNIC and PEG at N and C-terminus, respectively. The designed AHNP was chelated with Tc-99m through HYNIC and the isotope-labeled rate was analyzed by iTLC. Then, a nanoSPECT/CT was used for tumor detection.
RESULTS: We found that HER2 was overexpressed in colorectal HCT-15 tumor cells and the tumors of HCT-15-induced xenograft mice using Western blots. AHNP labeled with fluorescent FITC was performed to detect the binding efficacy of AHNP to HCT-15 in vitro using flow cytometry. The results revealed that AHNP specifically bound to HER2-positive HCT-15 cells compared to HER2-negative gastric MKN45 tumor cells, indicating that AHNP can be applied to diagnose HER2-positive tumors. Therefore, we labeled nuclear isotope, Tc-99m, with AHNP coupled with PEG to prolong the half-life of peptide in animals. The labeled rate of Tc-99m with AHNP through HYNIC chelating was measured $> 90\%$ using iTLC analysis. However we did not observe apparent difference in nuclear imaging for detecting tumors in HCT-15-induced xenografts, suggesting that peptide was unstable or rapidly metabolized in animals.
CONCLUSION: Our results showed that HER2 overexpressed in colorectal HCT-15 cells as a tumor target. HER2 specific binding peptide, AHNP, can be used to detect HER2-positive tumors as a good candidate tool in vitro, however, it was rapidly metabolized in animals.
Disclosure of Interest: None declared

P0373 BISULFITE-BASED DNA METHYLATION ASSESSMENT FROM RECENT AND ARCHIVAL FORMALIN-FIXED, PARAFFIN EMBEDDED (FFPE) COLORECTAL SAMPLES

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INTRODUCTION: Surgically removed formalin-fixed, paraffin-embedded (FFPE) specimens are routinely used for morphological and molecular diagnostics, although application of these samples in molecular biology analyses can be challenging. Methylation-sensitive high-resolution melting analysis (MS-HRM) is a cost-effective tool for the assessment of DNA methylation level alterations during several types of tumor formation including colorectal cancer (CRC).
AIMS & METHODS: We aimed to compare the applicability of recent and archive FFPE tissue samples for gene-specific MS-HRM using two different commercially available DNA isolation kits. Genomic DNA isolation was performed from two groups of FFPE blocks; archive samples older than 5 years ($n = 10$; 5 CRC, 5 normal adjacent tissue (NAT)), recent samples younger than 6 months ($n = 10$; 5 CRC, 5 NAT) using FFPE DNA Isolation Kits from Roche and Qiagen. The yield and purity of DNA samples were evaluated by spectrophotometry and by fluorometry. The integrity and applicability of DNA for PCR was examined by qPCR and a multiplex PCR experiment that contains primers producing four amplicons with different lengths. DNA samples were bisulfite converted and gene-specific DNA methylation analyses were performed for *MAL, SFRP1* and *SFRP2* genes by using MS-HRM analysis and GS Junior sequencing
RESULTS: Based on OD260 measurements the Qiagen method resulted in a slightly higher recovery in archive and a significantly higher recovery in fresh FFPE samples compared to the Roche method. More selective detection of RNA and DNA by fluorometric dyes revealed that Qiagen samples contain high amounts of RNA, more than the Roche isolated samples, which was also supported by the higher OD260/280 and OD260/230 ratios of Qiagen samples. The two isolation methods did not differ significantly in their DNA yield in case of archive samples, but Qiagen yielded about two times more DNA in average from fresh FFPE samples. The DNA integrity and amplificability of fresh FFPE samples were higher than the archive ones. Despite the equal DNA yield of Qiagen and Roche samples in the archive sample group, the integrity of Roche samples was higher, and their qPCR amplification was also significantly more effective. Identical DNA methylation pattern was detected by MS-HRM for Qiagen and Roche samples in the fresh FFPE group. However, in case of archive samples, more reproducible methylation results were obtained from Roche samples. The differences in the methylation level of selected tumor samples could be confirmed also by sequencing the PCR products of MS-HRM examinations.
CONCLUSION: Sufficiently reproducible MS-HRM results can be obtained from recently fixed, fresh FFPE samples, but less reliable results can be expected for archive ones. In case of archive samples more parallel reactions, and usage of highly effective primer assays is recommended.
Disclosure of Interest: None declared

P0374 COMPARISON OF AUTOMATED AND MANUAL DNA ISOLATION FOR DNA METHYLATION ANALYSIS OF BIOPSY, FRESH FROZEN AND FFPE COLORECTAL CANCER SAMPLES

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INTRODUCTION: A broad range of biological samples are being analysed with increasing number in the routine pathology; automated DNA isolation can be a promising solution to decrease the hands-on time.
AIMS & METHODS: Our aim was to analyse the performance of MagNA Pure 96 nucleic acid isolation system in DNA isolation from fresh frozen, biopsy and formalin-fixed, paraffin-embedded (FFPE) tissue specimens. Furthermore, we aimed to test the applicability of the isolated DNA in downstream DNA methylation analyses, and to compare results after automated and manual isolation. Fresh frozen ($n = 20$; 10 CRC, 10 normal adjacent tissue (NAT)) tissue specimens, biopsies ($n = 20$; CRC = 10, healthy colonic tissue = 10), FFPE blocks ($n = 20$; 10 CRC, 10 NAT) were collected. DNA isolation was performed from the fresh frozen and biopsy samples with QIAamp DNA Mini Kit (Qiagen) and with automated method with MagNA Pure DNA and Viral NA Small Volume kit (Roche Applied Science) on the MagNA Pure 96 system Kit in parallel, the FFPE samples were isolated with manual QIAamp DNA FFPET kit (Qiagen) and with automated MagNA Pure DNA and Viral NA Small Volume kit (Roche Applied Science). After DNA quantity and quality measurements, DNA methylation levels for MAL, SFRP1 and SFRP2 were analysed with methylation-specific high resolution melting analysis (HRM).
RESULTS: Yield of manually isolated samples were found to be equal in fresh frozen tissue samples and significantly higher compared to the automated method in the case of biopsy and FFPE samples. OD260/280 ratio was found to be similar in fresh frozen and biopsy samples, while manual isolation resulted in higher purity in FFPE samples. OD260/230 ratio was similar in fresh frozen tissue samples after both isolation methods, the automated method was superior in biopsy samples and the manual protocol in FFPE samples. DNA integrity was found to be the highest in fresh frozen samples, and half of the analyzed FFPE samples showed higher integrity after manual extraction, while the rest of samples had similar integrity after both methods. In biopsy and fresh frozen samples DNA methylation estimations were found to be highly similar after two isolation methods. In the FFPE samples the linearity of the assays lower even in FFPE samples SFRP1 and SFRP2 assays showed good correlation in the methylation percent data after the two different isolation methods.
CONCLUSION: Similar DNA methylation results were found after automated and manual DNA isolation, thus automation can be a suitable alternative in CRC diagnosis workflow beside manual protocols especially for laboratories with high sample throughput.
Disclosure of Interest: None declared

P0375 CORRELATION BETWEEN THE LOCATION OF THE INITIAL AND RECURRENT COLONIC POLYPS

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INTRODUCTION: The post-polypectomy surveillance colonoscopy is recommended because of the risk of synchronous and recurrent lesions. There are several factors used to stratify the probability of polyp recurrence. However, there are no studies correlating the location of the initial polyp and that of the recurrent one.
AIMS & METHODS: The aim of this study is to verify if the polyp location at the surveillance colonoscopy is correlated with the location of the previously excised polyps at the baseline colonoscopy.
We included all patients submitted to two total colonoscopies, with at least one-year interval and complete excision of the polyps detected in the baseline colonoscopy. We evaluated 346 patients, of whom 78 were excluded for not having polyps at the surveillance colonoscopy. We divided the intestine into cecum, ascending, transverse, descending, sigmoid and rectum and also evaluated the characteristics of polyps. We used the Kolmogorov-Smirnov test to determine the normality, Kappa for agreement and Chi-square, t-Test or Mann-Whitney as necessary.
RESULTS: We found a male predominance (64.9%) and a mean age of 64 ± 10 years. The number and size of the polyps at the initial and surveillance colonoscopy was 3 ± 1 *vs* 2 ± 1 polyps and 11 ± 9 *vs* 7 ± 5mm, respectively. The mean interval between the two colonoscopies was 37 ± 20 months. The overall agreement rate of polyp location between colonoscopies was 44%. Probability of recurrence in the several segments: cecum 50.0% [OR 6.4-62.4], ascending 57.0% [OR 2.3-7.2], transverse 46.4% [OR 1.9-6.9], descending 34.6% [OR 1.3-4.4], sigmoid 57.6% [OR 2.3-6.9], rectum 40.4% [OR 1.6-5.1], $p < 0.001$. No statistically significant difference was found between the rates of recurrence at the same location, taking into consideration: polyp morphology (sessile 59.8%; pedunculated 51.6%), size (11mm), polypectomy technique (biopsy forceps 64.3%; snare 54.0%; mucosectomy 70.4%), histology (low-grade dysplasia 54.7%, high-grade dysplasia 41.7%; hyperplastic 64.9%), resection (complete 48.6%; fragmented 58.3%). There was also no difference after stratification in

advanced adenoma (50.5%), non-advanced adenoma (56.8%) and hyperplastic (64.9%).
CONCLUSION: There seems to be a significant correlation between the initial location of polyps and the recurrence site in the surveillance colonoscopy. This may have future implications in terms of technical execution and accuracy of the procedure, including alerting for better scrutiny of the segment with previous polypectomy.
Disclosure of Interest: None declared

P0376 COMPARISON THE EFFICIENCY OF HIGH RESOLUTION MELTING ANALYSIS AND PYROSEQUENCING IN COLON CANCER DNA METHYLATION STUDIES

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INTRODUCTION: Identification of differentially methylated regions (DMRs) in the genome of cancer samples by comparing them with normal samples is a basic process in the course of epigenetic investigations. Methylation-sensitive high-resolution melting analysis (MS-HRM) and pyrosequencing of bisulphite modified DNA are two of the most popular technologies among single locus DNA methylation studies. Both techniques involve PCR amplification of bisulphite converted DNA, although they differ in their cost, hands-on time and in the output information they provide.
AIMS & METHODS: In order to test MS-HRM and pyrosequencing on colon cancer samples, fresh frozen tissue specimens were collected (20 CRC, 15 adenoma and 20 normal adjacent tissue (NAT)). After DNA isolation and bisulphite conversion, 12 different CpG rich regions of 9 genes were amplified by PCR (COL1A2, ENTPD5, PRIMA1, PTGDR, SFRP2, SOCS3, SULF1, SULT1A1 and THBS2). PCR amplification was carried out with primers designed to amplify both methylated and unmethylated templates. After amplification MS-HRM was carried out, and PCR amplicons were subsequently pyrosequenced.
RESULTS: In general, MS-HRM provided less accurate estimation, thus it is not suitable to detect very slight methylation level alterations. However, results of MS-HRM and pyrosequencing were in harmony with each other in 89% of cases. The number of hypermethylated tumours found by MS-HRM versus pyrosequencing was as follows: COL1A2: 5 vs. 7; PRIMA1: 5 vs. 7; PTGDR: 3 vs. 0; SFRP2: 13 vs. 13; SOCS3: 10 vs. 12; THBS2: 4 vs. 5, respectively. A promoter of an alternative variant of THBS2 was found to be hypomethylated in 4 vs. 5 tumour samples. The total number of DMRs found in the 20 CRC samples investigated was 44 by MS-HRM and 49 by pyrosequencing, which means that the efficiency of MS-HRM is 82% of the pyrosequencing. In contrast to pyrosequencing, MS-HRM was able to detect sample heterogeneity, especially in case of adenomas and tumour samples. Further experiments with laser captured microdissected cells from these samples revealed that epithelial cells were hypermethylated in tumours, while no DNA methylation level alteration could be detected in stromal cells.
CONCLUSION: Taken together, MS-HRM is cost-effective and needs less manual work than pyrosequencing, which makes it a suitable tool for DNA methylation screening study. The efficiency of MS-HRM is close to that of the pyrosequencing in DMR detection. Moreover, it gives information about sample heterogeneity. The major advantage of pyrosequencing is its higher sensitivity and the single CpG site information it provides.
Disclosure of Interest: None declared

P0377 TARGETED, NEXT GENERATION 454 SEQUENCING OF COLON CANCER BIOPSIES YIELDS THERAPEUTICAL AND DIAGNOSTIC DATA

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INTRODUCTION: Mutation analysis of certain genes is an essential procedure for an individualized therapy. The number of important target genes is gradually rising, pressing a requirement for continuous expansion of analytic methods. Fulfilling this goal in a time-efficient manner is a big challenge for diagnostic laboratories, using conventional sequencing procedures.
AIMS & METHODS: Creating a mutation sequencing panel helped us to reach the aim to investigate the potential of Next Generation Sequencing (NGS) in colon cancer genotyping. A multiplex PCR panel was designed to amplify mutation hot spots of 12 selected genes. Those genes were selected that are frequently mutated in colon cancer or that are investigated in routine oncodiagnostics (APC, BRAF, CTNNB1, EGFR, FBXW7, KRAS, MSH6, NRAS, PIK3CA, SMAD2, SMAD4, TP53). Amplicons were sequenced by a GS Junior Instrument (Roche) using ligated and barcoded adaptors. Eight samples could be sequenced in one single run. Altogether, control cell lines with known mutation profiles and 60 DNA samples were investigated by the panel (8 normal colon mucose; 33 adenomas and 17 adenocarcinomas).
RESULTS: In control cell lines (HT29 and Caco-2), 4 mutations were anticipated to be found by our panel; and three of them were successfully detected. Only one adenine insertion, which was located in an adenine homopolymer region, was not detected. We found one mutated normal of eight investigated samples (12.5%). This rate was much higher in adenomas and carcinomas (78% and 76%, respectively), indicating high sensitivity. The average number of mutations found in mutated samples was 1 in low grade adenomas; 1.8 in high grade adenomas; 1.9 in carcinomas and 2.3 in serrated adenomas. The only mutation found in normal samples was a germ line APC mutation. This typical gatekeeper suppressor gene was mutated in adenomas more frequently than in carcinomas (36% vs. 24%), in contrast with other caretaker or proto-oncogenes. The most frequently mutated genes were APC, TP53 and KRAS with 36%, 18% and 26% frequencies in adenomas and 24%, 47% and 45% frequencies in carcinomas, respectively. Interestingly, there was no sample found having APC and TP53 mutations together.
CONCLUSION: Our NGS based screening panel can be a useful and affordable tool to study the mutation profile of colon cancer. Additionally, not only can it detect sporadic, but many of frequent germ line mutations as well. Its application in diagnostic practice to predict therapeutic response is worth to consider.
Disclosure of Interest: None declared

P0378 REPORTED DELAY IN THE DIAGNOSIS OF COLORECTAL CANCER: ANALYSIS OF GP REPORTS OF AVOIDABLE DELAY FROM THE RCGP NATIONAL AUDIT OF CANCER

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INTRODUCTION: The UK has significantly poorer cancer survival rates than comparable countries(1) and diagnostic delay is perceived to be a significant contributory factor to this (2). In 2009/10 The RCGP undertook a National Audit of Cancer Diagnosis in Primary Care, obtaining data on 18,889 cancer patients, from 1120 practices (3). GPs also provided free text comments on any perceived avoidable delays within the patient's diagnostic pathway.
AIMS & METHODS: The aim of this study was to analyse the principal causes of delay, as reported by GPs.
The audit contained data on 2737 patients with colorectal cancer and avoidable delay was reported for 36%. Free text reports of the nature of the delay were available for 753 (28%) patients. These were transformed into quantitative data, utilising an extended version of The Model of Pathways to Treatment (4) as an analytical framework. Comments were independently categorised by CD and GR, with disagreements in categorisation reconciled through discussion. A proportion (10%) of cases were also coded by ET, as a data quality measure. In order to validate GP perceptions of diagnostic delay we compared categorised primary care and referral intervals for patients with and without perceived delay, using a chi-squared test.
RESULTS: GP reports of avoidable diagnostic delay were significantly associated with longer primary care and referral intervals ($p = < 0.0001$). The commonest reasons for delay were GP (mis)appraisal (29%), referral delays (e.g. routine rather than urgent) (13%) and investigation delays (28%). For colorectal cancer patients, help seeking delay was also a prominent factor (8%). Because these causes of delay were reported by GPs there was a potential reporting bias, with delays occurring prior to first consultation or in secondary care possibly being under-reported.
CONCLUSION: The causes of diagnostic delay for patients with colorectal cancer are complex. GP appraisal and type of referral appeared to be substantial contributors to cases of avoidable diagnostic delay. Interventions aimed at reducing the time to diagnosis should consider the specific causes of delay for colorectal cancer patients.
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Disclosure of Interest: None declared

P0379 CONFOCAL LASER ENDOMICROSCOPY FOR THE DETECTION OF EARLY MUCOSAL CHANGES IN RECTAL STUMPS OF PATIENTS WITH FAMILIAR ADENOMATOUS POLYPOSIS

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INTRODUCTION: Familial adenomatous polyposis (FAP) is an inherited, autosomal-dominant disease caused by a germline mutation of the adenomatous polyposis coli gene (APC). This condition inevitably leads to colorectal cancer. Prophylactic colectomy, or proctocolectomy with ileal pouch-anal anastomosis (IPAA) is recommended. Since any remaining rectal mucosa might still be at risk for malignancy, endoscopic surveillance of both the residual rectal stump and the ileal pouch is mandatory. Confocal laser endomicroscopy (CLE) is a novel technique that performs virtual histology of gastrointestinal mucosa with high accuracy, detecting in vivo early mucosal changes.
AIMS & METHODS: ***Aims:*** To assess the appropriateness of CLE for *in vivo* diagnosis of abnormal mucosal changes in rectal stumps of patients with FAP. ***Methods:*** Both white light endoscopy (WLE) and CLE were utilized in the examination of rectal stumps in 12 patients who had undergone proctocolectomy with IPAA. During WLE normal mucosa and polyps were classified according to both

Paris and Kudo classifications. CLE images were scored according to the MIAMI classification. Targeted biopsies were taken from normal mucosa and polyps were removed with biopsy forceps or polypectomy snares. CLE and histological findings of both background mucosa and polyps were compared.
RESULTS: WLE revealed that all but one patient had diminutive polyps (table 1) and the background mucosa always appeared normal. CLE confirmed that background mucosa was normal in all cases, whereas the diminutive polyps were classified adenomas in 9/11 patients and hyperplastic in 2/11 cases. After pathological examination, biopsies of the background mucosa always revealed normal colonic mucosa, while the diminutive polyps resulted to be 6/11 adenomas with low grade dysplasia (LGD), 3/11 adenomas with high grade dysplasia and 2/11 LGD adenomas with serrated features.

Patient	Polyp size (mm)	White light Endoscopy	Paris/Kudo Classification	MIAMI Classification	Histology
1	3	adenoma	Is-IIIL	adenoma	Low grade adenoma
2	4	adenoma	Is-IIIL	adenoma	Low grade adenoma
3	4	adenoma	Is-IIIL	adenoma	High grade adenoma
4	6	adenoma	Is-IIIL	adenoma	High grade adenoma
5	4	adenoma	Is-IIIL	adenoma	Low grade adenoma
6	7	adenoma	IIa-IIIL	adenoma	Low grade adenoma with serrated features
7	5	adenoma	Is-IIIL	adenoma	Low grade adenoma with serrated features
8	3	adenoma	Is-II	hyperplastic	High grade adenoma
9	5	hyperplastic	Is-IIIL	adenoma	Low grade adenoma
10	3	hyperplastic	Is-II	adenoma	Low grade adenoma
11	3	hyperplastic	Is-II	hyperplastic	Low grade adenoma

Table 1. Summary of findings in operated FAP patients undergoing surveillance with WLE and CLE
CONCLUSION: CLE showed good correlation with pathology in diagnosing diminutive polyps of rectal stumps in patients with FAP. Possibly, CLE could be useful for tailoring the surveillance in these patients. However, further studies are needed to confirm this hypothesis.
Disclosure of Interest: None declared

P0380 MICROMETASTASES IN THE SENTINEL NODE OF PATIENTS WITH STAGE I AND II COLON CANCER

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INTRODUCTION: According to the guidelines for TNM staging of colorectal cancer, occult nodal tumour cells are categorised as micrometastasis (MMs) and isolated tumour cells (ITCs). A recent meta-analysis demonstrated that MMs, but not ITCs, are prognostic for disease recurrence in patients with stage I/II colon cancer.
AIMS & METHODS: The objective of this retrospective multicentre study was to analyse the incidence of MMs in the sentinel node of patients with stage I/II colon cancer, to analyse the correlation between MMs, tumour differentiation and vaso-invasive growth, and to analyse the prognostic value of MMs for disease recurrence. Patients with elective surgery for stage I/II colon cancer were identified from databases about ex vivo sentinel lymph node mapping and ultrastaging, from three Dutch hospitals (2005-2012 Gelre Hospital (GH), 2011-2013 Leiden University Medical Center (LUMC) and 2010-2012 Jeroen Bosch Hospital (JBH)). Immunohistochemical staining was performed with antibody against pan-cytokeratin (LUMC, JBH) or cytokeratin-18 (GH) and findings were classified according to the 6th AJCC staging manual. Univariable analysis was applied for the correlation between MMs, tumour differentiation and vaso-invasive growth. Two year disease-free-survival (2yDFS) of patients with MMs, ITCs and patients without occult nodal tumour cells was compared with a Kaplan-Meier analysis.
RESULTS: A total of 214 patients were pooled in a multicentre database (GH n = 128; LUMC n = 19; JBH n = 67). MMs were found in twelve patients (5.6%), ITCs in 39 patients (18.2%) and occult tumour cells were absent in 163 patients (76.2%). Between these three groups, there were no significant differences in baseline characteristics or type of surgery. Tumour differentiation and vaso-invasive growth were comparable as well. Four patients with MMs received adjuvant therapy (33.3%) which was significantly more than patients with ITCs (n = 1; 2.6%) or patients without occult tumour cells (n = 7; 4.3%)(p = 0.004). After a median follow up of 20 months (IQR 20-47) recurrence of cancer was diagnosed in 12 patients (5.1%). Three recurrences were diagnosed in patients with MMs; one locoregional recurrence despite adjuvant treatment, and two distant metastases in patients who did not receive adjuvant treatment. Survival analysis showed a significantly reduced 2yDFS in patients with MMs compared to patients with ITCs or patients without occult tumour cells (p = 0.013).
CONCLUSION: In this study, the incidence of MMs in patients with stage I/II colon cancer was 5.6%, and was not correlated to tumour differentiation or vaso-invasive growth. Despite a relative large proportion of patients with adjuvant treatment, MMs were prognostic for disease recurrence.
Disclosure of Interest: None declared

P0381 PLASMA MICRORNAS AS SCREENING BIOMARKERS FOR COLORECTAL ADENOMAS

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INTRODUCTION: The identification and resection of colorectal adenomas during screening colonoscopy is the cornerstone of colorectal cancer prevention within bowel cancer screening programmes (BCSP).
Biennial faecal occult blood testing (FOBt) of patients aged 60-75 is the screening tool within the United Kingdom BCSP with a positive test identifying patients requiring colonoscopy. At screening colonoscopy, the yield for adenomas is 46.5% and for adenocarcinomas in 6%. [1] Whilst effective, FOBt lacks high sensitivity, specificity and accuracy. As a result, half of screening colonoscopies are normal or reveal other gastrointestinal disorders such as haemorrhoids and diverticular disease (that have lead to false positive FOBt results). This is a concern as colonoscopy is an invasive test which can cause patient harm. Another concern is the uptake of FOBt within screened populations is less than 60%. [1]
A biomarker screening test based on blood sampling may increase uptake – especially for individuals not keen to undertake faecal testing. If a biomarker had a high sensitivity, specificity and accuracy, the proportion of patients undergoing screening colonoscopy and having a non adenoma/ adenocarcinoma diagnosis would fall.
AIMS & METHODS: We plan to investigate microRNAs (miRs – short (18-24 nucleotides) evolutionary conserved non-coding RNA molecules) as potential biomarkers. 220 FOBt positive patients undergoing BCSP colonoscopy were recruited and samples of whole blood were taken (100+ patients with adenomas, 90+ controls – normal or non adenoma/ adenocarcinoma diagnosis). RNA was extracted from plasma and converted to complementary DNA. Pooled groups of patients with adenomas and controls were analysed using array cards. MiRs 19a, 98, 146b, 186, 331-5p, 452 and 625 were identified as candidate biomarkers. All cases were analysed for these candidates using quantative polymerase chain reaction.
RESULTS: All 7 candidate MiRs showed significant differences in expression in patients with colorectal adenomas when compared to controls.
MiRs 19a, 331-5p, 452 $p = <0.05$, miRs 98, 146b $p = <0.01$, miRs 186, 625 $p = <0.001$.
When ROC curve analysis was performed area under the curve was higher in patients with diverticular disease/ haemorrhoids than those without (0.866 vs 0.788).
CONCLUSION: This study suggest plasma miRs are potential screening biomarkers for patients with colorectal adenomas and also may help to identify patients with adenomas in the cohort of patients with background diverticular disease/ haemorrhoids. Further study and analysis is needed to validate these exciting findings.
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Disclosure of Interest: None declared

P0383 ACUTE TREATMENT OF MALIGNANT COLORECTAL OCCLUSION: SELF-EXPANDABLE METALLIC STENTS AS BRIDGE-TO-SURGERY OR PALLIATIVE TREATMENT VERSUS EMERGENCY SURGERY

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INTRODUCTION: Colorectal cancer presents as acute bowel occlusion in 10-40% of the patients. There are two main therapeutic approaches for decompression: emergency surgery and the endoluminal placement of self-expandable metallic stents (SEMS). Due to high mortality and morbidity rates associated to emergency surgery, SEMS placement as bridge-to-surgery or as palliation is being increasingly used with controversial results.
AIMS & METHODS: This study aimed to clarify the risk/benefit of the mentioned approaches. We conducted a retrospective longitudinal multicenter study, including 189 patients with acute malignant colorectal occlusion, diagnosed between January 2005 and March 2013. Demographic, clinical characteristics of the patients, tumor features and procedure details were analyzed.
RESULTS: Globally (85 patients – 35 bridge-to-surgery and 50 palliative) SEMS's technical success was 94.4%. Palliative SEMS had a limited clinical success (60.0%) and were associated to 40.0% of complications. SEMS occlusion (18.8%) was the more frequent, followed by migration (9.4%) and bowel perforation (7.1%). Elective surgery after stenting was associated to a higher frequency of primary anastomosis (93.8% *vs* 76.4%; $p = 0.038$), and a lower of colostomy (25.7% *vs* 54.9%; $p = 0.004$) and overall mortality (31.3% *vs* 56.7%; $p = 0.020$). However, no significant differences were identified concerning to postoperative complications. In palliative treatment, there was no difference in complications rate and overall mortality between SEMS and decompressive

colostomy. In this SEMS subgroup, we found a higher rate of reinterventions (40.4% vs 5.0%; $p=0.004$) and a longer hospital stay (14,9 *vs* 7,3 days; $p=0.004$).
CONCLUSION: SEMS placement as bridge-to-surgery should be considered in acute treatment of colorectal malignant occlusion, since it has advantages regarding to primary anastomosis, colostomy rate and overall mortality. However, the longer the SEMS stayed in place the higher the risk for complications. Therefore in palliative SEMS, despite the possible psychological effect of not having a colostomy, it does not seem to present significant advantages comparing to the decompressive colostomy.
Disclosure of Interest: None declared

P0384 THE EVALUATION OF NEW COLORECTAL CANCER TREATMENTS ON CHEMICALLY INDUCED COLON CANCER MODEL

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INTRODUCTION: Today new approaches for colorectal cancer treatment appear through traditional chemotherapy failure. The specificity of potential therapeutics, impact on malignant cells and/or their restraint within the tumor nodes, as well as the mininization of therapy and carcinogenesis side effects, are at the top of interests. Proteine kinase inhibitors are the most specific anticancer agents due to malignant cell peculiarities, whereas stem cells are the most specific anticancer drug vehicles due to tumor node metabolism. But the effects of the first and the last often are evaluated on xenograft models characterized by the immune deficient status of the host. So it is impossible to assess the state of the organism experiencing cancer adequately.
AIMS & METHODS: The investigation of the effects of new protein kinase inhibitors pyrrol derivates (PD) 5-amyno-4-(1,3-benzothyazol-2-yl)-1-(3-methoxyphenyl)-1,2-dihydro-3H- pyrrol-3-one and 1-(4-Cl-benzyl)-3-Cl-4-(CF_3- fenylamino)-1H-pyrrol-2,5-dione compared with therapeutic 5-fluorouracil (5FU) and the effect of allogenic trophoblast stem cells (TSC) on the tumor formation and growth and on the state of apparently healthy colon mucosa was undertaken. The 1,2-dimethylhydrazine (DMH) induced rat colon cancer model, which has histopathological and biochemical features similar to human colorectal cancer, was used. Carcinogenesis was initiated by 20 weekly injections of DMH (20 mg/kg) (up to tumor formation equal $T_{1\text{-}2}N_{0\text{-}1}M_0$ stage of human colorectal cancer) and followed by PD daily or 5FU weekly treatments for 7 weeks, or with TSC intravenous transplantation at 22nd week with no treatment for further 5 weeks. At 27th week of experiment the animals were euthanized, the colorectal tumors were counted and measured, the samples of colon walls with and without tumors were processed and examined under the light microscopy.
RESULTS: PD reduces the tumor number (N_t) and total tumor lesions area (S_t) at 27th week by preventing of new tumor formation and by regress of existing ones, as well as 5FU does (N_t and S_t at 27th week are less than these ones at 20th week). PD also diminishes the DMH-induced inflammation of the apparently healthy colon mucosa, whereas 5FU escalates this process. The data obtained suggest cell death predominantly by necrosis was caused by 5FU and by apoptosis one caused by PD. TSC transplanted at 22nd week at high dose ($1.5*10^6$ cells/kg) stops tumor growth compared to nontreated rats, as well as reduces mucosa inflammation, but does not cause regression of existing tumors (N_t and S_t at 27th week are the same at 22nd week). TSC transplanted at the same time at low dose ($0.5*10^6$ cells/kg) attenuates the inflammation features but doesn't affect tumor growth. We suppose TSC signals dominate the cancer stem cells ones and therefore contribute to normalization of cancer stem cells microenvironment and thus prevent further carcinogenesis.
CONCLUSION: Targeted therapy is suitable for non-metastatic stage of colorectal cancer, whereas the administration of stem cells could stop further carcinogenesis only but couldn't reduce the existing tumor nodes.
Disclosure of Interest: None declared

P0385 THE INDICATION FOR ADDITIONAL SURGICAL COLECTOMY WITH NODAL DISSECTION IN T1 COLORECTAL CARCINOMAS

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INTRODUCTION: With the introduction of screening programs for colorectal cancer and the recent advancement in EMR and ESD technology, a lot of T1 colorectal carcinomas are resected endoscopically with negative margins, and the percentage of early carcinomas amenable to endoscopic resection has increased. But, around 10% of the patients of T1 colorectal carcinoma have lymph node metastasis (LNM). Then, additional surgical colectomy with nodal dissection should be considered after endoscopic treatment. Therefore, it is critical to determine the criteria for curative endoscopic resection.
AIMS & METHODS: The aim is to clarify clinicopathological risk factors for LNM of T1 colorectal carcinomas and to establish the indication for additional surgical colectomy with nodal dissection.
A total of 19882 colorectal neoplasms excluding advanced cancers have been resected endoscopically or surgically at our unit from April 2001 to October 2013. Of these, 907 T1 carcinomas were included. Initial or additional surgical colectomy with nodal dissection was performed in 568 cases, and of which LNM was found in 55 cases (9.7%). We analyzed the clinicopathological risk factors as follows: age, gender, size, location, morphology, vessel permeation, tumor budding, poorly-differentiated or mucinous carcinoma (POR/MUC) component, desmoplastic reaction (DR) on the superficial layer, degree of SM invasion, and state of muscularis mucosae (MM grade). MM grade was evaluated into two conditions using the desmin immunostaining: MM grade 1 (complete or almost maintenance) and MM grade 2 (fragmentation or disappearance). Finally, based on significant factors, we stratified these T1 cancers into 3 groups at ultralow, low and high risk of LNM.
RESULTS: The existence of vessel permeation, tumor budding, POR/MUC component, MM grade 2 or the gender of female was significant. In contrast with MM grade 2, no lesions corresponding to MM grade 1 had LNM. Among T1 carcinomas with MM grade 2, male patients without vessel permeation, tumor budding or POR/MUC component showed low incidence (1/93: 1.1%) of LNM, while 54 (12.7%) of 433 patients with at least one factor had LNM.
CONCLUSION: The indication for additional surgical colectomy after endoscopic resection has been more clarified and simplified: MM grade 1 was suggested to be an anti-risk factor for nodal metastasis (Ultralow-risk group). T1 carcinomas with MM grade 2 and without female gender, vessel permeation, tumor budding or POR/MUC component may be acceptable for only monitoring (Low-risk group). For T1 carcinomas with MM grade 2 and with at least one factor, additional surgical colectomy with lymph node dissection should be recommended (High-risk group).
Disclosure of Interest: None declared

P0386 DOES THE TYPE OF COLECTOMY MODIFY THE RISK OF DESMOID TUMOR DEVELOPMENT IN FAMILIAL ADENOMATOUS POLYPOSIS PATIENTS?

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INTRODUCTION: Desmoid tumors represent one major complication of the disease in patients with familial adenomatous polyposis (FAP). Our aim was i) to study factors associated with the development of desmoid tumors in a large cohort of FAP patients and ii) to review the different treatment proposed with corresponding results.
AIMS & METHODS: We reviewed retrospectively 190 cases of patients with FAP, with complete medical records, followed at our institution between 1965 and 2013. There were 10 patients with biallelic MUTYH mutation (mean age 56,5 years) and 180 patients with either identified APC gene mutation, either a personal and family history suggesting APC-related polyposis (mean age 44,1 years, 22-85).
Treatment of desmoid tumor was proposed in those patients with progressive disease at radiological evaluation on a 4 to 6 month observational period. The response was evaluated retrospectively from the reports, according to RECIST criteria.
RESULTS: The median follow-up since the diagnosis of FAP was of 25 years. No patients (0/10) with MUTYH mutation ever developed desmoid tumor. In contrast, 31/180 (17.2%) patients with a mutation/phenotype of APC related polyposis (11 H, 20 F) developed 58 DT, at a mean age of 44,1 yrs (range 22-78 yrs). The localization of DT was: mesenteric 25, abdominal wall 25, extra-abdominal 3 (breast 2, gluteal muscle 1). From these 180 patients, a colectomy with ileo-rectal anastomosis had been performed in 104 (12 with DT, 11%) and proctocolectomy in 76 (19 with DT, 25%, $p=0.027$). There was no other factor associated with the development of DT, including the modality of surgery (laparotomy versus laparoscopy). As regards the treatment of DT: no treatment was proposed in 3 patients (mean FU 7,17 years); 12 patients (with 28 DT) had 29 medical therapeutic sessions with a mean duration of 12,8 months (range 3-24 months). Following RECIST criteria, a response was observed in 3 tumors (10.3%), a stabilisation in 17 cases (58.7%) and a progressive disease in 9 cases (31%). Medical treatment was: celecoxib (6 sessions), sulindac (9), tamoxifen (4), imatinib (8), sorafenib (1), bevacizumab (2). Surgical treatment of the DT was attempted for 32 tumors from 16 patients: 12 mesenteric (5 recurrences, 41.6%) et 21 extra mesenteric (6 recurrences, 28.5%).
CONCLUSION: This study suggests that the type of colorectal surgery (colectomy versus proctocolectomy) is a major determinant of the risk of developping desmoid tumors in APC type FAP patients. If confirmed, this may impact profoundly our surgical choices in these patients. On the other hand, we confirm the low efficacy of available medical treatments for desmoid tumors of FAP patients, and the high prevalence of post-surgical recurrences.
Disclosure of Interest: None declared

P0387 RADIATION PROCTOCOLITIS RESPONSE TO ARGON PLASMA COAGULATION

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INTRODUCTION: A mainstay in the treatment of prostate and some gynecological cancers is the use of external beam radiation therapy. Radiation proctitis is a well-recognized complication of pelvic radiation and Argon Plasma Coagulation (APC) is a very effective means of treatment. The literature supporting the use of APC is small.

AIMS & METHODS: The current study is a prospective analysis of patients with radiation proctitis referred from the Newfoundland and Labrador Bliss Murphy Cancer Centre. There were 81 patients referred to one gastroenterologist and 55 were treated with APC (Jan. 2010 to Dec. 2013). We studied the complete resolution of symptoms which was defined as the absence of rectal bleeding. A partial resolution was defined as a reduction in rectal bleeding.
RESULTS: This prospective cohort study was performed on all adults who underwent colonoscopy for radiation proctitis. In total, 81 patients were seen, 90.1% men and mean age = 68.4 (range: 48-87 years). The average time between the last dose of radiation and the development of symptoms of proctocolitis was 21.8 months (range: 0-132 months). Complete resolution of symptoms was reported in 75.9% of cases, partial resolution in 22.2% and only one patient (1.85%) showed no improvement. The mean sessions of treatment with APC was 1.86, (range 1-4). Furthermore, 61.5% of those with incomplete response had other potential sources of rectal bleeding identified such as hemorrhoids or an anal fissure. The rate of complications was 3.6% with 2 patients developing a rectal ulcer. Colonic adenomas were detected in 60.5% of individuals and colorectal cancer is 6.2%. Hemoglobin values before and after APC were available in ten patients and the mean increase was 9.6 g/L (range: -3 to 25 g/L).
CONCLUSION: APC is a safe and effective therapeutic modality for the treatment of radiation-induced proctitis. Pelvic radiation exposure can be associated with the development of symptoms of radiation proctitis. It is also associated with the development of adenomas and colorectal cancer. This is the largest reported case series to date regarding the utilization and efficacy of APC.
Disclosure of Interest: None declared

P0388 INHIBITION OF HUMAN AND MOUSE INTESTINAL AFFERENT MECHANOSENSITIVITY BY ACTIVATION OF GUANYLATE CYCLASE C

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INTRODUCTION: The guanylate cyclase C (GCC) agonist linaclotide reduces abdominal pain in constipation-predominant IBS (IBS-C). Its mechanism of action is via production and release of cyclic guanosine monophosphate (cGMP) by intestinal epithelial cells, which subsequently acts on high-threshold colonic afferent endings to reduce generation of pain signals in response to mechanical stimuli[1].
AIMS & METHODS: To determine 1. if inhibition of afferents by GCC agonism and by cGMP is seen also in a tubular preparation of mouse colon; 2. if this translates to inhibition of responses to the same stimulus in human appendix. Electrophysiological responses were recorded from human-extrinsic nerve bundles innervating tubular preparations of appendix[2]. A similar preparation was used in mice to record responses of lumbar splanchnic afferents innervating the distal colon.
RESULTS: Distension of mouse colon caused reproducible, stimulus-dependent excitation of splanchnic afferents up to 60mmHg. Administration of cGMP (500uM) or GCC agonist (linaclotide 1uM) significantly reduced the response to medium-level (40mmHg; N = 7, p = 0.01) and high-level distension (60mmHg; N = 7, p = 0.02). No effect was seen on response to low-level distension (20mmHg; N = 7, p = 0.9). In recordings of human appendix afferent responses to ramp distension (0-60mmHg), we attempted to release endogenous cGMP by activating GCC maximally with intraluminal enterotoxin ST (100nM). This had a similar pattern of effect as activation of GCC on mice on responses to distension, inhibiting only at high levels of distension (25% reduction, N = 5, p = 0.008).
CONCLUSION: GCC agonists inhibit mechanosensory responses to distension in intact *in vitro* preparations of both human and mice large intestine, but only at high intensities that correspond to those that would evoke pain *in vivo*. This provides important validation of the mechanism of action of linaclotide in relieving pain in IBS-C via peripheral inhibition of nociceptors in human intestine.
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P0389 PATHOPHYSIOLOGICAL CHARACTERIZATION OF SYMPTOM-BASED CLUSTERS OF PATIENTS WITH IRRITABLE BOWEL SYNDROME FOLLOWING A COMBINED NUTRIENT AND LACTULOSE CHALLENGE TEST

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INTRODUCTION: We recently demonstrated that a combined nutrient and lactulose challenge test allows symptom-based clustering of patients with irritable bowel syndrome (IBS) unrelated to exhaled gas and Rome III subtype (Le Nevé *et al* Am J Gastro 2013; oral communication UEGW 2013).
AIMS & METHODS: The aim was to further characterize the two IBS clusters previously identified. We included 100 patients with IBS (Rome III) and 38 healthy controls. The fasted subjects were served a test meal consisting of a 400ml liquid breakfast (Nutridrink®, 1.5 kcal/ml) containing 25g lactulose. The severity of gastrointestinal (GI) symptoms, fatigue, somatization, anxiety and depression were evaluated by questionnaires before the test (IBS-SSS, GSRS, VSI, FIS, PHQ-15, HAD), as well as visceral sensitivity (barostat) and fecal microbiota composition (16S rRNA pyrosequencing). The intensity of eight GI symptoms, the overall level of digestive comfort and the amount of exhaled H_2/CH_4 were assessed every 15min during 4h after meal intake. A mapping of the eight GI symptoms was done using a Principal Components Analysis (4h mean score). Independently, a hierarchical cluster analysis was performed on the same parameters to identify GI symptom-based IBS clusters.
RESULTS: The combined nutrient and lactulose challenge test discriminated IBS from healthy controls. The challenge also allowed clustering of IBS patients in two subgroups i.e "High GI symptom" (HGS) and "Low GI symptom" (LGS) based on intensity of GI symptoms, in line with our previous study. Patients in the HGS group (n = 39; mean 4h pain = 9.3, bloating = 10.3, distension = 11.2, discomfort = 11.8) displayed higher IBS-SSS score (353.7 vs. 236.8; $p < 0.0001$) and higher levels of anxiety (9.0 vs. 7.0; $p < 0.05$), fatigue (71.3 vs. 42.2; $p < 0.001$) and somatization (14.7 vs. 11.8; $p < 0.01$) as well as lower overall digestive comfort (8.0 vs. 12.8; $p < 0.001$) than patients in the LGS group (n = 61; mean 4h pain = 2.4, bloating = 3.0, distension = 3.4, discomfort = 4.8; $p < 0.001$). Patients in the HGS group displayed significantly higher rectal sensitivity compared to both LGS patients and healthy controls ($p < 0.001$ for pain intensity at 12 and 24mm Hg). No significant difference was seen between IBS clusters for fecal microbiota composition.
CONCLUSION: A test meal containing 25 g of lactulose allows clustering of IBS patients according to their GI symptom response, which reflects visceral sensitivity, IBS severity and psychological co-morbidity. This clustering cannot be predicted by fecal microbiota composition. The lactulose challenge test appears to be a promising tool to better define postprandial symptoms and the pathophysiology of IBS, and to non-invasively assess visceral sensitivity.
Disclosure of Interest: B. Le Nevé Other: Danone Research employee, R. Brazeilles Other: Danone Research employee, M. Derrien Other: Danone Research employee, J. Tap Financial support for research from: Danone Research, D. Guyonnet Other: Danone Research employee, H. Törnblom: None declared, L. Öhman: None declared, M. Simrén Financial support for research from: Danone Research, Consultancy for: Danone Research

P0390 NORMAL SIGMOID PENETRABILITY TO FLUORESCENT BEADS THE SIZE OF BACTERIA IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Altered intestinal barrier function has been suggested to play an important role in the pathophysiology of IBS, but the properties of one of the most important components of the intestinal barrier, the intestinal mucus layer, have not been studied in IBS. The colonic mucosa is covered by a thick mucus layer consisting of an inner adherent layer and an outer loose layer. The inner layer is normally devoid of bacteria. We tested the hypothesis that the penetrability of colonic mucus in situ to fluorescent beads the size of bacteria is increased in patients with irritable bowel syndrome (IBS).
AIMS & METHODS: Sigmoid biopsies were taken from unprepared colon in 12 healthy controls (mean age 28 years, 5 males and 7 females) and 14 IBS patients (2 males and 12 females), 2 IBS-C, 2 IBS-D and 10 IBS-M). 21 patients who underwent colonoscopy for other reasons (e.g. bleeding of unknown origin), with prepared colon, and 27 patients with ulcerative colitis (UC) in remission served as positive controls. The biopsies were mounted horizontally in an oxygenized perfusion chamber. After 20 minutes, a standardized amount of fluorescent beads with a size similar to that of bacteria (2 and 1 and 0.5 um) were added on the mucosal side. 40 minutes later, bead distribution was assessed by confocal laser microscopy at three laser frequencies, 488, 555 and 639 nm. The confocal images were transferred into Matlab and were processed by customized software. Mean bead intensity per 10 μm slice was calculated as a function of distance from end of crypt openings and the distance of this slice from end of tissue was used as a marker for bead penetrability. Mucus thickness was also measured repeatedly over time in a horizontal perfusion chamber using a micropipette after addition of charcoal particles to the apical side of the biopsy.
RESULTS: When measured repeatedly over time using carbon powder and a micropipette ruler, mucus thickness after 60 min was 540±65 μm in the controls and 610±50 in the IBS patients (p = 0.19). When studied with fluorescent microbeads, the distance of the slice with maximal bead intensity from the mucosa at 60 minutes was 400±60 μm in the controls and 470±80 μm in the IBS patients (p = 0.50). In the control patients, with prepared colon, the corresponding value was 500±60 μm (n.s.). In contrast, in prepared colon from UC patients in remission the distance was 280±60 μm ($p < 0.01$ versus other groups). Three different bead sizes were used to test the occurrence of size-dependent

permeability. However, no significant differences in impermeable layer thickness were found between the three bead sizes in any of the groups.
CONCLUSION: The values for mucus thickness in unprepared colon obtained with the micropipette ruler + carbon powder and the data obtained with the fluorescent microbeads agree closely, with slightly lower values obtained with the microbeads. In this small sample, sigmoid mucus from patients with IBS symptoms tended to have a mucus layer slightly thicker than in healthy controls (n.s. with both techniques), while the UC patients in remission had a markedly reduced thickness of the bead-impenetrable mucus layer.
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Disclosure of Interest: None declared

P0391 A PILOT RANDOMIZED PLACEBO-CONTROLLED MULTICENTER STUDY ON THE EFFECT OF PALMITOYL-ETHANOLAMIDE AND POLYDATIN IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Intestinal immune activation and mast cell intestinal infiltration play a pathophysiological role in the irritable bowel syndrome (IBS). Palmithoylethanolamide (PEA), the saturated fatty acid ethanolamide of palmitic acid, structurally related to the endocannabinoid anandamide, exerts anti-inflammatory and anti-nociceptive actions and inhibits mast cell activation. Polydatin (PD) acts synergistically with PEA in reducing mast cell release of cytokines and related T cell activation.
AIMS & METHODS: We designed a pilot, phase 2, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of PEA/PD in patients with IBS. Patients with Rome III confirmed IBS and healthy age- and gender-matched subjects (HC) were recruited from 5 European study centers (Bologna, Nantes, Barcelona, Tuzla, and Zagreb). After a 2-week run-in, the patients were randomly assigned to oral tablets micronized PEA/PD 200 mg/20 mg or placebo, b.i.d for 12 weeks. The efficacy evaluation included the assessment of: 1) mast cell infiltration and endocannabinoid system in patients with IBS *vs.* HC. 2) the effect of active treatment *vs.* placebo on mast cell infiltration, endocannabinoid system, and symptoms in patients with IBS. Colonic mucosal biopsies were obtained during at screening visit and at the end of the study. Biopsies were processed for quantitative immunohistochemistry for mast cells, and for biomolecular analysis of the endocannabinoid system (by liquid chromatography and western blot).
RESULTS: A total of 54 patients with IBS (29 allocated to PEA/PD and 25 to placebo) and 12 HC were recruited in the study. Mast cell counts were significantly increased in patients with IBS in comparison with HC (5.3%±2.7% vs. 3.2±1.3; $p = 0.013$). Compared to HC, expression of the peripheral cannabinoid receptor CB_2 in the tissue was higher in IBS ($p = 0.012$) while the fatty acid amide oleoylethanolamide was significantly reduced ($p = 0.007$). The logistic model for repeated measures did not reveal statistically significant effects of PEA/PD on mast cells and endocannabinoid system. Nonetheless, compared with placebo, PEA/PD improved abdominal pain severity (repeated measure ANOVA test; $P < 0.05$).
CONCLUSION: Our study suggests that PEA/PD is a promising effective treatment in the management of pain in patients with IBS. Whether the PEA/PD effect is secondary to mast cell stabilising or to modulation of the endocannabinoid system remains to be further investigated. ClinicalTrials.gov Identifier: NCT01370720.
Disclosure of Interest: None declared

P0392 ASSOCIATION BETWEEN CHANGES OF INTESTINAL MICROBIOTA, CHARACTERISTICS OF ANORECTAL MOTILITY AND RECTAL SENSITIVITY DISTURBANCES USING HIGH-RESOLUTION ANORECTAL MANOMETRY (HRAM) IN PATIENTS WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME

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INTRODUCTION: At present the role of changes of the intestinal microbiota in pathogenesis of irritable bowel syndrome (IBS) is widely discussed. Impact of microbiome on the gastrointestinal motility and visceral hypersensitivity is assumed. However the relevant data have been investigated insufficiently.
AIMS & METHODS: To estimate correlation between changes of the composition of intestinal microbiota, anorectal motility disorders and visceral hypersensitivity in patients with diarrhea-predominant IBS (IBS-D).
31 patients with IBS-D (clinical type was determined according to the ROME III criteria) and 15 healthy volunteers were studied. All subjects were analysed by examining sequencing data of the 16s rRNA from fecal samples, the hydrogen breath test with lactulose to determine small intestinal bacterial overgrowth (SIBO), high-resolution anorectal manometry (HRAM) using 20 channel water-perfused catheter with a polyethylene balloon (Solar GI, MMS, the Netherlands).
RESULTS: By sequencing of the 16s rRNA differences were found in the composition of intestinal microbiota between the IBS-D patients and healthy volunteers. In patients with IBS *Bacteroides* (18.9%), *Coprococcus* (7.2%) and *Blautia* (5.4%) were detected more often, the control group showed prevalence of *Blautia* (17.1%), *Prevotella* (8.3%) and *Faecalibacterium* (6.9%) ($p < 0.05$). A positive result of breath test (the presence of SIBO) was found in 20 patients with IBS-D (62.5%) and was not detected in the control group. A negative correlation was revealed between positive result of the breath test and the following parameters of rectal sensitivity and function of the anal sphincter: average pressure of the anal sphincter, average maximum compression pressure of the anal sphincter, the threshold for strong urge to defecate and maximum tolerable volume ($p < 0.05$).
CONCLUSION: Disruptions in the qualitative and quantitative composition of intestinal microbiota are found in patients with IBS-D; these changes are correlated with the parameters of anorectal motility and rectal sensitivity.
Disclosure of Interest: None declared

P0393 INSULAR HTR1A-NR2B PATHWAY MEDIATE THE VISCERAL HYPERSENSITIVITY INDUCED BY CHRONIC STRESS IN RATS

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INTRODUCTION: In many clinical studies, 5-HT1A receptor (HTR1A) of the central nervous system (CNS) was thought to be important in the pathogenesis of chronic stress related functional gastrointestinal disorders (FGIDs), but its potential mechanism is still not clear. Some studies thought the abnormality of HTR1A in CNS, through changing neuron activities of visceral sensory area such as insular cortex, mediated visceral hypersensitivity which was an important pathophysiological mechanism of stress-related FGIDs. NR2B was perhaps one key downstream signaling molecule of HTR1A. Insular HTR1A-NR2B pathway is inferred to be important in modulating the visceral hypersensitivity induced by chronic stress.
AIMS & METHODS: This study aimed to determine if insular HTR1A-NR2B pathway influences the activity of insula and mediates the visceral hypersensitivity induced by chronic stress in rats. Chronic water avoidance stress (WAS) was used to establish visceral hypersensitivity rat models. Visceral sensitivity was determined by measuring the visceromotor response (VMR) amplitude to 60mmHg colorectal distention (CRD). The HTR1A agonist 8-OH-DPAT and the HTR1A antagonist WAY100635 were microinjected into the left or right insular cortex. The expression levels of 5-HT, HTR1A, NR2B and c-fos were observed by RT-PCR, Western Blot or immunohistochemical staining.
RESULTS: Compared with sham WAS and normal rats, the expression levels of 5-HT and HTR1A in the bilateral insular cortex of WAS rats were significantly lower ($p < 0.05$), but the expression levels of c-fos and NR2B were significantly higher in the bilateral insular cortex of WAS rats ($p < 0.05$). After 8-OH-DPAT intervention of left or right insular cortex, the VMR amplitudes to 60mmHg CRD could be significantly reduced in WAS rats ($p < 0.01$). After WAY100635 intervention of left or right insular cortex, the VMR amplitudes have no significant changes in WAS rats ($p > 0.05$). The expression levels of bilateral insular NR2B and c-fos in 8-OH-DPAT intervention group were significantly lower than that in WAY100635 intervention group ($p < 0.05$).
CONCLUSION: Through regulating the activity of insular neuron, HTR1A-NR2B pathway has a critical role in mediating the visceral hypersensitivity induced by chronic stress in rats.
Disclosure of Interest: None declared

P0394 HIGHER FREQUENCY OF NEGATIVE SELF-ESTEEM AND INFERIOR COPING STRATEGIES FOUND AMONG IBS PATIENTS

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INTRODUCTION: A positive self-image is one of the key components for good health and wellbeing. Irritable Bowel Syndrome has been reported to be associated with altered psychological and cognitive functioning such as mood disturbances somatization, catastrophizing or altered visceral interoception by negative emotions and stress (1,2).
AIMS & METHODS: Aims to investigate the psychosocial constructs of self-esteem and sense of coherence among IBS patients compared to non-IBS patients. A case-control study in primary care setting among IBS patients meeting the ROME III criteria ($n = 140$) compared to controls i.e non-IBS patients ($n = 213$) in primary care without any present or previous gastrointestinal complaints. The data were collected through self-reported questionnaires of psychosocial factors.
RESULTS: IBS patients reported significantly higher frequency of more negative self-esteem than controls ($p < 0.0001$), had lower scores on the positive self-esteem measurement ($p < 0.0001$), and lower sense of coherence ($p < 0.0001$) than the controls. The IBS cases were also less likely to report 'good' health

status ($p<0.0001$) and less likely to report a positive belief in the future ($p<0.0001$). After controlling for relevant confounding factors in multiple regressions, the more negative self-esteem for IBS patients remained statistically significant ($p=0.02$), as were the lower scores for sense of coherence for IBS cases ($p=0.04$).

CONCLUSION: The more frequently reported negative self-esteem and inferior coping strategies among IBS patients found in this study suggest the possibility that psychological therapies such as cognitive behavior therapy might be helpful for these patients. However these data do not indicate the causal direction of the observed associations. More research is therefore warranted to determine whether these psychosocial constructs are more frequent personality traits in IBS patients or if the disease itself lowers self-esteem and leads to inferior coping strategies.

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P0395 LABOUR PRODUCTIVITY LOSS BECAUSE OF IRRITABLE BOWEL SYNDROME COMPLAINTS

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INTRODUCTION: Irritable Bowel Syndrome (IBS) is the most prevalent chronic functional bowel disease. IBS often results in a substantial disease burden for the patient and leads to considerable medical costs. Systematic reviews reporting economic consequences of IBS focus on direct medical costs and indirect societal costs, such as loss of productivity. When calculating indirect costs for IBS most researchers only take the costs for loss of labour days into account. In our view disease-related loss of labour productivity should also consider the IBS-related impact on work productivity on the days that the IBS patient is present at work.

AIMS & METHODS: We report the overall impact of IBS on labour productivity, i.e. the combined number of sick leave days and the loss of efficiency during the days IBS patients did work with active IBS complaints.

207 adult patients (18-65 years of age) with IBS, meeting Rome III criteria, who were recruited for a randomized controlled trial on hypnotherapy were selected. The impact of IBS on work was measured with four questions of the Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness (Tic-P): question 1 is about absenteeism from work because of IBS in the past two weeks (yes/no), Q2 about absenteeism for more than two weeks (yes/no),Q3 assessed if one was hindered by IBS complaints when working in the past two weeks (no, not at all; yes, somewhat; yes considerably) and Q4 assessed how efficient one has worked with the IBS complaints (from zero, indicating maximally inefficient up to 10: as efficiently as normal).

RESULTS: Of the 140 patients who had a job, 104 (74.3%) were women and 36 (25.7%) men. Of these female IBS patients 19 (18.2%) were absent from work because of IBS complaints, 10 (9.6%) less than two weeks, 9 (8.7%) more than two weeks. Eleven of these patients had moderate and 8 patients had severe IBS. Five of the male IBS patients (13.9%) were absent from work because of IBS complaints, 3 (8.3%) less than two weeks, 2 (5.6%) more than two weeks; one had moderate and four severe IBS. IBS subtype was known of 131 working IBS patients, 21 (16%) had IBS-Constipation, 33 (25.2%) had IBS-Diarrhea and 77 (58.8%) had IBS-Mixed type. Of the patients with IBS-C 2 (9.5%) were absent less than two weeks, 0% more than two weeks; of the patients with IBS-D 3 (9.1%) were absent less than two weeks and 2 (6.1%) more than two weeks; of the patients with IBS-M 8 (10.4%) were absent for less than two weeks and 8 (10.4%) for more than two weeks. In 20% of the female and 7% of the male working IBS patients IBS complaints had no impact on their labour productivity, 64% of women and 23% of men were hindered to some extent and 16% of women and 23% of men were hindered very much by their IBS complaints in performing their job; 33.3% of women and 52.8% of men indicated that they worked less efficiently than normal (score ≤ 6) because of their IBS complaints.

CONCLUSION: IBS complaints do not only result in substantial absenteeism from work, but also in severe loss of efficiency among those IBS patients who do not report sick, but continue working. When quantifying disease-related loss of labour productivity both aspects should be taken into account.

Disclosure of Interest: None declared

P0396 EXTENSIVE OVERLAP AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION, CHRONIC IDIOPATHIC CONSTIPATION, FUNCTIONAL DYSPEPSIA, AND GASTROESOPHAGEAL REFLUX DISEASE: A CROSS-SECTIONAL, POPULATION-BASED SURVEY

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INTRODUCTION: Individuals with functional gastrointestinal disorders (FGIDs) may report symptoms of more than one FGID as well as symptoms of gastroesophageal reflux disease (GERD). This US cross-sectional Internet-based survey assessed overlap of these disorders and sufferers' symptom experience.

AIMS & METHODS: A random sample of 10,030 US citizens completed an online screening questionnaire to identify those meeting Rome III criteria for irritable bowel syndrome with constipation (IBS-C), chronic idiopathic constipation (CIC), and/or functional dyspepsia (FD), and/or who reported GERD (defined as heartburn or regurgitation $\geq$twice/week in the absence of treatment). Survey responses were weighted for age and gender to be representative of the US census. Respondents who met criteria for $\geq$1 condition completed a detailed questionnaire including a symptom checklist and questions about bothersomeness, severity and frequency of symptoms and healthcare-seeking behaviour. Respondents reported symptoms experienced in the past 12 months, rating them on a scale from "less than 5 days a year" to "everyday." Overall and individual gastrointestinal (GI) symptom bothersomeness was reported on a 5-point scale from "not at all" to "extremely" bothersome.

RESULTS: A total of 2641 respondents met criteria for $\geq$1 condition. Including those with overlapping conditions, 328 met criteria for IBS-C, 552 for CIC, 1690 for FD and 1337 for GERD; 56.5%, 39.9%, 44.7% and 44.2%, respectively, reported very/extremely bothersome GI symptoms. Overall, 1592 (60.3%) met criteria for a single condition, 832 (31.5%) met criteria for 2 conditions and 217 (8.2%) met criteria for 3. Of the 4 conditions, respondents with IBS-C were the most likely to have overlapping conditions. Overall bothersomeness of symptoms increased with condition overlap: 22.5-30.4% of respondents with 1 condition had very/extremely bothersome symptoms, compared to 37.1-65.7% of those with 2 conditions, and 65.1-73.5% of those with 3 conditions. With the exception of heartburn/acid reflux, the frequency and bothersomeness of individual symptoms—including abdominal pain, bloating, diarrhea, and constipation—also increased with condition overlap.

TABLE 1. Condition Overlap

N (total = 2641)	IBS-C (n = 328)	CIC (n = 552)	FD (n = 1690)	GERD (n = 1337)
One Condition Only	57 (17%)	207 (38%)	721 (43%)	607 (45%)
and IBS-C[1]			247 (15%)	137 (10%)
and CIC[1]			289 (17%)	160 (12%)
and FD[1]	247 (75%)	289 (52%)		650 (49%)
and GERD[1]	137 (42%)	160 (29%)	650 (38%)	
3 conditions	113 (34%)	104 (19%)	217 (13%)	217 (16%)

CONCLUSION: Functional GI disorders frequently overlap with each other and with GERD. Patients with overlapping FGIDs have more frequent and bothersome symptoms and greater symptom burden. Results of clinical trials in FGIDs may be modified by overlapping FGIDs; baseline symptom severity may be affected by FGID overlap and global response measures may mask therapeutic response in one or the other FGID. (*Study sponsored by Forest Laboratories, Inc., and Ironwood Pharmaceuticals, Inc.)*

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P0397 THE PATH FROM GI SYMPTOMS TO DEPRESSED MOOD AND ELEVATED STRESS: IS IT SPECIFIC TO IBS?

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INTRODUCTION: The irritable bowel syndrome (IBS) has been associated with depressed mood[1] and elevated levels of perceived life stress[2], presumably via the adverse effects of the gastrointestinal (GI) symptoms associated with the disorder. However some degree of GI symptoms are also present in non-IBS individuals, including healthy community members.

AIMS & METHODS: We aimed to determine whether the path from GI symptoms to disordered mood leading to elevated perceived stress was different in IBS and non-IBS or undifferentiated between these groups.

Subjects (n = 192, 16% IBS, 84% controls) were all patients at primary health care clinics in one of three Swedish cities as part of the "Twin Cities" study based at Linköping University. Rome II criteria were assessed by the standard Rome Foundation questionnaire. GI symptom burden was assessed by 14 day diary and measures included percent of days with record of nausea, bloating, any abdominal pain (AP), moderate AP and intense AP. Maximum recorded pain intensity was also noted. Mood was assessed via questions addressing depression symptoms and the EuroQol 5 questionnaire. Stress was measured via the Perceived Stress Scale (PSS). A Structural equation model (SEM) was used to model latent variables for GI symptom burden predicting mood, which then predicted stress. Standardized path coefficients are reported along with measures of model fit.

RESULTS: In the combined sample GI symptom burden was found to predict mood ($b=0.184$, $SE=0.076$) and mood was found to predict stress ($b=0.591$, $SE=0.080$). When stratified, the model path coefficients were not different in any significant respect between IBS and non-IBS patients. GI symptoms

predicting mood yielded: IBS (b = 0.163, SE = 0.176) and control (b = 0.219, SE = 0.090) while for mood predicting stress: IBS (b = 0.708, SE = 0.141) and control (b = 0.582, SE = 0.089). Model fit did not differ significantly between the combined and stratified models, indicating that the subtle observed differences in path coefficients were consistent with random chance. The latent variables representing GI symptoms and mood provided an adequate representation of the GI and mood constructs (c^2/df = 1.73, CFI = 0.99, RMSEA = 0.06). This was equally true in the IBS and control groups.

CONCLUSION: Our data support the general hypothesis that symptom experience is associated with elevated mood disturbance which is associated with elevated levels of psychological stress. However while it has been assumed that there is something special about IBS symptomatology that induces mood disorder, our data suggests that while IBS is associated with higher levels of symptoms, the association between GI symptoms and mood, thence perceived stress exists equally in IBS and non-IBS individuals.

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P0398 FUNCTIONAL SYMPTOMS IN THE GENERAL POPULATION – DIARY VERSUS QUESTIONNAIRE

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INTRODUCTION: Previous studies have found discrepancies between recall and diary reports of symptoms[1]. While questionnaires are commonly used and convenient they can also be prone to recall bias [2]. Since the standard Rome criteria are symptom recall based, if the source of symptom information tangibly changes the clinical picture it calls into question diagnostic criteria.

AIMS & METHODS: We investigated the concordance between the IBS-supportive criteria ''pain relieved by defecation'' and ''onset of stools associated with a change in stool consistency'' between questionnaire recall and prospective diary reports. The present study population consists of 272 participants of a random population based colonoscopy study. Pain relieved by defecation (PRBD) was identified in 7 day diary records by selecting all hours when defecation was reported then checking whether pain was reported in a two-hour window prior to the hour in which defecation was reported but was absent in the two hour window after defecation was reported. The Rome II IBS criterion of stool consistency altered by pain was assessed by comparing the distribution of Bristol stool scores (Bristol) on days when pain was reported to the distribution on days when no pain was reported. Statistical contrasts, based on unconditional logistic regression, are adjusted for repeated measurements on individuals using the linearization method to yield correct standard errors and p-values.

RESULTS: *Pain relieved by defecation*: The PRBD pattern was ever identified in 3.4% of participants compared with the corresponding questionnaire item asking whether pain was ever relieved by defecation in a 3-month recall period where the prevalence was 55.3%. However concordance between diary and questionnaire was only 66.1% and kappa was close to zero (0.07). The PRBD diary pattern was seen significantly more often in persons who reported pain relieved by defecation on the questionnaire (7.2%) than persons who did not (1.3%) indicating that diary and questionnaire are not completely disconnected. *Change in stool form with pain*: Among all participants, hard stools were more often reported on pain days (OR: 4.06, 95% CI: 2.14-7.71, $p < 0.001$ for Bristol score 1 and OR: 2.67, 95% CI: 1.61-4.42, $p < 0.001$ for Bristol score 2). However this was true for all participants, regardless of whether they reported onset of pain or discomfort associated with hard stools on the questionnaire. No difference in the occurrence of loose stools on pain versus non-pain days was observed, not even in participants who reported onset of pain associated with loose stools.

CONCLUSION: The poor concordance between prospective diary and retrospective questionnaire might be due to any of: 1) poor recall when completing questionnaires, 2) symptoms fluctuate over short time scales or 3) a 7 day diary is too short to accurately capture low prevalence conditions. Given the apparent central importance of measurement methodology to prevalence of disease the reasons for this poor concordance needs to be elucidated.

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P0399 EFFECT OF THE FODMAP-RESTRICTED DIET ON COLONIC GAS PRODUCTION CAPACITY IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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INTRODUCTION: The FODMAP-(fermentable oligo-, di-, and monosaccharides and polyols) restricted diet is used as a treatment for functional gastrointestinal disorders such as irritable bowel syndrome (IBS) [1], with the goal of reducing fermentation and gas related symptoms. We wanted to investigate whether the capacity for gas production changed over time when consuming a FODMAP-restricted diet among patients with IBS or functional dyspepsia (FD).

AIMS & METHODS: 29 patients with IBS (n = 19) or FD (n = 10), were diagnosed according to ROME III criteria for IBS and FD (24F/5M, age 34±11y). Participants were instructed thoroughly about the diet from a clinical dietician and followed closely for 6 ± 1 weeks. Repeated 4 days prospective food records (baseline and 6 weeks) were used to measure diet changes and adherence to the diet. Lactulose breath test was performed before, and during the last week of the diet. Participants were adviced to not drink/eat/smoke 10 hours before the test (usually at 8:30). After baseline breath test they consumed 10 g of lactulose dissolved in 120 ml water and breath samples were collected every 15 min for 180 min. Hydrogen and methane gas was analysed in a Model SC Quintron Gas Chromatograph. The area under the curve (AUC) was used as a measurement for gas production, and breath samples before lactulose intake were used to study adherence with the diet. Statistical test used were paired t-test, Wilcoxon signed rank and Spearman and Pearson correlation test.

RESULTS: The FODMAP intake significantly decreased from median 8 g/d to 0.25 g/d ($p < 0.0001$), and good adherence was also verified by baseline breath samples for hydrogen which decreased from median 6 to 2 ppm ($p = 0.0124$), and methane from median 25 to 18 ppm (n.s. $p = 0.6797$). 28 (18 IBS/10 FD) had hydrogen production and there was a significant reduction from median 4418 to 1710 ppmxmin ($p = 0.0035$) during the diet intervention. 9 (7 IBS/2FD) participants had methane production, with a reduction from median 9495 to 6750 ppmxmin (n.s. $p = 0.5415$). Correlation between the change in FODMAP intake and the change in hydrogen ($r = -1609$, $p = 0.4045$) or methane production was not significant ($r = -0.1019$, $p = 0.7943$).

CONCLUSION: The FODMAP-restricted diet was associated with a reduction in the capacity for hydrogen gas production in patients with IBS or FD, which might indicate a shift in colonic microbiome

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P0400 WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN IBS: A MULTIFACETED PROBLEM

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INTRODUCTION: IBS is one of the most prevalent functional gastrointestinal disorders. Earlier studies have shown that IBS patients are more likely to be impaired at work and during daily activities compared to non-IBS patients. However, factors of importance for this impairment have not yet been fully examined.

AIMS & METHODS: Our aim was to investigate the relationship between work impairment and other factors related to IBS. We included 533 patients with IBS (median age 34 (17-80) years, 420 females). The patients completed the Work Productivity and Activity Impairment Questionnaire:IBS (WPAI:IBS), as well as questionnaires to assess IBS symptom severity (IBS-SSS), GI-specific anxiety (VSI), somatic symptoms (PHQ-15), depression and anxiety (HAD), and fatigue (MFI). Uni- and bivariate analyses were performed, as well as linear regression analyses to determine factors independently associated with the work productivity and activity impairment measures.

RESULTS: The IBS patients reported 7±19% (mean±SD) absenteeism (actual work time missed), 33±25% presenteeism (impairment while at work), 36±27% overall work productivity loss and 46±27% activity impairment. Female IBS patients reported greater activity impairment than males (47±27 vs. 41±27%; $p < 0.05$), but no other gender differences were found. A weak, but statistically significant negative association was noted between age and activity impairment ($rho = -0.11$; $p < 0.05$), but otherwise age was not associated with the work productivity and activity impairment. No differences between IBS-subtypes were found. With increasing severity of IBS symptoms, somatic symptoms and GI-specific anxiety, higher degrees of absenteeism, presenteeism, overall work productivity loss and activity impairment were seen ($p < 0.0001$ for all). Among the fatigue measures, physical fatigue, general fatigue and reduced activity demonstrated the strongest associations with the work productivity and activity impairment ($rho = 0.28$-0.47; $p < 0.01$). Weaker, but still statistically significant associations were seen between general anxiety and depression and presenteesim, overall productivity loss and activity impairment ($rho = 0.19$-0.30; $p < 0.05$). Using linear regression analysis, IBS symptom severity, GI-specific anxiety and general fatigue were independently associated with presenteeism ($R^2 = 0.36$; $p < 0.05$) and overall productivity loss ($R^2 = 0.42$; $p < 0.05$), while activity impairment was independently associated with IBS symptom severity and general fatigue ($R^2 = 0.40$; $p < 0.05$).

CONCLUSION: Work productivity and activity impairment is a substantial problem in patients with IBS. A combination of IBS and somatic symptom severity, fatigue and psychological factors seem to impact the IBS patients' ability to be active and productive at work. Based on this, a multidimensional treatment approach for IBS patients seems logical.

Disclosure of Interest: None declared

P0401 THE SEVERITY OF SYMPTOMS RELATED TO IRRITABLE BOWEL SYNDROME IS A RISK FACTOR FOR THE MISCLASSIFICATION OF SIGNIFICANT ORGANIC DISEASE

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INTRODUCTION: The diagnosis of Irritable Bowel Syndrome (IBS) is based mainly of clinical evaluation. The reported incidence of misclassification of significant organic diseases in previously diagnosed IBS patients differs between studies.
AIMS & METHODS: We examined the incidence and risk factors for the diagnosis of significant organic diseases (inflammatory bowel disease (IBD), Celiac disease, gastrointestinal malignancy and thyroid dysfunction) in a cohort of 2645 IBS.
RESULTS: During follow-up, organic disease was diagnosed in 27 subjects (1.03%): IBD in 23, Celiac disease in 2, IBD and Celiac disease in one and hypothyroidism in one. The mean interval from the diagnosis of IBS to the diagnosis of an organic disorder was 13.08±8.51 months. Increased symptom severity was the only significant risk factor for the misclassification of an organic disease (HR 2.26, 95%CI 1.01-5.05 $p = 0.047$). The risk ratio for misclassification of organic diseases in moderate to severe IBS was increased by 2.575 (95%CI 1.10-6.51, $p = 0.027$) in relation to mild IBS.
CONCLUSION: The incidence of misclassification of major organic disease in IBS patients was low. Increased symptoms severity was the only significant risk factor for the misclassification of organic disorders. Further gastrointestinal evaluation should be considered when symptoms are moderate to severe.
Disclosure of Interest: None declared

P0402 BILE ACID DIARRHOEA MASQUERADES AS DIARRHOEA-PREDOMINANT IRRITABLE BOWEL SYNDROME: RESULTS FROM A DUAL CENTRE PROSPECTIVE STUDY

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INTRODUCTION: Several studies have suggested that bile acid diarrhoea (BAD) can present with symptoms that are compatible with diarrhoea-predominant irritable bowel syndrome (IBS-D). However, uncertainty exists as these have often been retrospective, have not defined IBS-D according to accepted diagnostic criteria, or have included patients with chronic diarrhoea in the analysis. We have examined this issue in a well-characterised cohort of patients with rigorously defined IBS-D.
AIMS & METHODS: This was a prospective cross-sectional survey conducted among consecutive patients with IBS-D attending Gastroenterology clinics in two hospitals in Sheffield and Leeds, UK. All patients underwent 23-seleno 25-homo-tauro-cholic acid (SeHCAT) scanning according to local protocol, with a retention of $<15\%$ at day 7 used to confirm BAD. The degree of BAD was classed as severe if retention $<5\%$, moderate if $5.0\% > 9.9\%$, and mild if $10.0\% > 14.9\%$. Presence of IBS-D was defined according to the Rome III criteria. Patients with other known risk factors for BAD, including previous cholecystectomy, terminal ileal Crohn's disease, terminal ileal resection, pelvic or abdominal radiotherapy, coeliac disease, or microscopic colitis, were excluded. Participants completed the patient health questionnaire-15, a validated somatisation score, and the hospital anxiety and depression score. Demographic data, including age, gender, lifestyle, and body mass index (BMI) were collected. The effect of all these factors on presence or absence of BAD was examined by multivariate logistic regression analysis, with results expressed as odds ratios (ORs) with 99% confidence intervals.
RESULTS: This is an interim analysis of an ongoing study. In total, 51 patients with IBS-D according to the Rome III criteria have been recruited to date (37 (72.5%) female, mean age 47.0 years). In total, 14 (27.5%) were found to have BAD following SeHCAT scanning. Of these, nine (17.6%) had severe BAD, four moderate, and one mild. Mean age, BMI, anxiety, depression, and somatisation scores were not significantly different among those with, compared with those without, BAD. No predictors of presence of BAD were identified following multivariate logistic regression.
CONCLUSION: Our data suggest that more than one-in-four IBS-D patients, if investigated, have definite evidence of BAD. In the majority, this is severe. Failure to investigate patients to exclude BAD as an underlying cause of symptoms compatible with IBS-D results in misdiagnosis and a failure to institute effective therapy, in the form of bile acid sequestrants. This suggests that future IBS management guidelines should advocate diagnostic testing to exclude BAD before a diagnosis of IBS-D is made.
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P0403 VALIDATION OF THE USE OF THE ICD-10 DIAGNOSTIC CODE FOR IRRITABLE BOWEL SYNDROME IN THE SWEDISH NATIONAL PATIENT REGISTER

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INTRODUCTION: Irritable bowel syndrome (IBS) is a diagnosis based on symptom criteria. In order to perform epidemiologic studies based on national health-care registers there is a need to assess the accuracy of the diagnostic code in clinical practice at different time points.
AIMS & METHODS: The aim of this study was to evaluate the positive predictive value of the ICD-10 (International Classification of Diseases, version 10) code for IBS in Sweden in hospital based outpatient care during 2005 (using the Rome II criteria) and 2010 (Rome III criteria). We identified all Swedish adults that had received the ICD-10 code for IBS as the main diagnosis during hospital-based outpatient care in 2005 and 2010 by use of the Swedish National Patient Register. We excluded individuals from the IBS cohort if they had been diagnosed with predefined diagnoses, incompatible with IBS, during a time span of 6 months before or after the IBS diagnosis. The National Board of Health and Welfare generated a random sample of 300 identities. Each medical record was retrieved and read by two of the authors (N. J. and H. T.) who noted if symptoms compatible with IBS according to Rome II criteria (2005 cohort) or Rome III criteria (2010 cohort) could be identified.
RESULTS: We received a total of 248 medical records (2005, $n = 127$; 2010, $n = 121$). In 173 patients (70%), the diagnosis fulfilled diagnostic criteria with a high certainty and in 75 patients (30%) it did not. The proportions of valid diagnoses were similar in 2005 (Rome II criteria, 68%) and 2010 (Rome III criteria, 72%) ($\chi_2 = 0.67$, $df = 1$, $p = .41$). Out of the 75 cases that did not fulfill diagnostic criteria, 24 were labeled "probable IBS" because of insufficient medical data. There was no difference when comparing tertiary (72% correct) and secondary care (69% correct) ($p = .62$), but a significant difference in accuracy was noted comparing departments of internal medicine (155/210, 74%) and non internal medicine departments (18/38, 47%) ($p = .001$). The most common reasons for a diagnosis being judged as not valid were: insufficient patient data available in 33 patients (13%), symptoms only including abdominal pain/discomfort *or* abnormal bowel habit in 19 patients (8%), an obvious misuse of the diagnosis in 12 patients (5%) and too short duration of symptoms in 11 cases (4%).
CONCLUSION: The use of the ICD-10 diagnostic code for IBS in Swedish secondary and tertiary care has a high validity in departments of internal medicine but less so in other departments. This finding needs to be addressed when planning and interpreting epidemiologic studies of IBS.
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P0404 ALTERATIONS IN ENTERIC GLIA CELL PHENOTYPE AND FUNCTIONS IN IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Irritable bowel syndrome (IBS) is a complex disease characterized by symptoms including chronic abdominal pain or discomfort and alteration of bowel habit. Increasing evidence demonstrates a central role of intestinal epithelial barrier (IEB) dysfunction, and especially increased paracellular permeability, in the pathophysiology of IBS. The enteric nervous system (ENS), and in particular enteric glial cells (EGC) play a pivotal role in the maintenance of IEB.
AIMS & METHODS: The purpose of this study was to characterize the lesions of the EGC in IBS patients and the putative causative role of soluble factors produced by the colonic IEB microenvironment in these lesions. ***Methods*****:** Eighteen IBS patients (6 constipation-predominant IBS (IBS-C), 6 diarrhea-predominant IBS (IBS-D) and 6 mixed bowel habits IBS (IBS-M) patients) and 9 healthy controls (HC) were included. For each patient gastrointestinal symptoms were assessed using the Rome III questionnaire and colonoscopy was performed with 12 biopsies of left colon. Paracellular and transcellular permeability was measured on 3 biopsies using the Ussing chambers. Supernatant was obtained by incubation of 4 biopsies in Krebs-Hepes solution during 25 minutes at 37°C. At the end of the incubation time, biopsies were processed for Western blot analysis. Both total Glial fibrillary acidic protein (GFAP) expression and the 55-kDa band as well as S100b were analysed. The mRNA expression levels of glial markers (Sox-10; S100b) and inflammatory cytokine TNF-a were measured using real-time PCR. Intracellular calcium flux in response to adenosine triphosphate (ATP) stimulation was measured using Fluo-4 probe in culture of rat EGC after 48h incubation with patients and HC supernatants or protease-activated receptor agonists (SLIGRL and Thrombin), serotonin or histamine.
RESULTS: Paracellular and transcellular permeability of biopsies from all subtypes of IBS patients was similar as compared to HC, except in the IBS-C subtype for which transcellular permeability was significantly increased. No difference in S100b, total GFAP and the specific 55-kDa band expression was observed for any subtype. Sox-10 and S100b mRNA expression was similar in biopsies of all IBS subtypes as compared to HC. Interestingly, we observed a

significant increase in TNF-a mRNA expression in IBS-M but not C or D subtype as compared to control. Intracellular calcium responses (maximal amplitude and half max duration) to ATP were significantly decreased in rat EGC cultures incubated with supernatants of IBS-D and M but not C subtypes as compared to control. No difference in calcic response to ATP was observed in EGC cultures after incubation with different SLIGRL, thrombin, serotonin and histamine concentrations.

CONCLUSION: Our study demonstrates that enteric glial phenotype and functions are altered in IBS in a subtype dependent fashion. The mediators responsible for these changes as well as the functional consequences of these changes remain to be identified.

Disclosure of Interest: None declared

P0405 ABDOMINAL PAIN VERSUS ABDOMINAL DISCOMFORT: IMPLICATIONS FOR DIAGNOSTIC ASSESSMENT OF IRRITABLE BOWEL SYNDROME (IBS)

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INTRODUCTION: Diagnostic questions in the current Rome criteria for IBS inquire about frequency of abdominal "discomfort or pain", whereas the U. S. Food and Drug Administration guidelines for IBS clinical trials only reference abdominal pain frequency. It is unknown to what extent people perceive abdominal pain and discomfort differently or whether both are needed in GI diagnosis questions.

AIMS & METHODS: We compared abdominal pain and discomfort ratings in a U. S. nationwide internet community survey of 328 adults, containing the Rome III diagnostic questions for IBS in the new response formats planned for Rome IV diagnoses (Gastroenterology 2013;144(5) Suppl.1:S-916), including the standard "in the past 3 months, how often did you have discomfort or pain anywhere in your abdomen?" and alternative forms of that question replacing "abdominal discomfort or pain" with only "pain" or only "discomfort". Also included was a multiple-choice question about the extent to which abdominal pain and discomfort are experienced as separate sensations, and demographic questions. To avoid over-estimating agreement between alternative question forms, responses from people who reported having neither pain nor discomfort in the abdomen in the past 3 months were excluded from analysis, as well as those inconsistent on either of two repeated quality-check questions, leaving 218 for analysis. Analysis calculated percent agreement between alternate question forms, and also Cohen's Kappa (K-values) for diagnostic performance as this controls for rate of chance agreement (K > 0.8 = excellent agreement).

RESULTS: The subjects (52.8% females; mean age = 45.8, range 19-85 years) varied widely in their perception of the relationship between abdominal pain and discomfort: 33.9% stated they were entirely or mostly independent sensations, 27.1% that they were mostly or entirely the same sensation, and 39.0% that both were equally true – i.e., they could be either separate sensations or discomfort a mild version of pain. Only about half of subjects rated frequency of pain alone (52.8%) and discomfort alone (55.5%) as identical in intensity (i.e., same response option chosen on the 9-point frequency scale) to ratings on the standard "pain or discomfort" question. However, when the diagnostic frequency threshold for IBS (>3 days a month in the past 3 months) was compared, the agreement with "pain or discomfort" on that threshold being met (when met by either version) was 72.4% (K = 0.63) for the pain alone and 76.8% (K = 0.66) for discomfort alone, and 81.3% between the latter two (K = 0.74). When full IBS criteria were examined using the 3 different question versions, the agreement with the standard question version when at least one method qualified subjects as IBS was 80.8% (K = 0.85) for the pain-only version and 87.7% (K = 0.90) for discomfort-only, with the latter two also showing 87.7% agreement (K = 0.90). IBS diagnosis with discomfort alone diagnosed a slightly higher rate of IBS (71 cases) compared to the other 2 versions (66 cases each).

CONCLUSION: The use of abdominal "discomfort or pain" as a criterion for IBS diagnosis is ambiguous because there is no agreement among U. S. adults regarding whether these are qualitatively different sensations. However, in 4 out of every 5 cases the same individuals would be diagnosed IBS regardless of which descriptor is used. [Supported by a grant from Salix Pharmaceuticals]

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P0406 PREVALENCE OF ORGANIC GASTROINTESTINAL DISEASE IN SUSPECTED IRRITABLE BOWEL SYNDROME (IBS) VARIES ACCORDING TO SUBTYPE

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INTRODUCTION: In patients who report symptoms compatible with IBS in the absence of alarm symptoms, guidelines suggest the diagnosis can be made without investigations. However, there are few validation studies of the current gold-standard, the Rome III criteria, and the prevalence of organic gastrointestinal (GI) disease in people with suspected IBS is unclear.

AIMS & METHODS: We evaluated consecutive patients with Rome III-defined IBS, and examined whether prevalence of organic GI disease varied according to IBS subtype, or the presence or absence of alarm symptoms. Demographic and symptom data were collected from 4224 patients with GI symptoms attending outpatient clinics at two hospitals in Hamilton, Ontario. Participants completed the Rome III diagnostic questionnaire for the functional GI disorders, which was used to categorise IBS subtype. Individuals underwent colonoscopy, with assessors blinded to symptom status. Patients with normal colonoscopy and no evidence of coeliac disease were classed as having no organic GI disease. Prevalence of organic GI disease was compared according to IBS subtype, and in patients who did, compared with those who did not, report alarm symptoms (weight loss, rectal bleeding, anaemia, or family history of colorectal cancer) using a χ^2 test.

RESULTS: 537 patients met Rome III criteria for IBS (mean age 42yrs, 404 (75.2%) females). Organic GI disease was present in 138 (25.7%), with the commonest finding Crohn's disease (n = 46 (8.6%)). 63 patients had IBS-C, 209 IBS-D, and 265 IBS-M. Prevalence of organic GI disease was significantly lower in IBS-C (n = 8 (12.7%)) versus IBS-D (n = 67 (32.1%)) or IBS-M (n = 63 (23.8%)) (p = 0.005) (Table). In the 410 patients who reported ≥1 alarm symptom, prevalence of organic GI disease was significantly higher (n = 116 (28.3%)) compared with 127 patients who did not report any alarm symptom (n = 22 (17.3%)) (p = 0.013). In IBS-D, there was a significantly higher prevalence of organic GI disease in those with alarm symptoms (36.0%) compared with those without (17.85%) (p = 0.02). However, IBS-C and IBS-M prevalence of organic GI disease in patients with alarm symptoms versus those without was not significantly higher (IBS-C 11.6% versus 15.0%, p = 0.708; IBS-M 25.6% versus 17.7%, p = 0.202

	Total IBS (n = 537)	IBS-D (n = 209)	IBS-C (n = 63)	IBS-M (n = 265)
No organic GI disease (%)	399 (74.3)	142 (67.9)	55 (87.3)	202 (76.2)
Ulcerative colitis (%)	34 (6.3)	19 (9.1)	1 (1.6)	14 (5.3)
Crohn's disease (%)	46 (8.6)	21 (10.0)	2 (3.2)	23 (8.7)
Colorectal cancer (%)	14 (2.6)	5 (2.4)	2 (3.2)	7 (2.6)
IBD unclassifiable (%)	24 (4.5)	11 (5.3)	2 (3.2)	11 (4.2)
Microscopic colitis (%)	12 (2.2)	8 (3.8)	0 (0)	4 (1.5)
Coeliac disease (%)	8 (1.5)	2 (1.0)	2 (3.2)	4 (1.5)

CONCLUSION: Patients with suspected IBS-C are unlikely to have underlying organic GI disease, compared with IBS-D or IBS-M. Although the incorporation of the absence of alarm symptoms into the diagnostic criteria for IBS reduced the likelihood of organic GI disease, this was only for IBS-D and, because alarm symptoms are so common, ≥60% of patients still have normal investigations. Better ways of diagnosing IBS are needed.

Disclosure of Interest: None declared

P0407 SOMATISATION LEVEL VARIES ACCORDING TO IRRITABLE BOWEL SYNDROME (IBS) SUBTYPE AND DRIVES BLOATING SEVERITY

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INTRODUCTION: Literature suggests that somatisation is strongly associated with IBS. However, it remains unclear whether the degree of somatisation varies according to IBS subtype. Furthermore, whether there is an association between higher levels of somatisation and more severe IBS symptoms is unknown.

AIMS & METHODS: Demographic and symptom data were collected from 4224 adult patients attending gastrointestinal (GI) outpatient clinics at two hospitals in Hamilton, Ontario. Participants completed the Rome III diagnostic questionnaire for the functional GI disorders. Somatisation data were collected via the Patient Health Questionnaire-15 (PHQ-15), comprising 15 somatic symptom items. To avoid overestimation of the severity of somatisation we excluded the 3 GI items from the original PHQ-15 questionnaire to form the PHQ-12. Somatisation severity was categorised according to total PHQ-12 (minimal ≤3, low 4-7, medium 8-12 and high ≥13) with a maximum somatisation score of 24. Mean somatisation score and total number of somatic symptoms reported were compared between IBS subtypes (diarrhoea-predominant (IBS-D), constipation-predominant (IBS-C), and mixed stool pattern (IBS-M)) using analysis of variance. The effect of level of somatisation on the severity of individual IBS symptoms, including lower abdominal pain or discomfort, stool frequency, stool consistency, bloating or abdominal distension, tenesmus, and urgency was compared according to IBS subtype using a χ^2 test with P values of <0.01 denoting statistical significance.

RESULTS: 840 patients met the Rome III criteria for IBS and provided complete somatisation data (mean age 38.3 years, 702 female (83.6%)). Of these, 289 patients had IBS-D, 138 IBS-C, and 413 had IBS-M. Mean PHQ-12 scores were significantly higher in those with IBS-M (n = 10.35), compared with IBS-C (n = 8.94) or IBS-D (n = 9.24) respectively (P < 0.001). Mean number of PHQ-12 symptoms reported was also significantly higher in IBS-M patients (7.2) compared with patients with IBS-C (n = 6.2) or IBS-D (n = 6.4) respectively (P < 0.001). High level of somatisation was present in 222 patients (26.4%).

The prevalence of a high level of somatisation was significantly greater in patients with IBS-M (131 patients (31.7%)) compared with IBS-C (31 (22.5%)) or IBS-D (60 (20.8%)) respectively ($p = 0.003$). For all subtypes of IBS, high levels of somatisation were associated with a greater severity of bloating or abdominal distension ($P < 0.001$ for IBS-M and IBS-D, and $p = 0.004$ for IBS-C respectively). For patients with IBS-M, high levels of somatisation were also associated with a significantly greater prevalence of likelihood of reporting < 3 stool per week ($p = 0.001$). No other significant associations between somatisation severity and symptom severity were observed.

CONCLUSION: IBS-M is strongly associated with higher levels of somatisation. The number of reported somatic symptoms reported is higher in IBS-M compared with other IBS subtypes. Severity of bloating or abdominal distension reported by all patients with IBS is strongly associated with high levels of somatisation. This suggests psychological stress may drive the severity of this commonly reported symptom in IBS, and may partly explain why it can be difficult to treat.

Disclosure of Interest: None declared

P0408 INTESTINAL AND SYSTEMIC IMMUNE MARKERS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Immune activation (low grade inflammation) and an altered intestinal microbiota are postulated to be involved in the multi-factorial pathophysiology of Irritable Bowel Syndrome (IBS), especially in the diarrhea predominant subtype. Fecal calprotectin and plasma cytokines, as markers of intestinal inflammation and systemic immune activation, respectively, and the antimicrobial protein human beta defesin-2 (HBD-2), have previously been assessed in IBS patients, but results were inconsistent and numbers were too small for subtype analyses.

AIMS & METHODS: The aim of our study was to compare fecal calprotectin, HBD-2 and plasma cytokines levels of a large well characterized IBS cohort to healthy controls (HC), and to assess differences between subtypes.

Fecal and blood samples were obtained from IBS patients (Rome III) and age- and gender-matched HC. Calprotectin and HBD-2 levels in fecal samples were analyzed by ELISA, while non-stimulated levels of IL-1β, IL-6, IL-8, IL-10, IL-12P70 and TNF-α were assessed by Luminex assay. Kruskal Wallis test was used for multi-group comparison and Mann-Whitney U test for 2-group comparisons, with post-hoc Bonferroni correction (for multiple testing).

RESULTS: We included 164 HC and 264 IBS patients (IBS < SUB > TOTAL < / SUB >): 92 diarrhea predominant (IBS-D), 48 constipation predominant (IBS-C), 105 with mixed stools (IBS-M) and 19 with undefined subtype (IBS-U). IBS-U was not analyzed separately due to small numbers. Calprotectin was higher in IBS < SUB > TOTAL < /SUB > compared to HC (median [IQR]: 40.3 [19;81] vs. 20.4 [5-48] ug/g, $p < 0.001$, resp), and in all IBS-subtypes compared to HC. HBD-2 levels were lower in IBS < SUB > TOTAL < /SUB > compared to HC (31.0 [18;48] vs. 37.5 [27;60] ng/g, $p < 0.01$), which was also true for IBS-D vs. HC. The cytokines IL-1β (0.11 [0.11;1.12] vs. 0.11 [0.11;1.46] ug/l, $p < 0.01$) and IL-6 (0.19 [0.19;0.19] vs. 0.52 [0.19;3.13] ug/l, $p < 0.01$) were lower in IBS < SUB > TOTAL < /SUB > vs. HC, while IL-12p70 (0.08 [0.08;3.52] vs. 0.08 [0.08;1.53] ug/l, $p < 0.01$) and TNF-α (0.45 [0.26;0.69] vs. 0.67 [0.38;8.32] ug/l, $p < 0.01$) were higher IBS < SUB > TOTAL < /SUB > compared to HC. The IL10/12 ratio was also lower in IBS_{TOTAL} compared to HC (0.45 [0.26;0.69] vs. 0.67 [0.38;8.32], $p < 0.01$). The findings were consistent for all subtypes, apart for TNF-α being only increased in IBS-D and no differences found between all subtypes and HC for IL-1β. No significant differences were found for IL-8 and -10.

CONCLUSION: Calprotectin levels were significantly higher, but mildly elevated, in IBS patients and all subtypes compared to HC, pointing to low grade mucosal inflammation in IBS. The overall cytokine levels were low, but combined systemic cytokine data point to a pro-inflammatory state in the total group of IBS patients as well as in all subtypes. Interestingly, HBD-2 levels were lower in IBS patients compared to HC, especially in IBS-D, suggesting an altered host-microbe interaction.

In conclusion, our data point to a low-grade mucosal and systemic inflammatory state with reduced intestinal defensin levels in IBS patients when compared to healthy controls. The findings did not depend on dominant bowel habits, indicating that immune activation may plays a role in the pathophysiology of all IBS subtypes.

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P0409 ENDOSCOPIC FINDINGS AND CLINICOPATHOLOGIC CHARACTERISTICS OF ISCHEMIC COLITIS: A PORTUGUESE CENTER EXPERIENCE

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INTRODUCTION: Ischemic colitis (IC) is the most common vascular disorder of the intestinal tract and the second most common cause of lower digestive bleeding. The clinical disease course of ischemic colitis may vary from self-limiting to life-threatening and has a wide spectrum of endoscopic findings.

AIMS & METHODS: In this study, we made a retrospective analysis of endoscopy findings and clinicopathologic characteristics of IC in the endoscopy center of our hospital during the last 10 years (2002 to 2012) and try to identify the predictors of endoscopic severity of IC. The data collected included demographic (age, gender), clinical (symptoms, comorbidities and medication), laboratory (hemoglobin, leucocytes, C-reactive protein, lactate dehydrogenase), and endoscopic findings (localization, extension, severity of the lesions) and outcomes (length of hospitalization stay, treatment and death).

RESULTS: The study included 194 patients (92 women; 62 men), with mean age of 75 years. The most common comorbid disease was hypertension (56.5%), followed by cardiovascular disease (21.5%), arrhythmias (14.8%) and cerebrovascular disease (6.6%). The majority of patients had a history of drug use (89.6%), 23.4% of them nonsteroidal anti-inflammatory agents and 13.6% digitalis preparations. Hematochezias (79.2%) and abdominal pain (73.3%) were the most common presentation symptoms. The average elapsed time between the beginning of the symptoms and the diagnosis was 2,1 days. Ischemic lesions were located mainly in the left colon (77.3%) and were found in more than 2 colonic segments in 42.9%. The endoscopic lesions were grade I in 57.1%, grade II in 39.6% and grade III in 3.2% of patients. The involvement of more than 2 colonic segments ($\rho < 0.0001$), the involvement of sigmoid and descendent colon ($\rho < 0.0001$), anemia ($\rho < 0.04$), and mortality ($\rho < 0.0001$) were significantly higher in patients with severe endoscopic lesions. Death occurred in 4 patients (2.6%) and surgery was performed in only 1 patient. The mean length of hospital stay was 7.5 days. The involvement of more than 2 colonic segments ($p > 0.0001$), longer elapsing time between the beginning of symptoms and the diagnosis ($p > 0.0001$), antibiotics use ($p > 0.009$) and age higher than 80 years ($p < 0.001$) were related to longer hospitalization.

CONCLUSION: In our study, the majority of patients were female, over 50 years of age and with several risk factors. The clinical disease course was self-limiting and was associated a low mortality. The involvement of more than 2 colonic segments, the involvement of sigmoid and descending colon and anemia may be predictive factors of endoscopic severity in IC. An intimate knowledge of endoscopic findings and pathologic characteristics of ischemic colitis plays a pivotal role in decreasing the misdiagnosis rate of ischemic colitis.

Disclosure of Interest: None declared

P0410 THE CLINICAL CHARACTERISTICS OF PATIENTS WITH PNEUMATOSIS CYSTOIDES INTESTINALIS IN JAPAN

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INTRODUCTION: Pneumatosis cystoides intestinalis (PCI) is a relatively rare disease, in which multilocular or linear pneumatic cysts developed under the mucosa or serosa of the intestinal wall. In recent years, with the advances in imaging technologies, the number of reported cases of PCI has been increasing. Here, we investigated the clinical characteristics of patients with PCI.

AIMS & METHODS: 55 patients were diagnosed as PCI at Kyorin University Hospital during the 6-year period from September 2007 to August 2013. We conducted a retrospective analysis of the clinical characteristics of these patients, including sex, age, the site of lesion, symptoms and treatments.

RESULTS: The male to female ratio was 29:26 and the median age was 64.7 years. The diagnosis was made by CT(47 cases), or colonoscopy (8 cases). In regard to the site of lesion, the stomach was 2 patients, small intestine was 18 patients, ascending colon was 26 patients, transverse colon was 4 patients, descending colon was 2 patients and the sigmoid colon was 2 patients. 31 patients complained of symptoms of abdominal pain (18), abdominal distension (9), fever (2), diarrhea (2), and melena (1). There were 20 patients whose condition was idiopathic and 35 patients whose condition was secondary to other underlying diseases including diabetes (12), malignant tumors (9), intestinal tract necrosis (9), collagenosis (7), constipation (1), chronic obstructive pulmonary disease (1) and ileus (1). Eleven patients had a history of steroid use, and 12 patients had a history of treatment with α-glucosidase inhibitors. Thirty-four patients received in hospital treatment including conservative treatments such as nil by mouth, treatment with prokinetic agents, supplemental oxygen in 24 patients—and abdominal operation in 11 patients. Portal venous gas (HPVG) was observed in 9 patients, and 8 of these had underlying intestinal tract necrosis.

CONCLUSION: In most patients, PCI is mild, asymptomatic and resolves spontaneously. The principally used treatment strategy for PCI is conservative treatment. Appropriate consideration of the indications for operation is important for avoiding unnecessary invasive treatment. However, especially in cases of PCI complicated by HPVG, underlying intestinal tract necrosis should be borne in mind and it seems to be important to promptly determine whether emergency surgery is needed. There are numerous unresolved issues in respect of the pathological characteristics of PCI, therefore, further accumulation and examination

of cases are necessary. Further elucidation of the pathological characteristics and establishment of suitable treatments are expected.
Disclosure of Interest: None declared

P0411 PROFILE AND OUTCOME OF PATIENTS WITH ISCHEMIC COLITIS

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INTRODUCTION: - Ischemic colitis incidence is most likely underestimated because the mild form often is of transient nature and misdiagnosed when patients suffer from other diseases such as inflammatory bowel disease or infectious colitis.
AIMS & METHODS: We prospectively studied patients referrd for colonoscopy for lower gastro-intestinal bleeding from January 2013 until January 2014.
There were enrolled 74 patients (27 females and 47 males), aged between 20 to 75 years old, with a median age of 51 years old.
The findings at colonoscopy will depend on the stage and severity of ischemia. In the early stages of ischemia, petechial hemorrhages are interspersed with areas of pale, edematous mucosa. Later, segmental erythema, with or without ulcerations and bleeding, may be observed. The colon single-stripe sign, a single longitudinal ulcerated or inflamed colon strip, may characterize milder disease. With more severe ischemia, the mucosa appears cyanotic, dusky, gray, or black. Pseudopolyps and pseudomembranes may be appreciated, as well. A chronic stage of ischemia characterized by stricture, decreased haustrations, and mucosal granularity may occur several weeks or months later.
There are no endoscopic findings that are specific for ischemia, thus the clinical setting must be considered.
RESULTS: Conditions mandating anticoagulation, such as atrial fibrillation or dilated cardiomyopathy, were identified in 32% of case patients. Conditions requiring antiarrhythmic therapy were identified in 25% of case patients; in 4 of the patients, cocaine was identified as the leading cause.
Of 74 patients, 5 required immediate surgery and 3 of them were positive for clostridium difficile.
CONCLUSION: Ischemic colitis occurs as the result of a compromise in intestinal blood flow that can produce a spectrum of injury from transient self-limited ischemia to fulminant ischemia or transmural infarction. Its diagnosis requires a high index of suspicion, and the clinician should consider the diagnosis in patients with acute abdominal pain and bloody stools.
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Disclosure of Interest: None declared

P0412 CHRONIC KIDNEY DISEASE AND HIGH ECOG PERFORMANCE STATUS ARE RISK FACTORS FOR SEVERE ISCHEMIC COLITIS

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INTRODUCTION: Ischemic colitis is most frequent form of intestinal ischemic disease. However, there have been debates about prognostic factors of ischemic colitis
AIMS & METHODS: The aim of this study was to identify risk factors of severe ischemic colitis. From January 2000 to December 2011, a retrospective study was undertaken of patients with ischemic colitis hospitalized at 4 university hospitals and 2 secondary hospitals at Busan, Korea. Patients with colon ischemia were divided into two groups: those with mild disease and those with severe disease. Data collected included age, sex, symptoms (abdominal pain, hematochezia and abdominal angina), cormobidity (hypertension, diabetes mellitus, ischemic heart disease, stroke, arrhythmia, congestive heart failure, peripheral vascular disease, chronic obstructive lung disease, chronic kidney disease, hemodialysis, peritoneal dialysis, hyperthyroidism, hypothyroidism and irritable bowel syndrome), laboratory findings (total cholesterol, TG, LDL, HDL, total protein, albumin, Hg, WBC count, Platelet count, ESR and CRP), endoscopic fidings (location of lesions), and ECOG performance status.
RESULTS: A total of 292 patients were enrolled (mild group: 259, severe group: 33). In univariate analysis, location (involving Rt. Colon), chronic kidney disease (stage V), ECOG, Platelet count, CRP were significant risk factors for severe ischemic colitis. In multivariate analysis, chronic kidney disease (stage V) (OR, 5.289; 95% CI 1.308-21.378; $p = 0.019$), ECOG (OR, 1.690; 95% CI 1.108-2.579; $p = 0.015$) were significant risk factors for severe ischemic colitis.
CONCLUSION: Chronic kidney disease (stage V) and high ECOG performance status were independent risk factors for severe ischemic colitis. More caution would be necessary when treatment of patients with ischemic colitis having these factors.
Disclosure of Interest: None declared

P0413 RESECT AND DISCARD (RD) STRATEGY FOR COLONIC POLYPS- AN ASIAN PERSPECTIVE, ARE WE READY?

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INTRODUCTION: The current practice of routinely resecting all diminutive (1-5mm) and small (6-9mm) colonic polyps and submitting them for histopathologic assessment has several disadvantage in terms of cost-effectiveness and risks from repeated colonoscopies. The resect-and-discard (RD) strategy has been proposed to reduce retrieval of diminutive polyps (1-5mm) for histology which has been deemed not to have advanced histologic features. RD strategy for small polyps (6-9mm) are still controversial. The prevalence of advanced histologic features in the diminutive and small polyp category remains small but not clearly defined.
AIMS & METHODS: In this cross-sectional study, we aim to find the prevalence of small & diminutive polyps resected that shows advanced histologic features such as high grade dysplasia (HGD) or carcinoma to determine if RD policy is feasible in the local Asian tertiary setting. Data was retrieved from Jan-Dec 2009 with assistance from the Pathology Department to identify all submitted colonic polyp specimens. Each patient also had their colonoscopy report (s) and detailed histology report reviewed by 2 separate colleagues within the team to ensure data consistency. The variables captured include demographics, total polyp number, polyp distribution in the colon, histology, polyp size and respective number in each histology subtype and concurrent colorectal carcinoma (CRC).
RESULTS: There were a total 1482 polypectomy specimens retrieved for histology from 871 patients. The colonic distribution of the polyps was 45.4% right sided, 46.1% left sided and 8.5% rectal.
Please refer to Table 1 for summary of polyp distribution and dysplasia.

Colonic polyp histology	Tubular Adenoma (TA)	Tubulovillous Adenoma (TVA)	Villous Adenoma (VA)	Serrated Adenoma (SA)	Hyperplastic
Low grade dysplasia (LGD)	79.2%	26.7%	0.0%	83.9%	NA
High grade dysplasia (HGD)	20.8%	73.3%	100.0%		
No dysplasia	NA	NA	NA	16.1%	100.0%
Total number (1482)	1067(72%)	150(10.1%)	3(0.2%)	118(8.0%)	144(9.7%)

There were 844 diminutive polyps (1-5mm), 447 small polyps (6-9mm) and 191 large polyps (≥10mm). The proportion of HGD seen in each of these groups were 18.7%, 37.6% and 56.5% respectively. The percentage of HGD present in diminutive and small polyps was relatively high and significant. There were no concurrent carcinomatous features seen in all the polyps.
CONCLUSION: These findings showed that a significant proportion of diminutive polyps (18.7%) and small polyps (37.6%) harboured features of HGD, which is significantly higher than previous findings of 1% for diminutive polyps in some literatures. Based on size alone without the aid of narrow band imaging (NBI) or other forms of image enhanced endoscopy (IEE), we find that RD strategy for diminutive or small polyps may miss a significant group of patients with advanced neoplastic histology who needs earlier colonoscopic surveillance. There may be merits in the RD approach but this would require incorporation of other real-time endoscopic modalities such as IEE and more robust evaluation
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P0414 THE STRAY PATIENT DEMOGRAPHIC LABEL: IMPLICATIONS FOR PATIENT SAFETY AND QUALITY IN THE ENDOSCOPY UNIT

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INTRODUCTION: Over a 6-month period, 3 separate incidents occurred in our unit where the wrong patient demographic labels were affixed to the endoscopy biopsy requisition form (EBRF), the biopsy specimen container (BSC) or both. This type of incident can have a significant impact on patient safety and is an indicator of poor quality in the specimen control process.
AIMS & METHODS: The purpose of this study was to identify factors contributing to this medical error and to develop a process to prevent future occurrences. A Quality Assurance Review (QAR) was conducted to determine the systems issues that contributed to the incidents. This review was carried out at the Royal Alexandra Hospital in Edmonton, Canada. The endoscopy unit at this hospital performs about 18,000 procedures per year. A QAR using Systems Analysis Method of Review (SAM) was conducted to identify issues that contributed to the patient-specimen mismatches. SAM identified the following system issues: a) variation in the set-up of nursing workspaces, b) variation in where and when the EBRF was completed, and c) the occurrence of stray patient demographic labels. The QAR identified several recommendations to prevent future mislabeling: a) standardize how nursing workspaces are set up, b) develop a checklist to ensure proper patient identification prior to procedure initiation, proper labeling of EBRF and BSC, completion of EBRF, and c) remove all patient demographic labels from the theatre immediately after the conclusion of the procedure.

RESULTS: Since EBRF and BSC mislabeling incidents are rare events; we utilized indicators of EBRF information quality as surrogate markers for effectiveness of the QAR recommendations. We deemed the following factors as key quality indicators of EBRF information: a) completion of clinical history by physician, b) correct identification of specimen anatomic site, c) avoidance of ambiguous terminology, and d) correct patient label on EBRF and BSC. We tracked these indicators daily. We reported the data weekly to physician leaders and other healthcare providers in order to engage them in this initiative. We used the Reporting and Learning System (RLS) for patient safety to monitor reporting of similar incidents prior to implementation of the QAR recommendations, the average number of EBRF containing deficient information was 16.6/month. Subsequent to the implementation of QAR recommendations, this number decreased to 6.4/month ($p = 0.02$). However, in the 7 months subsequent to the QAR recommendation implementation, we had 4 further incident of mislabeling with the wrong patient label and 3 episodes of unlabeled specimen containers.
CONCLUSION: Stray patient data labels are a significant contributing factor to EBRF and BSC mislabeling. QARs can reduce the incidence of this medical error and improve quality of EBRF completion; however, without health care provider engagement, serious incidents may still occur.
Disclosure of Interest: None declared

P0415 A NOVEL SAMPLING DEVICE FOR COLLECTING MUCOCELLULAR MATERIAL FROM THE UNPREPARED RECTUM

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INTRODUCTION: Earlier detection of colorectal and other gastrointestinal malignancies is an urgent objective. Currently much effort is directed at the development of in vitro diagnostic tests that evaluate informative protein or DNA biomarkers in blood or stool samples. Stool samples are relatively inconvenient to collect, require special handling facilities, and additionally suffer from contamination that may interfere with molecular assays. Blood samples, while more convenient, may not be as informative early in the disease process. Several studies have shown that significant numbers of exfoliated cells and their products are retained in a muco-cellular layer overlying the colonic mucosa but distinct from the stool itself, and that this material flows toward the rectum, where it can be captured for analysis
AIMS & METHODS: Origin Sciences has developed a novel sampling device, which incorporates an inflatable nitrile membrane. Following insertion into the unprepared rectum via a standard proctoscope, the membrane is inflated to make contact with the rectal mucosa for 10 seconds. The membrane is then deflated and retracted into the device prior to removal from the patient. Upon retraction the material sampled from the rectal mucosa is retained on the inverted membrane, which acts as a receptacle for the addition of buffer to preserve the material for subsequent analysis.
RESULTS: The sampler has now been tested in over 2000 patients and healthy volunteers, and has shown excellent patient acceptability. Tests and in vitro experiments with monolayers of cultured human cells indicate that the membrane captures intact cells, which are easily washed off the membrane for further investigation. Detailed evaluation of the mucous-associated soluble material captured by the device in both normal and diseased states, shows it to be rich in protein and nucleic acids. Levels of soluble protein material present in the buffer vary between 90 and 3000 μg/mL, with a mean of 710 μg/mL. As part of a programme to identify novel cancer biomarkers, Origin Sciences has evaluated the presence of auto-antibodies in the proteinaceous component of the preparation, and has detected informative auto-antibody isotypes IgA, IgG and IgM by ELISA. The preparation is also rich in nucleic acids. DNA is found in amounts ranging from 0.5 to 21.9 ug/mL. Laboratory experiments have shown that this DNA retains a high degree of integrity and is suitable for PCR amplification, and subsequent sequencing, since we have been able to detect a number of genes by quantitative PCR.
CONCLUSION: The sampling device represents a novel and minimally invasive means of capturing biomarker-rich material from the unprepared rectum. Since there is minimal contamination by stool, the material collected is readily analysable, in principle lending itself to Point of Care tests for a wide range of indications, including infectious and inflammatory diseases of the GI tract in addition to malignancy. The device can be used as a robust means of collecting material for later analysis by a wide range of technologies.
Disclosure of Interest: None declared

P0416 SYMPTOM-SPECIFIC REFERRAL CONTENT: WHAT DOES THE GASTROENTEROLOGIST NEED?

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INTRODUCTION: Low quality referrals are a challenge for gastroenterologists when assessing and prioritizing the patients. However, it is not known which information the gastroenterologists rely on for this task. We wanted to identify what gastroenterologists considered the most important variables to include in the referral letters for 9 common indications.
AIMS & METHODS: 25 Norwegian gastroenterologists completed a web-based survey where they were asked to select the 15 most important variables out of a list of 29-36 potential variables.
RESULTS: For all 9 indications, information about duration, current medical treatment and weight loss were selected. The remaining selected variables were for:
Dyspepsia: Medical history, nausea/vomiting, reflux, hematemesis, dysphagia, abdominal pain, effect of anti-acid treatment, general condition, abdominal palpation (AP), previous gastroscopies and lab-analyses for anaemia and faecal occult blood (FOBT).
Dysphagia: Progression (intermittent, stable, progressive), texture provoking dysphagia, subjective localization of obstruction, hematemesis, regurgitation of undigested foods, presence of reflux, stimulantia, ulcerogenic medication, general condition, previous endoscopies and radiology and lab-analyses for anaemia.
Diarrhoea: Hematochezia, nocturnal diarrhoea, recent antibiotic treatment, general condition, digital rectal exploration (DRE), previous endoscopies and lab-analyses for anaemia, FOBT, celiac disease, infection/inflammation, inflammatory bowel disease (IBD) and faecal bacteria/parasites.
Bowel changes: Type of change, hematochezia, abdominal pain, B symptoms (fever, night sweat, weight loss), AP, DRE, general condition, previous endoscopies and lab-analyses for anaemia, celiac disease, IBD and FOBT.
Hematochezia: Blood colour, location of blood (on paper/on faeces/in faeces), percentage of bowel movements with observed blood, bowel changes, symptoms from upper or lower GI-tractus, hematemesis, AP, DRE, previous endoscopies and lab-analyses for anaemia, IBD and FOBT.
Chronic abdominal pain: Medical history, characterization and location of pain, nocturnal pain, relation to meals, presence of bowel changes, AP, general condition, previous radiology/endoscopies and lab-analyses for anaemia, liver/pancreatic function, IBD and FOBT.
Constipation: Main complaint (hard/ rare/slow etc), frequency and consistency of bowel movements, hematochezia, abdominal pain, effect of treatment-attempts, predisposing factors, AP, DRE, previous endoscopies and lab-analyses for anaemia, thyroid disease and FOBT.
Jaundice: Medical history, exposure liver-toxic substances, stimulantia, colour changes urine/faeces, abdominal pain, AP, liver stigmata, previous radiology and lab-analyses for liver/pancreatic function, hepatitis serology, specific liver diseases and infection/inflammation.
Weight loss: Presence of any abdominal symptoms, B symptoms, abdominal pain, appetite, food intake, general condition, AP, symptoms/findings from other organ-systems, previous radiology and lab-analyses for anaemia, celiac disease and FOBT.
CONCLUSION: We identified 15 variables considered essential by gastroenterologists for each of the 9 most common reasons for referrals. Validation of the relation between the findings and the quality of referrals remains unknown, and need further assessments.
Disclosure of Interest: None declared

P0417 PREVIOUS SCREENING EPISODE PREDICTORS OF REPEAT PARTICIPATION IN THE NHS BOWEL CANCER SCREENING PROGRAMME

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INTRODUCTION: Effective colorectal cancer (CRC) screening using faecal occult blood (FOB) tests requires adherence to a programme of repeat participation. This study investigated previous screening episode predictors of screening uptake among previous responders.
AIMS & METHODS: The NHS Bowel Cancer Screening Programme (BCSP) in England offers biennial screening using a guaiac FOB test. Uptake data for the second (R2) and third (R3) biennial invitation round were studied among 62,099 individuals (aged 60-64) in the Southern Hub of the BCSP. R3 invitees comprised three subgroups: 'Consistent Screeners' (screened in R1 and R2), 'Dropouts' (screened in R1, not screened in R2) and 'Late Entrants' (not screened in R1, screened in R2). Predictors of uptake derived from previous screening episodes included late return of the test kit (after more than 28 days), test results and compliance with follow-up investigations (usually colonoscopy). Age, gender, area-level socioeconomic deprivation and screening history were included in multivariable logistic regression analyses.
RESULTS: Overall uptake among previous responders was 86.6% in R2 and 88.6% in R3. In R3, repeat uptake was 94.5% among 'Consistent Screeners', 59.8% among 'Dropouts' and 78.0% among 'Late Entrants' (differences between groups, $p < 0.001$). Returning the test kit after more than 28 days in a previous episode was associated with a reduced likelihood of repeat uptake in R2 (82.3% vs. 88.7%, $p < 0.001$) and R3 (84.5% vs 90.5%, $p < 0.001$). Receiving an abnormal test result was also strongly associated with reduced repeat uptake in R2 (61.4% vs. 86.8%, $p < 0.001$) and R3 (65.7% vs. 88.8%, $p < 0.001$). Furthermore, repeat uptake in R2 and R3 was particularly low among subjects who had not attended their follow-up test (R2: 24.3% vs. 67.1%, $p < 0.001$; R3: 43.2% vs. 69.9%, $p < 0.001$).
CONCLUSION: Previous screening episode factors related to various stages of the screening process have been implicated in subsequent uptake. These previous screening episode predictors could be used to identify individuals at risk of dropping out of screening and provide an opportunity to tailor invitation and reminder letters to elicit increased uptake by selected sub-populations.
Disclosure of Interest: None declared

P0418 CAN WE EXPLAIN THE APPARENT DECLINE IN UPTAKE OF INVITATIONS FOR COLORECTAL CANCER SCREENING IN ENGLAND?

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INTRODUCTION: The NHS Bowel Cancer Screening Programme (BCSP) provides biennial guaiac-based faecal occult blood test (gFOBT) screening for colorectal cancer (CRC) to individuals aged 60-74 years (inclusive). Uptake of screening invitations in England, which averages about 55%, is affected by individual factors that include screening history, sex and level of social deprivation. Data for 2013 indicate a marked decline in uptake in England during the second half of 2013. The BCSP in England is co-ordinated by five regional Hubs; each works with local screening centres that provide follow-up investigations (usually colonoscopy) for individuals with a positive gFOBT result. The Southern Hub provides the screening service to about 26% of the population in England (14.6 million); it sends over one million invitations for screening and analyses about ¾ million test kits every year. Uptake in the Southern Hub averages 61% (2012/2013) but demonstrates the decline since June 2013 reported across the rest of the country, an observation investigated by the Southern Hub research team.
AIMS & METHODS: All BCSP screening activity is recorded on the Bowel Cancer Screening System (BCSS). Data for the period 2009-2013 were analysed to investigate patterns of uptake according to age, sex, screening episode, index of multiple deprivation (IMD) and screening centre.
RESULTS: Amongst individuals aged 60-74 years, although subject to marked fluctuations throughout each year, the overall trend was towards increased uptake until June 2013, after which uptake declined sharply. Uptake amongst first-time invitees aged 60 years was the most consistent (55%) between 2009 and 2012, although a marked fall in uptake was evident from mid-2013. The most deprived showed the greatest fall in the first invitation episode (60-year-olds) and there was no change in uptake by the least deprived individuals. Different patterns observed across screening centres may reflect different start dates resulting in a different mix of episodes, with the population with the longest screening history possibly subject to 'screening fatigue'.
CONCLUSION: We have not explained the decline in uptake of CRC cancer screening invitations during 2013. A decline in CRC screening uptake has been observed by the other BCSP Hubs and by the NHS screening programmes for the breast and cervix (personal communication), although the decline in uptake of breast and cervix screening has been more gradual. It may be that the public is reacting to adverse publicity about the benefits of screening surrounding breast screening, in particular, although data from the Scottish programme do not demonstrate the decline observed in England (personal communication). The benefits of CRC screening are well-recognised and efforts to improve uptake of screening invitations and close monitoring of uptake should continue.
Disclosure of Interest: None declared

P0419 PATIENT PREFERENCES FOR TERMINOLOGY USED TO IDENTIFY FECAL INCONTINENCE

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INTRODUCTION: Fecal incontinence (FI) affects 9% of non-institutionalized U. S. adults, but fewer than 30% have discussed this problem with their physician. This is unfortunate because effective treatments are available. Two factors that may contribute to low consulting rates are embarrassment about this taboo topic and unfamiliarity with the terms used by physicians.
AIMS & METHODS: Our goal was to identify terms that are the most acceptable and understandable to FI patients to make it easier for clinicians to inquire about and discuss FI with patients, and easier for patients to disclose the problem. Thirty patients with FI (29 women) recruited by advertisement participated in internet chat rooms of 1-5 persons. They were asked: "What words do you use to describe your FI when you are talking to doctors, family members, or friends?" with requests to rate 3 domains on a 0-10 scale: 1) the understandability of these terms, 2) their appropriateness for discussions with others, and 3) the patient's level of discomfort (embarrassment) in using the term. Based on focus group input, 29 terms were selected for participants to evaluate for a national survey. Thirty-one terms were not included because the investigators deemed them to be offensive (e.g., squirts, shits, taco butt) or because they were adjectives describing emotional reactions to FI or characteristics of FI (e.g. Embarrassing, Disgusting). This sample was stratified by FI status, age, sex, and race/ethnicity.
RESULTS: The national survey recruited 560 participants (42% with FI). Sixty-four participants were excluded for answering identical questions inconsistently. The remaining 496 participants had a mean age of 47.5 (range 18-91) years, 48% of participants were males, and race/ethnicity was 69.6% Caucasian, 15.7% Hispanic, and 14.7% African American. Participants were also divided into three age groups for analysis: 35 and younger (n = 146), 36-64 (n = 243) and 65 and older (n = 106). Appropriateness ratings are reported here. When we compared the ratings from participants with FI and without FI, four of the top five rated terms were the same for both groups (Bowel Incontinence, Bowel Control Issues, Accidental Bowel Leakage, and Diarrhea). Women rated all of these terms as significantly more Appropriate than men did. A consistent race/ethnicity pattern showed highest Appropriateness ratings for Caucasians, then Hispanics, and lowest by African Americans on all of these terms. Ratings also differed significantly by age group, increasing with age across the three groups for all of these terms. Ratings differed on only one of these terms due to Education level (Bowel Control Issues) or Income (Bowel Incontinence).
CONCLUSION: We recommend excluding the term Diarrhea as it is not specific to leakage of diarrhea. The remaining top three terms were ranked identically for participants with and without FI: 1) Bowel Incontinence, 2) Bowel Control Issues, 3) Accidental Bowel leakage. All three terms scored below the median on the Uncomfortableness domain. The term used most often by providers, fecal incontinence, did not score in the top 10 on any of the 3 domains. Accidental Bowel leakage, recently described as patients' preferred term, ranked 3rd. This information may help improve communication between patients and providers and enable more patients to receive treatment. Supported by Salix Pharmaceuticals.
Disclosure of Interest: None declared

P0420 SORD OVEREXPRESSION AND OTHER ASPECTS OF DYSREGULATED PROTEIN EXPRESSION IN HUMAN PRECANCEROUS COLORECTAL NEOPLASMS: A QUANTITATIVE PROTEOMICS STUDY

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INTRODUCTION: Colorectal adenomas are cancer precursor lesions of the large bowel. A multitude of genomic and epigenomic changes have been documented in these preinvasive lesions, but their impact on the protein effectors of biological function has not been comprehensively explored.
AIMS & METHODS: Using shotgun quantitative MS, we exhaustively investigated the proteome of 30 colorectal adenomas and paired samples of normal mucosa. Total protein extracts were prepared from these tissues (prospectively collected during colonoscopy) and from normal (HCEC) and cancerous (SW480, SW620, CACO2, HT29, CX1) colon epithelial cell lines. Peptides were labeled with isobaric tags (iTRAQ 8-plex), separated by OFFGEL electrophoresis, and analyzed by LC-coupled tandem MS. Non-redundant protein families (4325 in tissues, 2017 in cell lines) were identified and quantified. Principal component analysis of the results clearly distinguished adenomas from normal mucosal samples, and cancer cell lines from HCEC cells.
RESULTS: Two hundred twelve proteins displayed significant adenoma-related expression changes (q-value < 0.02, mean fold change vs. normal mucosa +/- 1.4), which correlated (r = 0.74) with similar changes previously identified by our group at the transcriptome level. Fifty-one (~25%) proteins displayed directionally similar expression changes in colorectal cancer cells (vs. HCEC cells) and were therefore attributed to the epithelial component of adenomas. Although benign, adenomas already exhibited cancer-associated proteomic changes: 69 (91%) of the 76 protein upregulations identified in these lesions have already been reported in cancers. One of the most striking changes involved sorbitol dehydrogenase (SORD), a key enzyme in the polyol pathway.
CONCLUSION: Validation studies revealed dramatically increased SORD concentrations and activity in adenomas and cancer cell lines, along with important changes in the expression of other enzymes in the same (AKR1B1) and related (KHK) pathways. Dysregulated polyol metabolism may represent a novel facet of the metabolome remodeling associated with tumorigenesis.
Disclosure of Interest: None declared

P0421 KNOWLEDGE AND PERCEPTION OF DOCTORS ON RISK FACTORS AND SCREENING OF COLORECTAL CANCER (CRC)

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INTRODUCTION: CRC has claimed 214,675 lives Europe and is expected to rise by 12% by 2020[1]. Knowledge and perception of doctors is important to future success of CRC screening program as early detection of CRC improve survival. However, little is known about doctors' knowledge and perception towards CRC. We aim to determine current knowledge and perception of colorectal cancer screening amongst junior doctors.
AIMS & METHODS: 169 junior doctors practicing across 7 specialties at a local academic institution were recruited from July -September 2013. Standardized questionnaires consisting of 44 questions were administered during structured resident teaching sessions that were unrelated to CRC. Individual responses were collected. Absent doctors were contacted via email. Standard statistical techniques were employed.
RESULTS: 74% (125/169) of junior doctors responded. Respondents' mean age was 27.7 years (23-35). Mean duration of practice locally was 3.2 years (1-8). Majority (97.6%) were aware that CRC is curable if treated early, and 85.6% recognized that CRC screening reduces mortality. Only 78.4% recognized CRC as the commonest cancer locally. Most CRC risk factors (CRC-RFs) such as age, family history, smoking, inflammatory bowel disease and colonic polyps were correctly identified (84.8-100%). However, knowledge of modifiable CRC-RFs was poor. Few recognized diabetes mellitus (5.6%), sedentary lifestyle (39.2%) and obesity (43.2%) as CRC-RFs. In addition, 10.4% wrongly identified traditional medicine as a CRC-RF, and only 45.7% correctly identified the recommended age for CRC screening according to local guidelines. More fresh graduates (PGY1) correctly identified ≥80% of CRC-RFs compared to the rest (40% vs 21.9%; p = 0.044). Only 90.4% and 88% identified colonoscopy and fecal occult blood test (FOBT) as acceptable CRC screening methods. 94.2% felt FOBT had poor test performance. Physician's concerns for colonoscopy included cost (76.9%), risk of perforation (61.5%), bleeding (46.2%), and inconvenient bowel preparation (66.7%). In spite of this, 80.8% will offer colonoscopy while only 68% will offer FOBT for CRC screening to their patients. There was

no difference in attitudes and practice patterns between doctors of different postgraduate years.
CONCLUSION: Majority of junior doctors correctly identified CRC as a significant healthcare burden, and that CRC screening and early detection reduces mortality. However, knowledge on modifiable CRC-RFs is still lacking. Many had concern about FOBT test performance, and more will offer screening colonoscopy. Continual medical education for junior doctors on modifiable CRC-RF and importance of CRC screening should be emphasized for continual success of CRC screening.
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Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
NERVE GUT AND MOTILITY I – POSTER EXHIBITION – HALL XL

P0422 OSMOTIC LAXATIVES ARE ASSOCIATED WITH LOWER RIGIDITY IN IDIOPATHIC PARKINSONISM

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INTRODUCTION: In idiopathic parkinsonism (IP), flexor rigidity is greater the higher the circulating natural-killer cell count, an effect modulated by CD4+ count.[1] These counts are higher with hydrogen-breath-test positivity for small-intestinal-bacterial-overgrowth. Two-thirds of IP-patients are positive at presentation.
AIMS & METHODS: Improving intestinal transit with laxatives might reduce rigidity by reducing overgrowth.
Relationships of interventions for constipation to rigidity and overgrowth were explored using generalised linear mixed models. Surveillance yielded 1378 objective measures of arm rigidity in 74 IP-patients over 343 person years, with 437 2-h lactulose-hydrogen-breath-tests in 48. Maintenance osmotic laxative (macrogols) was exhibited in 50 (176 person years); bulk-forming laxative (ispaghula husk/methylcellulose/sterculia) in 52 (196); enterokinetic agent (prucalopride) in 25 (45); and guanylate cylase-C receptor agonist (linaclotide) in 8 (12).
RESULTS: Osmotic laxative was the only intervention associated with a change in rigidity. Flexor rigidity increased (by 6.8 (4.3, 9.4) % per year, $p = 0.001$) where not exhibited, stabilised where exhibited (1.4 (95% CI -0.9, 3.8) % per year, $p = 0.2$). Bulk-forming laxative had no additional effect on rigidity ($p = 0.5$). Similarly, the ratio, flexor to extensor rigidity, indicating tendency to simian posture, increased (3.2 (0.7, 5.7) % per year, $p = 0.01$) where osmotic laxative was not exhibited, stabilised where exhibited (-1.6 (-3.9, 0.8) % per year, $p = 0.2$). Bulk-forming laxative had no additional effect on the ratio ($p = 0.6$).
Only bulk-forming laxative was associated with change in breath-hydrogen. Peak hydrogen was lower by 11 (1. 20) ppm ($p = 0.03$) where exhibited, with no differential effect of time ($p = 0.9$). (Odds ratio for a positive breath-test where exhibited compared with where not: 0.55). Osmotic laxative had no additional effect on peak hydrogen ($p = 0.3$).
CONCLUSION: Osmotic laxative may reduce rigidity by reducing inflammation, directly, or by removing an inhibitory effect on anti-parkinsonian medication. Any effect of overgrowth on rigidity may relate to organisms not flagged by hydrogen-breath-test.
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Disclosure of Interest: None declared

P0423 DOES BODY POSITION MODIFY ANORECTAL PRESSURE VALUES RECORDED BY THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY?

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INTRODUCTION: Anorectal manometry is the gold standard in the physiological exploration of anorectal disorders. In recent years, three-dimensional high-resolution anorectal manometry (3DHRAM) was developed. However, exams (conventional manometry or 3DHRAM) are traditionally made in the left lateral decubitus position while anorectal symptoms (dyschezia and anal incontinence) occur in the standing or sitting position.
AIMS & METHODS: The aim of our prospective study was to compare the pressure values obtained by 3DHRAM in the lying position (left lateral decubitus position) and in the standing position.
All patients referred to our center to explore anal incontinence or dyschesia by 3DHRAM and EUS were eligible. Patients with a history of anorectal surgery or suffering from anal pain were excluded. The 3DHRAM was performed by the same operator successively in the left lateral decubitus position and in the standing position. The EUS was perfomed the same day. KESS and Wexner scores were routinely rated, as well as size and weight of the patients. The calculated number of patients required for this study was 40.
RESULTS: These are preliminary results (20 patients included in the 40 to be included). 17 females and 3 males, with a median age of 41 years (20-73) and a median body mass index of 23 kg/m^2 (17-36) were included. The indication of examinations was anal incontinence in 8 patients and constipation in 12 cases, with a median KESS score of 20 (9-32) and a median Wexner score of 9 (7-20). No manometric measured parameters was significantly different in the supine or standing position, whatsoever in the subgroup of incontinent patients or in the subgroup of constipated patients.
CONCLUSION: These preliminary results showed no significant difference between the pressure values measured by 3DHRAM in the supine and standing position. At this stage of study, two hypotheses can be advanced: 1) the lack of power related to the low effective since we have included only half of the patients required; 2) no difference whatever the position of the patient when the measurements are made with 3DHRAM. Analysis of the results when all patients will be included will provide the answer to this question.
Disclosure of Interest: None declared

P0424 BUSERELIN INDUCES ENTERIC NEURONS TO EXPRESS CORTICOTROPIN-RELEASING FACTOR

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INTRODUCTION: Treatment with gonadotropin-releasing hormone (GnRH) analogs have led to severe dysmotility, which implicates roles for the reproductive peptide/hormones in the gastrointestinal tract. Administration of the GnRH analog buserelin to rats leads to neurodegeneration and ganglioneuritis. During these experiments, we have observed that the treated rats have exhibited a more stressed behavior than controls. Stress has been shown to increase secretion of corticotropin-releasing factor (CRF) and to increase intestinal permeability in humans, and to increase locomotion, rearing, pellet excretion, and altered colonic microbiota in rodents. CRF is highly expressed in the enteric nervous system in humans and rodents, and has been shown to abolish the vasoactive intestinal peptide (VIP)-induced neuronal survival.
AIMS & METHODS: The aim of the present study in rat was to evaluate the effect of the GnRH analog buserelin on enteric neurons immunoreactive to CRF and the intestinal microbiota.
Forty rats were given either buserelin (B) (20 μg, 1 mg/ml) or saline (C) subcutaneously, once daily for five days, followed by three weeks of recovery, representing one session of treatment. Two weeks after the fourth session, the animals were euthanized. Gastrointestinal tissue were collected and analyzed for neuronal survival and CRF immunoreactivity. Microbial DNA (16S rRNA genes) was extracted from the colonic mucosa and analyzed with molecular genetic methods. The Terminal Restriction Fragment Length Polymorphism (T-RFLP) method was used to analyze microbial diversity. Bacterial abundance of the bacterial groups *Clostridium leptum* and *Enterobacteriaceae* was estimated using separate quantitative PCR assays.
RESULTS: Body weight transiently increased by buserelin treatment at week 5 and 9 ($p < 0.001$). Enteric neurons were reduced in number by approximately 40% in both submucous and myenteric ganglia of ileum and colon. Enteric neurons in colon immunoreactive to CRF increased in submucous ganglia (C = 10 (6-16)%, B = 21 (14-25)%, $p < 0.05$) and in myenteric ganglia (C = 7 (5-9)%, B = 19 (18-23)%, $p < 0.01$) due to buserelin treatment. In submucous ganglia, the number of neurons immunoreactive to both nitric oxide synthase (NOS) and CRF increased due to buserelin treatment ($p < 0.05$). In the myenteric ganglia, the number of neurons immunoreactive to NOS or VIP, in addition to CRF, tended to increase after buserelin treatment ($p < 0.14$ and $p < 0.08$, respectively). The CRF fiber density was unaffected by buserelin treatment throughout all the different layers of the bowel wall. The total amount of bacteria and diversity in colon did not differ between groups. The number of bacteria in the group of *Enterobacteriaceae* was significantly lower in buserelin-treated rats compared to saline-treated rats ($p < 0.05$), whereas the total amount of bacteria in the groups of *Clostridium leptum* did not differ between broups.
CONCLUSION: The relative number of enteric neurons expressing CRF was increased after induction of enteric neuropathy. The enteric nervous system shows proof of plasticity, since NOS-immunoreactive neurons starts to express CRF after buserelin treatment. Despite a marked enteric neuropathy, no signs of bacterial overgrowth or diminished diversity are at hand in colon.
Disclosure of Interest: None declared

P0425 FUNCTIONAL CONSEQUENCES AFTER BUSERELIN-INDUCED ENTERIC NEUROPATHY IN RAT

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INTRODUCTION: Women treated with gonadotropin-releasing hormone (GnRH) analogs develop in some cases enteric neuropathy with ensuing severe

dysmotility. Administration of GnRH analog to rats leads to similar degenerative changes and ganglioneuritis.
AIMS & METHODS: The aim of the present study in rat was to evaluate the enteric neuropathy, in terms of affected neuronal subpopulations and gastrointestinal function, and to investigate levels of zonulin and titers of GnRH and luteinizing hormone (LH) and their receptors in plasma.
Forty rats were given either the GnRH analog buserelin (B) (20 μg, 1 mg/ml) or saline (C) subcutaneously, once daily for five days, followed by three weeks of recovery, representing one session of treatment. Two weeks after the fourth session, the animals were euthanized. Prior to sacrifice, feces were analyzed for weight and fat, and GI transit time and galactose absorption were studied. Neuronal subpopulations and survival were analyzed in GI tissue. Blood samples were analyzed for zonulin, GnRH and LH and their receptors.
RESULTS: Body weight transiently increased by buserelin treatment at week 5 and 9 ($p < 0.001$). Buserelin increased estradiol in plasma and uterine muscle layers were thickened, implicating high estrogen activity. Enteric neurons were reduced in number by approximately 40% in both submucous and myenteric ganglia of ileum and colon. Feces weight decreased in buserelin-treated rats (C = 4.3 (3.4- 5.9) g; B = 3.2 (2.4-3.6) g, $p < 0.01$) whereas fat content in feces increased (C = 2.8 (2.9-3.9)%; B = 3.6 (2.6-3.2)%, $p < 0.01$), compared to saline-treated rats. Total GI transit time and galactose absorption were not affected by buserelin treatment. Studies on the various neuronal subpopulations in colon showed increased relative number of somatostatin immunoreactive neurons in submucous, but not myenteric, ganglia while the numbers of cocaine-amphetamine-related transcript (CART), calcitonin gene-related peptide (CGRP), galanin, gastrin-releasing peptide (GRP), neuropeptide Y (NPY), nitric oxide synthase (NOS), serotonin, substance P (SP) and vasoactive intestinal peptide (VIP) were unchanged. The levels of zonulin in plasma and the titers of antibodies against GnRH, LH or their receptors were unaffected by buserelin treatment.
CONCLUSION: A marked enteric neuropathy is at place with only modest effects on gastrointestinal function after buserelin treatment. Altered feces weight and fat content is suggested as early signs of dysfunction.
Disclosure of Interest: None declared

P0426 CHARACTERIZATION OF BIOMECHANICAL PROPERTY OF INTESTINAL SMOOTH MUSCLE USING HILL-TYPE MUSCLE MODEL; ANIMAL STUDY

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INTRODUCTION: Various treatment modalities for GI motility disorders have been developed so far including medications and electrical stimulation. But little is known about biomechanical properties of gastrointestinal smooth muscle, in contrast to vascular or respiratory smooth muscle. In this study, we made a novel actuator model for characterization of biomechanical property of small intestinal smooth muscle.
AIMS & METHODS: In the order to characterize active and passive properties of intestinal smooth muscle, we performed tensile test and isometric, isotonic experiments using viable small intestines of 3 month old pig. In the tensile testing, we connected excised intestinal samples to the universal testing machine developed by our own group only for soft tissue measurement. In isometric and isotonic experiments, porcine small intestine was bathed in HTK-solution for preservation of energy source. After connection of the sample to sensor, muscle contraction was induced by acetylcholine chloride. Contractile force and velocity were measured by isometric force transducer and isotonic transducer.
RESULTS: In tensile experiment, tensile stress was maximum at the 1.67 times its original length and 0.702N at break point. In isometric experiment, maximum contractile force was observed at the resting length which was 12.35±0.5 mN after 50min of acetylcholine stimulation. Intestinal smooth muscle contraction was sustained for 55min. In isotonic experiment, intestinal smooth muscle was 10 to 100 times slower than skeletal muscle contraction. We calculated contractile velocity for various loads and acquired load free contractile velocity by curve fitting method (0.4952 mm/min). Finally, we combined previously acquired passive and active parameters of intestinal smooth muscle to make a comprehensive intestinal smooth muscle model.
CONCLUSION: In this study, we characterized active and passive parameters and applied them to modified Hill type muscle model for making a novel actuator of intestinal smooth muscle. This study would provide basic tool for understanding biomechanical properties of intestinal smooth muscle, and we can utilize this as basic data for development of a more efficient GI electrical stimulator.
Disclosure of Interest: None declared

P0427 5HT SELECTIVE RECEPTOR AGONISTS AND GALLBLADDER MOTILITY IN PATIENTS WITH MIGRAINE

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INTRODUCTION: Some 5HT selective receptor agonists (triptans) are reported to have gastric motor effects but less is known about their role on gallbladder (GB) motility.
AIMS & METHODS: Assessment of GB motility in patients treated with orodispersable triptans .30 patients diagnosed with mild to moderate migraine: 15 with with aura (3 men, 12 women, mean age = 43.13±17.72 years) and 15 without aura ((1 man, 14 women, mean age = 47.73±18.50 years), with an ejection fraction (EF) of GB < 60%, previously measured by elipsoid ultrasound Dodds method, without prokinetic treatments, collagen or thyroid disease, diabetes mellitus, cardiac, liver or kidney failure, undertook this study. The same measurements were made while having a migraine attack, before and every 15 minutes till 90 minutes after receiving 5 mg of orodispersable zolmitriptan.
RESULTS: There was no statistical significant difference between initially EF of the two groups ($p = 0.8190$). Patients with migraine with aura showed before therapy a mean EF = 42.53±4.31%; after therapy the mean EF improved significantly: 48.80±3.23% ($p = 0.0001$). Patients with migraine without aura displayed an initially mean EF = 42.53±3.27% and had a very statistically significant response to therapy with increasing of EF to 61.47±7.07% ($p < 0.0001$). There was also a statistically significant difference of respose to therapy in patients with migraine without aura (61.47±7.07% vs 48.80±3.23%; $p < 0.0001$).
CONCLUSION: 5HT selective receptor agonists increased GB motility in migraine attacks with a better response in patients without aura.
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Disclosure of Interest: None declared

P0428 NEUROPATHOLOGICAL ANALISYS AND CLINICAL FEATURES OF CHRONIC CONSTIPATION IN PATIENTS WITH PARKINSON DISEASE

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INTRODUCTION: Chronic constipation (CC) represents one of the most common gastrointestinal (GI) complaints in Parkinson's disease (PD), being diagnosed in about 80% of patients. Furthermore, CC often precedes the somatic motor impairment in PD. The enteric nervous system (ENS), controlling gut functions, can be a target of the PD although the precise neurochemical ENS abnormalities underlying CC/PD patients remain largely unknown.
AIMS & METHODS: In CC/PD patients we aimed to: 1) characterize constipation by assessing colonic transit time (TT) and anorectal manometry (AM); 2) analyze colonic submucosal neurons of PD patients *vs* controls, particularly assessing the secretomotor neuron component.
GI symptoms were evaluated by the Rome III questionnaire, while PD was established by a Unified Parkinson's Disease Rating Scale (part III). CC was studied in 25 PD patients (7F, 18M; age range: 64-85 yrs) by TT, AM and colonoscopy; 14 control subjects (4F, 10M; age range: 33-77 yrs) undergoing screening colonoscopy were also enrolled in the study. Using routine biopsies during colonoscopy, we obtained submucosal specimens with related neural network in 10 CC/PD patients and 10 controls. The submucosal plexus was studied by immunohistochemistry on whole mount preparations using a mouse monoclonal anti-HuC/D as pan-neuronal marker (Invitrogen, 1:50) and two rabbit polyclonal anti-VIP (vasoactive intestinal peptide-7913; CURE/DDRC, UCLA, 1:2500) and anti-pChAT (peripheral choline acetyl transferase, Justus-Liebig-University Giessen, Germany; 1:100) antibodies.
RESULTS: Four groups of CC/PD patients were characterized: a) 55% with a delayed TT and altered AM; b) 15% with a delayed TT; c) 20% with an altered AM; d) the remaining 10% with no evident functional impairment. There were no significant differences in the number of HuC/D immunoreactive (-IR) neurons/ganglion between CC/PD (4.7±0.8) and controls (5.5±1.5); however, a reduced number of HuC/D/VIP-IR neurons was found in CC/PD (73.3±17.1) *vs* controls (86.0±10.9) ($P < 0.05$). No significant changes were detected for HuC/D/ChAT neurons in both groups (85.6±11.1 *vs*. 91.2±10.1).
CONCLUSION: Most (90%) of CC/PD patients has a marked impairment of colonic motor and rectal sensory functions. Neurochemical changes in a subset of VIP containing secretomotor neurons suggest that altered secretory mechanisms may accompany sensorymotor dysfunction in PD-related CC pathophysiology.

Disclosure of Interest: None declared

P0429 EHLERS-DANLOS SYNDROME AND IBS - SAME GI SYMPTOMS, DIFFERENT DISEASES

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INTRODUCTION: Ehlers-Danlos syndrome (EDS) is usually an autosomal derived disease with defects in the collagen synthesis. It is divided into six subgroups according to the Brighton criteria. The most common subtype gives hypermobility of the joints, frequent luxations and fractures. It is also connected with gastrointestinal symptoms, most commonly abdominal pain and other symptoms that are included in the functional symptom spectrum. Patients with EDS fulfil the Rome III criteria for functional gastrointestinal disorders in 84%. So far there are no systematic studies of GI physiology and treatment for GI-disorders in these patients.
AIMS & METHODS: To evaluate symptoms, gastrointestinal work up, opioid therapy, treatment response to octreotide, and findings on 24h ambulatory small bowel manometry in patients with EDS.
Information obtained from patient database and retrospectively acquired information from the medical record system in the out- and inpatient clinic in Center of Digestive Diseases, Karolinska University Hospital, Stockholm, Sweden.
RESULTS: The search found 24 patients from 2001 to 2014, all but one were female. Abdominal pain was present in 100%, change of bowel habits in 19/24. Ten had done small bowel manometry, 3 of them were classified as enteric dysmotility and 5 patients had some changes of MMC phase III. Ten of the patients had tried octreotide and seven of them had clinical response and continued the octreotide treatment. Eleven patients were unable to do small bowel manometry due to use of opioids and three are on the waiting list for the manometry.
CONCLUSION: We show that patients with EDS have a high frequency of changes in small bowel manometry and high prevalence of enteric dysmotility. Treatment with octreotide is effective, even without having enteric dysmotility. Abdominal pain in patients with EDS should not be considered as IBS but EDS should be considered in patients with joint hypermobility and abdominal pain. Further studies are needed for evaluation of gastrointestinal physiology of patients with EDS.
Disclosure of Interest: None declared

P0430 COMBINED EFFECT OF EARLY LIFE STRESS AND ACUTE STRESS AS A NEW MODEL FOR FUNCTIONAL DYSPEPSIA

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INTRODUCTION: Functional dyspepsia (FD) is one of the most common GI disorders. Because of the chronic relapsing nature & lack of effective treatment options, FD is associated with significantly impaired quality of life and considerable health care costs.
Based on the central role stress seems to be playing in functional GI diseases, available animal models for FD rely on exposing animals to various types of stress either in the neonatal period or in adulthood.
However, clinical studies have shown that adverse physiological or psychological experiences in early life are associated with the development of FD symptoms, as well as acute stressful conditions in adulthood. Hence, childhood traumatic experiences followed by later exposure to acute stress may play key roles in the development & in modulation/ maintenance of FD.
AIMS & METHODS: In the present study, we tried to mimic this situation by combining early life stress (neonatal maternal separation, NMS) and acute stress in adulthood (restraint stress, RS) in rats, in the hope of developing a multidimensional experimental model of FD with closer resemblance to the clinical situation.
To explore the validity of this sequential stress model in trying to develop new drugs for FD, we tested the effects of STW5, a multicomponent herbal preparation widely used to treat FD with strong clinical evidence, as a standard drug.
RESULTS: Fundus strips from rats subjected to the combined stress showed significantly reduced responses to adrenaline, carbachol, KCl and 5HT as compared to those from normal rats or animals subjected to either stressor. Animals treated with STW5 showed normalized response to adrenaline, carbachol and 5HT. Combined stress also markedly increased plasma levels of CRF to twice as much as either stressor alone. The elevation of CRF was associated with a corresponding increase in plasma corticosterone. Pretreatment with STW5 protected against the increase in both CRF and corticosterone. None of the treatments significantly affected active plasma Ghrellin.
CONCLUSION: These data indicate that combined early life stress and acute stress effectively induce stomach motility disorders as well as hormonal derangements that might be more representative of the complex clinical situation and might represent a model for the screening of new FD drugs.
Disclosure of Interest: H. Abdel-Aziz Other: Employee of Steigerwald Arzneimittelwerk GmbH, W. Wadie: None declared, H. Zaki: None declared, J. Müller Other: Employee of Steigerwald Arzneimittelwerk GmbH, M. Khayyal Financial support for research from: Steigerwald Arzneimittelwerk GmbH

P0431 RECIPROCAL MODULATION OF INTESTINAL SMOOTH MUSCLE CELL CONTRACTILITY BY TH17 AND TH1 CYTOKINES

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INTRODUCTION: Gastrointestinal motility disorders, such as infection, IBD, ileus, achalasia and functional gastrointestinal disease, have been associated with immune activation. We have previously reported that the hypercontractility of small intestinal (SI) smooth muscle cells (SMC) is mediated by IL-17A-induced NFkB/IkBz-RGS4 signaling resulting in down regulation of RGS4 activity. RGS4 is known to suppress Gaq/11 signaling triggered by stimulation of the acetylcholine (muscarinic 3) receptor. On the contrary, IL-1β, which is known to induce hypomotility of SMC, upregulates RGS4 expression and function. However, these opposite effects by IL-17A and IL-1β both have been found to be mediated by NFkB/IkBz activation. In the present study, we have investigated the mechanism by which IL-17A- and IL-1β-induced NFkB/IkBz activation produces the different outcomes.
AIMS & METHODS: Murine SMCs were isolated, cultured, and treated with various chemical probes, IL-17A, IL-1β, and IL-4 (10–50 ng/ml). Contraction was assessed using a cell imaging analyzer on a temperature-responsive UpCell 96-well plate. Activation of NFκB was evaluated by the strength of the nuclear NFκB p65 immunosignal. Activation of RGS4, myosin light chain (MLC) and MAPKs were determined by immunoblotting.
RESULTS: IL-17A significantly enhanced carbachol-induced contractile responses, concomitant with increased phosphorylated MLC (p-MLC) and decreased RGS4 activity. IL-1β significantly decreased p-MLC and increased RGS4 activity. These effects of IL-17A and IL-1β were both abrogated by an NFκB inhibitor and IκBζ siRNA. Screening of activated MAPK using a proteome profiler revealed that IL-1β activated p38MAPK and JNK but IL-17A activated p38MAPK only. The effect of IL-17A was abrogated by p38MAPK inhibitors but not by JNK inhibitors. The effect of IL-1β was abrogated by JNK inhibitors but enhanced by p38MAPK inhibitors. Anisomycin, a p38MAPK activator induced hypercontractility.
CONCLUSION: These data suggest that the balance of relative activity levels of JNK and p38MAPK is critical for determining the direction of contractile response and that NFκB/ IκBζ signaling fuels the movement of MAPK-triggered molecular events toward/against hypercontractility of SI SMC. The relatively stronger activation of p38MAPK may result in hypercontractility, induced by IL-17A, and that of JNK may result in hypocontractility, induced by IL-1β. Our findings may lead to the development of new pharmacotherapeutic strategies for gastrointestinal motor dysfunctions.
Disclosure of Interest: None declared

P0432 EXPECTATIONS OF PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS): A PROSPECTIVE SURVEY OF THE FRENCH ORGANIZATION OF IBS PATIENTS

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INTRODUCTION: IBS may be responsible for an impaired quality of life (QoL) and represents an economic burden for society. Efficacy of treatments is poor and patients often feel isolated and dissatisfied with medical care[1]. This work aims to describe the characteristics of IBS in members of the French organization of IBS patients (APSSII, www.apssii.org) and to compare their expectations to their past experiences with health care providers.
AIMS & METHODS: From January to June 2013 all members of APSSII were asked (once, by mail or online) to answer a questionnaire with a description of: IBS, treatments, impact on QoL, expectations and experiences in relation to the disease and health care system.
RESULTS: 222 out of 330 members (67%) responded (women 68.5%, age 46.5±17.7 years, disease duration 8.8±0.7 years, IBS-D 33.6%, IBS-C 26.7%, IBS-A 38.2%). A colonoscopy was performed in 87%, and diagnosis was made by a physician in 88%. Patients were followed up by a doctor in 65% (specialist 57% or GP 38%), and 82% had consulted for IBS in the last 12 months. Past or current treatments were antispasmodics (46%), laxatives (25%), antidepressants (25%), probiotics (38%), homeopathy (34%), hypnosis (15%), relaxation (31%), osteopathy (28%), acupuncture (25%) and 46% were on a diet. IBS was severe (IBS-SSS $>$ 300) in 53% and major depression was present in 45% (HAD score $>$ 19). QoL was impaired (FDDQL score 41±14), more frequently in women (44.9±14 vs. 40.2±14.4 ($p = 0.039$), with no difference according to IBS subtype, and was correlated with disease severity and HAD score ($r = -0.707$ and $r = -0.484$, $p < 0.001$; respectively). Patients' expectations about IBS were "improved health", "information on the causes and treatments" for 94%, and "better disease recognition" for 86%. Expectations vs. experiences (%) in relation to the medical providers were: "sufficient information" (94% vs. 16%), "listening with empathy" (97% vs. 36%), "providing hope" (85% vs. 9%), "improved health"

(95% vs 15%). Patients thought that their doctors had ''good knowledge on IBS'' in 18%, ''believed in their symptoms'' in 47% and suggested to them that "it was in their head" in 65%. Only 16% were satisfied with the health care system for IBS management and 68% considered that an improvement in the management of symptoms would have an impact on overall IBS cost. There was a discrepancy between the desired information sources on IBS (more information via the doctor) and the reality: internet 84%, specialist 47.9% and GP 32%.
CONCLUSION: These French data on expectations of IBS patients from a survey conducted among members of a patients' organization show 1) a severe disease with frequent psychological impact and impaired QoL, 2) many unsatisfied expectations with respect to the disease and health care professionals, and 3) a need for improving the quality of patient-physician relationship.
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Disclosure of Interest: None declared

P0433 PROTECTIVE EFFECTS OF SACRAL NERVE STIMULATION AGAINST TNBS-INDUCED ACUTE INTESTINAL INFLAMMATION

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INTRODUCTION: Inflammatory Bowel Diseases (IBD) dramatically alter the quality of life for the young adult and have a high societal cost. Treatments of IBD have made recent progress but their adverse side effects are numerous and relapse prevention remains a problem. Enhancing intestinal epithelial barrier (IEB) functions emerges as a promising new therapeutic approach. The enteric nervous system (ENS), a key regulator of gut homoeostasis, exhibits major barrier protective effects. Sacral nerve stimulation (SNS), probably via activation of the ENS, has been reported to enhance IEB resistance (1) but its putative protective effects in response to inflammatory challenge remain unknown.
AIMS & METHODS: Therefore, the aim of this study was to determine whether SNS protects barrier dysfunction as well as modulates intestinal inflammation induced by an acute inflammatory stress induced by TNBS. Twelve pigs were implanted for percutaneous bilateral SNS (S3 stimulation) (Medtronic 041828-004, Minneapolis, USA; 14 Hz, 210ms). Six pigs were stimulated 3 hours prior and 3 hours after administration of rectal enemas of TNBS (15 mg/ml). Control animals (CT) were implanted but not stimulated and also received TNBS enema. Rectal panparietal biopsies were performed before (T0) and 1h, 3h, 24h after enema. Intestinal para- and transcellular permeability was assessed in Ussing chambers. *In vivo,* intestinal inflammation was evaluated by endoscopy and confocal endomicroscopy (CEM) scores. Impact of SNS upon the mucosal changes induced by TNBS was evaluated by combining histological and transcriptomic approaches.
RESULTS: In CT, a significant and transient increase in rectal para- and transcellular permeability was measured as early as 3h following TNBS enema. 24h after enemas permeability was still increased in CT as compared to its T0 value. In SNS pig, a significant and transient increase in para- and transcellular permeability occurred as early as 1h following TNBS enema. However, 24h after enemas permeability was similar to its T0 value. At 24h, similar results were observed at the rectosigmoidal hinge level. Consistently, the SNS pigs exhibited a trend toward a lower UCEIS score ($p = 0.07$, $n = 5$) as compared to CT. At 24h, CEM scores revealed that TNBS induced alterations in crypt circularity, tortuosity and brightness were significantly reduced by SNS as compared to control ($p = 0.05$, $n = 6$; $p = 0.008$, $n = 6$, respectively). Furthermore, epithelial desquamation and edema formation was significantly larger in CT as compared to SNS pigs ($p = 0.03$, $n = 6$, both measures). Finally, mRNA expression of key tight junction proteins such as Claudin-1 ($p = 0.04$, $n = 6$) and ZO-1 ($p = 0.03$, $n = 6$) were significantly increased in SNS ($p = 0.04$, $n = 6$; $p = 0.03$, $n = 6$, respectively) as compared to CT pigs. Western blot analysis of ZO-1 also showed that ZO-1 protein expression was increased in SNS as compared to CT animals ($p = 0.018$, $n = 6$).
CONCLUSION: Altogether these results show that SNS exhibit major reparative properties on mucosal lesions induced by acute inflammatory stress. These identify SNS as a putative alternative or complementary therapy targeting diseases such as IBD.
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Disclosure of Interest: None declared

P0434 FAECAL INCONTINENCE IN TYPE 2 DIABETICS: COMPARISON WITH NON DIABETIC HEALTHY INDIVIDUALS AND ANALYSIS OF RELATED FACTORS

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INTRODUCTION: Faecal incontinence is a complaint that some type 2 diabetic patients frequently refer[1]. The factors involved with are not well known.
AIMS & METHODS: The aim of this study was to compare the frequency of faecal incontinence between type 2 diabetic patients and non diabetic healthy individuals and to analyse some factors involved in this perturbation in diabetics. A questionnaire of Gastrointestinal Symptoms Rating Scale[2] was completed by to 140 type 2 diabetics and 132 non diabetic healthy individuals, matched by age and gender.
RESULTS: The frequency of faecal incontinence in diabetics vs. non diabetics was 14.3% vs. 3.1%, $p < 0.01$. According to the severity, the frequency of faecal incontinence between diabetics vs. non diabetics was as follows: minor symptoms, 3.6% vs. 2.3%; moderate symptoms, 7.9% vs. 0.8%; severe symptoms, 2.1% vs. 0.0%; very severe symptoms, 0.7% vs. 0.0%, $p = 0.03$.
When analysing the frequency of faecal incontinence in diabetics according to the disease duration, $</= 10$ years vs. > 10 years the results was 9.5% vs. 24%, $p < 0.01$. The symptoms for severity was also significantly higher in diabetics with more than 10 years of disease, $p = 0.01$. In diabetic patients, age, gender and glycaemia control did not influence the frequency and severity of faecal incontinence.
CONCLUSION: 1- Faecal Incontinence is more frequent and severe in type 2 diabetics than non diabetic healthy individuals. 2- Diabetes duration influences the frequency and the severity of faecal incontinence. 3- Age, gender and glycaemia control did not influence the frequency and the severity of faecal incontinence in type 2 diabetic patients.
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Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS I – POSTER EXHIBITION – HALL XL

P0435 PHENOTYPIC PLASTICITY OF ALVEOLAR MACROPHAGES IN GASTROESOPHAGEAL REFLUX DISEASE WITH PULMONARY MANIFESTATIONS AND ITS COMBINATION WITH ASTHMA

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INTRODUCTION: To date it is known that in spite of different points of view on etiology and variety of cellular and molecular pathogenetic components of pulmonary manifestations in gastroesophageal reflux disease (GERD) and combination of GERD and asthma there is a key feature of inflammation and the immune response disorder in the form of Th1/Th2 imbalance in the pathogenesis of the disease. Th1 or Th2 direction of immune response is mainly predetermined by innate and adaptive immune response cells - macrophages. Considering the concept of M1/M2 programming in changing microenvironment, macrophages can obtain either pro-inflammatory M1 phenotype, or alternatively anti-inflammatory M2 phenotype and change their phenotype in the disease formation. So we can suppose that Th1/Th2 imbalance is mainly due to impairment ability of macrophages to adequate change their phenotype, i.e. with impaired phenotypic plasticity of macrophages.
AIMS & METHODS: Assessment of alveolar macrophages (AM) phenotypic plasticity in GERD and its combination with asthma and healthy volunteers under the influence of different serum (FBS) concentrations. **Methods:** In vitro experiments were carried out on AM, isolated from BALF of patients with GERD ($n = 15$, 46.41 ± 4.18 y.o.), combination of GERD and asthma ($n = 16$, 49.30 ± 3.64 y.o.) and healthy volunteers (HV) ($n = 10$, 51.83 ± 3.52 y.o.). AM phenotype was assessed by flow cytometry (Beckman Coulter, FC500) by cytokine production of proinflammatory M1, anti-inflammatory M2 and bivalent M1/M2 cytokines in culture medium (CM) of AM (BenderMedSystems, BMS810FF). Phenotypic plasticity of AM was measured as percentage change of markers during 36 hours of AM reprogramming in the presence of 0%, 10%, 40% standard fetal bovine serum, containing endogenous reprogramming factor – surfactant protein D.
RESULTS: Pooled analysis of M1 and M2 phenotypic plasticity in GERD and its combination with asthma against HV showed maximum of M1 phenotypic plasticity in GERD – M1/M2 index of the macrophages ability to change their phenotype towards M1 was 5.33 and this was 8.5 times increased vs combination of GERD and asthma ($p < 0.05$). Maximum macrophage phenotypic plasticity towards M2 phenotype was observed in combination of GERD and asthma and M1/M2 index of phenotypic plasticity was 5.45 times higher than in GERD.
CONCLUSION: The ability of AM to change their phenotype under the influence of the microenvironment in GERD and its combination with asthma was changed as compared to healthy volunteers. In GERD macrophages possess more possibilities to obtain M1 phenotype than M2, but the in combination of GERD and asthma macrophages are more predisposed to obtain M2 phenotype. So the studied ability of macrophages to adapt their phenotype to the microenvironment and to reprogram the phenotype of the cells can be thought of as the base for new therapy approach in personalized medicine influencing the initial links of inflammatory response and Th1/Th2 imbalance even in initial stages of pathological process.
Disclosure of Interest: None declared

P0436 INCREASED LEPTIN SIGNALING IN ESOPHAGEAL ADENOCARCINOMA CELL LINE TREATED WITH PERITUMORAL ADIPOSE TISSUE-DERIVED CONDITIONED MEDIUM

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INTRODUCTION: Obesity is associated with an increased risk of cancer and it has been hypothesized that the action of adipokines (e.g. leptin and adiponectin) may influence tumor invasiveness.
AIMS & METHODS: Our aim is to investigate if peritumoral adipose tissue may play a direct role by altering the expression of genes involved in migratory/mesenchymal transition processes in human esophageal adenocarcinoma cells.
Human esophageal adenocarcinoma cells (OE33) were cultured with conditioned medium (CM) derived from adipose tissue fragments of peritumoral and distal (omental) depots of 15 patients with esophageal adenocarcinoma, undergoing surgical resection. After 48h we measured mRNA levels of leptin receptor (ObR), adiponectin receptor (AdipoqR), alpha-smooth muscle actin (α-SMA) and E-cadherin (CDH1) in OE33 cells using Real Time quantitative PCR.
RESULTS: Gene expression of ObR, AdipoqR, α-SMA and CDH1 were dramatically increased in OE33 cells cultured with CM, compared to control cells. Moreover, expression of ObR, AdipoqR α-SMA and CDH1 was significantly higher in OE33 cells cultured with CM of peritumoral depot, compared to cells cultured with CM of omental depot. Interestingly, ObR and α-SMA expression was significantly increased in OE33 cells cultured with CM of peritumoral depot derived from patients with lymph node involvement (N+), compared to peritumoral CM of patients with no positive lymph node (N-).
CONCLUSION: Our results suggest that peritumoral adipose tissue may influence esophageal adenocarcinoma cells, through the action of secreted factors. In particular, leptin signaling may be involved in the induction of α-SMA expression in esophageal adenocarcinoma cells, possibly promoting a more aggressive behaviour of tumor.
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Disclosure of Interest: None declared

P0437 SURFACTANT PROTEIN D AND ALVEOLAR MACROPHAGES PHENOTYPE AS ADDITIONAL MARKERS IN DIAGNOSTICS OF GASTROESOPHAGEAL REFLUX DISEASE WITH PULMONARY MANIFESTATIONS AND ITS COMBINATION WITH ASTHMA

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INTRODUCTION: Actual pathogenesis studies of pulmonary manifestations in gastroesophageal reflux disease (GERD) and its combination with asthma showed that respiratory system inflammation and imbalance between Th1 and Th2 immune responses are the main pathologic components of the process. Considering the present-day concept of Th1/Th2 Paradigm and M1/M2 macrophages programming, immune response disorders depend largely on the balance of functional phenotypes of alveolar macrophages (AM). One of significant bivalent regulatory components of AM activity is surfactant protein D (SP-D). So we suppose that pooled analysis of AM phenotype with quantitative and qualitative analysis of SP-D composition in broncho-alveolar lavage fluid (BALF) will add to research in pathogenesis of pulmonary manifestations in GERD and can be used as additional biomarker in GERD and its combination with asthma.
AIMS & METHODS: This study evaluated pooled data of AM phenotype and quantitative/qualitative composition of SP-D in BALF in patients with pulmonary GERD manifestations and its combination with asthma in comparison with healthy volunteers. **Methods:** Pooled analysis of AM phenotype in patients with GERD ($n=15$, 46.41 ± 4.18 y.o.), combination of GERD and asthma ($n=16$, 49.30 ± 3.64 y.o.) and healthy volunteers (HV) ($n=10$, 51.83 ± 3.52 y.o.) was performed by flow cytometry (Beckman Coulter FC500) by expression of M1 and M2 AM phenotypes CD markers (CD25, CD80 and CD163, CD206, respectively) and cytokine production of proinflammatory M1, anti-inflammatory M2 and bivalent M1/M2 cytokines in culture medium (CM) of AM (BenderMedSystems, BMS810FF). Quantitative analysis of SP-D in BALF was performed by ELISA. Qualitative assessment of SP-D oligomeric forms in BALF was performed by western blot analysis using tris-acetate gels (Invitrogen, NuPAGE, # EA03752BOX).
RESULTS: Analysis of AM phenotype in patients with GERD, its combination with asthma vs. HV showed that pooled M1/M2 ratio of AM CD markers and cytokine production was 2.16 and 2.52, 0.91 and 0.84 vs. HV, respectively. The results indicates shift of AM towards M1 phenotype vs HV in GERD and towards M2 phenotype vs HV – in combination of GERD and asthma. SP-D level in BALF in patients with GERD was 2.66 times decreased vs patients with combination of GERD and asthma (155.83 ± 18.13 ng/ml vs 414.72 ± 50.22 ng/ml, $p<0.05$) and 3.42 times decreased vs. HV (155.83 ± 18.13 ng/ml vs 533.20 ± 21.12, $p<0.05$). Qualitative analysis of SP-D oligomeric forms in GERD and its combination with asthma showed predominance of monomeric forms vs HV with monomeric and multimeric SP-D oligomers.
CONCLUSION: In GERD with pulmonary manifestations and combination of GERD and asthma AM phenotype and quantitative and qualitative composition of SP-D in BALF vary against healthy volunteers and each other. Shift of AM phenotype towards M1 vs healthy and significant maximum decreased SP-D level in BALF are typical for GERD with pulmonary manifestations, whereas shift of AM phenotype towards M2 and less decreasing SP-D level in BALF are specific for combination of GERD and asthma. There were no significant differences in qualitative oligomeric composition of SP-D in BALF in GERD and its combination with asthma.
Disclosure of Interest: None declared

P0438 INITIAL EXPERIENCE WITH HEMOSPRAY IN THE TREATMENT OF ACUTE UPPER GASTROINTESTINAL BLEEDING

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INTRODUCTION: Upper gastrointestinal bleeding remains a medical emergency. Endoscopic therapies such as adrenaline injection, heater probe and clips are used to achieve haemostasis. However, accurate delivery of these endotherapies can be challenging. Hemospray (Cook Medical, Winston-Salem, North Carolina, USA), an inorganic haemostatic powder, is licensed for use in non-variceal acute upper GI bleeding. The delivery system allows a wide area of coverage, negating the need for accuracy, and has promising results.
AIMS & METHODS: Retrospective analysis of all upper GI bleeds utilising Hemospray following its introduction to Russells Hall Hospital in July 2013. Patients were identified using the Unisoft endoscopy database and endoscopy unit logbooks. Data on the use of Hemospray, bleeding lesion identified and use of other therapeutic modalities were collected. Outcomes including mortality, primary haemostasis and rebleeding were obtained. The aim of this study was to assess the effectiveness of Hemospray in the real-life setting.
RESULTS: Hemospray was used 17 times in 13 patients with acute upper GI bleeding (mean age 69 years, range 37-96 years; 69% male). The patients had a median Blatchford score of 10 (range 5-13) and Rockall score of 7 (range 3-8). Three patients had Hemospray used on more than one occasion.
The cause of bleeding was peptic ulcer in 10/17 patients (58.8%), upper GI malignancy in 6/17 patients (35.3%) and unknown source in 1/17 patients (5.9%). Hemospray was used as primary endotherapy in 11/17 patients (65%) achieving initial haemostasis in 16/17 cases (94%). Technical failure occurred in one patient with the cartridge failing to operate and deliver Hemospray. Rebleeding within 30 days occurred with 6/17 uses (35%); 5 of these in the context of peptic ulcer disease and 1 in upper GI malignancy. When Hemospray was used as primary therapy rebleeding occurred on 4 occasions compared to 2 when used as second line therapy ($p=0.57$). Blatchford scores were higher in those patients suffering from rebleeding (12 versus 10, $p=0.21$). No significant differences in rebleeding was noted between malignant and non-malignant causes of acute upper GI bleeding. 30-day mortality in this patient cohort was 2/13 (15.4%). There were no documented complications of Hemospray therapy.
CONCLUSION: Hemospray is a safe, and easy to use, endoscopic therapy with excellent initial haemostasis as both a primary or second line treatment. In the context of bleeding as a result of upper GI malignancy Hemospray provided good palliation. Although there appeared to be a higher rebleeding rate seen when Hemospray was used as primary therapy this was not significant and may reflect the low numbers in the study.
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Disclosure of Interest: None declared

P0439 CORRECT USE OF PROTON-PUMP INHIBITORS FOR STRESS ULCER PROPHYLAXIS IN INTENSIVE CARE UNIT: NO GI BLEEDING AND NO CL. DIFFICILE?

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INTRODUCTION: Despite limited data about their use in critically ill patients, proton pump inhibitors (PPIs) have become the first line therapy in stress ulcer prophylaxis (SUP). PPIs may increase the risk of hospital-acquired pneumonia and enteric infections, especially *Clostridium difficile* related diarrhoea. Many studies showed an overuse of acid suppressive therapy in Intensive Care Unit (ICU), with unintended consequences of therapy.
AIMS & METHODS: The aim of the study was to evaluate the current practice of SUP, the correlation with the evidence-based American Society of Health-System Pharmacist (ASHP) guidelines and the occurrence of GI hemorrhage, pneumonia, and CDI in critical care setting.

The study was made on 300 consecutive patients (186 men, 114 women, medium age 63.9 yrs, range 23-99 yrs, median ICU stay 11.42 days range 3-45 days) admitted to ICU of the teaching hospital Macchi Varese between January 1st and June 30th 2012 and January 1st and June 30th 2013; patients admitted to neurocritical care unit and children under 18 yrs were excluded. Data about clinical indications, drug assumption and outcomes (gastrointestinal haemorrhage, pneumonia and enteric infections) were collected during ICU stay.

RESULTS: Mechanical ventilation for more than 48h was the reason for initiating prophylaxis in 294 patients (98%); 6 pts. had a platelet count under 50.000/mm3.

281 pts (93.6%) used PPIs (omeprazole 40mg daily i.v.), 19 pts (6.3%) H2RAs (ranitidine 150 mg every 8 hours i.v.), 296 pts (98.6%) antibiotics, 166 pts (55.3%) vasoactive drugs.

32 patients (10.6%) developed nosocomial pneumonia; 26 of them had other risk factors (1 asthma, 14 chronic obstructive lung disease, 1 AIDS, 10 were older than 75 years). One pt had *Clostridium difficile* related dyarrhea. One pt with a history of active duodenal ulcer had ulcer bleeding.

CONCLUSION: All SUP were classified as appropriate according to the ASPH guidelines. PPIs represent the first line therapy. Bleeding from stress ulceration is extremely uncommon; *Clostridium difficile* related dyarrhea is unexpectedly rare too. Patients who developed hospital-acquired pneumonia during acid-suppressive therapy, usually had other risk factors linked to this kind of infection. In this prospective observational study, the occurrence of GI bleeding and symptomatic CDI in critically ill patients, treated following ASHP guidelines, is lower than reported in other studies. More data from well-designed randomized clinical trials are needed before any change in practice.

Disclosure of Interest: None declared

P0440 A COMPARISON OF THE GLASGOW-BLATCHFORD SCORE AND AIMS65 SCORE IN PREDICTING NEED FOR CLINICAL INTERVENTION AND MORTALITY IN ACUTE NON-VARICEAL UPPER GI BLEEDS: A RETROSPECTIVE COHORT STUDY

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INTRODUCTION: The early use of risk stratification scores is recommended by the International Consensus Upper Gastrointestinal (GI) Bleeding Group for patients presenting with acute non-variceal upper GI bleeds (ANVUGIB) [1]. Such models permit identification of patients who are suitable for early hospital discharge or even outpatient care. The most widely used is the Glasgow-Blatchford Score (GBS) [2]. The score ranges from 0 to 23 and the risk of requiring clinical intervention and death has been shown to increase with increasing score [3]. More recently a simpler scoring system known as AIMS65 was devised, which is based on serum **A**lbumin (<30g/dl), **I**NR >1.5, altered **M**ental status (GCS<14), **S**ystolic BP (<90) and age >**65**. One point is scored for the presence of each variable and it has been shown to accurately predict mortality, length of stay, and be superior to the GBS in predicting mortality [4,5]. However, its ability predict the need for clinical intervention has yet to be established.

AIMS & METHODS: The aim of this study was to examine the ability of the AIMS65 score in predicting the need for clinical intervention and mortality in comparison to the GBS. To do this we performed a retrospective analysis of 150 adults who presented to a single district general hospital in Scotland with a primary diagnosis of ANVUGIB and who underwent upper GI endoscopy between March 2008 & April 2013. GBS and AIMS65 scores were calculated and requirement for clinical intervention, defined as the need for endoscopic treatment, blood transfusion and/ or surgery was recorded. The area under the receiving-operator characteristic curve (AUROC) was calculated for each score.

RESULTS: Of the 150 patients 62% were male and 38% female. The mean age was 68 years (SD 16), GBS 7.9 (SD 4.6) and AIMS65 score 1.0 (SD 1.0). The overall mortality was 6%. The GBS had a high predictive accuracy and was superior to AIMS65 in predicting requirement for any clinical intervention (AROC 0.81 vs. 0.70), blood transfusion (AROC 0.85 vs. 0.67) and endoscopic therapy (AROC 0.67 vs. 0.58). With respect to mortality, AIMS65 was superior to the GBS (AROC 0.79 vs. 0.68). Patients with a GBS <4 experienced no mortality, GBS ≥4 <8 2.6% and for those with GBS ≥8 10.1%. For the GBS these cut off values maximised the sensitivity and specificity for inpatient mortality. Patients with low risk AIMS65 scores (0 or 1) experienced mortality (4%) questioning its use as a risk stratification tool for safe, early, hospital discharge.

CONCLUSION: In our population the GBS was superior to the AIMS65 score in terms of predicting the need for any clinical intervention, blood transfusion or endoscopic therapy. We identified potential cut off values for the GBS that allow stratification of patients into low, medium and high risk groups on the basis of predicted mortality. This warrants further investigation.

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P0441 OUTCOMES AND PREDICTIVE FACTORS OF TRANSCATHETER ARTERIAL EMBOLIZATION FOR NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

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INTRODUCTION: Transcatheter arterial embolization (TAE) has been considered a therapeutic option for upper gastrointestinal (GI) bleeding when endoscopic treatment fails.

AIMS & METHODS: We aimed to assess the efficacy and clinical outcomes of TAE for acute nonvariceal upper GI bleeding and to identify predictors of recurrent bleeding within 30 days.

Transcatheter angiography was performed in 66 patients (42 men, 24 women; mean age, 60.3 ± 12.7 years) who experienced acute nonvariceal upper GI bleeding during a 7-year period. Clinical information was reviewed retrospectively. Outcomes included technical success rates, complications, and 30-day rebleeding and mortality rates.

RESULTS: TAE was feasible in 59 patients. The technical success rate was 98.3%. Rebleeding within 30 days was observed in 46.6% and was managed with reembolization in 8 patients, endoscopic intervention in 5, surgery in 2, and conservative care in 12. The 30-day overall mortality rate was 42.4%. Of the 34 patients whose initial endoscopic hemostasis failed, 31 (91.2%) underwent angiographic embolization, which was successful in 30. Rebleeding occurred in 15 patients (50.0%), mainly because of malignancy. Two factors were independent predictors of rebleeding within 30 days by multivariate analysis: coagulopathy (OR, 4.37; CI, 1.25–15.29; $P=0.021$) and embolization in $^{3}2$ territories (OR, 4.93; CI, 1.43–17.04; $P=0.012$). Catheterization-related complications included hepatic artery dissection and splenic embolization.

CONCLUSION: TAE controlled acute nonvariceal upper GI bleeding effectively. TAE may be considered when endoscopic therapy is unavailable or unsuccessful. Coagulopathy and embolization of $^{3}2$ territories were significant predictors of angiographic failure. Correction of coagulopathy before TAE is recommended.

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P0442 DOES DISCHARGE HEMOGLOBIN AFFECT OUTCOME OF PATIENTS WITH ACUTE NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING?

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INTRODUCTION: Many patients with gastrointestinal bleeding show anemia and usually need red blood cell transfusion. Several studies suggested that restrictive transfusion strategy and low hemoglobin threshold for transfusion showed acceptable outcomes in patients with acute upper gastrointestinal bleeding [1,2]. But clinicians are concerned about low hemoglobin affects prognosis and clinical outcome after discharge. This study aimed to assess whether discharge hemoglobin influences on outcomes, or not, in patients with acute non-variceal gastrointestinal bleeding.

AIMS & METHODS: Retrospective analysis was carried out on patients who had upper gastrointestinal bleeding between January 2011 and December 2012. We analyzed the patients who had lowest hemoglobin below 10 g/dL during admission. Patients with variceal bleeding, stroke, or cardiovascular disease were excluded. We divided the patients into two groups by discharge hemoglobin (Low discharge hemoglobin group; 8 g/dL ≤ hemoglobin <10 g/dL, High discharge hemoglobin group; 10 g/dL ≤ hemoglobin <12 g/dL) and compared clinical outcomes and hemoglobin level changes.

RESULTS: A total of 212 patients with upper gastrointestinal bleeding had undergone the endoscopic hemostasis during study periods. One hundred two patients had satisfied the inclusion criteria. Fifty patients discharged with hemoglobin level under 10 g/dL and fifty two patients discharged with hemoglobin level over 10 g/dL. There was no significant difference of endoscopic findings between two groups. Patients in low discharge hemoglobin group showed a lower consumption of pRBC(Low discharge Hb group; 3.2 ± 1.4 pint, High discharge Hb group; 4.1 ± 1.8 pint, P Value = 0.01) and shorter hospital days (Low discharge Hb group; 4.3 ± 2.5 days, High discharge Hb group; 5.6 ± 4.2 days). Hemoglobin levels were not fully recovered at out-patient department until 7 days after discharge. But, most patients showed hemoglobin recovery at 45 days after discharge (Low discharge Hb group; Hb 12.2 ± 2.0 g/dL at OPD 45, High discharge Hb group;; Hb 11.9 ± 2.0 g/dL at OPD 45). Clinical symptoms after discharge were presented no significant difference between two groups.

CONCLUSION: In patients with acute gastrointestinal bleeding, discharge hemoglobin between 8 to 10 g/dL was showed favorable outcomes during outpatient department follow-up. It seems to be tolerable level without additional pRBC transfusion. Despite of high hemoglobin over 10 g/dL at discharge, there was no significant advantage in clinical outcome. Our result can increase the evidence available to support restrictive transfusion strategies in patients with acute non-variceal upper gastrointestinal bleeding.

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P0443 EVALUATION OF THE PREDICTIVE VALUE OF REBLEEDING RATE OF FORREST SIMPLIFIED CLASSIFICATION

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INTRODUCTION: A simplification of the Forrest classification (FC) into three levels (high risk: Ia; increased risk: Ib to IIc; low risk: III) has recently been proposed [(1)].

AIMS & METHODS: Our aim was to evaluate the prognostic value of this new simplified classification (SC) in predicting re-bleeding of peptic ulcer (PU) and to compare it with the traditional FC. We retrospectively identified patients admitted to our unit between 07/2012 to 02/2014 with upper gastrointestinal bleeding due to PU. Demographic, clinical, laboratorial and endoscopic data were collected. Therapeutic interventions and cases of re-bleeding and mortality within a 30 days period were registered. The predictive value of the FC and SC were compared using logistic regression and ROC curves.

RESULTS: 81 patients underwent upper gastrointestinal endoscopy due to bleeding PU; the mean age was 70 ± 16 years; 61 (75%) were men. Clinical presentation of PU bleeding was melena in 33 cases (41%), hematemesis in 29 (36%), symptomatic anemia in 8 (10%), hematochezias in 7 (9%) and hemodynamic instability in 4 (5%). The mean hemoglobin at admission and heart rate were 8.75 g/dL and 94 bpm, respectively. Forty-eight percent of the ulcers were located in the stomach and 52% in the duodenum. Endoscopic therapy was performed in 39 patients (49%), and was effective in 38. One patient (1.2%) required surgery. At the 30th day, re-bleeding occurred in 15 patients (19%) and the mortality rate was 6%. Re-bleeding occurred in 1 of 2 patients with Forrest Ia ulcer (high risk) and 8 (38%) with Forrest IIa (increased risk). The odds ratio for re-bleeding of high risk and increased risk ulcers was 33.00 and 14.30 ($p = 0.013$), respectively. The AUROC (for re-bleeding) was 0.733 for SC and 0.723 for FC.

CONCLUSION: FC maintains its predictive value in determining re-bleeding in PU. The proposed SC maintains the prognostic value of the FC, and therefore is an alternative to assess the risk of re-bleeding.

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P0444 SURVIVAL OUTCOMES AFTER IMPLEMENTATION OF THE UK IMPROVING OUTCOMES GUIDANCE' (IOG) FOR OESOPHAGEAL AND GASTRIC CANCERS

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INTRODUCTION: Oesophago-gastric (OG) cancer is the 3rd most common cause of cancer-related death in the UK. Historically, it has been suggested that the UK may have lagged behind European OG survival outcomes because of fragmentation of service provision, suboptimal access to leading specialist centres and delayed presentation and referral of patients from primary care. The 'Improving Outcomes Guidance' (IOG) for Upper GI Cancers (2001) and Manual for Cancer Services (2004, 2011) recommended centralising curative therapies, reconfiguring access to diagnostic/staging services and formalising the role of the 'Cancer Network' and peer-reviewed 'Network Site Specific Groups'. Lister and QE2 District Hospitals (part of the Mount Vernon Cancer Network) cover a catchment population of 600,000 people and reconfigured their upper GI cancer services in mid-2009.

AIMS & METHODS: Aims: To assess survival outcomes in patients with OG cancer over a 9-year period before and after the reconfiguration of a local upper GI cancer network.

Methods: The medical, endoscopic and computerised notes of multi-disciplinary team meetings of all patients diagnosed with OG cancer between 1 January 2004 - 31 March 2013 were retrospectively analysed. Age, sex, histology, tumour site, treatment intent and number of patients surviving at 6, 12, 24 and 42 months and at 1 April 2014 were noted. The χ^2 (Chi-Square) test was used to analyse the significance of survival outcomes.

RESULTS: From January 2004 - December 2008 there were: 139 gastric cancers (27% curative therapeutic intent) and 234 oesophageal cancers (23% therapeutic intent; 63.6% adenocarcinoma), with overall 12-month survival of 30% and 42% and 42-month mortality of 12% and 15%, respectively. From January 2009 – March 2013 there were: 111 gastric cancers (18% curative therapeutic intent; 68.5% male; average age 75) and 230 oesophageal cancers (26.5% therapeutic curative intent; 65.2% male; average age 72; 69.1% adenocarcinoma) with overall 12-month survival of 40% and 36% and 42-month mortality of 16% and 8%, respectively ($p > 0.05$ for all corresponding follow-up intervals). Sub-group analysis shows increased survival in the 2009-2013 gastric cancer cohort treated with curative intent at 6 months ($p < 0.05$) and palliative therapy at 12 months ($p < 0.05$). There was no significant decrease in survival outcome at any stage of follow up in both cancer groups and cohorts.

CONCLUSION: These findings are in keeping with national outcomes and show that the institution of recommendations from the IOG, including centralisation of curative therapies and access to specialist services, show no significant decrease in survival outcome for OG cancer. Indeed, there is a modest increase in short-term gastric cancer survival. The lower percentage of patients treated with curative intent, compared to national data, may reflect the late presentation of OG cancers and partially explain survival outcomes in this population.

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P0445 THE FLAME MODEL: SUPPORTING ENDOSCOPY TRAINING IN LOW RESOURCE SETTINGS

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INTRODUCTION: Simulation permits selective breakdown of key motor skills for a clinical procedure into basic steps, which is better for acquisition, teaching and assessing. (1, 2) Environment doesn't significantly affect skills transfer, implying endoscopy can be learnt outside the clinical setting. Basic endoscopic competencies can be taught with ex-vivo animal models. (3) The British Society of Gastroenterology supported an excursion to Kurdistan whose remit to 'train-the-trainers' required provision of a suitable model.

AIMS & METHODS: Develop and Validate: Flexible Lightweight Animal Model for gi Endoscopy (FLAME), to support hands-on endoscopy training in a low-resource setting, specifically, to facilitate training in GI haemostasis, variceal banding and polypectomy. Pilot prototyping indicated use of a lightweight, mouldable, plastic frame with selected ports for the attachment of premade animal tissue patches with bespoke defects. Potential port sites were analysed to optimise access and offer different technical challenges. A foil plate and cling film wrap-around supported use of diathermy and prevented fluid leakage. The model was housed in foam and enclosed in a lightweight box. External Velcro straps provided further anchorage. The model was validated during a hands-on training course conducted in Erbil, Iraq in February 2014. Attendees completed 11-point realism (visual, anatomical and mechanical) surveys based on a 7 point Likert scale,(4) separately for GI haemostasis, variceal banding and polypectomy. Analysis using Wlicoxon signed rank test (PASW Statistics 18) for non-parametric data reported scores against a hypothetical mean of 4.0 for statistical significance ($n = 17$ gave >90% power to detect a difference of 1 point).

RESULTS: 20 delegates (6 consultants, 14 trainees) completed the surveys. For polypectomy all scores were greater than 1 point above the 4.0 hypothethical mean, range 5.26-5.76 (score of 7 indicates strong agreement with realism). Mean overall score was 5.59 [$p < 0.05$; CI 4.96-6.22]. For both variceal banding and GI haemostasis, all mean scores were above 4.0 though the overall reality scores did not reach significant difference; variceal banding - range 4.62-5.31, overall score 4.62; GI haemostasis – range 4.5-5.83, overall score 4.56. Separate evaluation of the overall training course revealed high levels of delegate satisfaction, principally the hands-on model training elements.

CONCLUSION: The FLAME's initial evaluation in a course setting demonstrates face and content validity for polypectomy. Whilst banding and GI haemostasis values didn't achieve statistical significance ratings for all parameters, all were higher than the hypothetical mean. The model is cost-effective, easy to transport, robust in practice and was highly valued by delegates in course evaluation. We plan further adaptations with follow-up validation studies.

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P0446 THE FIRST REPORT ON THE GASTROPROTECTIVE EFFECT OF TRIPEPTIDE T-34 UNDER CONDITIONS OF WATER-IMMOBILISATION STRESS IN RATS

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INTRODUCTION: There is accumulating evidence that a number of short peptides are envolved in the regulation of the function of gut and may be considered as new pharmacological drugs for the prevention and treatment of gastric ulceration.
AIMS & METHODS: Objective of our research was to explore the effect of tripeptide T-34 (H-Glu-Asp-Gly-OH) on the area of water-immobilisation stress (WIS)-induced gastric lesions in rats and activities of NO-synthases (NOS) and lipid peroxidation processes in gastric mucosa (GM).
The studies were conducted on white male rats. 30 min before the exposure to WIS rats were pretreated with T-34 introduced intragastrically (IG) in dose 10μg ($n = 5$) or intraperitoneally (IP) - 2μg ($n = 5$). Control rats were injected 0.5 ml of saline ($n = 5$). After 5 hours of WIS, rats were sacrificed, gross inspection of GM was conducted and NOS activity, NO and MDA content in GM were determined. In blood plasma L-arginine concentration was measured.
RESULTS: WIS caused the formation of gastric lesions (18±1.9 mm), accompanied by acute rise of NO-synthase activity ($p < 0.05$), in particular its inducible isoform – iNOS ($p < 0.01$), increased production of NO and MDA ($p < 0.05$) in GM compared to intact rats. The concentration of L-arginine, NO precursor, in blood plasma decreased ($p < 0.05$). Pretreatment with T-34 IG caused 27% ($p < 0.05$) decrease of ulceration area, at that NOS activity decreased for 45% ($p < 0.05$), iNOS activity diminished for 60% ($p < 0.01$) in GM compared to control rats. Decrease of NO ($p < 0.05$) and tendency to decrease of MDA content in GM were also noted, whereas L-arginine concentration in plasma increased ($p < 0.05$). Pretreatment with T-34 IP also resulted in the decrease of iNOS activity in GM ($p < 0.05$) but no statistically significant difference of the area of GM damage was evaluated compared to saline-treated rats exposed to WIS.
CONCLUSION: T-34 decreased the indices of nitrooxidative stress in GM under the conditions of WIS-induced gastric lesions in rats. IG administration of T-34 was superior to IP injection of this compound towards reduction of gastric mucosa damage. Deeper studies on the elucidation of the cytoprotective effect of tripeptide T-34, optimization of dosage and route of application are required.
Disclosure of Interest: None declared

P0447 THE FREQUENCY AND TYPE OF HISTOLOGICAL GASTRIC CHANGES IN PATIENTS WITH FUNCTIONAL DYSPEPSIA

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INTRODUCTION: Though the symptoms of functional dyspepsia (FD) are not considered to correlate with mucosa changes the histopathological evaluation seems to be fundamental not to miss the early onset of atrophic-metaplastic transformation.
AIMS & METHODS: Our aim was to assess the frequency and type of histological changes in patients with functional dyspepsia. This work was a part of a randomized superiority trial in which combined treatment using eradication therapy (ET) plus antidepressant by comparison with ET for patients with FD was assessed. Adult patients (18 - 65 years) with confirmed diagnosis of FD by the Rome III criteria (2006) were eligible to participate. Exclusion criteria: the presence of "red flag" signs and other comorbidities that could explain the symptoms. Biopsy specimens were taken from stomach following the Houston-updated gastric biopsy sampling protocol for the next histological examination. One expert gastrointestinal pathologist, blinded to all patient clinical but not endoscopic information, assessed all tissue samples. The degree of inflammatory changes was scored by the 4-grade Visual Analogue Scale, atrophy - following Operative Link for Gastritis Assessment (OLGA) and metaplasia - following Operative Link on Gastric Intestinal Metaplasia (OLGIM) staging systems. All patients were tested for *H. pylori* using two methods (rapid urease test and by morphological examination).
RESULTS: 75 patients fulfilled all criteria and were included into the study. Mean age was 40.3±3.9; males – 26 (34.7%). *H. pylori* was detected in all 75 patients. The main location of *H. pylori* infection was antral part. Patients had mainly a mild degree of mucosal inflammation (84%) which in most cases was limited to antral part. Atrophy was statistically significant more frequently diagnosed in antrum (64.0%) than in corpus (12.0%) ($p < 0.0001$) and in all cases didn't exceed OLGA stage I. Metaplasia of intestinal type was found in 26 (34.7%) patients in antral part and was not detected in corpus ($p < 0.0001$). No case of dysplasia was detected. We also tried to collate the degree of gastritis and the stage according to OLGA (2008) in antrum and corpus with the presence of such clinical syndromes of FD as postprandial distress and epigastric pain. No statistically significant correlation was found ($p > 0.05$).
CONCLUSION: As in most studies, we also didn't find the correlation between stage and degree of gastritis and clinical symptoms of FD. But we shouldn't forget about possible microscopic changes of mucosa when dealing with "functional" patients, thus conducting a primary prophylaxis of gastric cancer.
Disclosure of Interest: None declared

P0448 THE IMPACT OF ERYTHROMYCIN ON MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS

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INTRODUCTION: Surface electrogastrography (EGG) is a non-invasive method for the assessment of gastric myoelectrical activity. Erythromycin, as a potent prokinetic drug, increases the dominant frequency of EGG both in humans and experimental pigs. The aim of this study was to evaluate the effect of erythromycin on the porcine EGG power (assessed by areas of amplitudes) and power ratio (simple fraction ratio of the areas of amplitudes after and before erythromycin administration).
AIMS & METHODS: Six mature female pigs (3 months old, mean weight 23.2±2.1, median 23 kg) were included in the study. All EGG recordings were performed under general anaesthesia in the morning after 24 hours of fasting (by means of the MMS EGG System, Enschede, the Netherlands). The baseline EGG recording lasted 15 min., erythromycin ethylsuccinate (1,500 mg) was subsequently administered by gastric tube into the stomach. The EGG trial recording lasted 150 min. (ten 15-minute intervals: P1 to P10) after erythromycin administration. Running spectral analysis (based on Fourier transform) was used for initial evaluation of the EGG. The gastric myoelectric activity was estimated by EGG power analysis and by power ratio assessment.
RESULTS: Erythromycin increased the EGG power significantly after 15 to 30 min. from the baseline mean value 828±633 (μV^2) to 1583±4238 (at P1) and 1102±2077 (P2 interval), $p = 0.003$. Afterwards, the EGG power decreased to its minimum at P4 (237±200), $p < 0.001$; and increased to 709±1213 μV^2 after 150 min. (at P10), $p < 0.001$. The EGG power ratio reached the highest values at P1 (1.64±3.98) and P2 (1.91±4.27), decreased significantly at P4 (0.29±0.27; $p < 0.001$) and balanced out after 150 min. at P10 interval (1.15±2.48; NS: $p = 0.668$).
CONCLUSION: A medium single dose of erythromycin caused a significant increase in the EGG power and power ratio after 15 to 30 min. after intragastric administration. Both myoelectrical markers decreased after 60 min. and returned close to the initial values after 150 min.
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Disclosure of Interest: None declared

P0449 FUNCTIONAL MOTOR-SECRETORY LIGAMENTS OF DIGESTIVE ORGANS

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INTRODUCTION: Definition of motor stomach and duodenum disorders role in gastroduodenal zone development process is interesting for peculiarities of digestive system disorder clinical realization. Phase structure of interdigestive motility reflects changes of digestive system activity and inactivity periods; influences interdigestive cycle duration and essentially changes during gastric and duodenum diseases.
AIMS & METHODS: Patients with functional diseases (65), chronic gastritis/gastroduodenitis (184) and duodenal peptic ulcer (55) took part in study of stomach and duodenum motility (GDM). Also 30 healthy men took part in this testing. GDM was studied by the special bougie. Electrodes were based in duodenum, antrum and in body of stomach. External probe ends were connected with polygraph strain gauge, which registered GDM and defined interdigestive cycle periods of inactivity (I phase) and activity (II phase – intermittent motility, III phase – rhythmic phase).
RESULTS: Correct alternation of GDM was diagnosed among healthy men: I phase 22.4±2.0; II phase – 42.6±2.6; III phase – 5.6±1.7 min, in case of interdigestive cycle total time is 69.7±2.3 min. Amplitude and frequency characteristics of stomach and GDM were lowest during I phase (1-4 low-amplitude contractions per min), but they became higher during II phase (3-8 contractions of different height per min) and during III phase (9-15 rhythmic amplitude signals per min). Phase research of intragastric pH in basal conditions showed, that stomach pH decreases till 1.0±0.10 during II phase and it increases till 1.7±0.12 during the third one, as maximal realization of acidogenesis stomach function at the beginning of working period. Patients were separated in 3 observation groups: with heightened, preserved and reduced acidogenesis stomach function. The I group endurance period of inactivity (1 phase) lasted for 15.6±1.0 min, working period of II and III phase was increased till 50.6±1.0 and 6.2±0.9 min, properly ($P < 0.05$). Patients of the II group had phase indexes, which essentially did not differ from control group results (20.6±1.6-42.3±2.3-5.2±1.3; $P > 0.05$). In the group motor indexes and interdigestive total time did not statistically differ from check ones ($P > 0.05$). Patients from the III group had these results: I phase lasted for 27.3±0.9 min, II phase – 38.5±0.7 and III phase was shortened to 4.1±1.1 min; the inactive period increase was determined by means of working period, which was equivalent to gastroduodenodyskinesia.
CONCLUSION: In case of inflammatory gastroduodenum pathology, GDM structure changes according to the picularities of stomach acidogenesis during intagastral cycle. This fact can be explained by secretory and motor function of digestive system functional correlation.
Disclosure of Interest: None declared

P0450 HIGH ONE-YEAR RESPONSE RATE TO PERMANENT GASTRIC ELECTRICAL STIMULATION AND IMPROVED QUALITY OF LIFE IN PATIENTS WITH NON-ESTABLISHED INDICATIONS FOR TREATMENT SELECTED BY A TEMPORARY STIMULATION PERIOD

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INTRODUCTION: Gastric electrical stimulation (GES) with the Enterra system is a therapeutic alternative for patients with therapy refractory nausea and vomiting secondary to diabetic or idiopathic gastroparesis (GP). Some patients with normal gastric emptying also benefit from GES (Andersson et al, 2011) after selection with a temporary percutaneous stimulation (TPGES) test.
AIMS & METHODS: The aim of this study was to assess response rate and quality of life after one year of treatment with GES in patients selected by a TPGES test period. We used the TPGES technique described by us previously in a randomized double blind crossover design with 2 weeks stimulation ON (5-7 mA range) followed by stimulation OFF, or the opposite order. Treatment response was defined as a symptom reduction $\geq$50% during the ON period compared to the OFF period for one or both of weekly nausea hours (WNH) and weekly vomiting frequency (WVF). Non-responders to blinded TPGES were offered an open treatment period with increased stimulation (5-10 mA as tolerated). The response to permanent GES was judged by the same response definition but comparing one-year data with baseline symptom registration. Quality of life was evaluated by use of the SF36 questionnaire at baseline and after 12 months of GES therapy.
RESULTS: Twenty-eight patients (22 female (78.6%), median age 43.5 years (range 20-70)) with therapy refractory nausea and vomiting were included. Gastric emptying was normal in 17 patients (61%) and delayed in 11 (39%). Ten patients (36%) were responders after blinded TPGES and 18 were not. Six accepted an open stimulation period during which two more were responders and two were judged as responders by patient preference, both of whom had diabetes mellitus. Thus, a total of 14 patients (50%) were offered and accepted a permanent device (Table 1). After one year of GES treatment, 11 patients (79%) were still responders. Response to treatment could not be predicted by gastric emptying status, neither after TPGES ($p = .70$) nor after GES ($p = .61$). Responders to GES had a significant improvement in quality of life after one year comparing with baseline in terms of bodily pain ($p = .017$), vitality ($p = .035$), social functioning ($p = .026$), role emotional ($p = .038$), mental health ($p = .024$) and general health ($p = .017$).
Table 1. Clinical diagnosis, gastric emptying status, TPGES response and one-year response number in patients selected for permanent GES.

Diagnosis (n)	Gastroparesis	Responders TPGES (open stim)	Responders 1 year GES
Diabetes mellitus (5)	0	3 (2)	3
Idiopathic gastroparesis (3)	3	1	1
Postsurgical nausea or vomiting (7)	5	3 (1)	2
Functional dyspepsia (9)	0	5 (1)	3
Enteric dysmotility (4)	3	2	2

CONCLUSION: TPGES is a good selection tool for patients with non-established indications for GES treatment and results in a high one-year response rate. A significant improvement in quality of life after 1 year of GES therapy was also shown in the responder group.
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P0451 EFFICACY OF PNEUMODILATION IN ACHALASIA AFTER FAILED HELLER MYOTOMY

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INTRODUCTION: Heller myotomy is an effective treatment for the majority of achalasia patients. However, a small proportion of patients suffers from persistent or recurrent symptoms after surgery and they are usually subsequently treated with pneumodilation (PD).
AIMS & METHODS: The efficacy of PD as secondary treatment for achalasia has scarcely been studied. This study therefore aimed to investigate the efficacy of PD as treatment for achalasia patients suffering from persistent or recurrent symptoms after Heller myotomy. 20 patients with recurrent or persistent symptoms (Eckardt score >3) after Heller myotomy were selected. Patients were treated with PD, using a graded distension protocol with balloon sizes ranging from 30 to 40 mm. After each dilation symptoms were assessed to evaluate whether a subsequent dilation with a larger balloon size was required. Patients with recurrent or persistent symptoms (Eckardt score >3) after treatment with a 40-mm balloon were identified as failures.
RESULTS: 12 patients presented with achalasia type I, 6 with achalasia type II and 2 with achalasia type III (Chicago classification). Median relapse time was 4 years after Heller myotomy (IQR: 7 years and 9 months). 3 patients were not suitable for PD; 1 patient was morbidly obese and 2 had a mega-oesophagus. 5 patients were successfully treated with one 30-mm balloon dilation (median follow-up time: 2 years; IQR: 7 years). 8 patients required dilations with 30- and 35-mm balloons (median follow-up time: 6 years; IQR: 6.5 years). 4 patients underwent 3 dilations with balloon sizes up to 40 mm, and all failed on the 40-mm balloon as well. Thus, PD was successful for 13 out of the 17 patients who could be treated, resulting in a success rate of 76% for treatable patients or 65% for all patients. Patients successfully treated with a 30-mm balloon all suffered from achalasia type I. Baseline LOS pressure (before dilation) was not different between successfully treated patients (Median: 15.0 mmHg; IQR: 11.5 mmHg) and those that failed (median: 12.5 mmHg; IQR: 6.5 mmHg) treatment ($p > 0.05$). Furthermore, baseline Eckardt scores were not predictors of successful treatment; there was no difference between successful (median: 6; IQR: 2) and failed (median: 5.5; IQR: 3.25) treatment. Baseline symptom pattern was not a predictor of successful treatment either.
CONCLUSION: Pneumodilation for recurrent symptoms after previous Heller myotomy has a success rate of 76%, using 30- and 35-mm balloons. Patients with recurrent symptoms after pneumodilation with 35-mm balloon are likely to also fail after dilation with a 40-mm balloon.
Disclosure of Interest: None declared

P0452 IS DIFFERENTIATING BETWEEN HIATUS HERNIA IIIA AND IIIB IN HIGH RESOLUTION MANOMETRY USEFUL IN CLINICAL PRACTICE?

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INTRODUCTION: Oesophageal high resolution manometry (HRM) is a useful tool for the detection of hiatus hernia (HH) as two high pressures zones, lower oesophageal sphincter (LOS) and crural diaphragm (CD) can be clearly identified. Two types of HH have been described in HRM, type IIIa, associated with a further decrease in LOS pressure during inspiration, and IIIb associated with an increase in LOS pressure during inspiration.
AIMS & METHODS: The aim of this study is to determine if these HRM classifications for hiatus hernia are useful in clinical practice.
39 consecutive patients with HH detected by HRM were included. HRM (Manoscan; Given) was performed in supine and analyzed according to 2012 Chicago classification criteria. HH was defined as a separation $>$ 2 cm between LOS and CD at inspiration. Upper endoscopy was performed on all patients and 24 hours pH-monitoring on 30 (76.9%) of them. Statistical analysis: U Mann Whitney; Chi-Square.
RESULTS: Clinical data, HRM and pH-monitoring results are expressed in the table. Hypotensive LOS (resting pressure $<$ 10 mmHg) was found in 42.8% HH IIIa and in 27.8% HH IIIb; oesophagogastric junction (OGJ) obstruction (IRP-4 $>$15 mmHg) at the level of the CD was found in 19.1% HH IIIa and in 16.7% IIIb ($p = 0.591$). There were no significant differences in oesophageal body motility (normal 76.2% in HH IIIa and 61.1% in HH IIIb; $p = 0.457$). Multiple water swallow test was normal in 47.4% in HH IIIa and in 75% in HH IIIb ($p = 0.055$).

	HH IIIa (n = 21)	HH III b (n = 18)	p-value
Clinical data			
Age	63.8 [57.4-70.1]	58.6 [51.8-65.3]	0.234
Sex (F)	13 (58.9%)	9 (50%)	0.455
BMI (kg/m2)	30.7 [27.9-33.5]	27.2 [25.2-29.2]	**0.037**
Abdominal perimeter (cm)	105.7 [100.8-110.6]	97.4 [91.2-103.5]	0.078
Co-morbidity	1 (4.8%)	2 (11.1)	0.873
No	20 (95.2%)	16 (88.9%)	0.424
Yes	19 (90.5%)	15 (83.3%)	0.311
Previous PPI treatment	10 (47.6)	12 (66.8%)	
Upper endoscopy	2 (9.5%)	1(5.5%)	
Normal	4 (19.1%)	4 (22.2%)	
Peptic esophagitis	2 (9.5%)	1 (5.5%)	
Barrett	1 (4.8%)		
Ring/Stenosis	2 (9.5%)		
Diverticulum			
Other (gastritis, ulcer)			
	HRM parameters		
Resting pressure (mmHg)	12.6 [8.7-16.5]	12.5 [9-12,3]	0.945
IRP-4s	8.9 [6.1-11.8]	6.7 [3.7-9.8]	0.112
OGJ total length (cm)	7.3 [6.3-8.3]	7.7[6.3-9.1]	0.791
Oesophageal length (cm)	20.5[19.4-21.7]	20.8[19-22.7]	0.813
Sac length	3.3 [2.5-4]	3.1 [2.1-4.2]	0.646
DCI (mmHg.cm.s)	1474.4 [1027.5-1921.2]	2070 [868.7-3272.7]	1
VFC (cm/s)	3.8 [2.8-4.8]	4.2[2.9-5.4]	0.626
IBP (mmHg)	18.6 [14.4-22.8]	23.1[14.9-31.3]	0.967
Distal Latency (s)	5.4 [4.8-6.1]	5.9[5.6-6.3]	0.119
	pH-monitoring result		
Abnormal	7 (43.8%)	7 (50%)	0.509
Positive symptom index	3 (18.7%)	3 (21.4%)	0.558

CONCLUSION: There were no significant differences between the two HH types in the clinical data, in upper endoscopy, HRM and pH-monitoring results although patients with HH IIIa are more obese and tend to have a more hypotensive LOS. The differentiation between both subtypes is therefore not useful for routine clinical practice.
Disclosure of Interest: None declared

P0453 MULTIPLE RAPID SWALLOWING IS A USEFUL COMPLEMENTARY TEST TO CORRELATE SYMPTOMS TO ESOPHAGEAL MOTILITY ABNORMALITIES

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INTRODUCTION: Although esophageal motor disorders (EMD) are associated with non-cardiac chest pain (NCCP) and dysphagia, minimal data support a direct relationship between abnormal motor function and symptoms. Indeed, a recent study failed to observe a correlation between high-resolution manometry (HRM) metrics and symptoms during the manometric protocol. On the other hand, multiple rapid swallowing (MRS) has been recently suggested as a complementary test during HRM in order to observe abnormalities in inhibitory or excitatory esophageal mechanisms that could potentially underlie esophageal symptoms. Limited data are available on the role of MRS in eliciting NCCP or dysphagia during HRM testing.
AIMS & METHODS: We aimed to evaluate the yield of MRS to provoke esophageal symptoms in patients with normal or abnormal standard manometry. Consecutive patients with NCCP or dysphagia without previous surgery were enrolled. All patients underwent HRM as follows: after a 5-min baseline recording to locate and assess the esophago-gastric junction, the subjects took 10 single water swallows (5 mL) at 30-s intervals (standard assessment) and two MRS (one swallow every 2–3s) while 10mL of water was injected steadily into their mouths through a syringe. Symptoms reported were recorded and graded based on a 5-point Likert scale (0-4) and a 10-cm visual analogue scale (VAS). The tracings were analyzed based on Chicago Classification (CC) criteria for EMD and, further, MRS were analyzed for completeness of esophageal body inhibition and for augmentation of contraction after the last MRS swallow. Also the last swallow during MRS was classified according to the CC criteria.
RESULTS: We enrolled 31 [18M/13F; mean age 55 (35-78)] patients complaining of NCCP (n = 14) and dysphagia (n = 17) as major symptom. Fourteen (45%) patients had incomplete esophageal body inhibition, whereas 13 (42%) patients failed to increase wave amplitudes after MRS. Overall, 18 (58%) patients had abnormal MRS, with 5 (16%) of them having normal peristalsis. No patient complained of NCCP or dysphagia during standard assessment. In contrast, 9 (29%) patients reported either NCCP [n = 5; mean Likert scale 3.0 (range 2.0-4.0) and VAS scale of 7.7 (6.6-9.2)] or dysphagia [n = 4; mean Likert scale 2.8 (range 2.0-3.0) and VAS scale of 7.6 (5.2-8.8)] during at least one MRS (p = 0.0020). Among them, at standard manometric assessment, we found normal peristalsis (n = 2), Jackhammer Esophagus (n = 3), distal esophageal spam (n = 2), outflow obstruction (n = 1), and absent peristalsis (n = 1), whereas MRS resulted to be abnormal in 8 cases. Interestingly, when symptoms were reported, they were always associated with an abnormal last MRS swallow according to CC criteria (premature swallow, n = 4; rapid contraction, n = 3; hypercontractile swallow, n = 1; failed, n = 1). This was observed also in the only case with normal MRS.
CONCLUSION: MRS was a useful complementary test during HRM in order to detect esophageal motility abnormalities in patients with either normal or abnormal standard manometry. Moreover, MRS was superior to standard assessment in provoking esophageal symptoms in patients with NCCP or dysphagia and permitted to correlate them to abnormal motor function.
Disclosure of Interest: None declared

P0454 VALIDATION OF THE CHICAGO CLASSIFICATION FOR THE DIAGNOSES OF PRIMARY ESOPHAGEAL MOTILITY DISORDERS BASED ON OUTCOME DATA

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INTRODUCTION: Early comparisons between 8-channel water-perfused (WP) conventional manometry and 36 pressure transducers solid-state (36-SS) high-resolution manometry (HRM) showed that high spatial resolution increases the diagnostic yield and accuracy for clinically relevant esophageal motility disorders (EMD). Thus, a new classification of EMD based on HRM findings, the Chicago Classification (CC), has been proposed. Limited data are available on the clinical impact of this classification in terms of patients' outcome.
AIMS & METHODS: We aimed to prospectively assess the clinical value of the CC comparing the diagnoses of EMD obtained by using the 36-SS and the 24-channel WP system in a group of patients with esophageal symptoms and evaluating their clinical outcome at 1-year after treating them based on 36-SS HRM findings. Diagnoses of EMD have been collected from a prospective, randomized, double blind, crossover study aimed to measure and compare normal values of conventional and high-resolution manometry metrics as well as to assess the inter-rater and inter-device agreement for the diagnoses of EMD between the 36-SS (Given Imaging, US) and the 24-WP system (EB Neuro, Italy). Twenty patients [11M/9F; 48 (43-55)] underwent both procedures blinded and in random order. Two expert reviewers (RS, ES) performed a blind analysis of the patients plots. Diagnoses based on CC were obtained. Inter-rater and inter-device agreement for each reviewer were evaluated. Then, according to CC-based diagnoses at 36-SS HRM plus impedance-pH features in case of suspected reflux disease, patients were empirically treated and followed-up for 1 year. Outcome was evaluated as positive (≥50% of symptomatic relief) or negative (<50%) based on validated disease-related questionnaires.
RESULTS: Diagnostic inter-device agreement was moderate for both reviewers [k (RS) = 0.5; k(ES) = 0.4], whereas diagnostic inter-rater agreement was higher for the 36-SS ($k = 1$) than for the 24-WP ($k = 0.68$) system. As to the outcome evaluation at 1-year, we found that 17/20 (85%) patients had a positive outcome. Among them, 7 patients had dysphagia with achalasia (type II, n = 5; type III, n = 1; type I, n = 1) and were surgically (n = 4) or endoscopically (n = 3) treated, 7 patients had reflux symptoms with normal peristalsis (NP; n = 4) or frequent failed peristalsis (FFP; n = 2) or weak peristalsis (WP; n = 1) and were surgically (n = 2, Nissen Fundoplication) or medically (n = 5, PPI plus alginate) treated, 1 patient had chest-pain with WP and was treated with PPI plus prokinetic and, finally, 2 patients had dysphagia with FFP and outflow obstruction (OO) and were treated with prokinetic and endoscopic dilatation, respectively. Out of 3/20 (15%) patients with a negative outcome, 1 had dysphagia with NP (also at 24-WP HRM) and was treated with PPI plus prokinetic, 1 had regurgitation with OO (normal peristalsis at 24-WP HRM) and was treated with PPI plus prokinetic, and 1 had chest-pain with distal esophageal spasm (FFP at 24-WP HRM) and was treated with endoscopic dilatation.
CONCLUSION: The 36-SS HRM was more accurate and reproducible than the 24-WP system for diagnosing clinically relevant EMD based on the CC. Moreover, the Chicago classification has been found greatly useful as diagnostic tool in order to obtain good outcome in patients reporting esophageal symptoms.
Disclosure of Interest: None declared

P0455 CLINICAL AND ENDOSCOPIC CHARACTERISTICS CAN HELP DISTINGUISH PSEUDOACHALASIA FROM ACHALASIA

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INTRODUCTION: Pseudoachalasia is a condition in which clinical and manometric signs of idiopathic achalasia are mimicked by another abnormality, most often a malignancy. An underlying malignancy should be recognized early to prevent inappropriate therapeutic intervention and delay in appropriate treatment. However, clinical identification of pseudoachalasia can be challenging.
AIMS & METHODS: The aim of our study was to identify characteristics that suggest potential pseudoachalasia caused by malignancy. Patients diagnosed with achalasia by manometry were retrospectively included between 2000 - March 2014 in a single centre. Manometric criteria for achalasia were defined as aperistalsis and dysrelaxation of the lower oesophageal sphincter (LOS). Pseudoachalasia was diagnosed in patients with clinical and manometric signs of achalasia that were found to have an underlying malignancy. Clinical (Eckardt symptom score), manometric, endoscopic and radiological findings were reviewed and compared between patients with pseudoachalasia versus achalasia.
RESULTS: In total 205 patients with achalasia were included (116 male, median age 52 (39-64) (median (IQR)). Pseudoachalasia was diagnosed in 10 patients (4.9%, 8 male) and caused by oesophageal adenocarcinoma (n = 3), oesophageal

squamous cell carcinoma (n = 3), adenocarcinoma of the cardia (n = 3) or pancreatic adenocarcinoma (n = 1). The underlying malignancy was found at EUS (30%), at a second or third endoscopy with biopsies (20%) or during a treatment session (30%; 2x Heller myotomy, 1x pneumodilation). In 20% of the patients a CT-scan after achalasia treatment, performed because of quick recurrence of symptoms, eventually showed the malignancy. Patients with pseudoachalasia were older at time of diagnosis compared to achalasia patients (68 (50-72) vs 51 (38-63), $p < .05$)), had a shorter clinical history (6 (5-12) months vs 24 (11-68) months, $p < .01$) and lost more weight (12 (10-20) kg vs 6 (0-10) kg, $p < .01$). The Eckardt symptom score was higher in the group with pseudoachalasia (9 (8-10) vs 7 (6-9), $p < .05$). However when the score was corrected for weight loss no difference was seen (6 (6-7) vs 5 (5-7), $p > .05$). Manometries in both groups showed aperistalsis and dysrelaxation of the LOS, with no difference in LOS pressure (33 (19-35) mmHg vs 23 (18-32) mmHg, $p > .05$). In 80% of patients with pseudoachalasia a barium oesophagography was performed and in 75% it was suggestive of achalasia showing an enlarged diameter, narrowing of the LOS and stasis of contrast compared to 91% in idiopathic achalasia. All patients with pseudoachalasia underwent 1 or more endoscopies and in 80% the LOS was difficult or even impossible to pass. In achalasia patients the LOS was difficult to pass during endoscopy in only 22%.

CONCLUSION: Advanced age, short clinical history, considerable weight loss and difficulty in passing the LOS during endoscopy are characteristics that should arouse a higher suspicion of pseudoachalasia and warrant additional investigations. It is not possible to distinguish pseudoachalasia from achalasia with the conventional diagnostics used for achalasia such as manometry and barium oesophagography.

Disclosure of Interest: None declared

P0456 DEVELOPMENT OF AN ENDOSCOPY- AND HISTOLOGY-BASED ACTIVITY INDEX FOR EOSINOPHILIC ESOPHAGITIS

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INTRODUCTION: A validated instrument to assess severity of eosinophilic esophagitis (EoE) in clinical trials and observational studies is urgently needed. The international Eosinophilic Esophagitis Activity Index (EEsAI) study group is currently developing an activity index for adult EoE patients. Three instruments have been developed to assess endoscopic, histologic, and clinical EoE activity.

AIMS & METHODS: We aimed to develop instruments that assess endoscopic and histologic findings and the corresponding score based on the items that best explain the variability in the physician global assessment (PGA) of EoE severity. To assess whether items of the patient-reported outcomes (PRO) instrument, which is designed to assess symptom severity, also help to explain the variability of the PGA. We sought input from the experts and patients to generate the item list to be included into 3 different instruments. Physicians provided PGA that took into account symptoms, endoscopy, and histology and was assessed on a Likert scale from 0 to 10. Using the physician instrument, severity of EoE-associated endoscopic features including white exudates, rings, edema, furrows, and strictures was graded. Severity of EoE-associated histologic findings including peak eosinophil counts, eosinophil abscesses, basal layer enlargement, and subepithelial fibrosis was assessed by the means of histopathology instrument. The dysphagia characteristics and behavioral adaptations associated with consumption of foods of different consistencies, among others, were assessed using the PRO instrument. Linear regression and analysis of variance (ANOVA) was used to evaluate the extent to which variations in the severity of EoE-associated endoscopic and histologic features explain the variability in PGA. ANOVA was used to examine the extent to which variations in symptom severity help to explain the variability in PGA over and above variations in severity of endoscopic and histologic features.

RESULTS: The physician, histopathology, and PRO instruments were evaluated in 153 adult EoE patients (72.5 % males, median age 38 years) recruited in Switzerland and in the United States. Variations in severity of endoscopic features including white exudates, rings, edema, furrows, and strictures explained 52 % of the PGA variability. Variations in severity of histologic features including the peak esophageal eosinophil numbers and eosinophilic microabscesses explained additional 9 % of the variability in PGA. Variations in symptom severity (7 items of the PRO module recalled over the last 7 days) explained an additional 10 % of the variability in PGA.

CONCLUSION: The variations in severity of EoE-associated endoscopic and histologic features explained most variability in physician global assessment of EoE severity (total of 61 %).

Disclosure of Interest: None declared

P0457 DIETARY TREATMENTS FOR INDUCING REMISSION OF EOSINOPHILIC ESOPHAGITIS. A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Eosinophilic esophagitis (EoE) is a chronic esophageal immune/allergy-mediated disorder, which represents a distinctive form of food-allergy. Various dietary interventions have been used to treat patients with EoE, yielding varied results.

AIMS & METHODS: This systematic review assesses the efficacy of different dietary therapies in inducing disease remission of EoE in adult and pediatric patients with the disease.

A systematic search was performed in MEDLINE, EMBASE, and SCOPUS for studies investigating the efficacy of various dietary interventions in inducing remission (< 15 eosinophils/hpf) of inflammatory infiltration as observed in esophageal biopsies from both pediatric and adult EoE patients. Summary estimates, including 95% confidence intervals (95% CI), were calculated for exclusive feeding with amino acid-based elemental formulas, allergy testing-directed food elimination diets, and six-food elimination diets (SFED). A fixed or random effects model was used depending on heterogeneity (I^2); publication bias risks were assessed by means of funnel plot analysis.

RESULTS: The search yielded 578 references, of which 30 were included in the quantitative summary. All told, the studies described 1,285 EoE patients (1,124 children and 161 adults) undergoing different dietary treatments. Elemental diets were effective in 90.4% of cases (95% IC: 84.7–95.5%, I^2: 2.3%), SFED in 73% (66.6–78.9%; I^2: 0%), and allergy testing-directed food elimination induced remission in 46.3% of cases (35.6–57.1%; I^2: 7 6.4%). Additional dietary therapy strategies (elimination of cow's milk and gluten-free diets) were also evaluated. Overall, no significant differences in remission rates were documented between children and adults (67.4% *vs.* 71.5%).

CONCLUSION: Dietary treatment is effective in achieving histological remission in patients with EoE. Elemental diets and SFEDs were the most consistent alternatives, achieving < 15 eosinophils/hpf in 90.4 and 73% of treated patients, respectively.

Disclosure of Interest: None declared

P0458 IS EOSINOPHILIC ESOPHAGITIS CORRELATED WITH ALLERGIC RHINITIS?

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INTRODUCTION: Eosinophilic esophagitis (EoE) is a rare disorder and is reported to be associated with concurrent allergic disorders. In this study, we aimed to evaluate the prevalance EoE in patients with allergic rhinitis and to assess clinical features in those patients having EoE.

AIMS & METHODS: Patients with allergic rhinitis were questioned with respect to esophageal and gastric symptoms (i.e., epigastric pain, gastroesophageal reflux (GER), dysphagia), and underwent upper gastrointestinal (GI) endoscopy and serum IgE level measurement. Multiple tissue samples were taken from the upper, middle and lower esophagus, gastric corpus and antrum, and duodenum during upper GI endoscopy. EoE was defined as the presence of eosinophilic

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Dietary Treatment		Overall effect	N	Children	N	Adult	N
All		67.9% (57.9% – 77.1%)	42	67.4% (55.9% - 78%)	34	71.5% (53.3% - 86.7%)	6
Elemental diets		90.8% (84.7% - 95.5%)	13	90.4% (83.5% - 95.5%)	12	94.4% (17/18)	1
Allergy testing-direct elimination diets		46.3% (35.6% - 57.1%)	13	47.9% (36.8% - 59.1%)	12	26.6 (4/15)	1
SFED		73% (66.6% - 78.9%)	6	72.8% (62.5% - 82%)	4	73.1% (64.8% - 80.7%)	2
Gluten-free diet		52.2% (15.3% - 87.8%)	6	45.5% (2.6% - 93.8%)	4	100% (1/1)	1
Milk elimination diet		68.2% (47.8% - 85.6%)	3	66.6% (44.7% - 84.8%)	2	100% (1/1)	1
Subgroups according to quality	**Medium/High - High**	69.8% (58.4% - 80.1%)	32	70.3% (56.5% - 82.4%)	26	70.6% (51.1% - 86.8%)	5
	Low – Medium/Low	60.6% (35.3% - 83.1%)	10	58.5% (32.2% - 82.3%)	9	100% (1/1)	1

infiltration in the squamous epithelium of the esophagus (eosinophil number ≥15/HPF for patients using PPI and ≥20/HPF for patients not using PPI) and the absence of eosinophilic infiltration in corpus, antrum and duodenum. Reexamination with upper GI endoscopy was performed after a 2-month proton pump inhibitor (PPI) therapy. Allergy test results were recorded. Symptoms, serum IgE levels, allergy test positivity, *Helicobacter pylori* positivity, endoscopic findings and histologic findings were compared between patients with EoE and those without EoE.
RESULTS: Sixty seven patients were included in the study. Of them, 15 were male. Mean age of male and female patients were similar (p = 0.129). Histopathological diagnosis of EoE was made in 7 patients (10.4%) and none of them had a history of PPI usage prior to diagnosis. Symptoms of GER and dysphagia were present in 71.4% and 28.57% of patients with EoE, while they were present in 28.30% and 1.67% of those without EoE. In patients with histologically proven EoE (n = 7), 4 had endoscopic findings compatible with EoE (57%), 2 had grade A reflux esophagitis (28.6%) and 1 had normal endoscopic findings. In patients without EoE (n = 60), 1 had endoscopic findings compatible with EoE and 3 had grade A reflux esophagitis. All patients with EoE had eosinophil number ≥20/HPF in tissue samples from upper and middle portion of the esophagus. Serum IgE levels were significantly higher in patients with EoE than in those without EoE (281.59±204.12 vs 105.75±161.6) (p = 0.013). *H. pylori* positivity were similar (p = 0.816). Allergy test positivity was 85.7% in patients with EoE and 50% in those without EoE.
CONCLUSION: GER is the most common symptom in patients with EoE.
EoE may be present even in patients with normal endoscopic findings
Serum IgE levels are higher and allergy test positivity are more common in patients with allergic rhinitis and EoE.
EoE is common in patients with allergic rhinitis.
It is important to question patients with respect to EoE symptoms in patients with allergic rhinitis and high serum IgE levels, especially when corticosteroid therapy is considered.
Disclosure of Interest: None declared

P0459 CLINICAL AND HIGH RESOLUTION MANOMETRY DATA SUPPORT THE HYPOTHESIS THAT PROTON PUMP INHIBITOR-RESPONSIVE ESOPHAGEAL EOSINOPHILIA REPRESENT A GERD-RELATED PHENOMENON

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INTRODUCTION: Eosinophilic esophagitis (EoE) and Proton Pump Inhibitor-response esophageal eosinophilia (PPI-REE) present similar phenotypic appearance, similar histopathology but different response to antisecretory therapy. Thus, it is unclear if PPI-REE is a gastro-esophageal reflux disease (GERD)-related phenomenon, a subtype of EoE, or a completely unique entity. High resolution manometry (HRM) is a novel technique that has been recently shown to provide new insights on GERD pathogenesis. In particular, esophago-gastric junction (EGJ) morphology different from type I and weak peristalsis have been strongly associated with GERD.
AIMS & METHODS: We aimed to compare HRM features of patients with EoE and PPI-REE. Consecutive patients with symptoms suggestive of EoE underwent upper endoscopy in order to assess the presence of at least 15 eos/hpf on oesophageal biopsies at mid/proximal esophagus and, then, were treated with twice-daily PPI for at least 8 weeks. Thereafter, patients repeated upper endoscopy and were stratified into two groups: EoE, in case of persistence of at least 15 eos/hpf on oesophageal biopsies, and PPI-REE, in case of less than 15 eos/hpf and a 50% decrease from baseline. Patients underwent also HRM with a 5-min baseline recording to assess the EGJ and 10 single water swallows (5 mL) at 30-s intervals to evaluate the esophageal peristalsis. Tracings were analyzed based on Chicago Classification and each EGJ was classified as: Type I, no separation between the Lower Esophageal Sphincter and the Crural Diaphragm; Type II, minimal separation (>1 and <2 cm); Type III, >2 cm of separation.
RESULTS: Thirty-one patients were identified as having EoE [24M/7F; mean age 28 (18-75)], whereas 10 patients were diagnosed with PPI-REE [9M/1F; mean age 38 (20-64)]. The two cohorts had similar dysphagia for solids (EoE 71% vs. PPI-REE 66%, p = 0.6979), bolus impaction (65% vs. 60%, p = 1.000) and chest-pain (23% vs. 20%, p = 1.000), but different heartburn (26% vs. 60%, p = 0.0485) and regurgitation (16% vs. 50%, p = 0.0446). Endoscopic features had the same frequency between EoE and PPI-REE: rings (45% vs. 50%, p = 1.000), furrows (26% vs. 10%, p = 0.4101) and plaques (23% vs. 40%, p = 0.4132). Esophageal strictures tended to be more frequent in EoE (52% vs. 10%, p = 0.0592). At HRM testing, EoE patients had higher mean integrated relaxation pressure [9 (2-16) vs. 6 (2-16), p = 0.0616] and LES basal pressure [26 (10-54) vs. 17 (1-34), p = 0.0388], but similar mean distal contraction integral [1094 (522-2653) vs. 1763 (483-5281), p = 0.5613] compared to patients with PPI-REE. Type II and III EGJs were less common in EoE than in PPI-REE patients (9% vs. 50%, p = 0.0129). Manometric diagnoses were similar between EoE and PPI-REE: weak peristalsis including large or small breaks and frequent failed peristalsis (16% vs. 40%, p = 0.2221), absent peristalsis (3% vs. 10%, p = 1.0000) and distal esophageal spasm (3% vs. 0%, p = 1.0000).
CONCLUSION: Typical reflux symptoms and HRM features GERD-related are more common in patients with PPI-REE than in patients with EoE. These data support the hypothesis that PPI-REE may represent a GERD-related phenomenon rather than a subtype of EoE or a separate entity. Further larger studies are needed to confirm these findings.
Disclosure of Interest: None declared

P0460 LONG-TERM EFFICACY OF PROTON-PUMP INHIBITOR THERAPY IN ADULT PATIENTS WITH PPI-RESPONSIVE ESOPHAGEAL EOSINOPHILIA

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INTRODUCTION: Proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) is diagnosed in at least a third of patients with a phenotype suggestive of eosinophilic esophagitis (EoE). However, neither long-term response to PPI therapy in PPI-REE patients nor influencing factors have been evaluated yet.
AIMS & METHODS: We aimed to determine the long-term efficacy of PPI therapy in PPI-REE and its association to *CYP2C19* genotype status. Retrospective multicenter study in PPI-REE adult patients, defined by consensus guidelines. After a diagnosis of PPI-REE, PPI therapy was tapered and maintained at the lowest dose with the target endpoint of clinical remission. Histological remission was defined by < 15 eos/HPF. Follow-up endoscopy was performed at 12 months or longer on PPI maintenance dose. *CYP2C19*2* and *CYP2C19*17* were determined from blood samples in Spanish patients.
RESULTS: 46 PPI-REE patients were included (mean follow-up time: 27 months (12-79)). While on clinical remission on low-dose PPI therapy, 34/46 (74%) had sustained histologic remission (19 double-dose PPI, 21 single-dose PPI). In 8/12 relapsers (66%) on maintenance PPIs, esophageal eosinophilia recurred exclusively at the distal esophagus. Compared to patients with sustained PPI-response (n = 13), this subset of distal relapsers showed borderline significant higher rates of *CYP2C19*2* rapid metabolizer genotype (100% *vs.* 53%, P 0.07) and reflux esophagitis at baseline (50% vs. 0%, P 0.08). All distal relapsers re-achieved histological remission after PPI-dose intensification (omeprazole 40 mg bid).
CONCLUSION: 74% of adult PPI-REE patients had persistent clinico-histological remission on low-dose maintenance PPI therapy. While on clinical remission, two thirds of relapsers showed eosinophilic inflammation limited to the distal esophagus. Baseline reflux esophagitis and a CYP2C19 rapid metabolizer genotype were associated to this relapsing pattern and histological remission was re-achieved after PPI-dose intensification in all patients.
Disclosure of Interest: None declared

P0461 RESULTS OF LIQUID CYTOLOGY IN THE DIAGNOSIS AND MONITORING EOSINOPHILIC OESOPHAGITIS

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INTRODUCTION: Esophagoscopy with biopsy is considered the only method for diagnosis and monitoring EoE. Therefore it is important to find out less invasive diagnostic methods. Regarding this issue, obtaining oesophageal cytology is a way to explore to design in the future devices that allow to obtain samples without endoscopy and biopsy. The aim of the study was to analyze the accuracy of liquid-based cytology (LC) of the esophagus in the diagnosis and monitoring EoE histological activity.
AIMS & METHODS: LC specimens were obtained in patients with active EoE (AEoE) (≥15 eo/hpf) and EoE in remission (EoER) (<15 eo/hpf) by oesophageal aspirate samples collected after instillation of 50 cc of saline solution suctioned by bronchioalveolar lavage system adapted to the gastroscope. The samples were collected in Cytolyt solution (Hologic), obtaining Papanicolaou and May-Grünwald/Giemsa that were assessed by two independent pathologists. EoE specimens were compared with LC obtained from patients with GERD.
RESULTS: Specimens of 36 patients (69.4% male, mean age 30.88 years) were included. AEoE (17, 47.2%), EoER (11, 30.5%) and GERD (8, 22.2%). Eo / hpf proximal oesophageal biopsies (AEoE 28.58 vs EoER 2.09 vs GERD 1.25, p < 0.001) and distal (AEoE 23.33 vs EoER 2.36 vs GERD 2.50, p = 0.002). LC Eo/hpf (AEoE 9.23 vs EoER 1.54 vs GERD 2, p = 0.01). Linear correlation between Eo/hpf average biopsy and LC Eo/hpf: r = 0.57, p < 0.001. For diagnosis of EoE, ≥ 3 Eo/hpf in LC obtained a Sensitivity 70%, specificity 81%, PPV 86% and NPV 60% (AUC = 0.81, p = 0.01). For detection of AEoE, ≥ 3 Eo/hpf in LC obtained a sensitivity 70%, specificity 82%, PPV 81% and NPV 66% (AUC = 0.87, p = 0.001).
CONCLUSION: LC in oesophageal aspirate obtained by a cutoff in 3 eo/hpf seems to be effective for the diagnosis and monitoring activity in EoE. These results open the door to the development of non endoscopic devices that allow us the diagnosis and monitoring of disease noninvasively.
Disclosure of Interest: None declared

P0462 CORRELATION BETWEEN CLINICAL, HISTOLOGIC AND ENDOSCOPIC ACTIVITY IN EOSINOPHILIC OESOPHAGITIS. PRELIMINARY RESULTS OF SENECA PROJECT (SPANISH STUDY OF ENDOSCOPY AND EOSINOPHILS CORRELATION ASSESSMENT)

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INTRODUCTION: Esophagoscopy with biopsies is considered the gold standard for diagnosis and monitoring EoE. This is due to lack of correlation between histology, endoscopy and clinical manifestations of the disease. A novel endoscopic classification for assessment of eosinophilic esophagitis (EoE) activity has been recently proposed (EREFs). We aimed to address the correlation of clinical and endoscopic EoE activity scores with histological response after different therapeutic interventions.
AIMS & METHODS: Spanish multicenter prospective study in consecutive patients with EoE, according to consensus guidelines. Clinical (Dysphagia Symptom Score (DSS) Scale) and endoscopic (EREFS) disease activity, along with eosinophil peak count, were assesed at baseline and after topical steroids or elimination diet, including food reintroductions. Histological remission was defined by < 10 eos/HPF at both distal and proximal esophagus. Patients were subclassified: Group A (Baseline), Group B (No histological remission after therapy/food reintroduction) and Group C (Histological remission after therapy/food reintroduction).
RESULTS: 79 patients undergoing 128 upper endoscopies have been included so far (77.2% male, age 34.7 years-old, dysphagia 100%). Group A: 47 (36.7%), Group B: 61 (47.7%) and Group C: 20 (15.6%). DSS score was significantly higher in Group A (A = 7.16, B = 5.15, C = 3.70; p = 0.006), but no differences were observed between groups B and C (p = 0.12). Regarding endoscopic findings, inflammatory features were significantly decreased after histological remission (furrows: A = 63.8%, B = 72.1%, C = 40%; p = 0.034 / exudates (grade 2): A = 10.6%, B = 18%, C = 5%;p = 0.002), but not fibrostenotic features (pseudorings: A = 68.1%, B = 55.4%, C = 55%;p = 0.44/stricture: A = 10.6%, B = 9.8%, C = 5%;p = 0.75). Mucosal edema was common at baseline and persistent regardless of histological remission (A = 61.7%, B = 78.7%, C = 60%; p = 0.09).
CONCLUSION: EoE clinical activity significantly decreased after different therapeutic interventions, with no differences between patients showing eosinophilia remission or persistence after therapy. Histological remission was correlated with significant decrease of inflammatory endoscopic features, but not of fibrostenotic findings. Mucosal edema was mostly persistent regardless of histological remission, suggesting it might belong to the fibrotic remodelling spectrum.
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Disclosure of Interest: None declared

P0463 IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE, GLOBUS IS ASSOCIATED WITH ABNORMAL OROPHARYNGEAL ACID EXPOSURE

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INTRODUCTION: Globus, a persistent or intermittent non-painful sensation of a lump or foreign body in the throat, is frequently associated with gastroesophageal reflux disease (GERD): it is estimated that up to 68% of GERD patients suffer from globus. However, previous esophageal pH and pH-impedance studies failed to define a causative role of acid or non-acid reflux in globus pathophysiology.
AIMS & METHODS: The aim of this study was to investigate both distal and proximal, oropharyngeal acid exposure, with a new device, in patients with non-erosive reflux disease (NERD) with and without globus.
A group of 37 patients affected by NERD was enrolled. The presence of reflux symptoms was evaluated and severity was graduated by VAS. In eight patients, globus was the main symptom; in the other 29, globus was not present and they were thus considered the control group. Patients underwent standard stationary esophageal manometry (6 channels+sleeve) and 24-hr pH-impedance esophageal monitoring (Sleuth, Sandhill Scientific) combined with 24-hr oropharyngeal pH monitoring (Restech Dx-pH Measurement System).
RESULTS: Distal esophageal acid exposure (pH <4), number of acidic and weakly acidic reflux episodes and proximal extension of refluxate were similar between patients with and without globus. On the contrary, patients with globus showed a significantly longer oropharyngeal exposure to pH < 5.5 (total duration of acid exposure: 222 min ± 230 min vs 47 min ± 88 min, p < 0.05; and percent of recording: 16.07±16.2% vs 3.56±6.84%, p < 0.05), compared to patients without globus; the longest episode of oropharyngeal acid exposure was significantly longer in patients with globus than in patients without globus (110 min ± 115 min vs 15 min ± 25 min; p < 0.05). A higher score for heartburn was evident in the group of patients without globus (3.45±3.31 vs 1.31±1.44, p < 0.05); no difference was found in regurgitation, cough, sore throat, or thoracic pain score. Finally, the prevalence of esophageal motor disorders was similar in the two groups.
CONCLUSION: Oropharyngeal acid exposure could have an important pathophysiological role in globus onset. Oropharyngeal pH monitoring seems a more accurate diagnostic tool than the standard 24-hr pH-impedance study to define the role of acid exposure in this subgroup of patients.
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Disclosure of Interest: None declared

P0464 UNDERSTANDING THE CAUSE OF PERSISTENT GERD SYMPTOMS DESPITE PROTON PUMP INHIBITOR THERAPY: IMPEDANCE-PH MONITORING REVISITED

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INTRODUCTION: Non-response to proton pump inhibitor (PPI) therapy in patients with reflux symptoms and a normal gastroscopy remains a challenge. Impedance-pH (MII-pH) monitoring clarifies the symptom profile and evaluates patients objectively for acid reflux (AR) and non-acid reflux (NAR).
AIMS & METHODS: To study MII-pH characteristics in patients referred for GERD evaluation who remain symptomatic despite PPIs, and study mechanisms related to persistent symptoms. Methods: Between January 2009-December 2013, consecutive patients with typical symptoms (group 1); atypical symptoms (group 2) and non-cardiac chest pain (NCCP, group 3) underwent 24 hour MII-pH after PPI washout. Prevalence of (i) oesophageal acid exposure time (AET) > 4.2%; (ii) bolus exposure (BE > 1.4%), (iii) high reflux numbers (> 73) and/or (iv) positive symptom marker based symptom index (SI ≥50%) and/or symptom association probability (SAP ≥95%) for AR or NAR events was compared between groups by chi-square and student t-testing.
RESULTS: 208 patients (80M, mean age 45.9 ± 12.5) were studied (Table 1). Elevated AET occurred in 24 (11.5%). 120 (57.7%) recorded a positive study on MII-pH evaluation despite a normal overall AET. Group 1 and 3 patients had significantly more symptomatic AR events (p < 0.05) compared to group 2. Symptomatic NAR related events did not differ significantly different between groups. Patients with a positive symptom association for AR events were more likely to have abnormal BE (p = 0.01) and abnormal reflux numbers (p < 0.05). Table 1.
CONCLUSION: Use of MII-pH in PPI non-responders identifies AR and NAR events and serves as an important diagnostic modality to evaluate the symptom profile and guide appropriate therapy, which may extend beyond PPIs.
Disclosure of Interest: None declared

Table to P0464

	Group 1 Typical (N=39M,55F)	Group 2 Atypical (N=34M,50F)	Group 3 Non cardiac chest pain (N=7M,23F)
Raised AET	9/94 (9.6%)	13/84(15.5%)	2/30(6.7%)
No. of AR events (mean, SEM)	22.6 ± 2.3	21.2 ± 1.9	18.3 ± 3.0
No. of NAR events (mean, SEM)	26.1 ± 2.7 *p < 0.05 compared to group 3*	23.1 ± 1.5 *p < 0.05 compared to group 3*	17.1 ± 2.1
No of proximal reflux events (mean,SEM)	25.5± 2.3 *p < 0.05 compared to group 3*	23.7 ± 1.7 *p < 0.05 compared to group 3*	17.1 ± 2.8
Total no. of reflux events	48.6 ± 3.9 *p < 0.005 compared to group 3*	44.0 ± 2.5	35.4± 3.8
Total bolus exposure time (mean, SEM)	1.7 ± 0.2	1.5 ± 0.1	1.2 ± 0.2
Positive symptom association for acid reflux	45/94(47.8%) *p < 0.05 compared to groups 2*	23/84 (27.4%)	19/30(63.3%) *p < 0.05 compared to groups 2*
Positive symptom association for non-acid reflux	43/94 (45.7%)	39/84(46.4%)	10/30(33.3%)

P0465 ACID AND NON ACID REFLUXES MODIFY THE BASELINE IMPEDANCE VALUES IN A LARGE SERIES OF NERD PATIENTS

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INTRODUCTION: Esophageal baseline impedance (BI) may be considered as an indirect way to express macroscopic and/or microscopic mucosal integrity since recent evidence has shown that patients with both erosive or non erosive esophagitis have lower level of BI than healthy subjects.
AIMS & METHODS: The aim of our study was to evaluate how BI is transiently influenced by the nature of reflux events.
We studied 60 patients (28 M - mean age 45.8 ± 16.1) with typical GERD-symptoms (heartburn and regurgitation) and negative endoscopy, who performed a 24h-pH impedance monitoring from January to March 2014. Among these, 33 exams were performed on therapy with proton pump inhibitor, while 27 were off-therapy. For each patient, 24 hours esophageal BI was calculated during the first period of 60 seconds without an impedance event (swallow or reflux) every four hours. Then, we calculated BI immediately before and 1 minute after the end of the same reflux event. Pre and post-reflux BI for acid and non acid were calculated in off and on-therapy patients, respectively. Moreover, for each reflux episode, the minimum pH reached was also registered.
RESULTS: 24 hours BI and pre-reflux BI were similar for both acid and non acid events (2422±641 vs 2424±758mΩ and 2386±497 vs 2384±639 mΩ, respectively, all p = NS). On the contrary, a significant reduction between pre and post-reflux BI for acid and a significant increase was registered for non acid reflux (2424±758 vs 2130±721 mΩ, p = 0.001 and 2384±640 vs 2767±489 mΩ, p = 0.004, respectively). The same results were observed in the subgroups of subjects off and on therapy (Off-therapy: 2330±766 vs 2083±684 mΩ, $p < 0.01$; On therapy: 2187±478 mΩ vs 2713±503 mΩ, $p < 0.01$, respectively).
Most interestingly differences between pre and post-reflux BI of all patients were positively correlated to the pH nadir of each reflux event ($p < 0.0001$, $r^2 = 0.42$).
CONCLUSION: Baseline impedance may be transiently influenced by the nature of reflux episodes, being acid and non-acid refluxes respectively associated with a decrease and an increase of baseline impedance. Our data indicate that nature of refluxes is able to differently affect BI, likely, if this phenomenon underlies changes in mucosal integrity or it is associate with abnormal perception deserves further investigation.
Disclosure of Interest: None declared

P0466 PATIENTS WITH ACTIVE CELIAC DISEASE HAVE ALTERED INTERCELLULAR SPACES AND TIGHT JUNCTION STRUCTURE OF THE LOWER ESOPHAGUS THAT MAY EXPLAIN THE HIGH PREVALENCE OF REFLUX SYMPTOMS IN THESE PATIENTS

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INTRODUCTION: Patients with untreated celiac disease (CD) often complain of reflux symptoms, which in 30% of cases are considered moderate to severe (CGH 2011; 9: 214-9). The gluten-free diet leads to a rapid and persistent improvement in reflux symptoms and most cases do not require the use of proton pump inhibitors. The mechanisms involved in the expression of reflux symptoms in CD patients are unknown.
AIMS & METHODS: Objective: We explored symptomatic and mucosal markers of permeability of the lower esophagus in patients with newly diagnosed CD at the time of diagnostic endoscopy, patients with symptoms of GERD but no CD (GERD controls) and healthy controls without symptoms (healthy controls: HC).
Methods: A cohort of 23 consecutive patients with active CD at the time of diagnosis, 5 GERD control patients, and 11 HC subjects, were enrolled in the study. Nine out of 23 CD patients had GERD symptoms considered as moderate or severe (>2 points in the GSRS questionnaire). Endoscopic biopsies from the distal esophagus were obtained 2 cm above the z-line. Samples were assessed for histological damage, dilated intercellular space (DIS) scores by optical microscopy (OM) and electron microscopy (EM), and tight junction (TJ) mRNA expression for zonnula occludens-1 (ZO-1) and claudin-2 and -3 (CL-2; CL-3) using Real Time qRT-PCR.
RESULTS: Patients with active CD had increased DIS scores compared to HC subjects (OM: 8.0±3.1 vs. 2.2±2.5; $p < 0.003$ and EM: 31.7±9.5 vs. 15.0±5.1; $p < 0.04$) but similar to GERD controls. CD patients without GERD symptoms also had higher DIS scores compared to HC (OM: $p < 0.006$; EM: $p < 0.03$) but similar to those in CD patients with GERD symptoms. Overall CD patients had lower expression of ZO-1 than HC (CD patients with and without GERD symptoms: $p < 0.003$ and $p > 0.05$; respectively). A non-statistical trend for higher CL-2 and CL-3 expression was observed in CD patients compared with GERD controls and no differences were detected between CD subgroups with or without GERD symptoms. CD patients had similar expression of CL-2 and CL-3 compared to HC.
CONCLUSION: Our study suggests an impairment of mucosal permeability in the distal esophagus of patients with active CD irrespective of the presence of GERD symptoms. The altered expression of ZO-1, and CL-2 and CL-3 may underlie loss of TJ integrity in the esophageal mucosa, an expression pattern that is reminiscent of intestinal permeability abnormalities observed in CD, and that may contribute to reflux symptom expression and its reversion by the gluten-free diet.
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P0467 RECEPTOR MODULATION AND MAP-KINASE SIGNALING INDUCED BY STW5 AND BY THE PROTON-PUMP INHIBITOR OMEPRAZOL IN A RAT MODEL FOR GASTROESOPHAGEAL REFLUX DISEASE AND IN HET1A-CELLS

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INTRODUCTION: We had earlier demonstrated that STW5 affects multiple chemokine families on genome and proteome level reducing inflammation in the esophageal tissue in our rat model for gastroesophageal reflux disease (GERD)[1].
AIMS & METHODS: Here we investigated selected receptors and which signaling cascades are activated during the anti-inflammatory processes by STW5 and by the proton-pump inhibitor Omeprazole (O). **Methods:** Rats were pretreated with either STW5 (0.5 or 2ml/kg) or O (30mg/kg). Esophagitis was induced surgically followed by a further 10d treatment. On day 10 animals were sacrificed and whole cell lysates of the esophagi were evaluated by Western Blot analysis for the receptors GPR 84 and LOX-1 (lectin-like oxidized low density lipoprotein receptor 1) and the stress induced mitogen activated kinase (MAPK) p38. Further investigations were undertaken with the human esophageal squamous cell line HET-1A. Inflammation was induced with Capsaicin (50µM, 18hrs) and cells were treated with either STW5 (0.17; 0.5; 1.7; 5µl/ml) or O (10µg/ml; 30µg/ml). MAPKs p38, ERK1 and 2 were determined. Data were normalized either with the respected unphosphorylated protein or with ß-Actin.
RESULTS: The LOX-1 receptor was only detected in the esophagi of rats with esophagitis, but not in the esophagi of sham operated or treated rats. The GPR 84 receptor was increased in the esophagitis group compared to the sham group and down regulated by STW5 and O. In the sham group neither total p38 MAPK nor the phosphorylation of p38 was increased. The treatment of STW5 inhibited the phosphorylation of p38 MAPK in the tissue, but did not influence the increase in the total amount of p38 of the esophagitis group. In HET1A cells capsaicin slightly increased the expression of GPR84 which was reduced by the high concentration of STW5. Capsaicin induced an increase in the phosphorylation of ERK1/2 compared to the control. This increase was inhibited in the presence of STW5 as well as in the presence of O.
CONCLUSION: The LOX-1 and the GPR 84 receptor activation contribute to experimental GERD. They are targeted like P38, which is known to be acid sensitive in GERD[2], by STW5. Data further substantiate differential MAPKinase signaling in GERD. They support the classification of GPR84 as proinflammatory receptor with a link to the immune response in oesophageal tissue.
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P0468 EXPRESSION OF VEGF AND VEGFR IN EROSIVE AND NONEROSIVE REFLUX DISEASE

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INTRODUCTION: Up to 70% of patients with gastro-esophageal reflux disease do not have erosions visible in conventional endoscopy. They are classified as non-erosive reflux disease (NERD). Studies on endoscopy with optical magnification described a variety of minimal changes in NERD patients, also concerning vessels. Until now it is not clear why some patient develop erosions and others do not. Differences in self-defense mechanisms may matter. Vascular endothelial growth factor (VEGF) is a signal protein working through its receptor (VEGFR) promoting angiogenesis and wound healing.
AIMS & METHODS: We evaluated squamous epithelium above Z line in magnification up to 105 times in 20 patients with NERD, 12 patients with erosive esophagitis (EE) and 5 controls (patients without reflux disease). The magnified images were analyzed with respect to: visibility of palisade blood vessels, appearance of intrapapillary capillary loops (IPCLs) and white points seen as whitish pinpoint spots encirculating IPCLs or independent from IPCLs. Biopsy specimens for the histopathologic examination were taken 1-2 cm above Z line. In histology presence of inflammation was evaluated in a scale from 0 (absent) to 3 (severe). Expression of VEGF and VEGFR in squamous epithelium was

evaluated by immunohistochemistry method. The reaction of VEGF and VEGFR proteins was defined as low if positive in less than 33% of vessels, moderate if positive in 33-66% of vessels and high if positive in over 66% of vessels. Statistics was executed with Fisher exact test.
RESULTS: Expression of VEGF and VEGFR was significantly higher in EE than NERD group ($p < 0.05$). Control group had comparatively low expression of VEGF and VEGFR.

Number of patients	VEGF expression			VEGFR expression		
	Low *	Moderate	High *	Low **	Moderate	High **
EE	0 (0%)	5 (42%)	7 (58%)	1(8.3%)	4 (33.3%)	7(58.3%)
NERD	8 (40%)	8 (40%)	4 (20%)	11 (55%)	5 (25%)	4 (20%)
Controls	2 (40%)	3 (60%)	0 (0%)	3 (60%)	1 (20%)	1 (20%)

Enlarged IPCLs, white points or diminished visibility of palisade vessels seen in magnification endoscopy did not correlate with expression of VEGF and VEGFR, neither did the grade of esophagitis evaluated in plain histology.
CONCLUSION: VEGF and VEGFR expression is higher in EE than NERD patients. This phenomenon may be the part of esophageal mucosa healing in EE.
Disclosure of Interest: None declared

P0469 EXPRESSION OF EPIDERMAL GROWTH FACTOR RECEPTOR IN PATIENTS WITH GASTRO-OESOPHAGEAL REFLUX DISEASE AND IN THOSE WITH SYSTEMIC SCLEROSIS

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INTRODUCTION: Epidermal growth factor (EGF) and its receptor (EGFR), a tyrosine kinases receptors (TKs), are associated with epithelial proliferation and restitution, the two key mechanisms involved in oesophageal epithelial defense against reflux. It has been shown that EGFR expression increases with the progression from gastro-oesophageal reflux disease (GORD) to Barrett's oesophagus/adenocarcinoma. Systemic sclerosis (SSc) is characterized by deposition of collagen and other extracellular matrix proteins in the connective tissues, imbalance of the immune system, and microvasculature abnormalities. Besides TKs physiological roles, they are key players in various diseases, including SSc. Indeed, their pathological activation may drive carcinogenesis, vascular remodelling, and fibrogenesis. No studies investigated the EGFR expression on oesophageal mucosa of SSc patients.
AIMS & METHODS: We aimed to assess and compare the presence of EGFR expression on oesophageal mucosa of GORD and SSc patients. We studied 24 SSc (22F, median age 56yrs) and 22 GORD (9F, median age 64yrs) patients. They underwent upper endoscopy and multiple specimens ($n = 4$) were taken from the distal oesophagus (at the Z-line and 2 cm above it). Biopsies were fixed in formalin and embedded in paraffin. After preparation, anti-human EGFR monoclonal antibody, clone H11 (anti-EGFR) (Dako), was applied to the slides and EGFR expression was considered positive when staining was detected on the membrane. Patients were endoscopically classified as having erosive oesophagitis (EO), non-erosive reflux disease (NERD, in case of no mucosal breaks and GORD symptoms) or negative endoscopy (NE, in case of no mucosal breaks and absence of GORD symptoms). Microscopic oesophagitis (MO) was diagnosed by using a previously validated score.
RESULTS: At endoscopic evaluation, 3/24 (13%) SSc patients had EO, 11/24 (46%) had NERD and 10/24 (42%) had NE, whereas at microscopic evaluation 3 had evidence of erosive oesophagitis, 11 of MO and 10 of normal mucosa, respectively. Among GORD patients, we found at endoscopic and microscopic evaluation that 3/22 (14%) had EO with histological reply of 2 erosive oesophagitis and 1 MO, 12/22 (55%) had NERD with evidence of MO and 7/22 (31%) had normal findings at both measurements. Overall comparison of EGFR expression between SSc and GORD patients was not significant, whereas comparison of EGFR expression between the 10/24 SSc and 7/22 GORD patients without endoscopic and histological alterations was statistically significant ($p = 0.0068$). EGFR expression between the 14/24 SSc patients with erosive and microscopic oesophagitis was higher than in the 10/24 with normal mucosa ($p = 0.0177$) as well as in GORD patients with and without oesophagitis ($p = 0.0004$). In GORD patients EGFR expression decreases proximally, while in SSc patients it seems overexpressed.
CONCLUSION: In GORD patients, EGFR expression correlates with histological findings and seems to play a major role in maintaining epithelial integrity. In SSc patients, it is overexpressed and this can act as an inflammatory reactive stimulus, even in the absence of microscopic lesions.
Disclosure of Interest: None declared

P0470 ACID INFUSION INTO THE STOMACH DOES NOT AFFECT THE NUMBER OF MEAL-INDUCED TRANSIENT LOWER ESOPHAGEAL SPHINCTER RELAXATIONS (TLESR)

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INTRODUCTION: TLESRs are considered to be the most important mechanism of gastroesophageal reflux (GER). However, the regulation of TLESRs by acid is incompletely understood. We have recently reported that acid in the esophagus enhanced TLESR (Abstract Tu1868, Digestive Diseases Week, Gastroenterology Vol. 146[2014] suppl.). Specifically, we found that the acid infusion into the esophagus increased the number of meal-induced TLESRs by 60% compared to control infusion.
AIMS & METHODS: In the present study we evaluated the effect of acid infusion into the stomach on the meal-induced TLESRs. The study was carried out in healthy subjects (age 23 ± 0.3 years) None of the subjects had any esophageal motility abnormality as defined by Chicago criteria. TLESRs were evaluated by using high resolution manometry (HRM). The study was performed in sitting position. For infusions a tube (O. D. 1mm) was attached to the HRM catheter with the opening positioned in the stomach at least 5 cm below the manometrically identified lower esophageal sphincter. Each subject was studied at two occasions (control or acid infusion) separated by at least 7 days. Following a standard meal (chicken sandwich and soda drink), acid (0.15 M HCl) or water was infused into the stomach (8ml/min, 20 min) by using a perfusion pump. TLESRs were counted during 2h following the completion of the infusion. In some subjects TLESRs were also counted during 20 min of acid infusion. The study conformed to Declaration of Helsinki. All subjects gave informed consent.
RESULTS: 10 subjects (7M/3F) completed the study. We found that acid infusion into the stomach did not affect the number of meal-induced TLESRs. The number of TLESRs (median[interquartile range]) during 2h following the control vs. acid infusion was 17[12-18.75] vs. 15.5[12.25-20.25], $n = 10$, $p = NS$, Wilcoxon Signed-Rank Test). The average duration of TLESRs was not changed (16.3s±0.4s, $n = 153$ vs. 17.2s±0.7s, $n = 151$, $P > 0.2$, unpaired T-test). The number of TLESRs during the acid infusion was also not affected (quantified in 6 subjects, 4M/2F). The number of TLESRs during the 20 min of control vs. acid infusion was 5.5[2.75-6] vs. 4[3.25-4.75], $n = 6$, $p = NS$, Wilcoxon Signed-Rank Test).
CONCLUSION: We conclude that the acid infusion into the stomach does not affect the meal-induced TLESR. These results are consistent with the notion that the direct effects of acid in the stomach has limited role in the regulation of TLESR. Our results also indicate that the substantial enhancement of TLESR by acid infusion into the esophagus observed in our previous study was not due to acid effect in the stomach.
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P0471 EFFECT OF GHRELIN ON EXPERIMENTAL ESOPHAGITIS IN RATS

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INTRODUCTION: Both ghrelin and leptin are involved in the regulation of food intake but their effect on the development of experimental reflux esophagitis (RE) is unknown.
AIMS & METHODS: The present study was designed to assess; 1) the effects of pre-treatment with ghrelin and leptin on lesion score and esophageal blood flow in rats with RE; 2) the influence of ghrelin and leptin on mucosal gene expression and release of proinflammatory cytokines (IL-1b, TNF-a and IL-6) and 3) the influence of ghrelin and leptin on the expression of COX-2 and HSP70 in esophageal mucosa during development of RE. RE was induced in rats ($n = 6$/group) according to technique proposed by Nakamura et al (Jpn J Pharmacol 1982, 32:445) by two ligation of 1) the duodenum at the pyloric sphincter and 2) at the region between the forestomach and gastric corpus. Following treatment groups were used: A) intact rats; B) rats with RE pretreated 1h before with saline (control); C) rats pretreated with ghrelin (40 μg/kg i.p.) and D) leptin (40 μg/kg i.p.) 1 h before exposure to RE. The lesion score (scale 0-5) and esophageal blood flow using H2 gas clearance was measured. In addition, gene expression of IL-1b, TNF-a, IL-6 and release of these cytokines was analyzed by quantitative RT-PCR and ELISA. Furthermore, gene expression of COX-2 and HSP70 was measured by RT-PCR.
RESULTS: Both ghrelin and leptin significantly attenuated (by ~50%) the lesion score induced by RE and this effect was accompanied by a significant increase in esophageal blood flow. The expression of mRNA for COX-2 TNF-a, IL-1b and IL-6 was negligible in the intact esophageal mucosa but was upregulated in esophageal mucosa of rats with RE. The pretreatment with ghrelin and leptin decreased the expression of mRNA for COX-2, TNF-a, IL-1b and IL-6. In contrast, HSP70 was significantly downregulated in esophageal mucosa of rats with RE and this effect was reversed in rats pretreated with ghrelin or leptin. Ghrelin receptor (GHS-R) was detected both in intact and RE-inflamed esophageal mucosa.
CONCLUSION: Appetite hormones, such as leptin and ghrelin, significantly attenuate the inflammatory reaction in esophageal mucosa caused by pathologic reflux of gastric acid. The anti-inflammatory effect of ghrelin and leptin is may be attributed to their inhibitory effect on expression and release of proinflammatory cytokines, COX-2 and the restoration of protective Hsp70 inhibited due to RE.
Disclosure of Interest: None declared

P0472 ROLE OF ACID AND NON-ACID REFLUX IN ESOPHAGEAL MUCOSAL DAMAGE (EROSIVE ESOPHAGITIS AND BARRETT'S ESOPHAGUS)

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INTRODUCTION: The effect of acid reflux is commonly accepted nowadays. Substantial experimental and clinical evidence strongly supports the importance of acid and pepsin in causing esophageal mucosal injury. The role of weakly-acid and duodenogastroesophageal reflux as an etiological factor of esophageal mucosal injury is not clarified until recently. With introduction of combined esophageal pH-impedance monitoring, a precise diagnostic test for non-acid reflux is now available.
AIMS & METHODS: The aim of this study was to assess the role of acid and non-acid reflux in esophageal mucosal injury. 127 patients (75(59.1%) women and 52(40.9%) men, averaging 48.6 ± 14.9 years), off acid-suppressive therapy underwent diagnostic work-up including upper-GI endoscopy with biopsy and combined esophageal pH-impedance monitoring. According to data from pH-impedance study patients were subdivided into three groups by predominant characteristic of reflux: GERD with acid reflux (n = 65; AR); GERD with weakly-acid reflux (n = 36, WR), and GERD with duodenogastroesophageal reflux (n = 26, DGR).
RESULTS: The absence of endoscopically visible lesions or catarrhal esophagitis (NERD) was found during endoscopy in 55.4%, 86.1%, and 76.9% for AR, WR, DGR, respectively (p (AR-WR) <0.05). Erosive esophagitis (ERD) was found in 40%, 13.9% and 23.1% for AR, WR, DGR, respectively (p (AR-WR) <0.05). Esophageal ulcers were found only in AR group in 4.6%. Moreover, AR and DGR patients had significantly higher activity and degree of mucosal inflammation than patients in WR group ($p<0.05$). Endoscopic changes indicating Barrett's esophagus with histologic presence of esophageal intestinal metaplasia was found in 16%, 5.8%, and 42.9% for AR, WR, DGR, respectively (pAR-DGR <0.05; pWR-DGR <0.05).
CONCLUSION: Higher frequency of esophageal mucosal injury in AR group in comparison with patients in WR group suggests that acid is the key factor in causing esophageal injury. While weakly acidic reflux does not contribute significantly to esophageal mucosal damage. Similarly, the DGR patients had significantly higher rate of intestinal metaplasia which indicates the important role of duodenal content (bile or alkaline pancreatic secretions) in developing Barrett's esophagus.
Disclosure of Interest: None declared

P0473 IMPEDANCE-PH REFLUX PATTERNS IN PATIENTS WITH NON-EROSIVE REFLUX DISEASE AND EROSIVE REFLUX DISEASE

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INTRODUCTION: Non-erosive reflux disease (NERD) and erosive reflux disease (ERD) are the most common phenotypic presentations of gastroesophageal reflux disease.
AIMS & METHODS: To assess acid and non-acid reflux patterns in patients with NERD and ERD using combined esophageal pH-impedance monitoring. 133 patients (off acid-suppressive medication) complaining of reflux symptoms were underwent diagnostic work-up including upper gastrointestinal endoscopy and ambulatory 24-h esophageal pH-impedance monitoring. According to data of endoscopy patients were graded to NERD (90 patients (67.6%)) and ERD (43 patients, (32.3%)).
RESULTS: When compared to NERD, ERD patients showed a higher incidence of acid reflux episodes in 24 h (72 (43;103) vs. 47 (21; 68), $p<0.05$) and higher duration of total esophageal acid exposure (10.8% (6.6; 19.4) vs. 4.5% (1.4;7.1), $p<0.05$). Reflux-related acid exposure (pH drops associated with reflux detected by impedance) in ERD patients was twofold higher than in NERD patients (2.2% (1.6; 2.9) vs. 1.08% (0.5;1.9), $p<0.05$). Similarly, reflux-related alkaline exposure (pH elevation (pH > 7) [1] associated with reflux detected by impedance) was also higher in ERD patients (1.3% (0.8; 1.7) vs. 0.13% (0; 0.49), $p<0.05$). In contrast to ERD patients, NERD patients had significantly higher (1.08% (0.46; 1.86) vs. 0.04% (0; 0.2), $p<0.05$) reflux-related weakly – acid exposure (pH drops (pH < 7) [1] associated with reflux detected by impedance). When compared with accepted normal values [1] NERD patients had significantly higher mean number of weakly-acid refluxes (41(28;55)). Episodes of weakly-acid reflux in NERD patients happened mainly at postprandial period. Median acid (chemical) clearance time was twice higher in ERD patients (120 (76; 166) s.) in comparison to NERD's (60 (49; 116) s.) group. Meanwhile, there was no significant difference in median volume clearance time between ERD and NERD patients (23.3 (20.3; 27.6) vs. 19.1 (16.2; 23.6) s, $p>0.05$). In both GERD groups median volume clearance was significantly faster than median chemical clearance ($p<0.05$). Meanwhile, esophageal mucosa's exposure to reflux volume during 24 hour period, as assessed by impedance monitoring, was similar in both ERD and NERD patients (3.8% vs.3.1%, $p>0.05$).
CONCLUSION: While ERD and NERD patients have similar total esophageal bolus exposure, ERD patients have an increased level of esophageal acid exposure and reflux-related esophageal acid and alkaline exposure due to excessive number of acid and alkaline reflux as well as long duration of chemical clearance. Similarly, NERD patients have excessive number of postprandial weakly-acid reflux and increased level of reflux-related esophageal weakly-acid exposure. Consequently, this observation tends to support a notion that weakly-acid reflux is less damaging to esophageal mucosa than acid reflux. Significant differences between acid and bolus clearances' time may be caused by two different mechanisms of clearance. Volume clearance is achieved by peristalsis while chemical clearance requires neutralization by saliva.
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P0474 CHARACTERISTICS OF NIGHTTIME REFLUX ASSESSED BY USING MULTI-CHANNEL INTRALUMINAL IMPEDANCE PH MONITORING AND A PORTABLE ELECTROENCEPHALOGRAPH

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INTRODUCTION: Nighttime reflux is strongly associated with sleep disturbances; however, the detailed characteristics of nighttime reflux occurring during sleep have not been elucidated.
AIMS & METHODS: The present study aimed to analyze nighttime reflux by using multi-channel intraluminal impedance pH (MII-pH) monitoring and a portable electroencephalograph (EEG) in patients with gastroesophageal reflux disease. Seventeen patients with heartburn and/or regurgitation were examined by using MII-pH and a portable EEG simultaneously. Nighttime reflux was divided based on reflux type, acidity, and extent. Phases of nighttime at bed were divided as follows: (1) recumbent-awake before falling asleep; (2) nonrapid eye movement (NREM); (3) rapid eye movement (REM); (4) awakening from sleep; and (5) post-awakening in the morning.
RESULTS: A total of 184 nighttime refluxes were analyzed. Forty-three (23%) refluxes occurred during recumbent-awake before falling asleep; 28 (15%) during NREM; 14 (8%) during REM; 86 (46%) during awakening from sleep, with 50 (27%) during long awakening (≥ 5 min), and 13 (7%) during post-awakening in the morning. Liquid reflux was common during awakening from sleep, NREM, and REM. Prevalence of proximal migration was significantly lower in NREM and REM than in the other phases. There was no difference in acidity and bolus clearance time among the sleep phases. Nighttime reflux was highly prevalent during long awakening (19/24, 79%). Among them, eight (42%) refluxes occurred during the first epoch of long awakening.
CONCLUSION: Different reflux pattern at each phase during nighttime might explain the pathogenesis of GERD and its related sleep disturbances.
Disclosure of Interest: None declared

P0475 THE CIRCULATING LEVEL OF CYTOKINES IN PATIENTS WITH DIFFERENT FORMS OF GASTROESOPHAGEAL REFLUX DISEASE: NON-EROSIVE REFLUX DISEASE, EROSIVE ESOPHAGITIS AND BARRETT'S ESOPHAGUS

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is one of the most common diseases and, according to recent epidemiological studies, clinical and endoscopic GERD symptoms can be detected in 8-25% of the population depending on country, race and gender. In the Russian Federation, the prevalence of GERD reaches 11-15%. Despite improvements in diagnosis and treatment of GERD, there are still many unresolved issues. GERD is characterized by disorders in immune response presented by misbalanced cellular (Th1) and humoral (Th2) parts of immune response which depend on expression of cytokines.
AIMS & METHODS: To determinate the circulating level of cytokines in patients with different forms of gastroesophageal reflux disease (GERD): non-erosive reflux disease (NERD), erosive esophagitis and Barrett's esophagus. In prospective cohort study were included 55 patients and randomized in 4 groups: group 1 - 20 patients with NERD (11 men, 9 women; average age 37.75± 12.04), group 2 – 20 patients with erosive esophagitis (13 men, 7 women; average age 38.33±12.55), 3 group – 5 patients with Barrett's esophagus (5 men; average age 34.25±9.88) and group 4 (control group) – 10 healthy volunteers (5 men, 5 women; average age 33.37±9.39). In all enrolled patients were performed the upper gastrointestinal endoscopy and the determination of plasma cytokines (IL-4, IL-8, IL-10, IFN-γ, TNF-α) by flow cytometry. Statistical analyses were performed using SPSS 17.0 statistical package.
RESULTS: In patients with erosive esophagitis the median rate of IL-8 was 17.54 pg/mL (95% CI, 15.83 to 19.24), IFN-γ 72.97 pg/mL (95% CI, 15.24 to 130.7), TNF-α 16.31 pg/mL (95% CI, 14.03 to 18.58). The expression of IL-8 in patients with erosive esophagitis was 2,3 times higher than in patients with NERD ($p=0.02$) and 5,04 times higher than in patients with Barrett's esophagus ($p=0.02$). The expression of IFN-γ in patients with erosive esophagitis was 2,58 times higher than in patients with NERD ($p=0.03$) and 27,03 times higher than in patients with Barrett's esophagus ($p=0.03$). The expression of TNF-α in patients with erosive esophagitis was 2,22 times higher than in patients with NERD ($p=0.04$) and 2,26 times higher than in patients with Barrett's esophagus ($p=0.05$). In patients with Barrett's esophagus the median rate of IL-4 was 14.95 pg/mL (95% CI, 12.75 to 17.15), IL-10 9.2 pg/mL (95% CI, 8.75 to 9.68). The expression of IL-4 in patients with Barrett's esophagus was 2.36 times higher than in patients with erosive esophagitis ($p=0.03$) and 3.33 times higher than in patients with NERD ($p=0.05$). The expression of IL-10 in patients with Barrett's esophagus was 1.59 times higher than in patients with

erosive esophagitis ($p = 0.03$) and 2.53 times higher than in patients with NERD ($p = 0.03$).
CONCLUSION: In patients with erosive esophagitis in comparison with NERD and Barrett's esophagus we found overexpression of pro-inflammatory cytokines (IL-8, IFN-γ, TNF-α), that reflects their role in the Th1 immune response. In patients with Barrett's esophagus in comparison with NERD and erosive esophagitis was the overexpression of anti-inflammatory cytokines (IL-4, IL-10), that reflects their role in the Th2 immune response.
Disclosure of Interest: None declared

P0476 THE CIRCULATING LEVEL OF CYTOKINES IN PATIENTS WITH REFRACTORY TO PROTON PUMP INHIBITORS GASTROESOPHAGEAL REFLUX DISEASE

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is one of the most common diseases and, according to recent epidemiological studies, clinical and endoscopic GERD symptoms can be detected in 8-25% of the population depending on country, race and gender. In the Russian Federation, the prevalence of GERD reaches 11-15%. 50-60% of patients suffernig from refractory GERD who despite the received therapy do not have improved clinical and endoscopic picture, than can be explained with misbalance of Th1 and Th2 parts of immune response which depend on expression of cytokines.
AIMS & METHODS: To determinate the circulating level of cytokines in patients with GERD depending on the response to standard proton pump inhibitors (PPI) therapy. In prospective cohort study were included 50 patients randomized in 3 groups: group 1 - 20 patients with non- refractory GERD (the complete response to standard PPI therapy during 8 weeks which was defined on disappearance of complaints) - 11 men, 9 women; average age 37.66±10.02, group 2 - 20 patients with refractory GERD (the partial response or absence of response to standard PPI therapy during 8 weeks which was defined on maintenance of complaints) - 12 men, 8 women; average age 38.25±9.42, and group 3 (control group) – 10 healthy volunteers (5 men, 5 women; average age 34.25±9.88). In all enrolled patients were performed the upper gastrointestinal endoscopy and the determination of plasma cytokines (IL-4, IL-8, IL-10, IFN-γ, TNF-α) by flow cytometry. Statistical analyses were performed using SPSS 17.0 statistical package.
RESULTS: In patients with refractory to PPI gastroesophageal reflux disease in comparison with patients with non- refractory GERD were higher levels of IL-8 (18.10 pg/mL vs. 6.66 pg/mL; $p = 0.02$), IFN-γ (61.7 pg/mL vs. 24.10 pg/mL; $p = 0.022$), TNF-α (14.77 pg/mL vs. 7.97 pg/mL; $p = 0.03$). The high level of IL-8 is associated with relapse of erosive esophagitis within 2 years ($p \leq 0.01$).
CONCLUSION: In patients with refractory to PPI gastroesophageal reflux disease in comparison with non- refractory GERD was overexpressed IL-8, IFN-γ, TNF-α. Thus the high level of IL-8 was correlated with recurrent erosive esophagitis within 2 years, and this cytokine can be used as the marker defining the prediction of a course of a disease.
Disclosure of Interest: None declared

P0477 IS THERE A REAL RISK OF THE LONG TERM MEDICAL TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE?

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INTRODUCTION: A prolonged acid inhibition may be associated with the important consequences like nutritional defects, increased risk of fractures or infections and development of gastric polyps. The majority of data originate from retrospective epidemiological studies only.
AIMS & METHODS: The aim of the study was to prospectively evaluate the incidence of the possible risk events among patients during the long term acid suppressive treatment.
A prospective observational study in gastroesophageal reflux disease (GERD) patients requiring a long term treatment with proton pump inhibitors (PPI) was performed. The development of fractures, pulmonary and enteric infection and gastric polyps were recorded. The results were compared with control group recruited from endoscopy outpatients without any history of the proton pump inhibitor intake.
RESULTS: The cohort of 230 patients on maintenance GERD treatment (44% female, age 53.8 ±14.4) was followed-up for 7.1 years (1631 patient-years). Results were matched with 209 controls. The users of PPI were equally likely to develop fractures 3.5% (OR 0.53; 95% CI 0.21-1.32) and bronchopneumonia 0.4% (OR 0.29; 95% CI 0.03-2.87) as the controls. The development of infectious diarrhea was less frequent in PPI users than in controls (OR 0.11; 95% CI 0.01-0.09). No case of hypomagnesemia was diagnosed in PPI users. Only a development of fundic gland polyps was associated with PPI use in 12.6% of exposed patients (OR 2.7; 95% CI 1.07-6.63).
CONCLUSION: A long term acid suppressing treatment of gastroesophageal reflux disease did not increase the likelihood of fractures, infectious diarrhea, bronchopneumonia and hypomagnesemia. Our results could encourage the importance of prospective evaluation of risk events in subgroups according to the indication of PPI use.
Disclosure of Interest: None declared

P0478 30° MAY BE MORE APPROPRIATE THAN 45° FOR THE CRITICALLY ILL PATIENTS RECEIVING MECHANICAL VENTILATION AND ENTERAL NUTRITION

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INTRODUCTION: Semi-recumbent position plays a pivotal role in prophylaxis for the development of ventilator-associated pneumonia in the critically ills. In the present study, we aimed to find a more appropriate semi-recumbent position between 30° and 45° for the critically ill patients receiving mechanical ventilation and enteral nutrition on balancing their advantages in ventilator-associated pneumonia (VAP) prophylaxis and disadvantages in organ protection.
AIMS & METHODS: A prospective, randomized clinical study to investigate the effect of different HOB (30° or 45°) on all extent gastroesophageal reflux, proximal gastroesophageal reflux and development of VAP; intra-abdominal pressure (IAP), hemodynamic parameters [mean arterial pressure (MAP), abdominal perfusion pressure (APP), filtration gradient (FG)] and development of organ failure was conducted on 86 consecutive patients admitted to a comprehensive intensive care unit (ICU).
RESULTS: No significant differences in the incidence of VAP and number of all extent reflux were found between 30° group and 45° group. However, the number and percentage of proximal reflux in 45° group were unexpectedly higher than 30° group (Number: acid: $p = 0.022$; weakly acidic: $p = 0.257$; non acid: $p = 0.168$; Percentage: acid: $p = 0.000$; weakly acidic: $p = 0.000$; non acid: $p = 0.000$). Patients in 45° group had a trendency to develop new onset organ failure more easily (45° vs. 30°: 11/42 vs. 5/44, $p = 0.077$), accompanied with higher IAPs measurement (17.64±5.32 mmHg vs.14.98±5.34 mmHg, $p = 0.023$) and lower MAP, APP, and FG (MAP, $p = 0.001$; APP, $p = 0.000$; FG, $p = 0.000$).
CONCLUSION: For mechanically ventilated patients with enteral nutrition, keeping the HOB at 45° doesn't show superiority over 30°. Elevating the HOB from 30° to 45° can't reduce the incidence of VAP effectively but brings new onset organ failure more easily.
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Disclosure of Interest: None declared

P0479 DETECTION OF BURIED BARRETT'S GLANDS AFTER RADIOFREQUENCY ABLATION (RFA) WITH VOLUMETRIC LASER ENDOMICROSCOPY (VLE)

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INTRODUCTION: The prevalence and clinical relevance of Buried Barrett's (BB) epithelium after radiofrequency ablation (RFA) in Barrett's oesophagus (BO) is questioned. Recent studies using small optical coherence tomography (OCT) catheters for scanning underneath the neosquamous epithelium demonstrated a high prevalence of tissue structures that might correspond to BB. Histological correlation, however, is lacking. Volumetric Laser Endomicroscopy (VLE) is a novel balloon-based OCT imaging technique that provides a 6-cm long circumferential volumetric scan of the oesophageal wall layers to a depth of 3 mm with a resolution comparable to low-power microscopy.
AIMS & METHODS: To evaluate if post-RFA subsquamous structures, detected with VLE, actually correspond to BB and to pursue direct histological correlation of VLE images.
In-vivo VLE was performed to detect subsquamous structures suspicious for BB in patients with 100% endoscopic regression of dysplastic Barrett's epithelium after RFA. Areas with suspicious subsquamous VLE structures were marked with electrocoagulation after which in-vivo VLE was repeated to confirm that the correct area was demarcated. These areas were subsequently resected endoscopically, followed by immediate ex-vivo VLE scanning to reconfirm the presence of the subsquamous VLE structures. Extensive histological sectioning was then performed and all histopathology slides were evaluated by an expert BO pathologist (blinded for VLE images).
RESULTS: In 17 patients, 13 areas with suspicious subsquamous structures were seen on in-vivo VLE and resected. Ex-vivo VLE of these 13 ER specimens reconfirmed the presence of these subsquamous structures in 12 ER specimens. Extensive histological sectioning of these areas showed BB in one area. The other subsquamous VLE structures corresponded to dilated (ducts of) (sub)mucosal glands or blood vessels.
CONCLUSION: VLE may potentially detect BB under endoscopically normal appearing neosquamous epithelium. However, most post-RFA subsquamous structures identified by in-vivo VLE did not correspond to BB. Further studies

are required to identify VLE features that allow for differentiation of BB from normal subsquamous structures.
Disclosure of Interest: None declared

P0480 VOLUMETRIC LASER ENDOMICROSCOPY IN BARRETT'S OESOPHAGUS: A STUDY ON HISTOLOGICAL CORRELATION

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INTRODUCTION: Volumetric laser endomicroscopy (VLE) is a novel balloon-based optical coherence tomography (OCT) imaging technique. It provides a 6-cm long circumferential volumetric scan of the oesophageal wall layers to a depth of 3 mm with a resolution that is comparable to low-power microscopy. VLE has the potential for detection and delineation of early neoplastic lesions in Barrett's oesophagus (BO). In order to investigate this, it is important that structures identified on VLE can be correlated with histology and -vice versa- that of areas containing early neoplasia on histology the corresponding VLE features can be studied. Most previous OCT studies lack such a direct correlation between histology and OCT images.
AIMS & METHODS: To investigate the optimal approach for one-to-one correlation of VLE images with histology.
BO patients with and without early neoplasia underwent endoscopic resection (ER) of areas marked in-vivo with electrocoagulation markers (ECM). Subsequently ER specimens underwent additional ex-vivo marking with several different markers (ink, pin, ECM) followed by ex-vivo VLE scanning. Tissue blocks were carefully sectioned guided by the placed markers. After further histological processing a histopathology slide was sectioned from each block. When necessary, extensive sectioning of tissue blocks was performed in order to visualize all markers that were included in the tissue block on histology. All histopathology and VLE slides were evaluated by 2 researchers and considered a match if a) ≥ 2 markers were visible on both modalities and b) mucosal patterns aside from these markers matched on both histology and VLE. All slides were evaluated by an expert BO pathologist.
RESULTS: From 16 ER specimens (overall diagnosis: 7 non-dysplastic BO, 9 dysplastic BO (1 LGD, 4 HGD, 4 EAC)) 120 tissue blocks were sectioned of which 57 contained multiple markers and thus could potentially be matched with VLE. Based on several combinations of these markers in total 14 histology-VLE matches could ultimately be constructed. Markers that achieved the best yield of matches respectively were: in-vivo placed ECMs (8 matches with 12 markers), pins (7 with 11), and ink (4 with 5). Histopathological evaluation was not hindered by marker use. In this pilot study the last 6 ER specimens yielded 9/14 matches demonstrating a clear learning curve due to methodological improvements in marker placement and tissue block sectioning.
CONCLUSION: One-to-one correlation of VLE and histology is complex but feasible. The groundwork laid in this study will provide high-quality histology-VLE correlations that will allow further research on VLE structures and VLE features of early neoplasia in BO.
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P0481 SENSITIVITY TO OESOPHAGEAL MULTIMODAL STIMULATION IN BARRETT'S OESOPHAGUS PATIENTS

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INTRODUCTION: Oesophageal sensitivity to mechanical and acid stimulation in Barrett's oesophagus has previously been shown to be decreased.
AIMS & METHODS: The aim was to investigate the oesophageal sensitivity in Barrett's oesophagus using a multimodal (mechanical, thermal, electrical, acid) pain model.
Twenty-two patients with Barrett's oesophagus (mean age: 64.6 years) were compared to twelve healthy controls (mean age: 54.3 years) using oesophageal multimodal pain stimulation following upper endoscopy. A probe with a polyurethane bag was placed in the lower oesophagus. The probe was then used to apply mechanical, thermal, and electrical stimulation as well as a modified Bernstein test with infusion of 0.1 N HCl. All stimulations were stopped when the subject felt moderate pain, defined as 7 out of 10 on a visual analogue scale (VAS = 7).
RESULTS: Five of the Barrett's oesophagus patients had oesophagitis (Los Angeles grade A or B) on endoscopy.
For mechanical stimulation, the bag distension volume evoking VAS = 7 was significantly higher in the Barrett's group (mean volume 42 vs 28 mL, $P = 0.006$). For thermal stimulation, there was a non-significant tendency in the Barrett's group towards a higher "area under the curve" to reach VAS = 7 (949 vs. 677 s*°C, $P = 0.14$). The stimulus required to reach VAS = 7 during electrical stimulation was significantly higher in the Barrett's group (32.7 mA vs. 21.9 mA, $p = 0.03$. During the modified Bernstein test, the acid volume required to reach VAS = 7 or a maximum infusion volume of 200 mL was lower in the Barrett's group (mean 77 vs. 127 mL, $P = 0.03$). The time passed before feeling the first burning sensation during acid infusion was shorter in the Barrett's group, but just failed to be significant (181 vs. 329 seconds, $P = 0.056$).
The referred pain area defined by the subject immediately after sensing VAS = 7 was insignificant between groups ($P > 0.05$) for all 4 stimulation modalities.
CONCLUSION: Barrett's oesophagus patients showed *hypo*sensitivity to mechanical, thermal and electrical stimulation, but *hyper*sensitivity to acid stimulation. This is to some degree different from earlier findings, but the latter finding could indicate a sensitisation to acid because of oesophagitis underlying the disease.
Disclosure of Interest: None declared

P0482 SURVEILLANCE IN PATIENTS WITH BARRETT'S ESOPHAGUS: A COST-EFFECTIVENESS ANALYSIS

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INTRODUCTION: Surveillance is recommended for Barrett's esophagus (BE) to detect esophageal adenocarcinoma (EAC) at an early stage.
AIMS & METHODS: The aim of this study was to evaluate the cost-effectiveness of surveillance intervals and treatment strategies. 714 BE patients were included in a multicenter prospective cohort study and followed during surveillance according to the ACG guidelines. We used a multi-state-Markov model to calculate misclassification and true progression rates from no dysplasia (ND) to low-grade dysplasia (LGD), high-grade dysplasia (HGD) and EAC. These progression rates were incorporated in a decision-analytic model, which included costs and quality of life data associated with different surveillance strategies. We evaluated different surveillance intervals for ND and LGD, endoscopic mucosal resection (EMR) followed by radiofrequency ablation (RFA), RFA alone or esophagectomy for HGD or early EAC and esophagectomy with neoadjuvant chemoradiotherapy for advanced EAC. The incremental cost-effectiveness ratio (ICER) was calculated in costs per quality-adjusted life year (QALY). The willingness-to-pay threshold was set at €35.000 per QALY gained.

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	No dysplasia			Low-grade dysplasia		
Strategy	Costs	QALYs	ICER	Costs	QALYs	ICER
No surveillance	€5.695	12.62	€4.823	€21.806	10.95	€4.040
Surveillance every 5 years with RFA	€6.904	12.87	€61.821	€25.709	11.91	€28.741
Surveillance every 5 years with EMR and RFA	€7.139	12.87	€104.668	€27.447	11.91	€31.073
Surveillance every 5 years with esophagectomy	€13.965	12.64	€321.880	€50.909	11.33	€39.633
Surveillance every 4 years with RFA	€7.695	12.89		€28.006	11.99	€72.257
Surveillance every 4 years with EMR and RFA	€7.951	12.89		€29.959	11.99	
Surveillance every 4 years with esophagectomy	€15.229	12.63		€51.835	11.34	
Surveillance every 3 years with RFA	€8.868	12.90		€30.973	12.09	
Surveillance every 3 years with EMR and RFA	€9.148	12.90		€33.210	12.09	
Surveillance every 3 years with esophagectomy	€16.890	12.61		€52.851	11.34	
Surveillance every 2 years with RFA	€10.831	12.90		€34.956	12.19	
Surveillance every 2 years with EMR and RFA	€11.143	12.90		€37.575	12.19	
Surveillance every 2 years with esophagectomy	€19.325	12.59		€53.960	11.34	
Surveillance every year with RFA	€14.898	12.89		€40.542	12.27	
Surveillance every year with EMR and RFA	€15.257	12.89		€43.688	12.27	
Surveillance every year with esophagectomy	€23.686	12.54		€55.159	11.34	

RESULTS: The true annual progression rate for ND to LGD was 0.02, for LGD to HGD or early EAC 0.03 and for HGD or early EAC to invasive EAC 0.36. In patients with ND, surveillance every five or four years with RFA for HGD or early EAC and esophagectomy for advanced EAC had ICERs of €4.800 and €61.800 per QALY respectively. Strategies with shorter intervals provided higher costs with similar QALYs gained. In patients with LGD, surveillance every five to two years had ICERs of €4.040, €28.741, €31.073, and €39.633 per QALY respectively. EMR prior to RFA was slightly more expensive, but had additional value for tumor staging.
CONCLUSION: Surveillance with EMR and RFA for HGD or early EAC and esophagectomy for advanced EAC is cost-effective with 5-year intervals for patients with ND and 3-year intervals for patients with LGD, based on a willingness-to-pay threshold of €35.000 per QALY.
Disclosure of Interest: None declared

P0483 BOTH ESOPHAGEAL POSTERIOR AND RIGHT WALL ARE THE PREFERRED LOCALIZATIONS OF BARRETT'S ESOPHAGUS

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INTRODUCTION: Prevalence of Barrett's esophagus (BE) is higher in patient with gastroesophageal reflux disease (GERD) with a rate of prevalence of 10%. The risk of cancer associated to this condition is estimated to be approximately 0.5% per year. For this reason a careful endoscopic surveillance assumes a paramount importance. Only few literature data on the preferred esophageal location of BE are available to date.
AIMS & METHODS: The aim of this study is to identify the preferred area where BE can develop within esophageal circumference. We retrospectively analyzed patients with BE who underwent upper endoscopy between January 2010 and March 2014 at our Endoscopy Center. We included only patients with short BE. In the case of multiple BE tongues, each lesion was considered individually. The circumferential localization of the lesions was determined according to the numbers of a clock face.
RESULTS: In the study period, a total of 204 subjects were newly diagnosed of BE or had an endoscopic follow-up of BE. Twenty-four patients with circumferential lesions were excluded. Among the 180 remaining patients, multiple BE lesions were diagnosed in 110 of them, for a total amount of 332 areas of mucosal metaplasia. Our analysis of data showed a clear prevalence of BE in the position near 3 o'clock and 6 o'clock of the endoscopic image. The area between 5 and 7 o'clock (posterior wall) was the most affected (38.25% of the lesions). Other localizations were respectively the arc between 2 and 4 o'clock (right wall) with 27.71%, the arc 11 to 1 o'clock 23.80% (anterior wall) and the arc 8 to 10 o'clock 10.24% (left wall). For each of the four walls, difference between observed and expected (dividing equally the number of lesions for the number of quadrants) lesions was statistically significant ($P < 0.0001$ for each wall). Lesions were most commonly located in the right (1 to 6 o'clock) than in the left (7 to 12 o'clock) quadrant (207 versus 125 – two-tailed P value = 0.0189).
CONCLUSION: We first describe, in a large cohort of Italian patients, an uneven localization of BE in the distal esophageal circumference, with an higher prevalence on the posterior-right wall. Anatomical and environmental factors could explain this finding. The circumferential asymmetry of LES pressure (in particular, a lower pressure on the right quadrant) and the preference of supine position during sleep are two situations that may promote the reflux of gastric fluids preferably in the right and posterior wall of the distal esophagus. A more accurate observation of such areas during endoscopic surveillance is advisable in GERD patients.
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P0484 A STUDY ON THE LONG-TERM PROGNOSIS AND PERFORMANCE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGOGASTRIC JUNCTION ADENOCARCINOMA

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INTRODUCTION: Endoscopic submucosal dissection (ESD) was becoming widespread as a treatment option for superficial adenocarcinoma of the esophagogastric junction (EGJ) including Barrett's esophageal adenocarcinoma; however, its long-term and treatment outcomes have not been fully evaluated.
AIMS & METHODS: The aim of this study was to assess the long-term and treatment outcomes of ESD for patients with superficial adenocarcinoma of the EGJ.
Between September 2000 and December 2013, we performed ESD for 104 superficial adenocarcinoma of EGJ (type II tumor according to Siewert's classification) in 103 patients. The rates of en bloc resection, positive for lateral and/or vertical margin, curative resection, and overall and disease-specific survival rate after ESD were evaluated during follow-up (median observation period 55.6 months).
We divided all patients into two groups, the adenocarcinoma of Barrett's esophagus (BE group: 20 lesions in 20 patients) and other adenocarcinoma of EGJ (Non-BE group: 84 lesions in 83 patients), then each outcomes were evaluated.
RESULTS: All lesions were treated by en bloc resection. None of BE group were positive lateral margin and 7 of Non-BE group were positive lateral margin.
The rate of curative resection was 74% (77/104) in all patients, and BE group and Non-BE group were 74% and 75%, respectively. The most frequent cause of non-curative resection was tumor invasion into the deep submucosa.
Ninety three patients (93%) were traceable prognosis, and 5 year overall survival rate was 91.2%. When we limited to the curative resections, 5 year overall survival rates were 66.7% in BE group and 89.4% in Non-BE group. There was no death of adenocarcinoma of EGJ, meaning that the disease-specific survival rate was 100%.
There was no statistical difference of the rate of positive margin, curative resection and 5 year overall survival rates between BE and Non-BE groups.
CONCLUSION: The treatment outcomes of ESD for adenocarcinoma of EGJ were favorable regardless of the evidence of Barrett's esophagus. However, the curative resection rate was relatively low. It was assumed that pre-operative recognition of the tumor invasion into the submucosa might be difficult for adenocarcinoma of EGJ.
Disclosure of Interest: None declared

P0485 THE ROLE OF CONFOCAL LASER ENDOMICROSCOPY IN THE MANAGEMENT OF PATIENTS WITH BARRETT'S ESOPHAGUS: A CLINICAL EVIDENCE-BASED CONSENSUS REPORT

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INTRODUCTION: Confocal Laser Endomicroscopy (CLE) is a recent technology that provides microscopic imaging during endoscopy, thus *in vivo* and in real time. The currently recommended Seattle protocol is intended to provide a comprehensive mapping of the Esophagus, but its inherent constraints have impaired its application. CLE allows for unlimited sampling of the esophageal mucosa and several recently published studies have shown its ability to provide a comprehensive assessment of Barrett's Esophagus (BE) lesions.
AIMS & METHODS: The aim of thi study is to develop consensus recommendations on the role of CLE in the management of patients with BE.
Initial statements on the use of CLE for the characterization of BE were developed by a single CLE expert based on the available clinical evidence. Those preliminary statements were edited and submitted by an external group of 20 GI physicians experts in CLE using a modified Delphi approach. After two rounds of votes based on relevant data, quality of the evidence and strength of recommendation, statements were validated if the threshold of agreement was higher than 75%.
RESULTS: 12 recommendations were adopted and 4 were rejected. CLE should be considered in the evaluation of BE. CLE is clinically indicated in patients with BE dysplasia in lesions initially identified in surveillance, with or without electronic enhancement. CLE is able to distinguish cardia from intestinal metaplasia (IM), based on the presence/absence of goblet cells. CLE is superior to White-Light Endoscopy (WLE) in identifying IM. A negative CLE random sampling in an endoscopically benign appearing Esophagus is sufficient to reduce the need for a physical biopsy in patients with known BE. CLE can improve the yield for neoplasia compared to standard WLE and random biopsies. CLE and WLE targeted biopsies are superior to WLE targeted biopsies alone in the detection of dysplasia. A positive CLE random sampling in an endoscopically neoplastic appearing Esophagus is sufficient for therapeutic intervention. CLE can be used to define location and lateral extent of neoplasia prior to therapy. CLE should be cited as a valuable tool for an increased diagnostic yield in official surveillance guidelines. CLE should be combined with red flag techniques.
CONCLUSION: The panel of experts that participated in this initiative strongly believes that Confocal Laser Endomicroscopy is an important adjunct to the current endoscopy practice. This technique can improve the management of patients by more accurately characterizing neoplasia, identifying residual neoplasia in post-treatment surveillance and rationalizing the choice of the most appropriate treatment. This consensus report is based on a review of the clinical evidence and on a consensus opinion.
Disclosure of Interest: J. P. Galmiche Consultancy for: Mauna Kea Technologies, R. Arsenescu: None declared, H. Bertani: None declared, F. Caillol: None declared, D. Carr-Locke: None declared, K. Chang Other: Medical Advisory Board Mauna Kea Technologies, E. Coron Consultancy for: Has served as a consultant for Mauna Kea Technologies, A. Dlugosz: None declared, S. I. Gan: None declared, M. Giovannini: None declared, F. G. Gress: None declared, K. Ho: None declared, V. Konda Other: Honorary for Mauna Kea Technologies, H. Neumann: None declared, F. Prat: None declared, P. Sharma: None declared, S. Singh: None declared, K. Wang: None declared, H. Wholfsen: None declared

P0486 COST-EFFECTIVENESS OF CONFOCAL LASER ENDOMICROSCOPY (CLE) FOR THE MANAGEMENT OF BARRETT'S ESOPHAGUS

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INTRODUCTION: The clinical impact of CLE has been demonstrated for the management of patients undergoing surveillance or treatment of Barrett's Esophagus. This study is the first one evaluating the economic impact of using CLE in clinical practice in a European healthcare system.
AIMS & METHODS: The aim of this study was to evaluate the cost-effectiveness of a CLE-based strategy compared to the standard Seattle protocol for the management of patients with Barrett's Esophagus and suspicion of neoplasia, in the setting of the French public healthcare system.
We used the data published by Canto et al (1) on a multicentric randomized controlled trial which compared 2 strategies: (i) high definition white light endoscopy (HD-WLE) + CLE and targeted physical biopsies (CLE-based strategy) and (ii) HD-WLE and random physical biopsies (Standard strategy). In that study, the CLE-based strategy had a higher sensitivity for the diagnosis of HGD/EC (95 versus 40%) without significant change in specificity (92% versus 98% respectively). The average number of biopsies performed was reduced from 5.91 to 1.26 per patient by the use of CLE. These data were entered into a health economics model (piggyback study) to compare the costs of both strategies when performed in public academic hospitals. French costs were associated to each procedure in order to estimate the medical cost of the two strategies from a public health payer perspective. CLE was priced as a therapeutic endoscopy procedure that is valued 20% more than a standard diagnostic endoscopy.
RESULTS: In spite of a higher procedure cost, the total costs for a cohort of 100 patients associated to the CLE-based strategy were 89,313.29 € compared to 90,658.90 € for the standard strategy. The cost per patient adequately diagnosed and treated was also inferior for the CLE-based strategy (960.36 € vs. 1,054.17 €). Different sensitivity analyses (including a Monte-Carlo modeling) were performed which confirmed the robustness of previous results.
CONCLUSION: In the restricted context of this evaluation, the CLE-based strategy is not only more effective but also less costly than the standard strategy i.e. corresponding to the definition of a dominant strategy.
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P0487 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL BARRETT'S ESOPHAGUS ADENOCARCINOMA: CLINICAL OUTCOMES IN A LARGE SERIES OF EUROPEAN PATIENTS

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INTRODUCTION: The role of endoscopic submucosal dissection (ESD) in Barrett's neoplasia has not yet been well defined, although this technique could potentially achieve a higher curative resection rate and improved histological assessment compared to endoscopic mucosal resection (EMR).
AIMS & METHODS: This study sought to assess ESD efficacy, safety, and long-term results in a large patient cohort. Seventy-five consecutive Barrett's esophagus (BE) patients who underwent ESD between January 2007 and February 2014 were retrospectively analyzed. ESD was performed for either visible lesions that were multiple, over 15mm, or poor-lifting, or for suspected submucosal infiltration. Primary endpoint was curative resection rate of carcinoma (CRC).
RESULTS: Median patient age was 68 years (IQR, 61-76), median patient follow-up was 20 months (IQR, 8.5-37.5), and median maximum specimen diameter was 52.5mm (IQR, 43-71). Median maximum diameter of visible lesion was 20mm (IQR, 10-30). *En bloc* resection and CRC rates were 90% and 85%, respectively. G3 differentiation and invasion >pT1m2 were observed in 25% and 55% of cases, respectively. Five early (<48h) adverse events occurred (two delayed hemorrhages; three perforations), all treated endoscopically. No ESD-specific death was observed. Esophageal strictures manifested in 60% of patients, all treated endoscopically. Additional treatment methods for residual BE were proposed to 64% of patients, with a median number of two sessions (IQR, 2-3). At latest follow-up, complete remission of neoplasia and intestinal metaplasia was achieved in 92% and 73%, respectively.
CONCLUSION: ESD appears to be safe and effective, with a high curative resection rate. ESD should be the favored treatment for Barrett's neoplasia cases at risk of incomplete resection or poor pathology assessment with conventional EMR.
Disclosure of Interest: None declared

P0488 AUTOFLUORESCENCE-TARGETED PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY CAN DETECT THE FIELD OF MOLECULAR CHANGE IN BARRETT'S OESOPHAGUS

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INTRODUCTION: Probe-based confocal laser endomicroscopy (pCLE) allows optical biopsies in Barrett's oesophagus (BO) to predict histological outcome but it is subject to sampling error if performed in a random fashion. We used autofluorescence imaging (AFI) to direct pCLE and added molecular biomarkers to the histopathological diagnosis.
AIMS & METHODS: The aims of this study were to assess the diagnostic accuracy for dysplasia of AFI-targeted optical biopsies and to investigate the correlation between pCLE patterns and field of molecular change.
53 patients with BO (non-dysplastic BO n = 22, indefinite for dysplasia (ID) n = 5, low grade dysplasia n = 13, high grade dysplasia (HGD) or intramucosal cancer (IMC) n = 13) were recruited at a single centre. Patients underwent high-resolution endoscopy followed by AFI and then pCLE was performed on AFI positive (AFI+) areas. Targeted biopsies were taken from AFI+ areas, followed by random biopsies as per Seattle protocol. pCLE sequences were graded according to published criteria. Cyclin A and p53 expression were assessed by immunohistochemistry and aneuploidy by flow-cytometry on AFI-targeted biopsies. Statistical analyses were performed using chi-square test
RESULTS: AFI-targeted pCLE correctly classified all the HGD/EC patients and had a sensitivity and specificity for any grade of dysplasia of 94% and 86%, respectively. The Seattle protocol had similar sensitivity for HGD/IMC and any grade of dysplasia (85% and 92.5%, respectively). For the per-location analysis, a total of 185 endoscopic areas were analyzed with pCLE and molecular biomarkers. pCLE had a sensitivity and a specificity for HGD/IMC and any grade of dysplasia of 100%/67% and 77%/77%, respectively. Overall, 40% of pCLE irregular sequences corresponded to non-dysplastic areas (false positive). We found a statistically significant enrichment ($p < 0.001$) of the three molecular biomarkers in pCLE irregular areas. After exclusion of dysplastic areas, a significant correlation between pCLE irregularity and biomarker positivity was retained ($p = 0.008$). The presence of at least 1 positive biomarker significantly correlated with dysplasia both in pCLE irregular ($p = 0.01$) and pCLE regular areas ($p = 0.05$). Using a cut-off of two positive biomarkers, this panel classified as high risk all the patients with HGD/IMC and 45% of patients with LGD, but none of the patients with ID and non-dysplastic BO
CONCLUSION: AFI-targeted pCLE has a high diagnostic accuracy for dysplasia in BO. Tissue biomarkers are a useful adjunct to characterize the field of molecular abnormality associated with optical dysplasia. These results suggest that the presence of pCLE irregularity, even in the absence of histological dysplasia, relates to molecular changes and may warrant close follow up. A 3-biomarker is a useful adjunct to optical biopsy to provide further stratification
Disclosure of Interest: None declared

P0489 ROLE OF BODY COMPOSITION AND METABOLIC DYSFUNCTION IN BARRETT'S OESOPHAGUS AND PROGRESSION TO CANCER

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INTRODUCTION: Oesophageal adenocarcinoma (OAC) arises within Barrett's oesophagus (BE). Obesity is associated with metabolic syndrome (MS) and cancer progression. Body composition has a direct impact in obesity-related diseases. Normal weight individuals with increased fat mass are considered metabolically obese.
AIMS & METHODS: To evaluate the prevalence of obesity, altered body composition and metabolic indexes in patients (pts) with and without BE; and association with cancer progression in BE.
In sequential pts undergoing gastroscopy, MS, waist/hip ratio (WHR) and body fat% (BF by bioimpedance analysis) were obtained. In BE pts, histological findings were correlated with metabolic data. Pts were classified according to Body Mass Index (BMI), abdominal obesity (AO by WHR) and in females, Normal Weight Obese (NWO). Identified risk factors significantly associated with BE at univariate analysis were subsequently entered into a multivariate logistic regression analysis.
RESULTS: 250 cases and 230 controls (F/M: 193/287) were enrolled. Age (cut off: 57 years) and male gender (M/F 193/57; OR 5.01, $p < 0.0001$) were identified risk factors for BE. AO (76 *vs* 51%; OR 3.13; $p < 0.001$), increased BF% (30.7 *vs* 17.6%; $p = 0.001$), higher BMI (overweight: 39.6 *vs* 30%; OR 2.09; $p = 0.0008$; obese: 32 *vs* 22%; OR 2.3; $p = 0.004$) and MS (33.2 *vs* 20%; OR 1.95; $p = 0.0017$) were significantly associated with BE. A positive trend, possibly related to the small number of female cases, was demonstrated for NWO (28.1 *vs* 19.1%; OR 1.06; $p = 0.1$). More cases were affected by hypertension (37.4 *vs* 21.3%; OR 2.4; $p < 0.001$) and hyperlipidaemia (72.8 *vs* 53.9%; OR 2.28; $p < 0001$) but not diabetes.
When adjusted by gender, age and race into a multivariate analysis, independent risk factors for BE were BF% (OR 1.90; $p = 0.01$) and AO (OR 1.67; $p = 0.03$).

Metaplasia and dysplasia were present in 57.2 and 42.8%. AO was the only metabolic parameter independently correlated with high grade dysplasia (38 *vs* 21%; OR 2.44; p = 0.001).

CONCLUSION: Abdominal obesity, and body fat mass are strong risk factors for BE. A positive trend association was demonstrated in NWO. Furthermore, abdominal adiposity plays a role in progression to OAC. BE might therefore be considered in the metabolic syndrome spectrum and as such, in this group screening interventions may be considered.

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P0490 A NOVEL ENDOSCOPIC CLASSIFICATION SYSTEM USING I-SCAN IMPROVES DYSPLASIA DETECTION IN BARRETT'S OESOPHAGUS

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INTRODUCTION: Dysplasia arising in Barrett's oesophagus (BE) can lead to oesophageal adenocarcinoma. Endoscopic surveillance is performed to detect dysplasia in BE so early treatment can be offered. Current practice relies on white-light endoscopy (WLE) to obtain random quadrant biopsies every 2cm from the BE segment, sampling less than 5% of the surface and therefore potentially missing areas of dysplasia.

An endoscopic image enhancement technology, *i-Scan* (PENTAX HOYA, Japan), has been developed to help improve lesion recognition in the gastrointestinal tract. *i-Scan* utilises post-processing light filtering technology to provide real-time analysis and enhancement of different elements of the mucosa and microvasculature to improve dysplasia detection.

Previous endoscopic classification systems for BE have used image enhancement technologies combined with magnification endoscopy. We report the accuracy of a novel classification system using *i-Scan* without magnification amongst expert endoscopists based at 3 high-volume European tertiary referral centres for detecting BE dysplasia.

AIMS & METHODS: High definition (HD) video recordings were collected from patients with non-dysplastic (ND-BE) and dysplastic (D-BE) BE undergoing endoscopy at University College London Hospital. A protocol was used to record areas of interest and a corresponding biopsy was taken to confirm pathology.

A simple classification system based on mucosal (M) and vascular (V) patterns was used: M1 or M2 - regular oval or villous pits respectively (ND-BE), M3 – irregular or featureless mucosa (D-BE); V1 – regular vessels (ND-BE), V2 – irregular (dilated, corkscrew) vessels (D-BE).

In a blinded manner, videos of normal and abnormal lesions were interpreted by 3 expert endoscopists using the above classification. Predicted pathology was also recorded for each lesion. Acetic acid (ACA) chromoendoscopy was used in some cases. Agreement in relation to predicted histology was calculated using κ statistics.

RESULTS: Videos from 47 patients (including 13 before and after ACA to generate 60 videos in total) were analysed. 24 were ND-BE and 23 D-BE. Cases in which ACA was used, 7 had ND-BE and 6 D-BE.

Experts' accuracy for detection of D-BE and ND-BE was 69% (62–72%) and 68% (39-80%) respectively. The sensitivity and specificity for dysplasia detection using our classification system were both 68%. ACA improved the sensitivity and specificity to 78% and 71% respectively. Inter-observer agreement for dysplasia prediction in all cases was 'moderate' ($\kappa = 0.42$) but improved to 'good' ($\kappa = 0.70$) with ACA.

CONCLUSION: Using a simple non-magnification endoscopic classification system combined with i-Scan and ACA, experts are able to accurately diagnose D-BE in 78% of cases. ACA chromoendoscopy appears to improve the sensitivity and inter-observer agreement for dysplasia detection over HD-WLE alone. These data are comparable to similar classification systems using zoom enhanced imaging and ACA previously published and could be used by the general endoscopists performing BE surveillance to target sampling and improve dysplasia detection. The addition of zoom endoscopy to i-scan has the potential to increase the accuracy further.

Disclosure of Interest: None declared

P0491 IMPACT OF ABLATION VS. SURVEILLANCE ON QUALITY OF LIFE AND ILLNESS PERCEPTION IN PATIENTS WITH BARRETT'S OESOPHAGUS CONTAINING LOW-GRADE DYSPLASIA: A MULTI-CENTER RANDOMISED CONTROLLED TRIAL

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INTRODUCTION: Patients with a confirmed histological diagnosis of low-grade dysplasia in Barrett's oesophagus have an increased risk of neoplastic progression to high-grade dysplasia and oesophageal adenocarcinoma. We recently reported on a multi-center randomised controlled trial, in which endoscopic radiofrequency ablation reduced neoplastic progression from 26.5% to 1.5% compared to endoscopic surveillance. As part of this trial, we prospectively investigated whether these approaches also lead to differences in quality of life and illness perception.

AIMS & METHODS: Patients with a confirmed histological diagnosis of low-grade dysplasia in Barrett's oesophagus were randomly assigned to ablation or endoscopic surveillance. Quality of life and illness perception were assessed at baseline, 2, 8, 14, 26, and 38 months follow-up. QOL was measured with the SF-36 (general), the EORTC-QLQ-C30 (cancer-specific), and the EORTC-QLQ-OES18 (esophageal cancer-specific). Illness perception was measured with the brief-illness perception questionnaire (8 dimensions (scale 0-10); overall score (scale 0-80)). To compare ablation with surveillance for longitudinal data with repeated measurements, a linear mixed model was used.

RESULTS: Quality of life and illness perception were investigated in 96 patients (47 ablation, 49 surveillance) with a median follow-up of 36 months. There were no significant differences between the groups for SF-36 (general) and the EORTC-QLQ-C30 (cancer-specific). Apart from less reflux symptoms in the ablation group, there was no difference between the groups for EORTC-QLQ-OES18 (esophageal cancer-specific).

Compared to surveillance patients, ablation patients perceived their disease as lasting for a significantly shorter period of time (6.2 out of 10 vs 8.1 out of 10; $p < 0.001$), experienced fewer symptoms (2.4 out of 10 vs 3.3 out of 10 $p < 0.001$), had fewer concerns about their illness (3.6 out of 10 vs 5.2 out of 10; $p < 0.001$), and were less emotionally affected by their illness (2.8 out of 10 vs 3.3 out of 10; $p = 0.012$). As a result, ablation patients experienced their disease as less threatening compared to surveillance patients (overall illness perception score 26.6 out of 80 vs 34.2 out of 80; $p < 0.001$).

CONCLUSION: In this multi-center randomised controlled trial of ablation versus surveillance for low grade dysplasia in Barrett's oesphagus, ablation not only reduced the neoplastic progression by 25% compared to surveillance, but also led to fewer concerns and a less threatening view of the illness during a median follow-up of 36 months. This further strengthens the indication for prophylactic ablation of confirmed low grade dysplasie in Barrett's oesophagus.

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P0493 CLINICAL SIGNIFICANCE OF MEAN PLATELET VOLUME, PLATELETCRIT, PLATELET-LYMPHOCYTE RATIO AND NEUTROPHIL-LYMPHOCYTE RATIO IN THE DIFFERENTIATION OF PATIENTS WITH GASTRIC PRECANCEROUS LESIONS

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INTRODUCTION: Before gastric cancer becomes clinically noticeable, a prolonged precancerous process takes place which includes atrophic gastritis and intestinal metaplasia (IM). There is no validated evidence available to support surveillance of gastric intestinal metaplasia. Therefore, the aim of this study was to investigate whether systemic inflammatory response markers such as mean platelet volume, plateletcrit, platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) in peripheral blood may have a role in the differentiation of patients with gastric precancerous lesions.

AIMS & METHODS: 1139 patients with atrophic gastritis, intestinal metaplasia and gastric cancer were evaluated by means of mean platelet volume, plateletcrit, PLR and NLR. Patients were further divided into four groups according to updated Sydney classification: Group 0: IM negative, Group I: IM 1+, Group II: IM2+, Group III: IM3+, also two groups consisting of Group IV: gastric cancer and Group V: atrophic gastritis were included into the study in order to maintain appropriate comparisons.

RESULTS: As for PLR values, there were significant differences between groups indicating that PLR was significantly higher in group IV compared to groups 0, I, II, III, and V (209.4±216.6 vs 131.4±61.7, 131±60.4, 132.6±69.7, 131±76 and 141.9±53. p = 0.001, 0.001, 0.001, 0.001 and 0.048 respectively). NLR was also significantly higher in group IV compared to groups 0, I, II, III, and V (3.81±5.33 vs 2.4±1.65, 2.35±1.65, 2.42±1.91, and 2.34±1.57, p = 0.001).

Plateletcrit was significantly higher in group IV compared to group II (0.25±0.08 vs. 0.21±0.05%, p = 0.01). However, there were no statistically significant difference between groups by means of mean platelet volume. Receiver operating characteristic curve (ROC) analysis suggested that optimum PLR cut-off point according to Youden index was 137.6 (AUC: 0.718) with a sensitivity and specificity of 0.67 and 0.68 respectively, and optimum NLR ratio cut-off point was 2.2 (AUC: 0.702) with a sensitivity and specificity of 0.71 and 0.60 respectively.
CONCLUSION: No evidence from randomised studies exists to support surveillance of gastric intestinal metaplasia. Although sensitivity and specificity are not high enough, PLR and NLR may be used in clinical practice in order to decide which patients should be scoped and biopsied during the follow-up of patients with IM and atrophic gastritis.
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Disclosure of Interest: None declared

P0494 IMPACT OF CARCINOMATOSIS AND ASCITES STATUS ON LONG-TERM OUTCOMES OF PALLIATIVE TREATMENT FOR PATIENTS WITH GASTRIC OUTLET OBSTRUCTION CAUSED BY UNRESECTABLE GASTRIC CANCER: STENT PLACEMENT VERSUS PALLIATIVE GASTROJEJUNOSTOMY

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INTRODUCTION: Self-expandable metal stent (SEMS) placement and palliative gastrojejunostomy (GJJ) are palliative treatment options for malignant gastric outlet obstruction.
AIMS & METHODS: We aimed to compare clinical outcomes of palliative treatments for gastric outlet obstruction caused by unresectable gastric cancer to identify optimal treatment modalities according to carcinomatosis and ascites status. We analyzed 217 and 39 patients who underwent SEMS placement and palliative GJJ, respectively, for gastric outlet obstruction caused by unresectable gastric cancer.
RESULTS: Treatment modality was not an independently associated factor of clinical success ($P = 0.992$). Treatment modality, however, affected re-obstruction after clinical success ($P = 0.001$). In addition, carcinomatosis with ascites was an independent associated factor of clinical success ($P = 0.006$) and re-obstruction ($P = 0.045$). In a subgroup of patients with good performance who had neither carcinomatosis nor ascites, patency duration and overall survival duration did not differ between the two groups. In patients with good performance who had carcinomatosis without ascites, patency duration was longer in the palliative GJJ group than in the SEMS placement group. Overall survival, however, did not differ between the two groups. In a subgroup of patients with good performance who had carcinomatosis with ascites, both patency duration and overall survival were longer in the palliative GJJ group than in the SEMS placement group.
CONCLUSION: Long-term clinical outcomes of the palliative treatment modality for gastric outlet obstruction caused by unresectable gastric cancer were affected by carcinomatosis and ascites status, according to which a palliative treatment modality can be chosen.
Disclosure of Interest: None declared

P0495 HIGH PREVALENCE OF GASTROINTESTINAL STROMAL TUMOURS (GISTS): A CASE SERIES IN UK SECONDARY CARE

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INTRODUCTION: Gastrointestinal Stromal Tumours (GISTs) are mesenchymal tumours, predominantly affecting the GI tract. Diagnosis and classification require specialist review and there are few published data on the incidence of GIST in the UK. Reported incidences elsewhere vary between 6.5/ million/ year in Norway and 14.5/ million/year in Sweden[1,2]. We have analysed our caseload of GISTs in a UK secondary care setting with a population of approx 350,000, in order to estimate incidence and review outcomes.
AIMS & METHODS: A retrospective case note reviews of all patients with GIST, as identified from upper GI cancer multidisciplinary team meeting (MDT) minutes, from 2008 to 2013 inclusive (6 years). The diagnosis of GIST was considered valid, if characteristic imaging and/ or pathological features were verified by CT scanning, endoscopic ultrasound (EUS) needle aspiration/ biopsy and/ or surgical resection.
RESULTS: We identified 34 cases with a final diagnosis of GIST. The observed incidence of presentation to hospital varied year on year, and estimated annualised incidence was calculated at 16.2 / million/year. The age range was 28-91 years (M 15, F19). Nineteen cases (59%) presented with signs or symptoms of GI blood loss; five (15%) with other GI symptoms and remaining cases were found incidentally. The size of GIST at presentation ranged from 1cm to 20 cm in diameter. One case had metastasised at the time of diagnosis. EUS was used for diagnosis and staging in 15 cases; 13 had fine needle aspiration, of which 10/13 were diagnostic. 26/34((76%) cases underwent resection surgery. 6 cases were treated with Imatinib (Glivec). Case follow up range from 3 months to 6 years. Two patients died, one patient presented with metastatic disease other was managed with palliative approach due to advance age and co-morbidities.
CONCLUSION: Our review suggests a higher than expected incidence of GISTs in this population compared with other published series[1,2]. Most cases present with GI blood loss and surgery is curative in most cases with good prognosis. The incidence of GISTs in the UK is deserving of further study.
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Disclosure of Interest: None declared

P0496 ENDOSCOPIC CHARACTERISTICS PREDICTING LYMPHOVASCULAR INVASION OF EARLY GASTRIC CANCER: A RETROSPECTIVE COHORT STUDY USING PROPENSITY-SCORE MATCHING

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INTRODUCTION: The most important factor concerning endoscopic resection (ER) for early gastric cancer (EGC) is the prediction of regional lymph node (LN) metastasis before treatment. Of the main risk factors associated with LN metastasis, lymphovascular invasion (LVI) of tumor is the strongest predictor for LN metastasis in EGC. However, risk factors of LVI have not been securely established. The purpose of this study was to evaluate endoscopic characteristics predictive of LVI of EGC treated by ER.
AIMS & METHODS: A total of 1214 consecutive patients with 1240 EGCs underwent ER between January 2007 to June 2013. The lesions studied were grouped into groups of either no LVI group (n = 1166) or LVI group (n = 74), according to the presence of LVI in ER specimen. Propensity-score matching for adjustment of confounding variables including lesion size and submucosal invasion yielded 148 matched patients. Endoscopic characteristics including macroscopic type, erythema, whitish discolorization, ulcer, marginal delineation, and folds change were investigated among the matched cohort.
RESULTS: Lymphovascular tumor invasion was diagnosed in 6.0% of enrolled lesions. Of clinicopathologic characteristics in the overall cohort, larger size ($P < 0.001$) and submucosal invasion determined by endoscopic ultrasound ($P < 0.001$) and histology ($P < 0.001$) were significantly higher in the LVI group. In the 148 matched cohort after propensity-score matching, endoscopic elevated macroscopic type ($P = 0.020$) and whitish mucosal discolorization ($P = 0.022$) were significant endoscopic characteristics related to LVI of EGC, while no significant difference of age, sex, lesion size, location of tumor, submucosal invasion, and histology were detected between the matched two groups.
CONCLUSION: Endoscopic elevated macroscopic type and whitish mucosal discolorization in EGC carry a significant risk for LVI of tumor, which results in non-curative ER for EGC. Further prospective studies of preoperative prediction for LVI are warranted.
Disclosure of Interest: None declared

P0497 MAGNIFYING ENDOSCOPY WITH CRYSTAL VIOLET STAINING HAS NO ADDITIONAL DIAGNOSTIC VALUE COMPARED WITH NARROW-BAND IMAGING IN THE DIAGNOSIS OF SPORADIC NONAMPULLARY DUODENAL ADENOMA/ CARCINOMA

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INTRODUCTION: Sporadic nonampullary duodenal adenomas rarely occur but are precancerous lesions [1]. It recently became clear that high-grade dysplasia (HGD) shows a high risk of progression to adenocarcinoma [2]. Therefore, HGD and intramucosal carcinoma (HGD/IMC) are indications for endoscopic resection. We previously reported that magnifying endoscopy with narrow-band imaging (NBI-ME) was extremely helpful in the differential diagnosis of sporadic nonampullary duodenal low-grade dysplasia (LGD) or HGD/IMC. Magnifying endoscopy with crystal violet staining (CV-ME) is useful for diagnosing colorectal adenomatous tumors [3], but no report has analyzed the utility of CV-ME in diagnosing duodenal tumors.
AIMS & METHODS: In this study, we analyzed whether CV-ME has additional diagnostic value compared with NBI-ME in the diagnosis of sporadic nonampullary duodenal adenoma/carcinoma. The final diagnosis was determined by histopathological analysis of endoscopically resected specimens. Nineteen patients with sporadic nonampullary duodenal adenoma or adenocarcinoma without polyposis syndrome who were treated by endoscopic resection between November 2012 and October 2013 were prospectively evaluated. Twenty lesions were diagnosed using CV-ME after NBI-ME and then resected. In NBI-ME, we evaluated the presence of the following: (a) irregular villi of various sizes, (b)

small villi area (alternatively tubule-like structures), (c) intravillous irregular microvessels, and (d) network-like microvessels. If any one of these findings was observed, we diagnosed HGD/IMC. On the other hand, we diagnosed the lesion that had none of these findings as LGD. In CV-ME, we made a final diagnosis by adding the findings of (a) and (b) using CV-ME in addition to NBI-ME.
RESULTS: Eight of the 20 lesions were LGD, while 12 were HGD/IMC. The following values were obtained for NBI-ME and integrated diagnosis, respectively: sensitivity, 1.0 and 1.0; specificity, 0.375 and 0.500; positive predictive value, 0.706 and 0.750; negative predictive value, 1.0 and 1.0; and accuracy, 0.750 and 0.800. No significant differences were noted between groups (chi-squared test).
CONCLUSION: CV-ME does not have additional diagnostic value compared with NBI-ME in the diagnosis of sporadic nonampullary duodenal adenoma/carcinoma.
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Disclosure of Interest: None declared

P0498 A ROLE OF PALLIATIVE SURGERY IN STAGE IV GASTRIC CANCER

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INTRODUCTION: Standard treatment for patients with Stage IV gastric cancer is systemic chemotherapy. Some patients receive palliative surgery before chemotherapy to relieve gastric obstruction or uncontrollable bleeding. However, few data is available about the impact of palliative surgery on following chemotherapy in patients with Stage IV gastric cancer.
AIMS & METHODS: We aimed to compare the clinical outcomes between patients with advanced gastric cancer who initially received surgical resection for their primary lesion and those who initiated palliative chemotherapy without surgery. Data of consecutive 123 patients with pathologically confirmed advanced gastric cancer who received palliative chemotherapy between January 2005 and March 2014 were reviewed. A total of 57 patients received palliative chemotherapy following surgical resection for their primary lesion (Group A) and 50 patients initiated palliative chemotherapy without surgery (Group B). Overall survival was defined as the period between the date of surgery or chemotherapy initiation and the date of death for any reason or the last follow-up visit.
RESULTS: Both groups were similar in age and gender. Median survival time was 13.2 months (95% CI 7.2-19.2) for Group A and 10.2 months (95% CI 8.4-12.1) for Group B. In group A, 10 patients could not proceed to palliative chemotherapy because of postoperative complications (n = 3) and/or deteriorated general conditions (n = 7). In group B, 15 patients (37.5%) developed adverse events related to residual primary lesion: gastric hemorrhage (n = 6), gastric stenosis (n = 6), gastric perforation (n = 3). Among these 15 patients, only 2 patients who developed gastric perforation could resume chemotherapy. Duration of chemotherapy did not differ between two groups.
CONCLUSION: Our data suggested that surgical resection of primary lesion before initiating palliative chemotherapy could reduce the risk of developing severe adverse events related to residual primary lesion during chemotherapy without hampering its efficacy.
Disclosure of Interest: None declared

P0499 CLINICAL APPLICABILITY OF PERIOPERATIVE CHEMOTHERAPY IN RESECTABLE GASTRIC CANCER – RESULTS FROM A PORTUGUESE CANCER INSTITUTE

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INTRODUCTION: The benefit of perioperative chemotherapy (POC) in patients with resectable gastric cancer (GC) and esophagogastric junction cancer (EGJC) was demonstrated in MAGIC trial (2006), which was associated to high morbidity.
AIMS & METHODS: Aims: To evaluate the clinical applicability of perioperative chemotherapy (POC) in patients with resectable gastric and esophagogastric junction (EGJ) cancer treated in a Portuguese cancer institute, as stated in the MAGIC Trial. **Methods:** Selection of patients with GC and EGJC referred to our institution from 2009 to 2013. Patients were staged with thoraco-abdomino-pelvic CT, endoscopic ultrassonography (if T < 3, N0 and M0) and laparoscopy (if T > 2 or N+ and M0). POC was proposed to those staged as T > 2 or N+ and M0 (3 pre and 3 postoperative cycles of epirrubicine, cisplatin and 5-fluorouracil; surgery with D2 lymph node dissection). Non-surgical candidates or stage IV patients received palliative care. Those staged as T1/2 and N0, age > 80 years or with an obstructive or bleeding tumor had direct surgery. Evaluation of clinical characteristics, adhesion, complications, survival and recurrence. Statistical analysis performed with chi2, t-Student tests, Kaplan-Meier.
RESULTS: We evaluated a total of 418 patients: 315 with GC and 103 with EGJC; 57% males; mean age 65.4 ± 21-93 years. POC proposed to 150 patients. *Preoperative chemotherapy* in 143 patients; not performed due to disease progression-5; obstructive symptoms-1; associated diseases-1; major morbidity-7%, mortality-3%. *Surgery* in 134 patients (94%); not performed due to death during chemotherapy-4, toxicity-1, disease progression-1, refusal-2. R0 surgery was performed in 102 patients (76.1%), R1 surgery in 5 patients and R2 surgery/unressecable in 28 patients; major morbidity-16%, mortality-3%. *Postoperative chemotherapy* in 74 patients (72.5%); not performed due to previous chemotherapy/surgery complications in 26 patients and disease progression in 2 patients; major morbidity-6%; mortality-0%. Median time from chemotherapy to surgery: 50 days; from surgery to chemotherapy: 35.5 days. Surgical complications were identical in those that had direct versus perioperative chemotherapy resections. Overall, 69 patients (47%) did not complete the proposed protocol. *Survival at 36 months*: a) general 37.4%; b) proposed to POC 51.2%; c) treated with curative intention-66.5%, d) completed the proposed protocol-70.7%.
CONCLUSION: In our series, one third of all patients were eligible for POC. The rates of treatment conclusion, R0 surgery and postoperative chemotherapy were higher in our series, compared with those described in the MAGIC study. POC is feasible and applicable in clinical practice, but similar to that described in the MAGIC study, only half of patients completed the proposed protocol, either due to complications of treatment, either due to disease progression.
Disclosure of Interest: None declared

P0500 THE PROGNOSTIC SIGNIFICANCE OF TUMOR ANGIOGENESIS IN GASTRIC CANCER

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INTRODUCTION: Angiogenesis, the process by which new blood vessels are formed, plays an essential role in the survival of the malignant cells, in the local expansion and tumor invasion, as well as in the appearance of distant metastases. The intratumoral microvessel density (MVD), which can be evaluated immunohistochemically, seems to have an influence on the prognosis of various malignant tumors. The forming of new intratumoral microvessels depends on the elaboration of the angiogenic growth factors by the malignant cells (such as vascular endothelial growth factor – VEGF). These factors' expression is correlated with the tumor angiogenesis, neoplasia progression and severe prognosis. Among the known angiogenic factors, VEGF plays a central role in angiogenesis process control in cancerous disease.
AIMS & METHODS: We evaluated the relation between MVD, VEGF expression, the clinicopathologic factors and the survival in patients with gastric cancer. A prospective study has been carried out, regarding the evolution and aggressiveness of gastric cancer, with a duration of five years, 61 patients that underwent a surgery for gastric cancer being included in the study. The immunohistochemical reactions for CD34 and VEGF were performed for all gastric cancers cases included in the study group.
RESULTS: MVD has shown in the gastric carcinomas an average value significantly higher in comparison to the normal mucosa (38.7 vs. 12.5, $p < 0.001$). In the intestinal type we have noticed a much lower average MVD than the average MVD in the diffuse type of gastric carcinomas (36.8 vs. 41.6) ($p = 0.024$). Anaplastic carcinoma and the signet ring cell carcinoma are differentiating as histological forms associated to an intense neoangiogenesis activity. The neoangiogenesis activity is correlated with the histologic grade, the lymphovascular invasion, the level of extend, the lymph node metastasizing, the distant metastasizing and the TNM stage. Positive immunoreactions for VEGF are significantly more frequent in gastric carcinomas, in comparison to the normal gastric mucosa (65.6% vs. 6.5%, $p < 0.001$). The immunoreactions to the VEGF protein were positive in 71.1% of the intestinal carcinomas, significantly more frequent in comparison to the diffuse type carcinomas (52.9%) ($p = 0.018$). Our results show a tight correlation between the histologic grade, the level of the tumor invasion and the VEGF expression. Our results prove the major correlation between the VEGF expression and the 5 year survival rate of the patients with gastric cancer, the survival rate for the carcinomas with VEGF +/++ being significantly lower than for the VEGF negative ones (12.5% vs. 23,8%) ($p = 0.027$).
CONCLUSION: Our study proves a tight correlation between the VEGF expression and the MVD ($p = 0.039$), these factors playing an important role in the tumoral biologic behaviour, in the progression and the prognosis.
Disclosure of Interest: None declared

P0501 GASTRIC CANCER IN PATIENTS WITH TYPE I GASTRIC CARCINOIDS

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INTRODUCTION: Type I gastric carcinoids (T1-GCs) are rare tumors which may arise in pts with atrophic gastritis (AG). These tumors are well-differentiated with low proliferative index and a generally benign behavior, and constitute up to 80% of all gastric carcinoids. A major pathogenetic factor for T1-GCs is hypergastrinemia due to AG. Gastrin acts as a growth type factor for enterochromaffin-like cells, which in AG are chronically induced to proliferate, through a

Table to abstract P0501.

Patient	Gender	Age, years	Type of lesion	Diagnosis of gastric cancer	Locali-zation	Time of occurrence after diagnosis of type IGC, months (years)	Outcome
# 1	F	40	Low-grade dysplasia (intramucosal, endoscopically normal mucosa, detected on random biopsies) Diffuse gastric cancer (signet-ring cells) in situ (endoscopically normal mucosa, detected on random biopsies)	Gastroscopy according to follow-up protocol	Antrum Antrum	17 (1.4) 156 (13)	Gastric surgery alive
# 2	M	78	Intestinal-type adenocarcinoma (gastric ulcer, 3 cm)	New onset of anemia	Angulus	80 (6.7)	No surgery due to comorbidities dead
# 3	F	58	Intestinal-type adenocarcinoma (gastric ulcer, 2 cm)	New onset of epigastric pain	Antrum	63 (5.2)	Gastric surgery dead (complications of surgery)
# 4	F	49	Intestinal-type adenocarcinoma in situ (endoscopically normal mucosa, detected on random biopsies)	Gastroscopy according to follow-up protocol	Antrum	61 (5.1)	Gastric surgery alive

multistep process passing from hyperplasia to dysplasia and then to carcinoid. Epidemiological data suggest that AG is associated not only with T1-GCs, but also with intestinal-type gastric cancer. The occurrence of gastric cancer in AG pts with type I gastric carcinoids has not yet been described.
AIMS & METHODS: The aim of this study was to describe in a retrospective case-series the occurrence of gastric cancer in AG pts with type I gastric carcinoid in a single tertiary referral center. Between 1994 and 2012, 17 new cases of T1-GCs were diagnosed amongst a cohort of AG pts. The clinical charts of these 17 T1-GCs pts were retrospectively evaluated for the occurrence of gastric cancer at follow-up (median 4.2 years, range 0.5-13). AG diagnosis was based on the presence of hypergastrinaemia and atrophy of the body mucosa. Diagnosis of T1-GCs was performed when enterochromaffin-like cells proliferation was $>500\mu$ (WHO 2010 criteria).
RESULTS: In 4/17(23.5%) T1-GCs pts (3F, age 40-78yrs), gastric cancer occurred (median follow-up 5.9 yrs, range 5.1-13; Table1). Three cases were intestinal-type adenocarcinomas and one a signet-ring cells diffuse gastric cancer, localized in 3 cases in the antrum. In two pts it was detected on random biopsies during follow-up-gastroscopy, in the other two gastroscopy was performed due to new symptoms. All pts with gastric cancer had associated autoimmune features (pernicious anemia, autoimmune thyroid disease and a spared antrum), compared to 77%, 46% and 54% of those without gastric cancer.
Table1. Pts with type I gastric carcinoid who developed an epithelial neoplastic lesion
CONCLUSION: This case-series shows that in pts with T1-GCs gastric cancer may frequently occur at long-term follow-up. Thus, these pts should be monitored by a long-term surveillance programme, including an accurate bioptic sampling of antral mucosa.
Disclosure of Interest: None declared

P0502 THERAPEUTIC OUTCOMES OF ENDOSCOPIC RESECTION IN FOREGUT NEUROENDOCRINE TUMORS

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INTRODUCTION: Endoscopic resection (ER) may benefit to treat the low grade foregut neuroendocrine tumors (NETs). This study aimed to evaluate therapeutic outcomes of ER for foregut NETs.
AIMS & METHODS: From January 2003 to February 2013, a total of 40 patients were confirmed histologically as foregut NETs from the ER (stomach = 16, duodenum = 13) and surgical resection (SR, stomach = 9, duodenum = 2). The clinicopathological characteristics and therapeutic outcomes were evaluated retrospectively.
RESULTS: Of 29 patients underwent ER (EMR = 23, ESD = 6), 28 were diagnosed as NET-G1 and 1 as NEC. Of 11 patients underwent SR, 9 were diagnosed as NET-G1 and 2 as NEC. Tumor size of ER group was significantly smaller than SR group (7.4 mm vs. 18.2 mm, $P<0.01$). Depth of invasion was limited to mucosa and submucosa in 28 NETs of ER group, However, all NETs of SR group invaded the submucosa or proper muscle. Complete resections were achieved in 22 patients (75.9%) of ER group and achieved in 11 patients (100%) of SR group. In ER group, immediate procedure-related complications occurred in 2 cases (bleeding = 1, perforation = 1), and they were successfully treated by conservative treatment. There was no complication in SR group. There was no recurrence in 7 NETs reported as incomplete resection in margin, but all of 3 NEC patients (ER = 1, SR = 2) had recurrence during follow up period. They were treated by additional chemotherapy and had no more disease progression. One metachronous recurrence occurred after complete ER, and it was treated by ER.
CONCLUSION: ER can be used as an effective method as treatment for a small sized and low grade foregut NETs. However, additional treatment should be considered in the patients who diagnosed as NEC from histological result after endoscopic treatment because it has high risk of recurrence rate.
Disclosure of Interest: None declared

P0503 SELF-EXPANDABLE METAL STENTS VERSUS SURGICAL GASTROENTEROSTOMY FOR PALLIATION OF MALIGNANT DUODENAL OBSTRUCTION

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INTRODUCTION: Surgical gastroenterostomy used to be the first line treatment for palliation of malignant gastroduodenal obstruction. Recently endoscopic placement of self-expandable metal stents (SEMS) has become a broadly accepted treatment for patients with advanced malignant gastroduodenal obstruction as a minimally invasive therapy.
AIMS & METHODS: We attempted to elucidate the current status of endoscopic SEMS for palliation of malignant duodenal obstruction in comparison with surgical gastroenterostomy. A total of 39 consecutive duodenal tumor obstruction patients who were treated at Okayama Saiseikai General Hospital from January 2006 to Dectmber 2011 were reviewed (23 pancreatic cancer, 5 gallbladder cancer, 4 duodenal cancer, 2 renal pelvis cancer, 2 colon cancer, 1 gastric cancer, 1 liver cancer, 1 occult primary cancer). 25 patients were treated by SEMS and 14 patients by surgical gastroenterostomy. We compared procedure time, time from the procedure to starting oral intake, time from the procedure to starting chemotherapy, technical success rate, complication, hospital stay, and mortality.
RESULTS: In each and every patients, treatment (eather endoscopic stent implantation or surgical gastroenterostomy) was clinically successful. Endoscopic stenting was found to be associated with a shorter time of procedure (mean 31.7 vs. 146 min, $P<0.01$), a shorter time from the procedure to starting oral intake (mean 2.96 vs. 6.64 days, $P < 0.01$) and a shorter hospital stay (mean 15.3 vs. 25.6 days, $P < 0.02$) than the surgical gastroenterostomy. There was no significant difference between the two groups in the analysis of mortality (mean 91.5 vs. 158.8 days, $p=0.107$) and time from the procedure to starting chemotherapy (mean 8.6 vs. 13 days, $p=0.177$). A single case of complication was seen in each group, one case of intestinal perforation in SEMS group (4%) and one case of intra-abdominal abscess in surgical gastroenterostomy group (7%). Both cases were able to recover by conservative treatment.
CONCLUSION: Endoscopic SEMS insertion was superior against surgical gastroenterostomy in terms of procedure time, start of oral intake period and the length of hospital stay. SEMS in duodenal obstruction is a feasible alternative of surgical gastroenterostomy for the palliation of inoperable malignant duodenal obstruction. With a high clinical success and low complication rate, endoscopic implantation of SEMS seems to be a safe and tolerable procedure for palliative treatment of malignant duodenal obstruction.
Disclosure of Interest: None declared

P0504 CLINICAL OUTCOMES OF SALVAGE ENDOSCOPIC THERAPY AFTER CHEMORADIOTHERAPY FOR ESOPHAGEAL CANCER

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INTRODUCTION: Chemoradiotherapy (CRT) for esophageal cancer, especially at stage I, has comparable survival rates to surgery, with a median survival rate of 5 years. Therefore, in some cases, it is chosen as a first-line treatment for stage I, II, and III esophageal cancer. However, about 30% of patients who are administered chemoradiotherapy experience a local recurrence after complete response, so it is important to consider salvage therapy to treat such recurrences. Commonly administered salvage therapies include surgery, endoscopic therapy, and argon plasma coagulation (APC).
AIMS & METHODS: The aim of this study is to illuminate the results of administering salvage endoscopic therapy in cases of recurrent esophageal cancer that had previously been treated with chemoradiotherapy. 161 patients with UICCI-III esophageal cancer who received chemoradiotherapy at the Cancer Institute Hospital between 2005 and 2013 without previously being treated were retrospectively studied. 11 of these patients had local recurrences after receiving chemoradiotherapy, and received salvage endoscopic therapy as treatment for the recurrence. Their overall survival (OS) and time of recurrence after CRT and salvage endoscopic therapy were studied. Kaplan-Meier analysis and Cox proportional hazard modeling were used for statistical analysis.
RESULTS: The median observation period for the 11 patients studied was 75.2 months (39.1-107.6). The clinical stages of esophageal cancer of the 11 patients studied were as follows (stage I/II/III: 6/1/4). The salvage endoscopic therapies administered were as follows (EMR/ESD/APC: 7/3/1). The clinical responses of the patients to chemoradiotherapy were as follows (CR/PR: 8/3). 5 patients experienced local recurrences again after salvage endoscopic therapy (EMR/ESD/APC: 4/0/1). Disease-free survival in patients who received salvage EMR therapy was a median 24 months (8.9-50.1). Patients who were administered salvage APC therapy experienced relapses twice, and recurrence-free survival among those patients was a median 9 months (3.4-14.6). None of the patients who were administered ESD experienced a relapse, and disease-free survival among those patients was a median 25.3 months (13.3-32). The complications usually associated with endoscopic therapies were also not observed. There was no significant difference between salvage therapies in terms of overall survival (EMR 74.8 months (46.1-100.1), ESD 78.9months (39.1-107.6), APC 66.5 months).
CONCLUSION: ESD can be considered to be a better salvage therapy than the other endoscopic therapies as the local recurrence rate was lower than that for either EMR or APC. Even for less serious cases of esophageal cancer, ESD is a preferable choice as a salvage endoscopic therapy after chemoradiotherapy. It should be noted, however, that there was no difference in the long-term prognoses among the different salvage therapies, even after recurrence. In some cases, ESD may not be ideal as a treatment, such as in patients who have other pre-existing diseases that make long-term treatment difficult, or in cases of esophageal stenosis, which renders it difficult to use ESD scopes. For such cases, other salvage therapies can be considered, including surgery and photo-dynamic therapy (PDT).
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
H. PYLORI I – POSTER EXHIBITION – HALL XL

P0505 LOW-DOSE ASPIRIN-ASSOCIATED GASTRIC AND DUODENAL ULCERS IN JAPANESE PATIENTS WITH NO PREVIOUS HISTORY OF PEPTIC ULCERATION

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INTRODUCTION: Long-term administration of low-dose aspirin (LDA) is associated with a greater risk of adverse events, including gastroduodenal ulcers and their potentially fatal complications (e.g., gastrointestinal bleeding and perforation). The identified risk factors for ulcer bleeding with aspirin use are history of ulcer bleeding; aspirin dose; advanced age (>70 years); concomitant use of NSAIDs or anti-coagulants; use of dual anti-platelet therapy; *Helicobacter pylori* infection; and history of alcohol abuse, diabetes, or renal failure. Proton pump inhibitors (PPIs) are used to decrease LDA-associated gastroduodenal mucosal and NSAID-induced injuries. In Japan, since 2011, treatment with half-dose PPI (lansoprazole 15 mg/day) has been permitted as a medical service under health insurance for the prevention of NSAID- or LDA-induced peptic ulcers in patients in the high-risk group who have a history of peptic ulcers. However, there are few reports in which the use of PPIs reduced the risk of LDA-associated peptic ulcers in patients without pre-existing peptic ulcers
AIMS & METHODS: AIM: To assess the risk factors and the efficacy of medications for development of peptic ulcer disease in Japanese with no prior history of peptic ulceration.
METHODOLOGY: We conducted a matched background study using esophagogastroduodenoscopy (EGD) record collected from January 2010 through December 2010. Consecutive 219 outpatients receiving LDA (75 mg) who had no peptic ulcer history were matched to 1 control by age and sex who were not receiving LDA and had no peptic ulcer history. Clinical parameters, concomitant drugs, the reason for endoscopy, and endoscopic findings were analyzed.
RESULTS: Of 219 patients receiving LDA, 20 (20%) was diagnosed endoscopically with peptic ulceration, which was significantly higher than 7 (3.2%) of 219 patients not receiving LDA (OR, 3.0; 95% CI, 1.26–7.35; $P=0.016$). From multiple logistic regression analysis, LDA smoking habit, NSAID, and PPI were detected as increased and decreased risk factors for peptic ulcer, respectively (OR, 9.6; 95% CI, 2.27–38.63; $P=0.002$), (OR, 3.9; 95% CI, 1.03–14.72; $P=0.045$), (OR, 7.4; 95% CI, 1.73–31.67; $P=0.007$), (OR, 0.11; 95% CI, 0.02–0.45; $P=0.002$). Age, current alcohol consumption, H_2-receptor antagonists, and abdominal symptom were not significantly associated with the presence of peptic ulcers.
CONCLUSION: Long-term administration of LDA increases the risk of peptic ulcer even in the patients who had no peptic ulcer history, and PPIs reduces the risk of developing gastric or duodenal ulcers. However this risk is significantly increased in patients with concomitant smoking habit and NSAID. These results may help identify patients who require more intensive prophylaxis against aspirin-induced ulcerations.
Disclosure of Interest: None declared

P0506 CORRELATION BETWEEN THE PREVALENCE OF GALLSTONE AND HELICOBACTER PYLORI INFECTION

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INTRODUCTION: Several studies have reported that the presence of *Helicobacter* DNA in human bile sample, although its pathological role is not clear. Moreover, little is known about the association between *Helicobacter pylori (H. pylori)* infection and gallstone.
AIMS & METHODS: The aim of this study was to determine whether *H. pylori* infection is associated with an increased risk of gallstone in an asymptomatic population.
We examined 2782 subjects (1635 men and 1147 women) who underwent both upper endoscopy with CLO test and abdominal ultrasound at the Health Examination Center at Chung-Ang University Yong-san Hospital in Korea from January 2007 to December 2009. We compared the prevalence of gallstone on ultrasound and endoscopic findings such as reflux esophagitis, gastric diseases in the *H. pylori* infected subjects with that of the *H. pylori* uninfected subjects.
RESULTS: The overall prevalence of *H. pylori* infection in our study was 45.6% (1271/2782). When the subjects were divided into two groups according to the *H. pylori* infection status, there was no significant differences of the baseline characteristics between the two groups. The prevalence of gallstone in the *H. pylori* infected subjects was higher than that of the *H. pylori* uninfected subjects (5.4% vs 3.2%, $P=0.032$). The prevalence of peptic ulcer in the *H. pylori* infected subjects was higher than that of the *H. pylori* uninfected subjects (8.2% vs 3.4%, $P<0.001$). The prevalence of reflux esophagitis in the *H. pylori* infected subjects was lower than that of the *H. pylori* uninfected subjects (6.2% vs 14.0%, $P=0.012$).
CONCLUSION: These findings suggest that *H. pylori* infection is associated with an increased risk of gallstone in asymptomatic population.
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Disclosure of Interest: None declared

P0507 HELICOBACTER PYLORI INFECTION AMONGST ARAB ISRAELI WOMEN WITH HYPEREMESIS GRAVIDARUM- A PROSPECTIVE, CONTROLLED STUDY

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INTRODUCTION: *Helicobacter pylori* has been associated with hyperemesis gravidarum in some geographical regions. The prevalence of *H. pylori* in Arab Israeli women in the Upper Galilee and its association with hyperemesis gravidarum, has not been previously studied.
AIMS & METHODS: The aim of this study was to examine whether *H. pylori* infection is associated with hyperemesis gravidarum in Arab Israeli women. Subjects with hyperemesis gravidarum carrying a singleton fetus, were prospectively recruited. Women with an uncomplicated pregnancy served as controls. All patients underwent C13-urea breath testing to assess for *H. pylori* infection.
RESULTS: A total of seventy two subjects, including 24 patients with hyperemesis gravidarum and 48 controls, aged 28.8±5.3 years, were included. *H. pylori* infection was identified in 73.9% (17/24), and 60.4% (29/48) of cases and controls, respectively (p = ns). *H. pylori* infection did not correlate with age or the number of previous pregnancies (p = ns). Control subjects with a history of early trimester vomiting were not more likely to be infected with *H. pylori*, compared to controls without a history of early trimester vomiting (p = ns).

CONCLUSION: *H. pylori* does not seem to increase the likelihood of hyperemesis gravidarum in Arab Israeli women. However, given the apparently high background prevalence of *H. pylori* in this population, a larger study is required to corroborate these findings.

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P0508 THE PREVALENCE OF HELICOBACTER PYLORI POSITIVITY IN THE GENERAL POPULATION IN SWEDEN HAS DECREASED FROM 38 PERCENT TO 16 PERCENT SINCE 1989

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INTRODUCTION: It is assumed that the prevalence of Helicobacter pylori (H.p.) is decreasing in wealthy countries. There are however no recent prospective population based studies confirming this.
AIMS & METHODS: We aimed to evaluate the prevalence of positive H.p. serology in random population sample in a Swedish community over 23 years. In 1989 we mailed the validated Abdominal Symptom Questionnaire (ASQ) (age 22-80), and 1097 (87%) responded. H.p.serology (HM-CAPTM immunoassay) was measured on a stratified sample (n = 145 with either dyspepsia, IBS or symptom free) (1). In late 2011 the ASQ was mailed again with the same sampling procedure in the same community (age 20+) and 1175 (64%) replied. A total of 388 out of 1034 participants 20-79 years of age and suitable for an upper endoscopy had an upper endoscopy spring 2012. H.p. serology (*H. pylori* IgA/IgG ELISA) was measured on 386, 32 of those had participated in 1989. The effect of time on H.p. prevalence was calculated using random effects logistic regression models using H.p. as the dependent variable and gender, age and time as independent variables. All participants in all surveys are included in the analyses (499 participants, 531 observations).
RESULTS: The prevalence of H.p. positivity in 1989 and 2012 in total and in age groups for the 499 participants who participated in either or both studies is presented in the table. H.p. positivity decreased significantly with time, the odds ratio for H.p. positivity corresponding to 0.25 per decade (OR:0.25; 95%CI:0.11-0.59, p = .001) independent of gender and age. There was no difference in H.p. prevalence between men and women (OR:0.92; 95%CI:0.40-2.08). The odds of H.p. positivity increased with age by 11% per year (OR:1.11; 95%CI:1.04-1.18, p = 0.001).
Table. Prevalence of Hp positivity in 1989 and 2012 in total and by age group

	1989 N hp positive/total	%	2012 N hp positive/total	%
Total	55/145	37.9	61/386	15.8
20-39	8/47	17.0	4/60	6.7
40-59	21/40	34.4	17/161	10.6
60-80	26/37	70.3	40/165	24.4

CONCLUSION: In this random sample of the adult general population in Sweden, H.p. prevalence has decreased radically over the last two decades across all ages. Among adults below 40 years it has reached the level where the "test & treat" strategy might be questioned (2). Among adults older than 60 years the risk of complications (3) is most probably reduced.

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P0509 OBESITY AND HELICOBACTER PYLORI INFECTION: IS THERE A LINK?

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INTRODUCTION: The incidence of obesity is increasing worldwide. The involvement of Helicobacter pylori (*H. pylori*) in the pathophysiology of obesity is still debated. Among the possible related factors reported, *H. pylori* infection has been proposed to play a role by interfering with the release of gastric hormones involved in the regulation of appetite and food intake. However, the data available until now are conflicting are derive from small series of cases.
AIMS & METHODS: To analyze the distribution of *H. pylori* infection in a large cohort of consecutive patients stratified according to sex, age and body mass index (BMI).
We enrolled 4653 subject referred to our Gastroenterology Unit between January 2006 to January 2014 to perform 13C-urea breath test (13C-UBT). In all cases we recorded: age, sex, weight, height, previous esophagogastroscopy results, previous eradication therapy and *H. pylori* status. BMI was calculated according to the following formula: mass (Kg)/height (m)2. The 13C-UBT was performed by administering a solution of 100 ml tap water containing 100 mg of 13C-urea and 1.4 g of citric acid. Breath samples were taken at baseline and 30 minutes after ingestion of the urea. The 13C enrichment in breath was determined by isotope ratio mass spectrometer. The 13CUBT was considered positive if the δ-value over baseline at 30 minutes was $> 5‰$.
RESULTS: Overall, there were 1916 (41%) male. Mean age was 43.75 years (range 3-88), 323 (7%) subject were ≤15 year-old. Forty-seven percent (2183) subjects reported previous eradication therapy. BMI was ≤ 18 in 188 (4%), ≥18.1-≤25 in 2322 (50%), ≥25.1-≤30 in 1576 (35%) and ≥30.1 in the remaining 514 (11%) of the cases. *H. pylori* infection was detected in 1892 (40.7%) with a progressive increasing trend according to BMI (≤ 18: 36%; ≥18.1-≤25: 34%, ≥25.1-≤30: 46% and ≥30.1: 56%; p < 0.0001).
CONCLUSION: *H. pylori* infection is significantly more frequent in obese than in normal weight individuals, irrespective of sex and age.

Disclosure of Interest: None declared

P0510 HELICOBACTER PYLORI, DECREASED PEPSINOGEN AND ATROPHIC GASTRITIS ARE NOT ASSOCIATED WITH BARRETTS ESOPHAGUS AND EROSIVE ESOPHAGITIS

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INTRODUCTION: Helicobacter pylori (*H. pylori*) infection has been suggested to protect against the development of erosive esophagitis (ERD) and Barrett's esophagus (BE). A possible explanation represents the development of corpus pre-dominant and/or atrophic gastritis in the natural course of *H. pylori* infection with an associated decrease in gastric acid secretion.
AIMS & METHODS: Aim of the study was to assess whether *H. pylori* infection, decreased serum pepsinogen levels as a marker for gastric atrophy and different forms of gastritis are associated with the occurrence of BE and ERD.
For this, we reviewed prospectively collected data of 332 patients with an age above 50 years that underwent gastro-duodenoscopy and colonoscopy. *H. pylori* status was determined by serology and serum pepsinogen I levels were measured in fasting state by commercially available assay. Intestinal metaplasia (IM), glandular atrophy and mucosal inflammation were diagnosed from histological specimens and graded according to the updated Sydney-classification.
RESULTS: In *H. pylori* infected patients (n = 101; 30.4%), the overall prevalence of ERD (20.8%) was comparable to non-infected patients (25.5%) (p = 0.215) and the same accounted for BE (7.9% vs. 11.7%) (p = 0.214). *H. pylori* infection was not associated with an increased risk for both ERD (OR = 0.76, 95% CI: 0.43-1.35) and BE (OR = 0.65, 95% CI: 0.28-1.49). The histological proof of intestinal metaplasia and/or gastric atrophy independently of the *H. pylori* status did not show an association to neither ERD (OR = 0.61, 95% CI: 0.28-1.49) or BE (OR = 0.73, 95% CI: 0.32-1.67). The same accounted for the different phenotypes of gastritis, including antrum- and corpus pre-dominant as well pangastritis for both ERD and BE. Furthermore, no association was seen between a decreased pepsinogen I level and the occurrence of ERD (OR = 0.75, 95% CI: 0.37-1.54) and BE (OR = 0.82, 95% CI: 0.31-2.22).
CONCLUSION: *H. pylori* infection does not show any association to the occurrence of ERD and BE. Furthermore, different types of gastric inflammation and a hypoacid gastric function do not have an influence on the development of ERD and BE.

Disclosure of Interest: None declared

P0511 A RETROSPECTIVE STUDY OF HELICOBACTER PYLORI AND PEPTIC ULCER DISEASE PREVALENCE IN AN UPPER GASTROINTESTINAL ENDOSCOPY REVIEW BETWEEN 2002 AND 2014

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INTRODUCTION: There is a well established association between *Helicobacter pylori* (*H. pylori*) infection and peptic ulcer disease (PUD). This association is known to be stronger in duodenal ulcers (DU) in comparison to gastric ulcers (GU). Over recent years, trends worldwide have shown a decreasing prevalence of *H. pylori* infection with some studies suggesting the rate of decline may be as high as 26% per decade[1]. Consequently due to its prominent association with PUD it would be interesting to identify the change in prevalence of PUD over the same timescale.
AIMS & METHODS: Using oesophagogastroduodenoscopy (OGD) as our chosen diagnostic tool, we have set out to determine whether the trend of decreasing *H. pylori* prevalence has been reflected in our sample population over the last 12 years and whether there has also been a decrease in PUD prevalence in particular with respect to duodenal ulcers.
1781 diagnostic OGD procedures carried out by the same endoscopist in a single District General Hospital in the South East of England were analysed retrospectively. For each procedure the age, gender, *H. pylori* status and PUD diagnosis were recorded. Prevalence data was calculated for three sequential time periods with comparable patient numbers: 2002 to 2005 (Period 1: n = 346), 2006 to 2010 (Period 2: n = 677), 2011 to 2014 (Period 3: n = 681).
RESULTS: The data showed that prevalence of *H. pylori* infection decreased in each successive period ($p = 0.0012$). The prevalence across the three time periods were as follows: period 1- 36 cases (10.4%), period 2- 38 cases (5.60%, $p = 0.005$ with respect to (WRT) Period 1) and finally period 3: 32 cases (4.70%, $p < 0.001$ WRT Period 1, $p = 0.446$ WRT Period 2).
The prevalence of PUD also decreased in each successive period ($p < 0.001$). The prevalence across the three time periods were as follows: period 1 - 27 cases (7.80%; DU = 24; GU = 3), period 2 - 32 cases (4.73%, $p = 0.046$ WRT Period 1; DU = 24; GU = 8) and period 3 - 11 cases (1.62%, $p < 0.001$ WRT Period 1, $p = 0.001$ WRT Period 2; DU = 8; GU = 4). The prevalence of duodenal ulcers decreased in each successive period ($p < 0.001$), however the prevalence of gastric ulcers remained consistently low ($p = 0.502$).
CONCLUSION: Prevalence of *H. pylori* has fallen significantly over the time period studied. Key reasons for this include continually improving sanitation and living conditions as well as more effective treatment of *H. pylori* infection, making recurrence less frequent. The falling prevalence of *H. pylori* is likely to have contributed to the significant decrease in prevalence of PUD in the same time period. Other reasons for this trend include the introduction of effective *H. pylori* treatment and increasing effective use of acid suppressive medication. Another possible factor for the decrease in PUD prevalence is more careful prescription of non steroidal anti-inflammatory drugs. The stronger association between *H. pylori* and DU may explain the significant reduction in the prevalence of DU in comparison to GU.
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Disclosure of Interest: None declared

P0512 SECOND-LINE RESCUE THERAPY WITH LEVOFLOXACIN AND BISMUTH AFTER FAILURE OF A HELICOBACTER PYLORI ERADICATION TREATMENT

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INTRODUCTION: The most commonly used second-line regimens for *H. pylori* eradication are bismuth-containing quadruple therapy and levofloxacin-containing triple therapy, both offering suboptimal results. Combining bismuth and levofloxacin in the same regimen may be an option as rescue regimen.
AIMS & METHODS: To evaluate the efficacy and tolerability of a second-line quadruple regimen containing levofloxacin and bismuth in patients whose previous *H. pylori* eradication treatment failed.
Design: Prospective multicenter study. *Patients*: Patients in whom a standard triple therapy (PPI, clarithromycin, and amoxicillin) or a non-bismuth quadruple therapy (PPI, clarithromycin, amoxicillin and metronidazole, either sequential or concomitant) had failed. *Intervention*: Esomeprazole (40 mg b.i.d.), bismuth (240 mg b.i.d.), levofloxacin (500 mg o.d.), and amoxicillin (1 g b.i.d.) for 14 days. *Outcome*: Eradication was confirmed using the ^{13}C-urea-breath test 4-8 weeks after therapy. *Compliance/tolerance*: Compliance was determined through questioning and recovery of empty medication envelopes. Incidence of adverse effects was evaluated by means of a questionnaire.
RESULTS: 78 patients were consecutively included. Mean age 46±16 years, 64% women, 14% peptic ulcer. Previous failed therapy included: standard clarithromycin triple therapy (57 patients), sequential (12), and concomitant (9). One patient did not return after treatment. 92% took all medications correctly. Per-protocol and intention-to-treat eradication rates were 89.5% (95%CI = 82-97%) and 87.2% (95%CI = 79-95%). Cure rates (per-protocol) were similar when compared depending on the diagnosis (peptic ulcer 100% vs. functional/uninvestigated dyspepsia 88%) and previous treatment (standard triple therapy 89% vs. sequential 83% vs. concomitant 100%). Adverse effects were reported in 60% of patients (95%CI = 49-72%), most commonly nausea (27%), metallic taste (26%), diarrhoea (23%), abdominal pain (22%), asthenia (17%), and vomiting (6.4%). In 2 cases, the adverse effects (nausea) were classified as severe (one patient discontinued the treatment), but none of them was serious.
CONCLUSION: 14-day bismuth-and levofloxacin-containing quadruple therapy is an effective (≈90% cure rate) and safe second-line strategy in patients whose previous standard triple therapy or non-bismuth quadruple (sequential or concomitant) therapy has failed, providing a simple and probably more effective alternative than bismuth-quadruple or levofloxacin-triple standard regimens.
Disclosure of Interest: None declared

P0513 NON-BISMUTH QUADRUPLE CONCOMITANT THERAPIES IN THE ERADICATION OF HELICOBACTER PYLORI: STANDARD VS. OPTIMIZED (14 DAYS, HIGH-DOSE PPI) REGIMENS IN CLINICAL PRACTICE

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INTRODUCTION: Non-bismuth quadruple "concomitant" regimen is increasingly used as first-line *H. pylori* eradication treatment.
AIMS & METHODS: To evaluate the efficacy and tolerability of the standard and optimized "concomitant" regimens.
Design: Prospective multicenter study. *Patients*: Consecutive *H. pylori*-infected patients. *Treatment*: In a first phase, patients received a standard concomitant therapy (CONC10): omeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg and metronidazole 500 mg for 10 days b.i.d. In a second phase, patients received the same regimen but with esomeprazole 40 mg b.i.d. and lasting 14 days (CONC14+). *Outcome*: Eradication confirmed with ^{13}C-urea breath test 4-8 weeks after therapy. *Compliance/tolerance*: Compliance and adverse events were determined through questioning and recovery of empty medication envelopes.
RESULTS: 827 consecutive patients were included (mean age 48 years, 46% males, 21% peptic ulcer): 356 in CONC10 and 471 in CONC14+. Compliance with treatment was 94% and 95% respectively (non-statistically significant differences). Per-protocol eradication rates with CONC10 and CONC14+ were 86%(95%CI = 83-91%) and 93%(91-96%) ($p < 0.01$). Respective intention-to-treat cure rates were 86%(83-90%) and 91%(90-92%) ($p < 0.01$). Adverse effects (mostly mild) were reported in 32% of patients in CONC10 and in 44% in CONC14+ ($p < 0.05$), the most common being metallic taste, diarrhoea, nausea and abdominal pain.
CONCLUSION: An optimized (fourteen-day and high-dose esomeprazole) non-bismuth quadruple "concomitant" regimen for the eradication of *H. pylori* is more effective than the standard one, and achieves over 90% cure rate. Although the incidence of adverse events is higher with the optimized treatment, these are mostly mild, and do not negatively impact the compliance.
Disclosure of Interest: None declared

P0514 SECOND-LINE RESCUE THERAPY WITH MOXIFLOXACIN AFTER FAILURE OF TREATMENT TO ERADICATE HELICOBACTER PYLORI INFECTION

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INTRODUCTION: Second-line bismuth-containing quadruple therapy is complex and frequently induces adverse effects. A triple rescue regimen containing levofloxacin is an alternative for *H. pylori* eradication. However, resistance to quinolones is rapidly increasing and may jeopardize its future efficacy. Moxifloxacin, a new generation quinolone, may be less affected by quinolone resistance than levofloxacin.
AIMS & METHODS: To evaluate the efficacy and tolerability of a second-line triple regimen containing moxifloxacin in patients whose previous *H. pylori* eradication treatment failed.
Design: Prospective multicenter study. *Patients:* Patients after failure of either:
- standard triple therapy (PPI, clarithromycin, and amoxicillin)
- non-bismuth quadruple therapy (PPI, clarithromycin, amoxicillin and metronidazole, either sequential or concomitant)
Intervention: Moxifloxacin (400 mg o.d.), amoxicillin (1 g b.i.d.), and esomeprazole (40 mg b.i.d.) for 14 days. *Outcome:* Eradication was confirmed using the 13C-UBT 4-8 weeks after therapy. *Compliance/tolerance*: Compliance was determined through questioning and recovery of empty medication envelopes. Incidence of adverse effects was evaluated by means of a questionnaire.
RESULTS: 250 patients were consecutively included. Mean age 48±15 years, 58% women, 11% peptic ulcer. Previous failed therapy included: standard triple therapy (179 patients), sequential (27), and concomitant (44). Four patients did not return after treatment. 97% of patients took all medications correctly. Per-protocol and intention-to-treat eradication rates were 85.7% (95%CI = 81-90%) and 82.4 (95%CI = 77-87%). Cure rates were similar when compared depending on the diagnosis (peptic ulcer 77% vs. functional/uninvestigated dyspepsia 82%) and previous treatment (standard triple therapy 83% vs. sequential 89% vs. concomitant 77%). In the multivariate analysis, age was the only variable associated with eradication success (OR = 0.957; 95%CI = 0.93-0.98). Adverse effects were reported in 25% of patients (95%CI = 20-30%), most commonly diarrhoea (9.6%), abdominal pain (9.6%), nausea (9.2%), metallic taste (4.5%), asthenia (4.5%), and vomiting (2.5%). In 13 cases, the adverse effects were classified as "intense", but none of them was severe.
CONCLUSION: 14-day moxifloxacin-containing therapy is an effective (>80%) and safe second-line strategy in patients whose previous standard triple therapy or non-bismuth quadruple (sequential or concomitant) therapy has failed, providing a simple alternative to bismuth quadruple or levofloxacin triple regimens.
Disclosure of Interest: None declared

P0515 THE ROLE OF A DUAL THERAPY CONTAINING HIGH-DOSE PPI IN ERADICATION IN PATIENTS WITH HELICOBACTER PYLORI POSITIVE DYSPEPSIA

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INTRODUCTION: *H. pylori* eradication rates vary by society and usually do not exceed 80%. Some publications have reported that this rate was even higher with dual therapies containing high-dose proton-pump inhibitors. *H. pylori* eradication is recommended in patients with dyspepsia. The objective of the present study is to determine eradication rates with dual therapy containing high dose omeprazole in *H. pylori*-positive patients with dyspepsia.
AIMS & METHODS: The patients were treated orally with either dual (n:74, omeprazole 20mg q.i.d and amoxicillin 1g b.i.d) or triple therapy (n:116, omeprazole 20mg b.i.d and amoxicillin 1g b.i.d and clarithromycin 500mg b.i.d) for 14 days. HpSA test was requested 3 months later. The results were evaluated statistically, p values <0.05 were considered significant.
RESULTS: The study included 190 patients (80♂,110♀, $p>0.05$). The mean age was 35.6±11 years ($p<0.001$). The mean duration of dyspeptic symptoms was 28.2±33.7 months (median:18, range:3–338). Bloating was more frequent in the triple therapy group ($p<0.01$) while epigastric pain/burning and early satiation did not differ significantly between the groups ($p>0.05$). Alcohol and smoking, endoscopic findings and *H. pylori* rates with pathological examinations were not significantly different between groups whereas there was a significant difference in *Hp*Fast tests ($p<0.01$). When examined with HpSA tests 3 months after the treatment, eradication rate was 81.1% in the dual therapy group versus 63.8% in the triple therapy group ($p=0.011$). Dual therapy was more economic compared to triple therapy (144USDvs.107USD,$p<0.001$).
CONCLUSION: Dual therapy in patients with dyspepsia was more successful, cost-effective and is less risky in terms of side effects compared to standard triple therapy.
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Disclosure of Interest: None declared

P0516 SECOND-LINE REGIMEN'S EFFICACY AGAINST HELICOBACTER PYLORI INFECTION AFTER STANDARD TRIPLE THERAPY WITH PPI, AMOXICILLIN & CLARITHROMYCIN: META-ANALYSES

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INTRODUCTION: *Helicobacter pylori* infection is usually treated with a proton pump inhibitor (PPI), amoxicillin and clarithromycin, but it fails in ≥ 20% of patients.
AIMS & METHODS: *Aim*: To estimate, by a systematic review and meta-analyses, the most effective rescue treatments after the failure of a first-line therapy with PPI, amoxicillin and clarithromycin in *H. pylori* eradication. *Methods*: *Selection of studies:* Meta-analyses were performed with randomized clinical trials (RCT) that assessed the efficacy of second-line regimens; the generic inverse variance was applied on prospective and retrospective studies. *Inclusion criteria:* Studies treating *H. pylori*-positive patients after clarithromycin-amoxicillin-PPI failure. *Exclusion criteria:* Second-line treatment based on the antibiotic sensitivity, or if the confirmation of eradication was made only by serology, PCR or polyclonal stool antigen test. *Search strategy:* Bibliographical searches were performed in PubMed, CINAHL, Cochrane Library, ClinicalTrials.gov, and several international congresses, up to April 2014. *Data synthesis:* Intention to treat eradication rate.
RESULTS: The efficacies of the second-line treatments are shown in the table attached. A meta-analysis comparing the triple therapy with levofloxacin-amoxicillin-PPI against the quadruple bismuth-metronidazole-tetracycline-PPI regimen showed a non-statistically significant tendency towards better results with levofloxacin (OR = 1.62; 95% C. I. = 0.84-3.14; p = 0.15; $I^2 = 75\%$; 7 studies; 1,158 patients).

SECOND-LINE TREATMENT	E. R.	N. S.	N. P.	95% C. I.	I^2
Levofloxacin + Amoxicillin + PPI					
-Overall	75%	21	2,919	70 - 80%	88%
-7 day treatment	69%	11	632	64 - 74%	53%
-10 day treatment	83%	11	1,946	77 - 89%	89%
-10 days with L(500 mg/24h) + A(1 g/12h)+PPI	87%	7	373	81 - 94%	77%
*Removing 1 outlier study	**92%**	6	273	89 – 95%	0%
-14 day treatment	74%	3	341	70 – 78%	96%
*Removing 1 outlier study	86%	2	151	81 – 92%	0%
Bismuth + Metronidazole + Tetracycline + PPI					
- Overall	77%	43	3,685	74 - 81%	86%
-7 day treatment	75%	31	2,345	71 - 80%	84%
-10 day treatment	77%	2	142	60 - 93%	76%
-14 day treatment	**81%**	15	1,187	76 - 86%	83%
Metronidazole + Amoxicillin + PPI					
- Overall	88%	24	1,642	85 - 91%	75%
-7 day treatment	75%	24	1,160	85 - 91%	75%
-7 days with M(250 mg/12h) +A(750 mg/12h)+PPI	**92%**	12	751	89 - 95%	48%
-10 day treatment	84%	4	314	77 - 91%	69%
-14 day treatment	81%	2	127	75 - 88%	0%
Amoxicillin + PPI (14 days –all the studies were done in Japan)					
- Overall	82%	5	200	69 - 95%	87%
-14 day with A (500 mg/6h) + PPI(10 mg/6h)	**93%**	3	106	88 - 98%	3%
-14 day with A (1 g/12h) + PPI (20 mg/12h)	66%	2	94	51 - 81%	58%

E. R.: eradication rate; N. S.: Number of studies; N. P.: number of patients.
CONCLUSION: The most effective second-line treatments, after a clarithromycin-amoxicillin-PPI failure, are the metronidazole-amoxicillin-PPI or a 10 day levofloxacin-amoxicillin-PPI therapy. More high quality trials, performed outside Japan, are needed to verify the efficacy of the 14 day dual therapy with amoxicillin-PPI.
Disclosure of Interest: A. Marín: None declared, A. McNicholl: None declared, J. Gisbert Other: Dr. P. Gisbert has served as a speaker, a consultant and advisory member for, and has received research funding from MSD and Abbvie.

P0517 SEVEN-DAY NON-BISMUTH CONCOMITANT QUADRUPLE THERAPY IS SUFFICIENT IN ACHIEVING A GRADE A REPORT CARD FOR FIRST-LINE ANTI-HELICOBACTER PYLORI THERAPY: A PILOT STUDY

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INTRODUCTION: The eradication rate of the standard triple therapy has generally declined to unacceptable levels (i.e., 80% or less) recently because the increasing incidence of clarithromycin-resistant strains of *Helicobacter pylori (H. pylori)*. **10-day** concomitant therapy (non-bismuth concomitant quadruple therapy) can achieve a promising success rate of 90-94% in the presence of clarithromycin resistance. This therapy is superior to standard triple therapy for *H pylori* eradication and less complex as this regimen does not involve changing drugs halfway through.
AIMS & METHODS: This study is to assess the efficacy of 7-day concomitant therapy and to investigate the host and bacterial factors influencing the treatment outcomes of all eradication therapies. One hundred and eighty consecutive *H. pylori*-infected patients are randomly assigned to a 7-day non-bismuth quadruple therapy (EACM group, Esomeprezole 40 mg bid., amoxicillin 1 g bid., clarithromycin 500 mg bid., and metronidazole 500 mg bid. for 7 days) or a 7-day standard triple therapy (EAC group, Esomeprezole 40 mg bid., amoxicillin 1mg bid., clarithromycin 500 mg bid., and for 7 days). Patients are asked to return at the 2nd week to assess drug compliance and adverse events. Repeated endoscopy with rapid urease test, histological examination and culture is performed at the 8th week after the end of anti- *H. pylori* therapy. If patients refuse follow-up endoscopy, urea breath tests are conducted to assess *H. pylori* status. Additionally, antibiotic susceptibility of *H. pylori* will be examined. Finally, the rates of eradication, adverse events and compliance will be compared between groups by chi-square test, and the host and bacterial factors influencing each efficacy of the regimen are assessed by multivariate analysis.
RESULTS: Our results demonstrated that the eradication rates for EACM therapy and EAC standard triple therapy in intention-to-treat analysis were 86.7% vs. 72.2%, $P=0.016$ and 95.1% vs. 79.2%, $P=0.002$) in the per-protocol analysis. Drug compliances were 100% in both groups although more adverse events were reported in the EACM group (35.3% vs. 18.3%, $P=0014$). Clarithromycin resistance was the only independent predictors of treatment failure in multivariate analysis. In the subgroup analysis according to antibiotics susceptibility, none of the patients with clarythromycin resistant strains and 33.3% with metronidazole resistant strains were eradicated in the EAC group while 75% of those with resistant strains were eradicated in the EACM group.
CONCLUSION: This study suggests that a 7-day non-bismuth concomitant quadruple therapy is sufficient in achieving a grade A report card for first-line anti-*H. pylori* therapy. Clarithromycin resistance was the factor responsible for eradication failures.
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Disclosure of Interest: None declared

P0518 EMPIRICAL RESCUE THERAPY AFTER *H. PYLORI* TREATMENT FAILURE. A 15-YEAR SINGLE CENTER STUDY OF 1,000 PATIENTS

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INTRODUCTION: The most commonly used empirical therapies for *H. pylori* eradication fail up to 20-30% on first line, and even more in "rescue" therapies. This is mainly due to increasing antibiotic resistances and poor compliance. Therefore it is necessary to evaluate the efficacy and safety of the overall eradicating strategy, including multiple and consecutive lines of treatment.
AIMS & METHODS: To evaluate the efficacy of different "rescue" therapies empirically prescribed during 15 years to 1,000 patients in whom at least one eradication regimen had failed to cure *H. pylori* infection.
Design: Retrospective single-center study. *Patients:* 1,000 consecutive patients who had failed at least one eradication therapy (1998-2013). *Intervention:* The most common eradication treatments were: 1) PPI-Amoxicillin-Levofloxacin (PPI-A-L), 2) Ranitidine bismuth citrate-Tetracycline-Metronidazole (Rcb-T-M), 3) Classic Quadruple therapy (PPI-Bismuth-Tetracycline-Metronidazole) (PPI-B-T-M), 4) Esomeprazole-Moxifloxacin-Amoxicillin (E-Mox-A), 5) PPI-Amoxicillin-Rifabutin (PPI-A-Rif). Rifabutin was prescribed only as 4th line, and the other treatments were used both as 2nd and 3rd line. As antibiotic susceptibility was unknown, "rescue" regimens were prescribed empirically. Rescue regimens were prescribed without retreating with the same drugs. *Outcome:* Eradication was defined as a negative ^{13}C-urea breath test 4-8 weeks after completing therapy. Modified "intention-to-treat" analysis was used, considering patients with poor compliance, but not those who were lost during the follow-up.
RESULTS: Overall eradication rates of *H. pylori* with 2nd, 3rd and 4th lines of "rescue" therapies were 74.6%, 71.1% and 50% respectively, with a cumulative eradication rate after consecutive administration of 4 treatments of 99.2%. Compliance with 2nd, 3rd and 4th line regimens was 95.6%, 93% and 93.5% respectively, with an overall compliance of 95.1%. The efficacy and adverse effects of treatments were 83.5% and 24.2% with E-Mox-A, 77.8% and 24% with PPI-L-A, 68.9% and 21.5% with PPI-B-T-M, 66% and 33.3% with Rcb-T-M, and 62% and 37.9% with PPI-A-Rif. The highest rate of eradication was achieved with E-Moxi-A (83%) as a 2nd line treatment, regardless of the first-line regimen prescribed.
CONCLUSION: *H. pylori* eradication rates may reach 99% without performing bacterial culture by using a rescue strategy of 4 consecutive empirical treatments. The best rescue strategy to eradicate *H. pylori* is the consecutive administration of quinolones (2nd line), PPI-B-T-M (3rd line) and PPI-A-Rif (4th line).
Disclosure of Interest: None declared

P0519 LETS TRY QUINTUPLE THERAPY AS A RESCUE ERADICATION REGIMEN FOR REFRACTORY *H. PYLORI* INFECTION

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INTRODUCTION:
To compare the efficacy, tolerability and side effect profiles of two quintuple regimens for helicobacter pylori (*H. pylori*) eradication in patients who failed the first line quadruple therapy.
AIMS & METHODS: Between April 2011 and March 2012, a total of 208 patients with dyspepsia who failed *H. pylori* eradication using the standard quadruple therapy with BOAC (Bismuth subcitrate, Omeprazole, Amoxicillin, Clarithromycin) or BOAM (Bismuth subcitrate, Omeprazole, Amoxicillin, Metronidazole) were recruited for this study. The patients were randomized into two equal groups using random block method. Patients in BOACT group were treated by omeprzole 20 mg, combined with bismuth subcitrate 240 mg, and three antibiotics clarithromycin 500 mg, amoxicillin 1000 mg and tinidazole 500 mg all twice daily for seven days. Patients in the BOTMO group were given omeprazole 20 mg and bismuth subcitrate 240 mg along with tetracycline 500 mg and ofloxacin 200 mg in the same manner as in BOACT group. The eradication was confirmed at 12 weeks after end of therapy by C14 urea breath test. Patients' compliance and drugs side effects were evaluated at the end of treatment. The success rates were calculated separating by intention-to-treat (ITT) and per-protocol (PP) analyses.
RESULTS: A total number of 208 patients were included in the study and 205 patients completed the treatment course. The intention-to-treat and per-protocol eradication rates were 75.5% and 76% in the BOACT group and 86.5% and 86.7% in the BOTMO group, respectively. The eradication rates of the BOTMO group was significantly higher than BOACT group ($p=0.04$). Side effects were reported from 33.2% of the patients which were mild and did not necessitate interfere with therapy although 3 patients (2 patient in BOACT group and 1 patient in BOTMO group were excluded from the study due to severe drug side effects.
CONCLUSION: Quintuple therapy with BOTMO could be an alternative second-line rescue therapy for Iranian patients who have failed one previous standard treatment for *H. pylori* eradication, but its efficacy needs to be confirmed in other populations before we can generalized our findings, considering regional antimicrobial resistance. Considering the short length of treatment in our study, further studies to assess the effects of quintuple therapies by BOTMO regimen with periods longer than 7 days is recommend
Disclosure of Interest: None declared

P0520 HELICOBACTER PYLORI ERADICATION RATES AND PLASMA PANTOPRAZOLE LEVELS IN TYPE 2 DIABETIC AND NONDIABETIC PATIENTS

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INTRODUCTION: The eradication rate of Helicobacter pylori has been reported as being lower in patients with type 2diabetes mellitus (DM) than in those without DM.
AIMS & METHODS: The first aim of this study was to compare the efficacy of a bismuth-based quadruple regimen as first-line therapy for Helicobacter pylori (HP) eradication in diabetic and non-diabetic patients. The second aim of the study was to compare plasma Pantoprazol levels in these patient groups during *H. pylori* eradication treatment.
Forty consecutive type 2 DM and 40 non-diabetic naïve *H. pylori* infected patients were enrolled in this study. All patients received Pantoprazole (40 mg b.i.d.), bismuth citrate (120 mg q.i.d.), tetracycline (500 mg q.i.d.), and metronidazole (500 mg t.i.d.) for 14 days as the eradication regimen. We used Square-Wave Voltammetry method to determine plasma Pantoprazole levels in both groups.
RESULTS: The overall compliance rates among the diabetic patients and control group were 90.0% (36/40) and 92.5% (37/40), respectively. The per-protocol HP eradication rates (63.9% vs 89.2%, $p=0.01$), Intention-to-treatment HP eradication rates (60% vs 87.5%, $p<0.001$) and Plasma Pantoprazole levels ($0.25\mu gmL^{-1}$ vs. $0.34\ \mu gmL^{-1}$, $p=0.005$) were significantly lower in diabetic patients.
CONCLUSION: Our study showed that diabetic patients had lower plasma Pantoprazole levels which led to lower *H. pylori* eradication rates with a bismuth and Pantoprazole including regimen. Clinical and pharmacokinetic investigations are required to improve plasma proton pump inhibitor levels in diabetic patients for satisfactory *H. pylori* eradication rates.

Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
SMALL INTESTINAL I – POSTER EXHIBITION – HALL XL

P0521 CAUSE-SPECIFIC MORTALITY IN PEOPLE WITH COELIAC DISEASE COMPARED TO THE GENERAL POPULATION: A COMPETING-RISK ANALYSIS

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INTRODUCTION: Quantifying excess cause specific mortality among people with coeliac disease (CD) compared to the general population accounting for competing risks (which takes into account that patients may die due to other causes before dying from the cause of death of interest) will allow accurate information to be given on prognosis and risks of adverse outcomes.
AIMS & METHODS: This study quantifies the excess cause specific mortality among people with CD by 10 year of diagnosis compared to the general population while accounting for competing risks. We identified from the Clinical Practice Research Datalink (CPRD), all patients with CD for whom linkage to Office of National Statistics (ONS) data to determine cause of death if it occurred was available. We selected controls by frequency matching from the registered GP population within 10 year age bands. We calculated the adjusted cumulative incidence (including adjustment for competing risks) for different causes of death up to 10 years from diagnosis. We also calculated the excess cumulative incidence (eCI) for each cause of death compared to controls.
RESULTS: Of the 5,310 patients with CD, 352 died within the study period. The overall mortality rateamong CD patients was 124 per 10,000 person-years compared to 111/10,000 in controls. By 10 years after CD diagnosis, the cumulative incidence of death (Table 1) from cardiovascular related deaths was slightly lower compared to those without CD diagnosis (CD 0.16% versus Controls 0.26%) with a corresponding eCI of 0.1% (95% CI -0.14 to -0.06). Overall there was no difference in the cumulative incidence of respiratory, digestive or cancer related death among cases and controls. However, CD patients had 0.1% excess risk (95%CI;0.01-0.16) of deaths death from non-Hodgkin's lymphoma or leukaemia.
Table 1: Cumulative incidence and excess risk by 10 years after diagnosis adjusted for competing risks, gender, age and social class

Cause of death	With CD	Without CD	Excess	95% CI	
Cardiovascular overall	0.16	0.26	-0.10	-0.14	-0.06
Ischemic heart disease	0.10	0.15	-0.05	-0.08	-0.16
Respiratory overall	0.07	0.07	0.00	-0.02	0.03
Neoplasm overall	0.78	0.72	0.06	-0.11	0.23
Non-hodgkins/leukemia	0.13	0.04	0.08	0.01	0.16
Digestive overall	0.15	0.11	0.05	-0.03	0.13

CONCLUSION: Overall, people with CD have no major excess risk of cancer, digestive, cardiovascular or respiratory related mortality compared to the general population over the 10 year period following initial diagnosis. In addition they have only a very small excess risk of dying of haematological malignancy. These findings should be reassuring to both patients with CD and clinicians managing their care.
Disclosure of Interest: None declared

P0522 NUTRIENTS INTAKE IN NON CELIAC PATIENTS ON GLUTEN FREE DIET BECAUSE OF PERCEIVED GLUTEN SENSITIVITY: COMPARISON WITH CELIAC PATIENTS AND WITH NATIONAL NUTRITIONAL GUIDELINES

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INTRODUCTION: Non celiac and non wheat allergic patients that spontaneously adhere to gluten free diet (GFD) because of adverse gastrointestinal and extra-intestinal reactions to gluten containing food are frequently encountered in clinical practice and are commonly referred to as "gluten sensitive" (GS) patients. In most cases GS patients do not seek dietician advice on GFD, and no information is available on the nutritional adequacy of their self-made diet.
AIMS & METHODS: We carried out a prospective clinical study to assess macro- and micro-nutrients of GFD in GS patients compared with that of a cohort of patients with celiac disease (CD) matched according to gender and age (range +/-4 years), and with the recommendations of the Italian nutritional guidelines (LARN 2012). Patients in the 2 study cohorts were asked to fill in a standardized 7-day food diary. Data from diaries were analyzed with Microdiet© software (Downlee systems, ltd. UK) that returns very detailed information on diet composition. Nutritional characteristics included: total Kcal, proportion of total energy values of CHO, free sugars, proteins, fats, SFA and PUFA, and total amounts of fibres, vitamins A, C, D, B12, folates, sodium, calcium, iron, zinc, selenium, magnesium and alcohol. For statistical analysis Fisher's exact test and Wilcoxon matched paires test were used as appropriate.
RESULTS: Twenty-two GS patients (mean ± SD 40 ±9 years, BMI 22±3) and 22 CD patients were enrolled. Total Kcal were 1767 ±501 Vs 1544 ±539 in GS and CD respectively, with no difference in % contribution of CHO, fats and proteins to total calories. The proportion of macro-nutrients in the diet that was correct according to the LARN recommendations was 54%, 59% and 32% in GS and 18%, 41% and 5% in CD for CHO, proteins and fats, respectively. Comparison of selected nutrient composition in GS Vs CD patients and Vs LARN are reported in the table.

Nutrients	GS	CD	GS Vs LARN %[§]
PUFA, % TEV	4.6±2.2	3.4±1.2*	- 50
Fibres, g	20.0±24.9	11.9±6.5	-86
Alcohol, g	2.3±4.4	4.0±8.9	NA
Vitamin B12, µg	3.9±1.8	1.0±1.6*	-14
Vitamin D, µg	2.2±1.2	1.5±0.9*	-100
Folates, µg	324.5±381.5	131.7±74.7*	-73
Magnesium, mg	146.7±101.4	44.6±64.4*	-77
Iron, mg	9.0±5.4	5.4±2.7*	-68
Selenium, µg	39.0±16.3	10.4±16.0*	-55

CONCLUSION: Patients spontaneously adhering to a GFD for perceived GS have, despite no dietetic instruction, a more balanced intake of macro- and micro-nutrients in comparison with CD patients. This phenomenon may be the result of a behavioural attitude towards healthy food more pronounced in GS than in CD patients, although LARN recommendations are not met for most nutrients.
Disclosure of Interest: None declared

P0523 SPLEEN DIAMETER/RDW AS A NOVEL INDICATOR FOR CELIAC DISEASE

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INTRODUCTION: Red cell distribution width (RDW) has been shown in previous studies to be a sensitive predictor for coeliac disease (CD), but it lacks specificity. Splenic hypotrophy is also noted frequently in celiac patients. Our aim was to evaluate if spleen size/RDW can be used as an indicator for celiac disease.
AIMS & METHODS: We evaluated 32 patients with small bowel disease (12 newly diagnosed CD patients and 20 patients with Crohn's disease, IBD-CD) and 32 age-matched patients with irritable bowel syndrome (IBS), admitted to our clinic over a one-year period. We evaluated the differences in spleen diameter, RDW and their ratio among the three groups.
RESULTS: Of the 32 patients with small bowel disease, 11 were males, with a mean age of 38.34 years. Mean RDW was significantly higher in the CD and IBD-CD groups than the IBS group (14.49 and 16.73 vs. 13.51, $p = 0.0099$), whereas mean spleen size was lowest in the CD patients (84.08, 107.85 and 112.62 mm respectively). The mean spleen diameter/RDW was 5.82 in the CD group, 6.65 in the IBD-CD group and 8.34 in the IBS group ($p = 0.0001$). A ratio under 6 had a sensitivity of 75% and a specificity of 88.46% in detecting CD.
CONCLUSION: Spleen diameter/RDW is a simple, widely available score, which can be used to select patients for futher diagnostic tests. This should be repeated in larger patient cohorts.
Disclosure of Interest: None declared

P0524 CELIAC DISEASE AND DRUG-BASED THERAPIES: INQUIRY INTO PATIENTS' DEMANDS

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INTRODUCTION: The gluten free diet (GFD) is the only available therapy for patients with celiac disease (CD). Medical research is actively focused on the search for drug-based solutions as an alternative to GFD, which requires lifelong, strict adherence.
AIMS & METHODS: We aimed at evaluating the actual need for other-than-GFD therapies perceived by CD patients, along with the impact of GFD itself on their life.
During the 2012 meeting of the Lombardy section of the Italian CD Patients Association, adult CD subjects on GFD were invited to fill in a questionnaire investigating their clinical profile in relation to GFD compliance, health status and quality of life as well as their opinion on GFD, alternative therapies and research priorities.
RESULTS: 372 patients (76 M, mean age at diagnosis and at entry 29.7 ± 16.9 and 41.7 ± 13.9 years, respectively) completed the questionnaire. 94% patients reported strict adherence to GFD. Patients reported a significant improvement in health status and quality of life after the diagnosis of CD was made and GFD was started ($p < 0.001$), with a greater improvement of health status than quality

of life (82% vs 56%, $p<0.001$). GFD was favourably considered and accepted by 88% patients, but a demand for alternative therapies was reported by 65% patients. Subjects expressing the need for a drug-based therapy showed a significantly lower increase of quality of life on GFD ($p=0.002$), but no differences were observed in health status changes. The preferred option for an alternative therapy was the "on demand" assumption of drugs, i.e. enzymes (145 subjects), followed by a vaccine-based strategy (111 subjects). Almost two thirds of the cohort stated they would accept to be enrolled in *ad hoc* designed clinical trials.
CONCLUSION: GFD is favourably accepted and followed by most CD patients, with significant health status improvement. Nevertheless, a considerable proportion of patients pronounce themselves in favour of the development of alternative drugs, although a chronic drug therapy is not considered a likely opportunity.
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Disclosure of Interest: None declared

P0525 IMPAIRED BONE MICROSTRUCTURE IMPROVES AFTER ONE-YEAR ON GLUTEN-FREE DIET. A PROSPECTIVE LONGITUDINAL STUDY IN WOMEN WITH ACTIVE CELIAC DISEASE

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INTRODUCTION: We have recently identified a significant deterioration of trabecular and cortical microarchitecture in peripheral bones of patients with undiagnosed celiac disease (CD) by using high resolution-peripheral quantitative computed tomography (HR-pQCT). Such finding may underlie bone fragility and lead to fractures in these patients. Up to now, the effect of the gluten-free diet (GFD) on microstructural parameters of peripheral bones has not been assessed.
AIMS & METHODS: Aim: To explore one-year changes of bone microstructure associated with the GFD in a prospective cohort of premenopausal women with newly diagnosed CD.
Materials: We prospectively enrolled 31 consecutive females with newly diagnosed CD. Up to now, 25 patients have been reassessed one-year after diagnosis. Clinical and biochemical status, CD specific serology, assessment of the degree of compliance with the GFD, bone densitometry and microstructural determinations (HR-pQCT) were performed at both time points. HR-pQCT bone volumetric and structural measurements were determined at the distal non-dominant radius and tibia. Parameters of patients were also compared with those of 22 healthy women of similar age and body mass index.
RESULTS: Compared with the baseline *z*-score, the one-year bone mineral density measured by dual energy x-ray absorptiometry (DXA) improved significantly at the distal radius (mean±SD) (-1.94±1.27 vs. -1.43±1.06; $p<0.02$) but not at the lumbar spine level. The microstructure of the trabecular compartment in the distal radius was significantly improved (trabecular/bone volume fraction, trabecular density and trabecular thickness: $p<0.0001$) at the one-year time point. At the level of tibia, treatment was associated with significant increment of the total volumetric density ($p<0.01$), cortical density ($p<0.002$), trabecular density ($p<0.0001$), trabecular/bone volume fraction ($p<0.0001$) and trabecular thickness ($p<0.002$). In contrast, the cortical thickness decreased significantly in both sites ($p<0.001$). Compared to the control group there were no statistically significant differences in most trabecular parameters measured by HR-pQCT.
CONCLUSION: This is the first study exploring the effect of a one-year GFD on microstructural parameters measured by HR-pQCT in patients with newly diagnosed CD. Our study shows that trabecular parameters impaired at the time of diagnosis improved significantly by treatment reaching values comparable to those in healthy controls. We postulate that bone microarchitecture improvement underlie the decreased risk of fractures observed after treatment with a GFD.
Disclosure of Interest: G. Longarini: None declared, M. Zanchetta: None declared, A. Costa: None declared, V. Longobardi: None declared, M. Temprano: None declared, H. Vazquez: None declared, S. Niveloni: None declared, E. Smecuol Financial support for research from: Astra Zeneca, Lecture fee(s) from: Astra Zeneca; Takeda, Consultancy for: Astra Zeneca, M. Moreno: None declared, H. Hwang: None declared, R. Mazure: None declared, A. Gonzalez: None declared, E. Mauriño: None declared, J. Bai: None declared

P0526 HOW DOES SPECIFIC SEROLOGY MATCH WITH ESPHGAN SEROLOGIC GUIDELINES FOR DIAGNOSIS OF CELIAC DISEASE IN A PROSPECTIVE COHORT OF ADULTS WITH HIGH PRETEST PROBABILITY?

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INTRODUCTION: Intestinal biopsy is considered mandatory for the diagnosis of celiac disease (CD). This has been recently challenged by several studies and the 2012 ESPGHAN guideline proposing an appropriate clinical and serological algorithm that could be used to reduce the need for duodenal biopsy. This provocative strategy has been confirmed by some studies but rejected by others. However, all these studies were performed on the basis of retrospective analyses of biased populations. Prospective evaluation of patients in whom diagnosis was based on histological grounds is important to clarify this controversy.
AIMS & METHODS: 1-To review the performance of serology tests in a prospective and consecutive series of adult patients with high pretest probability for CD; 2- to compare performance of serologic tests with the ESPGHAN serologic algorithm; and 3- to establish the best serologic algorithm for diagnosing CD using antibody tests detecting different antigens.
We performed a *post hoc* analysis of data from all patients enrolled in a previous prospective study (WJG 2010; 16: 3144) where consecutive adults suspected of intestinal disorders (high pretest population) were enrolled. Diagnosis of CD was based on histology (Marshs stages ≥3a) in all patients irrespective of serology. CD-related serology consisted of seven different assays but we only report the performance of tissue transglutaminase (tTG) IgA, deamidated gliadin peptides (DGP) IgG and the combination of both (INOVA Diag. Inc.). Serologic performance was compared with the ESPGHAN serologic criterion (cut-off >10 times the upper limit of normal -ULN-), the best cut-off (area under the ROC) and the cut-off suggested by the manufacturer.
RESULTS: Sixty-three of 161 patients (39%) had histological criteria for CD. According to the ESPGHAN criterion, IgA tTG sensitivity was 22% with 100% positive predictive value (PPV). The best cut-off value (34 AU/mL) would detect 93.6% of patients with 100% of PPV. Finally, the manufacturer cut-off (20 AU/mL) had 95.2% sensitivity and 97.9% PPV. The ESPGHAN criterion used for IgG DGP was 3.2% sensitive with a PPV of 100%. The best cut-off (was similar to that of the manufacturer: 20AU/mL) was 95.2% sensitive and had 100% PPV. Any test was positive (>20AU/mL) in all patients and both were concomitantly positive in 90.5% of cases with100% of PPV.
CONCLUSION: This prospective study indicates that, under particular clinical circumstances, a serologic strategy can be used to avoid duodenal biopsy in the diagnosis of adult patients with CD. The need for biopsy could be avoided in a minority of patients by using the ESPGHAN serologic criterion. Our results suggest that the best serologic strategy for a high pretest population seems to be the association of tTG IgA and DGP IgG. In such context, biopsy could be avoided in more than 90% of the cases when both tests are positive.
Disclosure of Interest: G. Longarini: None declared, E. Sugai: None declared, H. Hwang: None declared, F. Nachman: None declared, A. Cabanne: None declared, H. Vazquez: None declared, M. Moreno: None declared, A. Costa: None declared, M. Pinto: None declared, S. Niveloni: None declared, E. Smecuol Financial support for research from: Astra Zeneca, Lecture fee(s) from: Astra Zeneca; Takeda, Consultancy for: Astra Zeneca, R. Mazure: None declared, E. Mauriño: None declared, J. Bai: None declared

P0527 HIGH RATES OF PRIOR CELIAC DISEASE OVERDIAGNOSIS AMONG PATIENTS REFERRING TO AN ITALIAN TERTIARY CARE CENTER

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INTRODUCTION: Celiac disease (CD) was formerly considered a rare condition and frequently underdiagnosed. Interest in CD has grown in recent years, not only among gastroenterologists but also among general practitioners and patients. Furthermore, focus of media on gluten-free diet (GFD) is increasingly spreading worldwide. Therefore many patients are labeled as celiacs and start a GFD even without completing the correct diagnostic process.
AIMS & METHODS: Our aim is to assess the impact of overdiagnosis in an Italian tertiary referral center for CD. We reviewed the clinical history of all patients referring to our Centre from October 2012 to December 2013. We included only patients at their first examination. We questioned diagnoses for the following reasons: EMA/TTG absence or negativity; duodenal biopsy not performed or unclear; DQ2/DQ8 negativity. Following data of patients with a doubtful diagnosis were extracted: people who have diagnosed CD (physicians or patients); reasons for diagnosis (symptoms, DQ2/DQ8, specific antibodies, duodenal biopsy), gluten consumption status. Number of patients undergoing a proper diagnostic process was determined, as well as of patients with a prior undebatable diagnosis. Diagnosis was revaluated by repetition of serology and by second-reading of duodenal tissue slides by an experienced pathologist. DQ2/DQ8 was searched in pertinent cases.
RESULTS: Over the study period, 293 patients attended our Centre, of whom 150 for the first time. Of them, 47 (31.3%) presented with an undebatable diagnosis of CD, and 37 (24.7%) were newly diagnosed because of EMA/TTG positivity associated with duodenal Marsh lesions. In 15 patients (10%) referring for

family history of CD, gastrointestinal symptoms or anemia, CD was excluded by serology and histology assessment. The remaining 51 patients (34%) came for a revaluation of previously diagnosed CD. Forty-five of them (88%) were on a GFD at the time of the examination. Thirty-five patients (68.6%) were diagnosed of CD by their trusted doctor (gastroenterologist, gynaecologist, dermatologist or general practitioner), while the remaining 16 (31.4%) believed to be affected of CD on their own. Motivations for prior CD diagnosis were often multiple for each patient: serologic positivity (9 AGA, 5 EMA, 2 TTG) in 16 cases, histological features in 19 cases, DQ2/DQ8 positivity in 20 cases, amelioration of symptoms after GFD in 16 cases. Reasons for questioning previous diagnosis were also multiple for each patient: EMA/TTG absence or negativity in 45 cases; lack of duodenal biopsy in 20 cases; unclear histology in 24 cases; DQ2/DQ8 negativity in 2 cases. Diagnosis of CD was rejected in 78.4% of doubtful cases (n = 40), being confirmed in only 19.6% (n = 10) of them. In one patient, diagnosis is still ongoing.
CONCLUSION: Our retrospective study shows that a considerable number of patients referring to an Italian tertiary care center experience previous misdiagnosis and/or overdiagnosis of CD. Such behavior may lead to both a diagnostic delay of other diseases and a remarkable waste of economic resources (tax exemptions, gluten-free food vouchers, diagnostic exams), with damage for both patients and health services. Greater accuracy in the application of the adequate diagnostic process and a higher adherence to guidelines are needed to minimize misdiagnosis of CD.
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P0528 GLUTEN AVOIDANCE BEFORE A DEFINITE DIAGNOSIS IS MORE COMMON AMONG NON-CELIAC SUBJECTS THAN CELIAC ONES

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INTRODUCTION: Gluten is known to trigger not only celiac disease, but also other conditions, such as non-celiac gluten sensitivity (NCGS) and wheat allergy, recently grouped together as "gluten-related disorders". Gluten has recently shown to cause depression in subjects with NCGS. Furthermore, gluten is able to cause gastrointestinal (GI) symptoms and to alter bowel barrier functions in patients with diarrhea-predominant irritable bowel syndrome (IBS-D). Gluten-free claims are increasingly spreading on the Web and other media, and many subjects start a gluten-free diet (GFD) without any prior medical consultation. Such a behavior may lead to a considerable waste of resources and to diagnostic delay both in celiac and in non-celiac subjects.
AIMS & METHODS: Our aim was to assess the impact of gluten avoidance before a definite diagnosis in both patients with and without celiac disease. We reviewed the clinical history of all patients referring to our CD outpatient clinic from October 2012 to December 2013. We included only patients without a definite diagnosis of CD at their first examination at our Centre. Patients were grouped according to their gluten consumption status at the time of examination. Gluten was reintroduced for at least 2 months before any diagnostic assessment in all subjects already on GFD. The following data were extracted from patients on GFD at the time of examination: gender, age, reasons for gluten avoidance without definite diagnosis (GI/extraintestinal symptoms, DQ2/DQ8, specific antibodies, duodenal biopsy), proposer of GFD (physicians or the patient itself). All patients underwent blood dosage of EMA, TTG and total IgA levels, as well as upper endoscopy with duodenal biopsy. In all patients CD was diagnosed because of EMA and TTG positivity associated with Marsh-type intestinal lesions. Correlation between gluten avoidance and further diagnosis of CD was assessed by Chi-square test.
RESULTS: Over the study period, a total amount of 293 patients attended our Centre, of whom 150 (M 41, F 109 – mean age 39 y) for the first time. Ninety-two patients came without a definite diagnosis of CD. Of them, 32 (34.8%) were on GFD at the time of examination, and 60 (66.2%) were not. Reasons for GFD without definite diagnosis were: GI symptoms (12 cases), extraintestinal symptoms (7 cases), DQ2/DQ8 positivity (9 cases), antibody positivity (6 cases), histological features (9 cases). Sixteen patients started a GFD on their own (41%), and 23 upon medical advice (58%). Gender did not influence gluten consumption status ($p = 0.8376$). Respectively, CD was diagnosed in 21.9% (7/32) of patients on GFD and 71.8% (43/60) of patients on a gluten-containing diet at the time of first examination ($P < 0.0001$).
CONCLUSION: Our study shows that gluten avoidance before a clear definition of diagnosis is more common among subjects in whom CD is ruled out at a later stage than ones diagnosed of CD afterwards. The increasing interest of physicians and patients in gluten-related diseases, and unmotivated gluten-free claims may explain such reasons. Also symptom burden and gluten influence on mental component of patients may play a role in this phenomenon. However, the retrospective nature of our study represents a limitation in data analysis. Further, prospective trials are warranted to clarify this issue.
Disclosure of Interest: G. Ianiro: nothing to declare, G. Bruno: nothing to declare, S. Bibbò: nothing to declare, S. De Martino: nothing to declare, V. Arena: nothing to declare, A. Gasbarrini: nothing to declare, G. Cammarota: nothing to declare

P0529 IS VISCERAL ADIPOSE TISSUE A RISK FACTOR FOR SMALL BOWEL ANGIOECTAISA?

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INTRODUCTION: Small bowel angioectasia (SBA) is one of the major bleeding sources of obscure gastrointestinal bleeding (OGIB). Little is known about etiology of SBA. Visceral adipose tissue (VAT) expresses some bioactive molecules including vascular endothelial growth factor (VEGF), which is implicated in normal or pathological vessel formation. In the present study, we investigated VAT in association with the risk of small bowel angioectasia.
AIMS & METHODS: We retrospectively investigated 198 consecutive patients (male: female; 117: 81, mean age 65.8 ± 12.8 years) who underwent capsule endoscopy (CE) and CT for investigation of overt and occult OGIB at the University of Tokyo Hospital between January 2009 and September 2013. VAT and subcutaneous adipose tissue (SAT) were measured by CT, and medical history of concomitant disease and body mass index were obtained from their medical records. Logistic regression analyses were used to evaluate associations.
RESULTS: Out of 198 OGIB patients, CE found SBA in 18 patients (9.1%). Compared with patients without SBA, those with SBA had significantly higher VAT (96 ± 76.0 $cm^{2,}$ vs. 63.4 ± 51.5 cm^2, $p = 0.016$) and higher prevalence of liver cirrhosis (11(61%) vs. 41(23%), $p = 0.0011$). Prevalences of SBA progressively increased according to VAT; 7.2% in patients with VAT less than 100 cm^2, whereas 12.5% in those between 100 cm^2 and 150 cm^2, 21.4% more than 150 cm^2 ($p = 0.058$ by trend test), respectively. Multivariate analysis showed that VAT (odds ratio for each 10 cm^2 increment, 1.1; 95% confidence interval (CI), 1.01-1.19; $p = 0.025$), liver cirrhosis (odds ratio, 5.5; 95% CI, 1.98-16.6; $p = 0.0011$) were related to significant risk factors of SBA.
CONCLUSION: In addition to liver cirrhosis, visceral adipose tissue is one of the risk factors for small bowel angioectasia.
Disclosure of Interest: None declared

P0530 EVALUATION OF GASTRO-INTESTINAL LESIONS IN PATIENTS UNDERGOING ORAL ANTICOAGULANT THERAPY BY CAPSULE ENDOSCOPY

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INTRODUCTION: Small bowel bleeding is still poorly studied in patients with long-term anticoagulation therapy. Capsule endoscopy (CE) is the first-line method for evaluation of bleeding in patient after negative upper endoscopy and colonoscopy.
AIMS & METHODS: In this retrospective study, we had investigated the types and frequency of small bowel GI bleeding lesions in patients undergoing oral anticoagulant therapy, by CE. Of a total of 1085 CE obtained between January 2003 and June 2013, 679 were performed in patients with obscure gastrointestinal bleeding. Of these 96 were obtained in patients undergoing oral anticoagulant therapy, 55 males and 41 females, mean age 70.6 years (range 23-87 years). At the time of evaluation by capsule endoscopy, the mean level of haemoglobin was 8.3 g/dl for males (normal values 14-18 g/dl) and 6.7 g/dl for females (normal values 12-16 g/dl). The mean number of blood units used for transfusions was 5.7 per patient (range 2-20). All patients underwent upper and lower gastro-intestinal endoscopy, prior to capsule endoscopy (CE). If upper and lower examinations were negative, CE was performed. The following data were recorded in the data base: patient age, gender, indication for the examination, medical and surgical history, bleeding history (including type of bleeding, total number of transfusions, hospitalizations), number and type of prior diagnostic testing, and details of the capsule examination.
RESULTS: In the series of patients undergoing oral anticoagulant therapy: 35/96 (36.4%) patients had negative examination; 22/96 (22.9%) had small-bowel angiodysplasias, small bowel erosions 21/96 (21.8%), small bowel ulcerations 5/96 pts (5.2%), neoplasia 4/96 (4.1%). In the series of patients with OGIB without anticoagulant therapy: 102/583 (17.4%) had angiodysplasias, small bowel erosions 48/583 (8.2%), small bowel ulcerations 25/583 (4.2%), neoplasia 44/583 (7.5%)
CONCLUSION: Small bowel angiodysplasias remain the main cause of occult GI bleeding. In our series, patients undergoing oral anticoagulant therapy had high prevalence of small bowel angiodysplasias (36.4% for anticoagulant group and 17.4% for control group). Furthermore in the anticoagulant group we have seen a major occurrence of erosions (21.8% VS 8.2%).
Disclosure of Interest: None declared

P0531 FREQUENCY AND RISK FACTORS FOR REBLEEDING EVENTS IN PATIENTS WITH SMALL BOWEL ANGIOECTASIA

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INTRODUCTION: Small bowel angioectasia is reported as the most common cause of bleeding in patients with obscure gastrointestinal bleeding (OGIB). Although the safety and efficacy of endoscopic treatment have been demonstrated, rebleeding rates are relatively high. To establish therapeutic and

follow-up guidelines, we investigated the long-term outcomes and clinical predictors of rebleeding in patients with small bowel angioectasia.
AIMS & METHODS: A total of 68 patients were retrospectively included in this study. All the patients had undergone CE examination, and subsequent control of bleeding, where needed, was accomplished by endoscopic argon plasma coagulation. Based on the follow-up data, the rebleeding rate was compared between patients who had/had not undergone endoscopic treatment. Multivariate analysis was performed using a Cox proportional hazard regression model to identify the predictors of rebleeding. Rebleeding was defined as evidence of recurrent visible gastrointestinal bleeding (hematochezia or melena) with recent negative upper and lower endoscopic examinations and/or a reccurent drop of the hemoglobin level by more than 2 g/dl from the baseline. We defined the OGIB as controlled if there was no further overt bleeding within 6 months and the hemoglobin level had not fallen below 10 g/dl by the time of the final examination.
RESULTS: The overall rebleeding rate over a median follow-up duration of 30.5 months (interquartile range 16.5–47.0) was 33.8% (23/68 cases). The cumulative risk of rebleeding tended to be lower in the patients who had undergone endoscopic treatment than in those who had not undergone endoscopic treatment, however, the difference did not reach statistical significance ($P = 0.14$). In the majority of patients with rebleeding (18/23, 78.3%), the bleeding was controlled with additional endoscopic treatment by the end of the follow-up period. Multiple regression analysis identified multiple lesions (≥ 3) (OR 3.82; 95% CI 1.30–11.3, $P = 0.02$) as the only significant independent predictor of rebleeding.
CONCLUSION: In conclusion, patients with small bowel angioectasia show relatively high rebleeding rates. Although a single session of endoscopic treatment was not sufficient to control future rebleeding, in most cases, rebleeding could be controlled with repeated endoscopic treatment and/or iron replacement therapy. Careful follow-up is needed for patients with multiple lesions, which was identified as a significant risk factor for rebleeding.
Disclosure of Interest: None declared

P0532 GENE EXPRESSION LEVELS OF ANGIOGENIC FACTORS IN SMALL BOWEL ANGIODYSPLASIA

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INTRODUCTION: Angiodysplasias are known to account for 50% of small bowel bleeding sources, but diagnosis and effective treatment of these lesions is limited by a poor understanding of the pathophysiology of the condition. By measuring serum angiogenic factors in patients with small bowel angiodysplasias (SBA), we have already identified abnormalities in the angiopoietin pathway; with elevated levels of Ang2 and decreased levels of Ang1, associated with the condition. To determine the significance of these findings we need to determine whether these factors and their receptors are specifically located in SBA tissue.
AIMS & METHODS: The aim of this study was to measure gene expression levels of various angiogenic factors and receptors in SBA tissue compared to adjacent normal tissue and to normal SB tissue in controls. Following informed consent, patients aged 18-80 years of age undergoing double balloon enteroscopy for a variety of small bowel disorders at Tallaght hospital were invited to participate. From patients with SBA, one standard biopsy was taken from a single angiodysplasia lesion, and a further biopsy was taken from macroscopically adjacent normal mucosa. In controls, a single small bowel mucosal biopsy was taken at random. Biopsy samples were immediately placed in RNAlater solution and stored in a fridge overnight before being stored at -80°C for batch analysis. Using a standard technique, RNA was isolated and a reverse transcription reaction was performed on each sample using the Fermantas first strand cDNA synthesis kit (Thermo Scientific). The resulting cDNA was used in quantitative PCR reactions to determine the relative expression of Ang1, Ang2, Tie2, VEGF and TNF. Relative gene expression was calculated using the comparative cycle threshold (CT) method and was normalised to the control gene GAPDH. Statistical analysis was performed using SPSS version 20. Fold differences of each gene were expressed as a mean and compared between groups, with a p value of < 0.05 considered significant.
RESULTS: In total, 20 biopsy samples were collected; including 9 from angiodysplasia mucosa, 7 from adjacent normal mucosa, and 4 from normal mucosa in controls. Detectable levels of genes encoding Ang1, Ang2, Tie2, TNF and VEGF were found in all biopsy samples. There were significantly higher levels of Ang1 and its receptor Tie2 in angiodysplasia tissue compared to adjacent normal mucosa and to controls, with mean fold differences of 1.77 vs 0.82 and 0.81 for Ang1 ($p = 0.049$), and 1.66 vs 0.76 and 0.52 for Tie2 ($p = 0.02$) respectively. Levels of Ang2 appeared higher in angiodysplasias than both adjacent mucosa and controls, however; this was only statistically significant between the angiodysplasias and their adjacent mucosa ($p = 0.04$). There were no differences in levels of TNF or VEGF expression between any of the samples.

	Ang 1	Ang 2	Tie2	TNF	VEGF
Control	0.8175	0.5625	0.76	0.79	1.1
Angiodysplasia	1.7667	0.7333	1.66	0.82	1.1367
Patient normal tissue	0.8129	0.3957	0.9714	0.8057	1.4057
p value	<0.05	0.04	0.02	0.46	0.42

CONCLUSION: Expression of levels of genes encoding Ang1 and Ang2 and their receptor Tie2 are higher in the mucosa overlying small bowel angiodysplasias than unaffected mucosa. This further strengthens the identification of the angiopoietin pathway as a key factor in the pathophysiology of SBA formation.
Disclosure of Interest: None declared

P0533 WHAT IS THE LONG-TERM SAFETY OF A NEGATIVE CAPSULE ENDOSCOPY IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING?

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INTRODUCTION: Although capsule endoscopy (CE) is the investigation of choice in obscure GI bleeding (OGIB), the clinical outcomes of a negative capsule remain contradictory according to different studies.
AIMS & METHODS: The aim of the study was to compare the long-term outcome of patients with OGIB after a negative and a positive CE and identify risk factors for rebleeding.
Methods: Retrospective study of 173 patients who underwent CE for OGIB, from 2005 to 2013; patients with a follow-up time < 6 months were excluded. CE with no lesions or with lesions P0 (petechial lesions; mucosal congestion) or P1 (isolated erosions; small angiodysplasias) were considered negative. Rebleeding was defined as a documented fall in hemoglobin of 2 g/dL from baseline, evidence of melena or hematochezia, and the need for blood transfusion, at least 30 days after the index bleed.
We evaluated the demographic characteristics, type of OGIB (overt vs occult), medication, rebleeding rate after a negative and a positive CE, type of treatment (endoscopic/surgical) performed in patients with positive CE and the influence on rebleeding. Statistical tests: t-student, $\chi 2$.
RESULTS: The mean age was 61.7 years; 67% of patients underwent CE because of occult GIB; 54.3% of CE were negative; the mean follow-up time was 27 months ($\pm$ 23.4) and the overall rebleeding rate was 22.5%. The rebleeding rate after a negative CE was significantly lower than after a positive CE (16% vs 30.4%, $p = 0.024$). Patients who rebleed needed more transfusions of red blood cells (mean = 6.0) prior to CE when compared with those who did not rebleed (mean = 1.2, $p < 0.001$). Age, sex, anticoagulants or anti-agregants did not influence the rebeeding rate.
Almost 50% of patients with a positive study underwent endoscopic (56.4% - argon plasma coagulation) or surgical treatment (28.2%), with significantly lower rebleeding rate than patients who did not undergo any treatment (23.1% vs 37.5%, $p < 0.02$).
CONCLUSION: Conclusions: A negative CE study in patients with OGIB is associated with a low rate of recurrent bleeding in the long term (16%). It is reasonable to take an expectant approach with these patients, thus avoiding the need for unnecessary additional investigations. The endoscopic/surgical treatment decreases the rebeeding rate after a positive CE.
Disclosure of Interest: None declared

P0534 SMALL BOWEL CAPSULE ENDOSCOPY IN ELDERLY PATIENTS. INDICATIONS AND FINDINGS

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INTRODUCTION: Given the aging of the European population a growing number of elderly patients need to be subjected to small bowel capsule endoscopy. In our study we aimed to determine the indications and findings of patients aged > 80 years old subjected to small bowel capsule endoscopy in our Department, in comparison to those aged < 80 years old.
AIMS & METHODS: From March 2003 till August 2013, 3410 patients have been subjected to small bowel capsule endosopy (Given imaging) in our Department. Among them, 131 were > 80 years old. We analyzed the indications and findings of these patients in comparison to the rest of the patients subjected to the test.
RESULTS: Among the 131 patients aged > 80 years old, the 106 (80.9%) have been subjected to small bowel capsule endoscopy because of obscure gastrointestinal bleeding. The corresponding percentage for patients aged < 80 years old was 60.2%. The remaining patients have been subjected to the test because of suspected Crohn's disease (n = 9, 6.8%), chronic diarrhea (n = 9, 6.8%) and abdominal pain (n = 7, 5.3%). The corresponding figures for those patients aged < 80 years old were 21.7%, 3.7% and 4.3% respectively. The findings of the test in both age groups in cases of obscure gastrointestinal bleeding are presented in table 1. No patient aged > 80 years old had any complication due to the small bowel capsule endoscopy investigation.
Table 1. Findings of small bowel capsule endoscopy

	Patients > 80 years old	Patients < 80 years old
Angiodysplasias	86.3%	59.2%
Apthoid ulcers	0.9%	13.0%
Ulcerations	5.4%	12.0%
Polyps	2,7%	9.9%
Tumors	4,6%	5.8%

CONCLUSION: Small bowel capsule endoscopy in elderly patients is mainly done for the investigation of obscure gastrointestinal bleeding. The test appears to be safe in these cases and angiodysplasias are detected more frequently than in younger patients.
Disclosure of Interest: None declared

P0535 NON ANEMICS WITH EROSIVE GASTRITIS MORE FREQUENTLY PRESENT SMALL BOWEL ULCERATIVE LESIONS

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INTRODUCTION: Although erosive gastritis can cause iron deficiency anemia, its presence cannot prevent small bowel evaluation with capsule endoscopy.
AIMS & METHODS: Aim: To define the risk to find small bowel ulcerative lesions and anemia in patients with erosive gastritis.
Methods: 1010 patients undergone small bowel capsule endoscopy, gastroscopy and colonoscopy were evaluated. 537 were evaluated for iron deficiency anemia or recent obscure bleeding, 324 for diarrhea, 60 for unexplained abdominal pain and 89 for other causes. 176 patients excluded from the analysis, as they presented either inflammatory bowel disease or celiac disease and 81 because they presented a gastric or a duodenal ulcer, leaving a study population of 753 patients (mean age 64±16 years, 421 men, 159 active smokers). Erosive gastritis was present in 132 (mean age 65±15 years, 77 men, 32 active smokers). Stat: X2, logistic regression analysis.
RESULTS: 50 (38%) patients with erosive gastritis and 161 (26%) without presented small bowel erosions ($p = 0.006$). 27 (48%) patients with erosive gastritis consuming aspirin or NSAIDs and 50 (33%) NSAIDs consumers without erosive gastritis presented small bowel erosions ($p = 0.04$). 13 (41%) patients with erosive gastritis on clopidogrel and 23 (29%) clopidogrel consumers without erosive gastritis presented small bowel erosions ($p = 0.26$). Among patients not on antiplatelets, 10 (23%) with erosive gastritis and 88 (23%) without presented small bowel erosions ($p = 0.97$). Among anemics, 19 (42%) patients with erosive gastritis consuming aspirin or NSAIDs and 44 (34%) NSAIDs consumers without erosive gastritis presented small bowel erosions ($p = 0.04$). 12 (30%) patients with erosive gastritis on clopidogrel and 18 (28%) clopidogrel consumers without erosive gastritis presented small bowel erosions ($p = 0.26$). No patient with erosive gastritis not consuming antiplatelets and 40 (20%) without erosive gastritis presented small bowel erosions ($p = 0.048$). In logistic regression analysis old age, erosive gastritis, AF and use of aspirin were related with increased risk for small bowel ulcerative lesions and diabetes with reduced risk.
CONCLUSION: Non anemics with erosive gastritis are at risk for small bowel erosions, especially if they consume aspirin or NSAIDs, because small bowel mucosa is possibly more vulnerable to noxious stimula. On the other hand, among anemics erosive gastritis was related with less small bowel ulcerative lesions among no antiplatelet consumers. Possibly because erosive gastritis is an independent cause of iron deficiency anemia.
Disclosure of Interest: None declared

P0536 PATIENTS WITH ATRIAL FIBRILLATION ON CLOPIDOGREL ARE AT HIGH RISK TO DEVELOP SMALL BOWEL ULCERATIVE LESIONS AND ANEMIA

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INTRODUCTION: Patients with atrial fibrillation are usually on antiplatelet treatment or anticoagualants.
AIMS & METHODS: Aim: To define the risk to find small bowel ulcerative lesions and anemia in patients with atrial fibrillation on antiplatelet or anticoagulant treatment.
Methods: 1010 patients undergone small bowel capsule endoscopy, gastroscopy and colonoscopy were evaluated. 537 were evaluated for iron deficiency anemia or recent obscure bleeding, 324 for diarrhea, 60 for unexplained abdominal pain and 89 for other causes. 176 patients excluded from the analysis, as they presented either inflammatory bowel disease or celiac disease, leaving a study population of 834 patients (mean age 64±16 years, 476 men, 176 active smokers). Atrial fibrillation (AF) presented 78 patients (mean age 76±7 years, 41 men, 8 active smokers). Stat: X2, logistic regression analysis.
RESULTS: 246 (29%) patients presented small bowel ulcerative lesions; 164 (31%) anemic and 78 (26%) non-anemic ($p = 0.19$). 33 (42%) AF patients and 213 (28%) without AF presented small bowel ulcerative lesions. Small bowel ulcerative lesions were present in 14 (48%) AF aspirin/NSAID users, 13 (42%) AF clopidegrel consumers and 6 (33%) AF patients not receiving antiplatelets. In addition they were present in 132 (38%) aspirin/NSAID users without AF ($p = 0.31$), 23 (29%) clopidogrel consumers without AF ($p = 0.02$) and 109 (23%) patients without AF not receiving antiplatelets ($p = 0.33$). Thus small bowel ulcerative lesions were more common among aspirin users without AF ($p = 0.001$), but not those with AF ($p = 0.41$). Moreover there was no difference between aspirin and clopidogrel (AF: $p = 0.62$; no AF: $p = 0.14$). Among anemics small bowel ulcerative lesions were present in 14 (56%) AF aspirin/NSAID users, 14 (47%) AF clopidegrel consumers and 2 (17%) AF patients not receiving antiplatelets. In addition they were present in 67 (37%) aspirin/NSAID users without AF ($p = 0.08$), 17 (27%) clopidogrel consumers without AF ($p = 0.02$) and 109 (22%) patients without AF not receiving antiplatelets ($p = 0.33$). Thus small bowel ulcerative lesions were more common among aspirin users with ($p = 0.02$) and without AF ($p = 0.0006$). Moreover there was no difference between aspirin and clopidogrel (AF: $p = 0.49$; no AF: $p = 0.13$). In logistic regression analysis old age, erosive gastritis, AF and use of aspirin were related with increased risk for small bowel ulcerative lesions and diabetes with reduced risk.
CONCLUSION: Small bowel ulcerative lesions are more common among aspirin users. Clopidogrel is generally safer, nevertheless both presence of anemia and small bowel ulcerative lesions are more common among patients with atrial fibrillation, possibly because small bowel mucosa is more vulnerable to develop inflammatory lesions in this patient group.
Disclosure of Interest: None declared

P0537 REDUCTION OF NSAID-INDUCED SMALL INTESTINAL DAMAGE IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING SULFASALAZINE

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INTRODUCTION: Recent studies have demonstrated that nonsteroidal anti-inflammatory drugs (NSAIDs) often cause damage to the small intestine, and NSAID-induced enteropathy is mediated by different inflammatory cytokines. Sulfasalazine is being widely used in patients with rheumatoid arthritis (RA), and this drug have the potential to induce mucosal healing in patients with intestinal diseases such as inflammatory bowel diseases.
AIMS & METHODS: To evaluate the preventive effect of sulfasalazine against small intestinal damage due to chronic NSAID use in RA patients. Between March 2009 and June 2011, capsule endoscopy was performed in 51 consecutive RA patients who received NSAIDs for more than 3 months with or without sulfasalazine therapy over a period of 3 months. The findings were scored as follows according to the method described by Graham et al. (Clin Gastroenterol Hepatol. 2005): 0, normal; 1, red spots; 2, 1 to 4 erosions; 3, >4 erosions; and 4, large erosions/ulcers. Scores of 3 and 4 indicated severe damage. The relationship between the use of sulfasalazine therapy and risk of severe damage (score 3 or 4) or severest damage (score 4) were assessed using multiple logistic regression.
RESULTS: Comparative data were analyzed for 47 patients, and 4 patients were excluded because the entire small bowel could not be visualized in these patients. Of the 25 patients who did not receive sulfasalazine therapy, 12 (48%) had severe damage (score of 3 [n = 8] or 4 [n = 4]). On the other hand, of the 26 patients receiving sulfasalazine therapy, 5 (19.2%) had severe damage (score of 3 [n = 3] or 4 [n = 2]). On stratifying the patients by sulfasalazine therapy, we obtained a crude odds ratio (OR) of 0.26 for severe damage with a 95% confidence interval (CI) of 0.10 to 0.66, and of 0.38 for severest damage with a 95% CI of 0.17 to 0.88. This effect of sulfasalazine therapy on NSAID-induced enteropathy remained robust to adjustment for age, gender, history of peptic ulcers, disease activity score-28 (a disease activity index for RA), use of selective cyclooxygenase-2 inhibitors or steroids, blood hemoglobin concentration, and all these variables, with the adjusted ORs for severe damage ranging from 0.19 to 0.25 and those for severest damage ranging from 0.30 to 0.40.
CONCLUSION: Sulfasalazine therapy may protect against NSAID-induced small intestinal damage in RA patients and may be effective in the treatment of NSAID-induced enteropathy.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00-17:00
NUTRITION I - POSTER EXHIBITION - HALL XL

P0538 IS THE TRADITIONAL DIET DISAPPEARING AT THE SAME TIME AS THE PREVALENCE OF OBESITY IS INCREASING IN ITALY? EVALUATION OF EATING HABITS IN A GROUP OF ITALIAN OBESE FEMALE PATIENTS

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INTRODUCTION: The nutrition transition from traditional to Western dietary patterns could account for the dramatic rise in the prevalence of obesity in Italy (1).
AIMS & METHODS: We describe the dietary patterns in a group of obese Italian female patients. A retrospective survey was conducted on the records of 113 obese (BMI 40.2±7.0 kg/m2) female inpatients aged 19-60 y (mean 40.5 y). Anthropometric measurements and dietary patterns were obtained from the records. Dietary habits were recorded by detailed questioning and computed database determined the nutrient intakes. The recommended dietary allowances (RDAs) for the Italian population were used as the reference range. The sample was also divided, according to age, into three groups (19-35y, 36-45y, 46-60y). Statistical analysis was performed by PASW 18.0.
RESULTS: The table shows the variations, as percentages, of the nutrient intakes over or below the RDAs. The values are expressed as 50^{th} (25^{th}, 75^{th}) percentile. Animal protein intakes averaged 266% over the RDAs in the whole sample, with median variations from 241 to 278% among the age groups. The intake rates of total carbohydrates (CHO) were minimally higher on average (15-19%) than the RDAs. The simple CHO intake averaged 67-90% over RDAs. The ω-6/ω-3 fatty acid ratio was about 100% over the RDA, without significant differences among age groups. Moreover the intakes of ω-6 fatty acids was 64% over the RDA, but in the younger group the variation rate from the RDA was significantly higher (72%, $p < 0.05$) than in the older group (50%). Nutrients with protective effects, such as PUFA and ω-3 fatty acids, averaged 35-48% and 11-19% below RDAs, respectively.

Nutrient intakes	RDAs (g)	all (113)	19-35 y (37)	36-45 y (36)	46-60 y (40)
Protein	64 (59, 66)	100 (71, 132)	95 (75, 108)	119 (70, 166)	112 (80, 130)
Animal Protein	74 (55, 100)	266 (171, 349)	241 (171, 316)	248 (164, 385)	278 (214, 354)
Fat	136 (112, 165)	129 (88, 175)	151 (113, 175)	129 (85, 195)	118 (80, 162)
PUFA	10 (7, 13)	-44 (-57, -23)	-35 (-53, -15)	-35 (-57, -19)	-48 (-59, -31)
ω-3	1.2 (1.1, 1.3)	-16 (-34, 11)	-11 (-28, 44)	-19 (-43, 8)	-18 (-34, 9)
ω-6	4.8 (4.6, 5.3)	64 (27, 123)	72 (42, 164)	74 (27, 126)	50 (23, 90)
ω-6/ω-3	4	100 (66, 123)	89 (49, 119)	102 (69, 133)	102 (67, 123)
Total CHO	363 (347, 380)	19 (2, 40)	19 (-2, 42)	31 (9, 51)	15 (-2, 28)
Simple CHO	69 (66, 72)	84 (27, 146)	90 (32, 142)	84 (14, 166)	67 (33, 117)

CONCLUSION: We observed that the highest variation rates were not found for total carbohydrates or simple carbohydrates, as could be expected, but for fat and protein, and especially for animal protein. Moreover the excessive consumption ω-6 fatty acid, with unbalanced ω-6/ω-3 fatty acid ratio, could show a tendency to change the traditional Italian diet towards Western eating habits. However there was no significant difference between younger and older people.

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Disclosure of Interest: None declared

P0539 CAN INTERVENTION ON LIFESTYLE HAVE AN IMPACT ON CARDIORESPIRATORY FITNESS IN THE NON-OPERABLE SEVERELY OBESE PATIENT?

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INTRODUCTION: Severe obesity (BMI > 40 kg/m^2 or 35 kg/m^2 and complications) is associated with higher frequency of comorbidities such as respiratory failure and higher premature mortality compared to less obese patients. Diet change, physical exercise and lifestyle modifications are the only therapeutic options for a substantial proportion of patients. The literature on cardiorespiratory fitness in these patients is sparse.

AIMS & METHODS: To examine whether or not a systematic rehabilitation program providing lifestyle intervention has a significant positive impact on cardiorespiratory fitness in the non-operable severely obese patients.

Forty non-operable severely obese patients (F 29, M 11, mean age 44 y, range 23-62 y) were consecutively enrolled in a rehabilitation program. In total 33 patients stayed in the program 12 months after enrolment, but 6 of them did not complete all tests due to acute illness. Eligible for enrolment was patients in groups of 12-15, in all 4 groups. The first stay lasted 4 weeks, the consecutive stays 2 weeks every 6 months. At each stay a team of nurses, physician, dietician, psychologist and physical activity therapist provided education and physical exercise to each patient individually or to patients assembled as a group, including matched patient's conversations. At enrolment patients were classified as respiratory healthy or as having chronic respiratory illness. Furthermore at the beginning of each stay body weight, peak oxygen uptake (VO_2peak) and functional residual capacity % (FRC %) were registered and body mass index (BMI) calculated. The test was performed on a treadmill programmed in a standard fashion regarding velocity and inclination. All tested patients reached anaerobic threshold (VO_2peak).

Mean ± standard deviation are reported at inclusion and one year after inclusion. FRC% is regarded normal above 80 %.

RESULTS: We report on cardiorespiratory fitness in 27 patients (F 19, M 8, mean age 45 y, range 23-62) 12 months beyond baseline. Ten patients were respiratory healthy and 17 had respiratory illnesses; asthma (N = 4), chronic obstructive lung disease (N = 1) and obstructive sleep apnoea syndrome (N = 12). Body weight: 125.5 ± 21.7 kg vs 120.1 ± 23.1 kg, p = 0.004. BMI: 42.1 ± 3.9 kg/m^2 vs 40.6 ± 5.2 kg/m^2, p = 0.016. FRC%:76.9 ± 12.1 % vs 80.4 ± 13.8 %, p = 0.069. VO_2peak during exercise: 22.7 ± 3.0 ml*kg^{-1}min^{-1} vs 24.0 ± 4.5 ml*kg^{-1}min^{-1}, p = 0.032.

CONCLUSION: We found a significant improvement in cardiorespiratory fitness in a group of 27 non-operable severely obese patients that participated in a systematic rehabilitation program for one year. Our results should be verified in larger scale studies. This would also make it possible to stratify patients according to respiratory health.

Disclosure of Interest: None declared

P0540 THE RELATIONSHIP BETWEEN OSTEOPOROSIS AND LEPTIN IN OBESE FEMALES

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INTRODUCTION: The pathogenesis of decreased bone mineral density (BMD) in NAFLD is unclear. Hyperleptinemia, hormone mainly secreted by white adipose tissue, is associated with inflammatory process, suppress bone formation and increase bone resorbtion. Aim of our study was to correlate leptin level with decreased BMD in obese females.

AIMS & METHODS: We included obese females in postmenopausal period for at least 1 year: 54 with NAFLD and 56 without NAFLD, age, waist circumference (WC) and body mass index (BMI) matched. Exclusion criteria: diabetes mellitus, chronic use of corticosteroids, supplementation with calcium products, secondary obesity due endocrine diseases, renal disease, alcohol intake, smoking, previous fractures. Blood samples were collected in both groups for lipid profile, hepatic enzymes and leptin (references values 4.9-24ng/ml). Lumbar BMD was measured by DEXA and abdominal ultrasonography was performed by the same physician and steatosis was graded using a semi-quantitative scale of 1 (mild) to 3 (severe).

RESULTS: In NAFLD group mean age was 49.5 years, BMI 32,5±3 and WC 99±5cm, in second group mean age was 51,3 years, BMI 30,3±3 and WC 97±5, without statistic significance between the two groups. In NAFLD group 24 females had mild steatosis, 18 had moderate and 12 had severe steatosis. No evidence of steatosis in group B. Leptin level was 8.7ng/ml±1.2 in group B and 15.2ng/ml±5.1 in NAFLD group, with significance statistic differences between the two groups. In NAFLD group we found 9 patients with normal T score, 21 patients with osteopenia and 24 with osteoporosis. In group B we found 15 patients with normal T score, 25 with osteopenia and 16 with osteoporosis. BMD was lower in NAFLD women than these without NAFLD and osteoporosis in NAFLD group seemed to be associated a more severe liver disease. In NAFLD group the highest levels of serum leptin were found in moderate or severe steatosis with osteoporosis and we found a positive correlation with BMI and WC (p = 0.000 and p = 0.002). In the other group, leptin level had no significant differences in relationship with BMI, WC or decreased BMD.

CONCLUSION: In our study, leptin level was correlated with osteoporosis in NAFLD group. In obeses females without NAFLD, leptin level was similar despite the presence or absence of osteoporosis.

Disclosure of Interest: None declared

P0541 ENDOSCOPIC REMOVAL OF GASTRIC BANDS – A HEAVY ISSUE

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INTRODUCTION: One of the most popular methods in bariatric surgery is the gastric band. However, its migration into the gastric lumen has frequently been described as a long-term complication. There is no consensus on how to handle such cases, but its removal through endoscopy is increasingly being documented as a safe and effective alternative. The authors present a Gastroenterology department 5-year experience.

AIMS & METHODS: To describe our experience in a relatively novel endoscopic technique useful to handle a common bariatric surgey complication.
Review of clinical files and endoscopic imaging.

RESULTS: A total of eight procedures were undertaken in morbidly obese female patients (average age: 38.7 years old). Median time between initial surgery and band removal was about 69±31.9 months. Clinical manifestation was weight increase in 5 patients and upper abdominal pain in the remaining three. All cases were diagnosed through upper digestive endoscopy.

During such procedures, a 0.035 inch guidewire and a Soehendra lithotripter were used to cut through the band, which was then pulled with a polypectomy snare. Extraction of the cutaneous port was done by the assisting surgeon. Average duration of the procedure was about 30 minutes.

A peritoneal leak was the only major complication, due to the passage of air from the stomach lumen to the peritoneum through the band internal canal.

CONCLUSION: Considering the high number of gastric band procedures undertaken in the last few years, its intra-gastric migration will be a common clinical issue. This endoscopic approach, although technically demanding, is a safe and effective alternative, thereby avoiding morbidity associated with a major surgical intervention.

Disclosure of Interest: None declared

P0543 FIRST REPORTS OF THE NEW SPATZ 3 ADJUSTABLE BALLOON SYSTEM

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INTRODUCTION: The original Spatz Adjustable Balloon System for weight loss was introduced in 2010. It was the first intragastric balloon approved for 1 year implantation with the added feature of balloon volume adjustability. This enabled changes to balloon volume during the course of the 1 year implantation period. It contained a rigid catheter and metal chain that caused duodenal migration. The new Spatz 3 intragastric balloon device, CE Mark approval in 2012, has a soft catheter to simplify the procedure and decrease complications. In addition, reports of volume adjustments using a mean 177 ml yields additional 1.7 kg/month wt loss. It has been suggested that adjusting with larger volumes will yield better results. We report our experience with the Spatz 3 device in 7 centers.
AIMS & METHODS: To determine the difference between the reported results of the original Spatz Adjustable balloon System and the new Spatz3 Adjustable balloon System with respect to ease of use, complications, weight loss results and the effect of larger volume adjustments. 158 patients with mean BMI 40.1; mean weight 109 kg; mean age 37; were implanted with the Spatz3 device. Mean balloon volume was 473 ml (400-600). Adjustments were made for intolerance or weight loss plateau.
RESULTS: All endoscopists felt that the Spatz 3 device was easier to use than the original Spatz adjustable balloon system device. Mean wt loss at 12 weeks was 12.5 kg with an 11.7% wt loss and 28.8 % EWL (% excess wt loss). At 24 weeks mean wt loss was 16,2 kg; 16.7% wt loss, and 35,3 % EWL. 94 patients reached 9 months with a reported mean wt loss of 23.2 kg; 20.4 % weight loss; and 44.9 % EWL. And 48 patients after 12 months with mean wt loss of 24.1 kg; 20.6 % weight loss; and 48.1 % EWL. There were 49 balloon volume adjustments: 11 downward adjustments of 100 cc alleviated early intolerance, with added mean wt loss of 15.3 kg after the adjustment; 38 upward adjustments (mean 327 ml; range 150-500) at a mean month 4,1 yielded additional mean wt loss of 8.7kg after the adjustment. 7 balloons were extracted; early intolerance and refusal to adjust volume downward (4); gastric ulcer (2); deflation (1).
CONCLUSION: The Spatz 3 adjustable balloon is easier and less complicated than the original Spatz device. Complications associated with the original catheter have not been seen in the Spatz 3 device. Larger volume adjustments yield greater weight loss results.
Disclosure of Interest: E. Machytka: None declared, Z. Kowalczyk: None declared, S. Al Awadhi: None declared, M. Al Falasi: None declared, J. Mason: None declared, L. Bene: None declared, S. El Asala: None declared, V. Puig-Divi: None declared, M. Buzga: None declared, J. Brooks Shareholder of: Spatz FGIA

P0544 WEIGHT MAINTENANCE 2 YEARS AFTER EXTRACTION OF THE SPATZ ADJUSTABLE BALLOON

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INTRODUCTION: The Spatz Adjustable Balloon System was developed to provide an adjustable intragastric balloon approved for 1 year implantation. Weight loss results > 20 kg/year have been reported in the literature. The question is whether treatment with an intragastric balloon also leads to better weight loss maintenance after balloon removal. A prospective study on the BIB balloon has reported maintenance of > 10% weight loss in 25% of patients for up to 2.5 years after BIB balloon removal.
AIMS & METHODS: 79 patients from 3 centers who were implanted with the Spatz Adjustable Balloon for 1 year were contacted and asked to provide their weight 1 year and 2 years post balloon extraction. Net weight changes were recorded, and % weight loss was calculated based on weight prior to balloon implantation. Net weight loss > 10% was considered successful weight maintenance.
RESULTS: 70 of the 79 patients contacted (88.6%) were responsive in providing their weight data. The group's data at the original implantation was as follows: mean weight 120.3 kg (80-180); mean BMI 38.8 (30-65). At the time of balloon extraction (12 months) the group's mean weight loss was 24 kg with a 23.8% weight loss. All of the 70 patients had reached at least 12 months post Spatz balloon extraction. Fifty three of the seventy (75.7%) retained at least 10% weight loss at 1 year post balloon extraction. 34 of the 70 patients had reached 2 years post extraction, and 26 (76.4%) retained at least 10% weight loss. The group's mean weight change was +6.7 kg at 1 year and +3.4 kg at 2 years after balloon extraction.
CONCLUSION: The maintenance of > 10% Weight loss at 1 year and 2 years after Spatz Adjustable Balloon extraction has been retrospectively documented in 75.7% and 76.4% of patients, respectively. This study is limited by its retrospective review and the small numbers in year 2 and requires prospective review to confirm these findings. Nonetheless, it suggests a long term benefit to longer implantation time and/or adjustable balloon function and warrants further study.
Disclosure of Interest: None declared

P0545 SACCHAROMYCES BOULARDII ADMINISTRATION CHANGES GUT MICROBIOTA AND REDUCES HEPATIC STEATOSIS, LOW GRADE INFLAMMATION AND FAT MASS IN OBESE AND TYPE 2 DIABETIC DB/DB MICE

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INTRODUCTION: Obesity and type 2 diabetes are associated with an altered gut microbiota and inflammation. Growing evidence suggest that the gut microbiota is involved in the regulation of energy homeostasis. We and others have shown that gut microbiota modulation using prebiotics constitute an interesting target in the physiopathology of obesity.
AIMS & METHODS: So far, probiotic yeast have not been investigated in this context. The aim of this study is to evaluate the role of the most studied probiotic yeast (i.e., *Saccharomyces boulardii* Biocodex) on obesity and associated metabolic disorders. *S. boulardii* was administrated daily by oral gavage to leptin-resistant obese and type 2 diabetic mice (*db*/*db*) for 4 weeks.
RESULTS: We found that *S. boulardii* treated mice exhibited reduced body weight, hepatic steatosis, fat mass and both hepatic and systemic inflammation. These effects were associated with local effects in the intestine, such as an increased caecum weight and caecum tissue weight. Importantly, we also found that *S. boulardii* induced dramatic changes in gut microbial communities at the phylum, family and genus levels. We also found that microbial changes in response to *S. boulardii* were correlated with host metabolism response.
CONCLUSION: In conclusion, our study demonstrated that *S. boulardii* acts as a beneficial probiotic treatment in the context of obesity and type 2 diabetes.
Disclosure of Interest: L. Geurts: None declared, A. Everard: None declared, S. Matamoros: None declared, N. Delzenne: None declared, P. Cani Financial support for research from: Biocodex

P0546 CORRELATION BETWEEN DIET AND NON-ALCOHOLIC FATTY LIVER DISEASE: INVESTIGATION OF A COHORT OF ITALIAN PATIENTS

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INTRODUCTION: The Western diet is characterized by a high-energy intake, saturated fats and refined sugars. Excess calorie intake, associated with reduced physical activity, leads to obesity, type 2 diabetes mellitus, cardiovascular disease and non-alcoholic fatty liver disease (NAFLD).
AIMS & METHODS: Within the FP7 - European FLIP (Fatty Liver Inhibition Program) program we tried to investigate the role of diet in NAFLD, in a large cohort of patients from three different Italian Centers (Modena, Bologna and Turin). We used the EPIC questionnaire to investigate energy intake (Ei) and intake of food in a well-characterized series of 163 NAFLD patients. Anthropometric measurements, blood tests, insulin resistance, liver ultrasound (Hamagouchi score) and liver stiffness were analysed. Nutrient intakes were compared with Italian reference values.
RESULTS: The daily intake of simple sugars (18.4% *vs.* a reference intake <15%), saturated fats (12% *vs.* <10%) and the ratio between animal proteins/vegetal protein in the diet (68% *vs.* <50%) was higher than recommended, whereas the fiber intake was lower (19g *vs.* 25g). In the patients, a significant direct correlation ($p<0.005$) was observed between BMI, waist circumference, insulin resistance, transient elastography values, Hamagouchi score, and lipid intake.
CONCLUSION: The dietary intakes of NAFLD patients are systematically different from the recommended daily intakes for the Italian population. In particular the higher-than-recommended intake of simple sugars might be one of the possible causes of NAFLD (Supported by FLIP Project, (FP7/2007–2013) under grant agreement no. HEALTH-F2-2009-241762).
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Disclosure of Interest: None declared

P0547 FOOD INTOLERANCE AND OBESITY: NEW STRATEGY IN THE TREATMENT OF OBESITY

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INTRODUCTION: Challenges associated with the treatment of obesity still remain high, in spite of efforts made by professionals combating the public health issue. A low-calorie diet, which is considered as the most effective

treatment, is hard for many patients to incorporate due to the discomfort brought by hunger. An effective treatment should focus on increasing the quality of a patient's life, by creating a treatment that reduces symptoms associated with obesity, while allowing patients to not experience hunger during the treatment period.
AIMS & METHODS: The aim of the study was to compare the difference in effectiveness between the traditional low-calorie diet and the elimination diet. A Survey was completed by 60 patients, 30 women and 30 men, with the average age 37.6 ± 4.7 years. In addition to routine methods of investigation, all patients were analyzed on food intolerance using the FED- test, which is based on the immunetermistometrical principle, a new term we used to describe the conductivity and viscosity change in the blood after making contact with certain food extract. The FED- test uses 96 different food extractions to evaluate food intolerance. To evaluate the improvement of a patients condition, questionnaires were used before and after the treatment to receive any complaints patients had throughout the treatment period. Information about complaints was assessed on a Harington scale of a unit from 1 (no symptoms) to 0.1 (maximum symptom). Patients were divided into 3 equal groups - overweight, and 1 or 2 class obesity. Each group was divided into two subgroups. Patients in the (A) subgroup were on a low-calorie diet: 1200-1600 Kcal, depending on the age, sex, and physical activity. Patients of the (B) sub-group were on the individual eucalorie (with normal energetic value) elimination diet, based on the results from the FED- testing.
RESULTS: 1. The influence that the type of diet had on weight reduction. Among the first two groups with overweight patients, greater weight loss was observed in those patients who adhered to the elimination diet. The difference in BMI accounted for 0.776 ± 0.222 kg \ m2 in the group A and 1.788 ± 0.449 kg/m2 in the group B. In obese patients, the following similar results were observed: in the elimination diet weight loss was 3.764 kg \ m2 and 4.065 kg \ m2 in in patients with class 1 and 2 obesity accordingly. In low-calorie diet, BMI reduction was 1.291 kg \ m2 and 2.280 kg \ m2 in patients with class 1 and 2 obesity accordingly.
2. Improvements in patients' condition. On the elimination diet improvement of the patient's condition amounted to 0.292 in the obese group, and 0.222 in the overweight group. In groups in which patients followed the low-calorie diet, no significant dynamics in the state of the patients were observed: 0.046 in a group of obese patients and 0.034 patients in the overweight group.
CONCLUSION: Under the influence of elimination diet BMI reduction was significantly better in patients with 1 and 2 class obesity compared to the dynamics of BMI on the standard low-calorie diet ($p = 0.0037$). Between groups of patients who were overweight, no significant differences were found ($p = 0.087$).
The patients' quality of life after 6 months of treatment differed significantly in subgroups of those treated with the elimination diet, compared to the subgroups of those that received the standard low-calorie diet treatment ($p = 0.004$).
Disclosure of Interest: None declared

P0548 ARGON PLASMA FULGURATION TO TREAT WEIGHT REGAIN AFTER BARIATRIC SURGERY

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INTRODUCTION: The weight regain is a problem after bariatric surgery and occurs, in part, by dilatation of the gastro-jejunal anastomosis, which causes a faster gastric emptying and increased food intake.
AIMS & METHODS: Objective: To evaluate the efficacy of endoscopic fulguration of the anastomosis and of the gastric stump using argon plasma (APF) aiming to reduce the diameter thereof.
Methods: We analyzed 32 patients. 30 of them underwent at least 02 sessions of FPA. Two patients underwent only one session due to an immediate reduction of the anastomosis to a diameter smaller than 10 mm after the first session, wich is the procedure target. The coagulation was held at the anastomosis and in gastric stump. 80 w power was used in the 1st session, and 70w power FPA in the following, with an Agon flow of 2L/min. The objective is to obtain an anastomosis with a diameter less than or equal to 10 mm. Data were analyzed with descriptive statistics, student's t test and Spearman correlation.
RESULTS: Of the 32 patients, 87.5 % were women ($n = 28$). The mean regained weight in relation to the maximum weight lost (Nadir) after bariatric surgery was 46.9 % (14 to 76.9). The mean duration of treatment was 170 days (56-338). There was a significant reduction in body mass index (BMI) at the end of the analysis (32.42±4.45 kg/m2) compared to the initial mean BMI (mean BMI = 37.05±4.76 kg/m2) ($p < 0.0001$). The average loss of the regained weight was 66.92% (22.08-211.11). The average weight loss in Kg was 12.73 (6.3-25.5). There was significant correlation between the reduction in the BMI and the highest number of sessions of FPA ($p = 0.0003$) and between the longer duration of the treatment ($p = 0.0212$). The analyzed patients remain in treatment.
CONCLUSION: The FPA has demonstrated great efficacy in the treatment of weight regain after bariatric surgery of gastric bypass in Roux-Y.
Disclosure of Interest: None declared

P0549 ANALYSIS OF 1973 PATIENTS SUBMITTED TO ENDOSCOPIC TREATMENT OF EXCESS WEIGHT WITH AN INTRAGASTRIC BALLOON

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INTRODUCTION: Endoscopic methods, especially the intragastric balloon (IGB), have been shown to be effective for the treatment of excess weight.
AIMS & METHODS: OBJECTIVE: To assess the efficacy and complications of excess weight treatment with an IGB in patients seen at the Endogastro Med Service clinic, Gastro Obeso Center and Sander clinic.
METHODS: A total of 1973 patients were analyzed. An Allergan IGB (BIB®) with a volume of 600 to 700 ml was used. The patients had a minimum initial body mass index (BMI) of 27 kg/m2 and were followed up by a multidisciplinary team consisting of a nutritionist, a doctor and a psychologist. For statistical analysis, the patients were divided into groups according to sex and degree of excess weight (overweight and grade I, II and III obesity). Data were analyzed using descriptive statistical methods, the Student t-test, and analysis of variance followed by the Tukey post-test. The level of significance was set at $p < 0.05$.
RESULTS: 107 patients were excluded from the analysis: 70 (3.55%) due to early IGB removal, 13 (0.66%) due to absence of weight loss, 14 (0.71%) due to weight gain, and 10 (0.51%) due to incomplete data. The incidence of fungus was 0.2% ($n = 4$) and the incidence of leakage was 0.25% ($n = 5$), pregnancy was 0.1% ($n = 2$); Wernick Korsakoff syndrome due to excessive vomiting was 0.05% ($n = 1$), gastric perforation and upper digestive bleeding was 0.05% each ($n = 1$). Of the 1866 remaining patients, 1402 were women and 464 were men. Mean age was 37.32 years. The patients showed a significant weight loss, with a significantly lower final BMI (mean: 28.93±4.71 kg/m2; range: 18.98-57.38) than the initial BMI (mean: 36.47±5.61 kg/m2; range: 27-74.74) ($p < 0.0001$). Mean BMI reduction was 7.55±3.49 kg/m2 (range: 0.36-29.79). Mean percent weight loss was 20.43±7.82% and mean percent excess weight loss (EWL) was 73.48±36.71% (range: 2.22-431.1). Percent EWL was higher in the overweight group, followed by obesities grades I, II and III sequentially ($p < 0.0001$). Percent EWL was also higher in women than in men ($p < 0.0001$).
CONCLUSION: Endoscopic treatment of excess weight with an IGB has been established as an excellent therapeutic option for patients of both genders with overweight or different degrees of obesity.
Disclosure of Interest: None declared

P0550 PREDICTIVE RISK FACTORS FOR SUCCESS OF BARIATRIC THERAPY WITH BIOENTERICS INTRAGASTRIC BALLOON

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INTRODUCTION: In obese patients, a large amount of data shows that bariatric therapy with Bioenterics intragastric balloon (BIB) results in weight loss in some patients. However there is a paucity of data about predictive risk factors for BIB success.
AIMS & METHODS: The aim of this study was to determine the effectiveness of this device on weight loss and predictive risk factors for BIB success. A prospective study with 147 patients [(75.5% females, mean age 40 (±11.9)] submitted to BIB insertion, which was removed after 41.4 (±12.7) weeks. Anthropometric and laboratory parameters were assessed when BIB was positioned and when BIB was removed. BIB success was defined as weight loss ≥ 50% of the weight excess (pre BIB weight – calculated weight to lower the BMI to 24.9).
RESULTS: At baseline, mean weight was 97.2 Kg (± 16.1), mean body mass index (BMI) was 36.5 (±5.9) kg/m2, 19 (12.9 %) patients had type II Diabetes Mellitus and mean insulin resistance (HOMA-IR) was 2.9 (± 2). With BIB intervention, mean weight and mean BMI decreased, respectively, to 83.5 (± 16.9), $p < 0.001$ and 31.4 (±6.3), $p < 0.001$. Regarding laboratory parameters, cholesterol, triglycerides and HOMA-IR were significantly reduced ($p < 0.05$). There was no significant improvement in TGP, G-GT, HDL cholesterol and ferritin. BIB success was observed in 57 (38.8%) patients. Predictive risk factors for BIB success were mean pre-operative weight, 92.8 (±13) vs 99.7 (± 16.9)kg, $p = 0.011$ and mean pre-operative BMI, 35 (±3.5) vs 37.5 (±6.9), $p = 0.007$; a trend was observed for baseline HOMA-IR, 2.7 (±2.3) vs 3 (±1.7), $p = 0.056$.
CONCLUSION: BIB therapy achieves significant weight loss and significantly improves laboratory parameters of the metabolic syndrome in obese patients. BIB success is associated with baseline weight and baseline BMI further emphasizing that the endoscopic technic has major impact in mild obese, those that are not surgical candidates.
Disclosure of Interest: None declared

P0551 PREOPERATIVE ENDOSCOPY IN ASYMPTOMATIC BARIATRIC PATIENTS – IS IT STILL WORTH IT?

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INTRODUCTION: Obesity represents a major public health problem associated with increased risk of diabetes, cardiovascular and cerebrovascular disease and cancer. Surgery has shown to be an effective long term treatment. Preoperative endoscopy (POE) is recommended by the current "guidelines", but evidence supporting this recommendation in asymptomatic patients is scarce.
AIMS & METHODS: We sought to determine whether endoscopic findings justify routine POE before bariatric surgery. Obese (BMI > 30 kg/m2) and morbidly obese (BMI > 35 kg/m2) patients undergoing endoscopy in our institution were retrospectively selected. Endoscopic and histological findings and their impact on surgical strategy were assessed.
RESULTS: Of 557 patients (78.3 % female, mean age 46.9±11.5 years), 43.3 % had a normal endoscopy. Esophageal, gastric and duodenal disease were present in 22.6 %, 44.2 % and 11.0 % respectively. The most frequent esophageal findings were hiatus hernias (17.2 %) and esophagitis (8.0 %, 97.5 % Class A and B of Los Angeles). Gastric changes included erosive (18.3%) and non-erosive gastritis (19.7%), polyps (4.8%) and ulcers (1.6%, all Forrest III). Bulbitis (10.4%), ulcers (0.5%) and polyps (0.2%) composed most common duodenal findings. From a total of 218 gastric biopsies 46.3% revealed the presence of Helicobacter pylori (Hp) bacilli. In 3 patients Barrett's esophagus was diagnosed (without dysplasia) and in 2 gastric low grade MALT lymphoma (which regressed after eradication of Hp).
CONCLUSION: Our findings were of little relevance and did not alter the operative strategy. Given the high prevalence of Hp, which has been associated with higher postoperative complications, its screening by non-invasive methods prior to surgery may be a less expensive alternative. This study suggests that EPO might be dispensable in asymptomatic bariatric patients.
Disclosure of Interest: None declared

P0552 MODIFIED PROBIOTIC ESCHERICHIA COLI NISSLE INCREASES COLONIC SHORT CHAIN FATTY ACIDS AND FECAL BIFIDOBACTERIA AND LACTOBACILLI COUNT IN RATS

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INTRODUCTION: Short Chain Fatty Acids (SCFAs) are considered as one of the most important metabolite produced by commensal organism in the gut. Dietary consumption of complex carbohydrates such as inulin, fructo-oligosaccharides and sodium gluconate are known to increase SCFAs in the colon. However, they limit in their efficacy if not consumed daily. *E. coli* represents a major commensal population the human colon. *E. coli* expresses an apo- form of membrane bound enzyme, glucose dehydrogenase, which converts glucose to gluconic acid. However, it is unable to synthesize the cofactor, PQQ (Pyrroloquinoline quinone). *E. coli* produces gluconic acid when PQQ is supplied in the medium.
AIMS & METHODS: We hypothesized that, recombinant probiotic *E. coli* Nissle 1917 (EcN) expressing PQQ synthesis genes is able to synthesize large amount gluconic acid in the intestine and subsequently increased production of SCFAs.
pqqABCDE gene cluster was cloned and expressed in EcN. Rats were fed with starch containing diet along with recombinant probiotic EcN for 60 days.
RESULTS: Recombinant EcN expressing *pqqABCDE* gene cluster produces high amounts of gluconic acid in M9 minimal medium supplemented with glucose under laboratory conditions. Weekly treatment of recombinant EcN producing gluconic acid results in increased production of gluconic acid in the colon. Additionally, SCFAs (Butyrate and Acetate) concentration was also found to be elevated by approximately 3 fold and 1.6 fold respectively. mRNA profile of colon showed increased expression of mucin and intestinal trefoil factor genes in treated rats. The treated rats also had increased fecal *Bifidobacteria* and *lactobacilli* number.
CONCLUSION: The present study suggest that engineered probiotic could be a potent nutritional supplement against intestinal dysbiosis and other related pathologies.
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Disclosure of Interest: None declared

P0553 NUTRIENT INTAKES AT THE TIME OF DIAGNOSIS IN PATIENTS WITH HIV INFECTION: COMPARISON WITH NATIONAL NUTRITIONAL GUIDELINES AND WITH A COHORT OF HEALTHY SUBJECTS

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INTRODUCTION: Assessment of nutrient intake is an important key element in healthcare of HIV patients because nutritional status is a determinant of HIV outcomes and of many co-morbidities including gastrointestinal problems, osteoporosis, cardiovascular diseases, diabetes and other metabolic changes (1,2). Little is known about nutritional adequacy among HIV patients at the time of diagnosis and prior to pharmacological treatment.
AIMS & METHODS: We carried out a prospective clinical study to assess macro- and micro-nutrient components of diet in a cohort of HIV patients at the time of diagnosis, and to compare them with Italian recommended levels of nutrient intake (LARN 2012) and with those of a cohort of healthy subjects, matched with HIV cohort according to gender and age (range ± 4 years). Patients in the two cohorts were instructed to fill in a standardized 7-day food diary. Data from diaries were analyzed with Microdiet© software (Downlee system, ltd. UK) and nutritional characteristics studied were: total Kcal, proportion of total energy value of CHO, free sugars, proteins, fats, SFA and PUFA, and total amounts of fibre, vitamins A, B12, C, and D, folates, sodium, calcium, iron, zinc. For statistical analysis Fisher's exact test and Wilcoxon matched pairs test were used as appropriate.
RESULTS: 22 HIV patients signed informed consent, 21 returned the diary and 14 were at present analyzed. Eleven were male, age 42 ±1 year (mean ± SD), BMI 23.8 ±3.3 Kg/m2 with 4 patients in overweight class, 1 in grade 1 obesity class and 9 in normal BMI class. Comparison of selected nutrient composition with LARN and with healthy subjects are reported in the table.

Nutrients	HIV patients	Healthy subjects	HIV Vs LARN§ %
CHO, % TEV	48.2±6.9	40.0±5.6*	- 21
Fats, %TEV	33.2±6.0	37.0±3.4*	+36
Proteins, %TEV	16.3±2.2	16.6±2.6	+79
Vitamin B12, µg	3.7±1.4	2.5±0.8*	-21
Vitamin D, µg	2.5±1.8	3.4±1.6	-100
Folates, µg	191.6±44.6	140.3±49.8*	-100
Calcium, mg	508.9±133.0	771.0±253.9	-100
Iron, mg	7.0±1.4	9.7±2.3*	-100
Zinc, mg	8.4±1.5	8.8±2.1	-79

CONCLUSION: Daily intake is inadequate in HIV patients at time of diagnosis for most macro- and micro- nutrients, but is closer to LARN recommendations than in healthy subjects. Nutritional counseling must be provided in HIV naïve patients in order to improve their nutritional status and to contribute to prevention of gastrointestinal and metabolic co-morbidities.
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Disclosure of Interest: None declared

P0554 SUPPLEMENTATION WITH A PROBIOTIC MILK DRINK DOES NOT ALTER GUT MICROBIOTA COMPOSITION IN PATIENTS WITH METABOLIC SYNDROME

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INTRODUCTION: Metabolic syndrome (MetS) is associated with disturbances in gut microbiota including changes in the Bacteroidetes/Firmicutes ratio. In animal models, modulation in the composition of gut microbiota through supplementation with probiotics is possible. It is not known to date if this is also possible in humans.
AIMS & METHODS: We therefore aimed to study whether supplementation with a probiotic milk drink containing *Lactobacillus casei* Shirota (LcS) is able to modulate gut microbiota composition in patients with MetS. In a single-center, prospective, randomized-controlled pilot study, 28 subjects with MetS received either LcS (YAKULT® light 3 bottles a day, 65 ml each, containing LcS at a concentration of 10^8/ml) for 12 weeks (LcS group; n = 13) or received standard medical therapy (n = 15). 6 healthy subjects served as controls. Stool samples were collected at baseline and after 3 months. Gut microbiota composition was characterized using 454 pyrosequencing of the amplicon libraries from V1 to V3 hypervariable regions of 16S rRNA genes. Generated sequencing data was analyzed with Quantitative Insights Into Microbial Ecology (QIIME version 1.7.0) pipeline in stool samples.
RESULTS: No significant differences in Unifrac distances or Bray-Curtis distances between samples from the same patients in two time points were found

(p = 0.70 and 0 = 0.48, respectively). The Bacteroidetes/Firmicutes ratio was not different compared to healthy controls and was not influenced by probiotic supplementation (Controls: 0.783; LcS baseline: 0.961; LcS 3 months: 1.007; Standard baseline: 0.921; Standard 3 months: 0.995). Diversity (using Shannon index) and richness of gut microbiota in MetS showed similar distribution compared to healthy controls and was not influenced by probiotic supplementation. LcS was only detectable in 1 individual of the treatment group after 3 months of supplementation with LcS.

CONCLUSION: In our study no difference in gut microbiota composition was found between healthy subjects and patients with MetS. The supplementation of LcS did not change gut microbiota composition, so we conclude that the microbiota variations occurring in the treatment group were not larger than the normally expected variations during this time period. This is in accordance with our previous findings that supplementation with LcS did not influence clinical and biochemical parameters of glucose metabolism, inflammation and innate immune response.

Disclosure of Interest: None declared

P0555 QUANTIFICATION OF IN VIVO COLONIC SHORT CHAIN FATTY ACID PRODUCTION FROM INULIN

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INTRODUCTION: Short chain fatty acids (SCFA; acetic (Ac), propionic (Pr) and butyric (Bu) acid) are produced during bacterial fermentation of undigested carbohydrates in the colon. In this study, we determined the bioavailability of each SCFA and applied a stable-isotope dilution method to quantify the colonic production of SCFA after consumption of inulin.

AIMS & METHODS: Six healthy subjects (3F/3M; 29±7y) each performed 4 test days with minimal 1 week interval. On the first 3 test days they received either 400mg ^{13}C-Ac or 340mg ^{13}C-Pr or 990mg ^{13}C-Bu in a pH-dependent colon delivery capsule with a standard breakfast. After collection of a basal blood sample, they received a primed constant infusion of ^{2}H-labelled SCFA (Ac:20µmol/kg.h; Pr:2µmol/kg.h; Bu:1µmol/kg.h) for 12h. On the 4th test day, the SCFA production from inulin fermentation was quantified. The subjects received 15g of inulin (Raftilin HP, Beneo-Orafti) with a standard breakfast and an infusion with ^{13}C-SCFA (Ac:12µmol/kg.h; Pr:1.2µmol/kg.h; Bu:0.6µmol/kg.h) for 12h. Additional blood samples were collected at regular times during the day. Plasma total SCFA concentrations, ^{13}C- and ^{2}H-SCFA enrichments were measured using gas chromatography (GC), GC combustion isotope ratio mass spectrometry (IRMS) and GC pyrolysis IRMS, respectively. The bioavailability index (F) of the respective SCFA was calculated from the area under the curve (AUC) of the ^{13}C-SCFA concentration time curve (F = AUC x Cl x 100/administered dose). The clearance rate (Cl) was determined using the ^{2}H-SCFA infusion (Cl = infusion rate (i)/steady state (SS) ^{2}H-SCFA concentration). SCFA turnover was calculated using stable-isotope dilution. The infusion with ^{13}C-SCFA results in a constant ^{13}C-SCFA enrichment in the blood. After fermentation of inulin in the colon, SCFA enter the blood and dilute the ^{13}C-SCFA resulting in a decrease of ^{13}C-SCFA enrichment. The total turnover (T) of the SCFA at each time was calculated as follows: T = i x [(Tracer enrichment/Plasma enrichment)-1]. The turnover at SS was subtracted from the total turnover to obtain the exogenous SCFA turnover. The AUC was calculated to yield total SCFA appearance in plasma. Finally, the bioavailability index and SCFA plasma concentrations were used to quantify the SCFA produced in the colon. Results are expressed as medians and interquartile ranges.

RESULTS: The bioavailability index of Ac, Pr and Bu were 37 [30-57]%, 21 [17-25]% and 4 [3.5-9]%, respectively. SS turnover of Ac, Pr and Bu were 13 [8-16], 0.23 [0.19-0.31] and 0.26 [0.15-0.34] µmol/kg.min, respectively. The total amount of Ac in plasma was 661 [512-991] µmol/kg; corresponding to a production of 112 [88-194] mmol of Ac in the colon within 12h after inulin ingestion. The AUC of Pr and Bu were 14 [9-22] and 13 [10-15] µmol/kg, respectively. Twelve hours after inulin ingestion a total of 0.9 [0.6-1] and 0.7 [0.6-1] mmol of Pr and Bu appeared in the circulation. The colonic produced Pr and Bu levels were 4 [2-6] and 19 [11-24] mmol, respectively.

CONCLUSION: In conclusion, inulin is mainly fermented into acetate followed by butyrate and propionate. Stable isotope technology allows to quantify *in vivo* SCFA production from carbohydrate fermentation and will facilitate the evaluation of health benefits attributed to SCFA.

Disclosure of Interest: None declared

P0556 ABDOMINAL HEMODYNAMIC IN PATIENTS WITH MALNUTRITION AND HEREDITARY CONNECTIVE TISSUE DISORDERS

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INTRODUCTION: The aim of the research is to study the peculiarities of abdominal hemodynamic in patients with malnutrition and hereditary connective tissue disorders.

AIMS & METHODS: To study mechanisms of malnutrition at the patients with hereditary connective tissue disorders.

121 patients with hereditary connective tissue disorders were included in the research (The revised Ghent nosology for the Marfan syndrome, 2010). The control group was represented by 40 healthy subjects to be comparable by sex and age. The assessment of malnutrition and ultrasonic dopplerography of the abdominal vessels (vena portae, arteria *hepatica communis*, arteria mesenterial superior and arteria splenica) were performed for the patients. The investigation was undertaken with fasting after feeding test, with the ultrasound scanner Sonoace-8000 (Medison, South Korea).

RESULTS: The signs of malnutrition in patients with hereditary connective tissue disorders have been revealed in 70,9% of cases. The degree of malnutrition has been correlated with the expression of hemodynamic disturbances (r = -0,55; p < 0,001).

By estimating the abdominal blood flow in persons with hereditary connective tissue disorders more lower volume rates of a blood flow were recorded: along vena portae - 1853,0 [1688,0-2297,0] ml/min., in the group of comparison -2149,0 [1827,0-2400,0] ml/min (p < 0,05); along arteria mesenterial superior - 988,0 [837,0-1272,0] ml /min, in the group of comparison - 1136,5 [992,0-1465,0] ml/min (p < 0,05); along the vessels of a celiac trunk: arteria hepatica communis - 480,5 [425,0-587,0] ml/min, in the group of comparison - 591,5 [536,0-689,0] ml/min. (p < 0,001) and splenic arteries - 600,0 [452,0-709,0] ml/min, in the group of comparison - 700,0 [591,0-795,0] ml/min (p < 0,01). After meal the persons with hereditary connective tissue disorders had fewer high-speed indicators gain and it didn't exceed 30% from the initial indicators (p < 0,001).

The data of the abdominal blood flow were correlated with some central hemodynamic changes (minute volume of circulation): at the vena portae (r = 0.55, p < 0,05), at the arteria hepatica communis (r = 0.60, p < 0,05), at the splenic artery (r = 0.77 p < 0,05); by the extent of vegetative sympathetic influences on a vascular tonus: at the arteria hepatica communis (r = -0,48, p < 0,05), at the splenic artery (r = -0,27, p < 0,05), at the arteria mesenterial superior (r = -0,36, p < 0,05); by splanchnoptosis degree: at the portal vein (r = -0,210; p < 0,05), at the arteria hepatica communis (r = -0,38; p < 0,05), at the arteria mesenterial superior (r = -0,86; p < 0,05).

CONCLUSION: The signs of malnutrition in patients with hereditary connective tissue disorders have been revealed in 70.9% of cases. The degree of malnutrition has been correlated with the expression of systemic connecting tissue involvement. The postprandial period abdominal blood flow has been characterized by the low values of volume rate at the vessels of the celiac trunk, arteria mesenterial superior, and portal vein. Some disturbances of a cardiac hemodynamic, prevalence of sympathetic influences on vascular tonus, splanchnoptosis presence may be considered to be the main causes of blood flow decreasing.

Disclosure of Interest: None declared

P0557 OPTIMIZATION OF DIAGNOSIS AND TREATMENT OF NUTRITIONAL INSUFFICIENCY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Development of nutritional deficiency (ND) due to the loss of nutrients, water and electrolytes with frequent stools, nutrients malabsorption, anorexia and increased catabolism is typical for patients with IBD relapse. To determine the frequency and structure of ND in patients with IBD relapse and to evaluate the therapeutic effect of nutritional support (NS) of nutritive mixtures during the course of therapy.

AIMS & METHODS: Two-phase three step study with prospective monitoring in patients with IBD was conducted during 3 years in the period from 2010 to 2012. The first phase was carried out using a one-time screening scales MUST and NRS, further in phase 2, the NS structure was refined. 520 patients with IBD were examined: 410 with ulcerative colitis (UC) and 110 with Crohn's disease (CD).

RESULTS: The 1st, 2d and 3d degree of ND was detected in 111 (27.1%), 96 (23.4%) and 42 (10.2%) patients with UC, respectively. 2d and 3d degree of ND was recorded in 48 (43.6%) and 29 (26.4%) cases in patients with CD, respectively. At the second stage of the study, 80 patients with UC were randomized into two major groups, depending on the degree of NN, were divided into groups A (2d degree of ND) and B (3d degree of ND). On basic therapy, patients of the Ist group received a diet with a high amount of protein (HAPD) and increased calorage (2500 kcal / day), while to the patients of the IId group in addition to the basic therapy, nutritional mixtures: peptamen and modulen IBD (Nestle) in the amount of 1/3 of the daily calorage were prescribed. Efficacy of treatment was evaluated on the 3 d, 4th, 12th week. At the third stage of the study, during 3 years, the long-term results were studied using index of the relapse frequency (IRF). Pick of the IRF was in the 1st group and by the end of the study it was 15 (75%) and 17 (85%) cases, respectively. In the second group IRF was significantly lower: 9 (45%) and 12 (60%) (p < 0,05).

CONCLUSION: In patients with UC and CD relapse ND of the 1st and 3d degree was recorded an average of 20.3% and 35%, respectively. Use of NS provides a low rate UC relapse, and thus stable remission of the disease.

Disclosure of Interest: None declared

P0558 TEDUGLUTIDE FOR PATIENTS WITH SHORT BOWEL SYNDROME-INTESTINAL FAILURE. A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Teduglutide (TG) is a novel agent recently approved for the treatment of parenteral support (PS) dependent patients with short bowel syndrome (SBS). PS dependence is a major concern for patients with SBS because of PS caries a risk of serious complications and affects quality of life. In phase III

trial, TG use lead to significant reduction in PS volume in SBS patients. Limited data is available regarding clinical results outside the research protocols.
AIMS & METHODS: Aims: To evaluate short and long-term outcomes of SBS patients receiving TG and assess patients' interest in TG therapy. **Methods:** Retrospective medical chart review was conducted. 19 pts. with SBS were identified. Demographics, length of small bowel, primary diagnosis, past surgical history, PS (TPN/IV fluids) volume and duration, TG dose and related complications were collected. SBS patients who received TG from 04/2013 to 03/2014 were included in the final analysis.
RESULTS: 6 of 19 SBS pts. received TG (Females 4, Males 2); Race: Caucasian 4, Hispanic 1, African-American 1. Mean age: 45.8 yrs. (range 26-71). Cause of SBS: vascular 3, RYGB/strangulation 1, surgical resections 2. SB length: range 30-120 cm. Colon in continuity 4, stoma 3 (ileostomy 2, colostomy 1). TPN duration: range 1–14 years. PS volume/week 1-8 Liters. Duration of TG therapy:1-12 months. Complications: bowel obstruction (SBO) 1, stoma swelling 2, bloating 4 (subsided). TG discontinuation 1 (SBO*), TG dose reduction 1 (stoma swelling). PS discontinued 4. Volume reduction in 6/6 pts. Gain or stable weight in all while on TG. No biliary/pancreatic complications, TG injection aversion were seen. Reason for no TG therapy in 13 pts.: No TG candidates 4 (recent cancer 2, post surgery <12 months 1, massive small bowel dilation 1), no insurance approval 1, no interest in TG therapy 8. **Characteristics of SBS patients who received TG therapy**.

Pts.	Age	Sex	SB length (cm)	Colon present	PS Duration (years)	PS Volume (Week)	PS Reduction >20%	PS Stopped	TG duration (months)
1	52	F	90	N	1.5	8L	Y	N	1
2	29	F	~30	Y	14	7.2L	Y	Y	12
3	26	F	70	Y	5	6.4L	Y	Y	9
4	36	M	50	Y	2	7.5L	Y	Y	6
5	61	F	~120	N	2	1L	Y	Y	5
6	71	M	90	Y	2	7L	Y	N	4 (TG stopped*)

CONCLUSION: From our eligible SBS patients only 6/14 (43.8%) received TG and > 50% of them expressed no interest in TG therapy. Three PS/nutrient dependent patients with colon in continuity and one with end-stoma discontinued PS completely with TG therapy. All patients had >20% reduction in PS volume while on TG. All had significant reduction in stoma/stool output. TG was well tolerated. Further studies with a larger sample size are needed in SBS patients to assess clinical benefits of TG and address patient decision process regarding this therapy.
Disclosure of Interest: A. Ukleja Consultancy for: NPS, A. Alvarez: None declared, K. Alvarez: None declared, L. Lara: None declared

P0559 BEDSIDE ELECTROMAGNETIC GUIDED PLACEMENT OF NASOJEJUNAL FEEDING TUBES IN PATIENTS AFTER PANCREATODUODENECTOMY: PROSPECTIVE SINGLE-CENTER PILOT STUDY

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INTRODUCTION: Early oral feeding is now considered the routine feeding strategy after pancreatoduodenectomy. Some 35-45% of patients will develop delayed gastric emptying postoperatively and consequently require nasojejunal tube feeding. Endoscopic placement of a nasojejunal feeding tube by gastroenterologists is relatively labour-intensive and a cumbersome procedure for patients. Bedside electromagnetic (EM) guided placement using the Cortrak® Enteral Access System by nurses has been found to be a simple, safe and cost-effective strategy in several patient categories. To date, however, an altered anatomy of the upper gastrointestinal tract is seen as a relative contraindication for EM-guided tube placement.
AIMS & METHODS: The aim of this study was to determine the success rate of bedside EM-guided placement of nasojejunal feeding tubes in patients after pancreatoduodenectomy.
We performed a prospective single-center pilot study in all patients requiring a nasojejunal feeding tube after pancreatoduodenectomy between July 2012 and March 2014. EM-guided nasojejunal tubes were placed by two specialized nurses with extensive experience with the technique. EM-guided placement was not performed in patients with upper gastrointestinal stenosis or oesophageal varices or when it was not possible for logistical reasons. Primary endpoint was the success rate of primary tube placement confirmed on plain abdominal x-ray (AXR). Success was defined as the tip of the tube positioned in the efferent jejunal limb.
RESULTS: In our study period, 55 of 126 (44%) patients who underwent pancreatoduodenectomy required a nasojejunal feeding tube. In 36 patients the tube was placed under EM-guidance at a median of 8 (6-11) days after pancreatoduodenectomy. Initial tube placement was successful according to the nurse in 25 (69%) patients and on AXR in 21 (58%) patients. Median procedure time was 25 (15-35) minutes. 22 (61%) patients underwent 50 replacement procedures after previously failed placement attempts ($n=31$) or after luxation or blockage of the tube ($n=19$). 36 replacements were performed endoscopically, with a success rate of 67%, and 14 under EM-guidance, with a success rate of 71%. No tube (re)placement related complications occurred. There was no learning curve effect when comparing the first 10 with the subsequent 26 procedures concerning success rate, but median procedure time decreased from 33 (18-45) to 20 (15-30) minutes.
CONCLUSION: Bedside EM-guided placement of nasojejunal tubes after pancreatoduodenectomy was successful in 58% of patients, which seems acceptable given the potential benefits for the patient. Based on these findings we have included patients after pancreatoduodenectomy in an ongoing randomized multicenter trial focussing on the magnitude of benefits of EM-guided placement, such as reduced patient discomfort and costs as compared to endoscopy.
Disclosure of Interest: None declared

P0560 PROSPECTIVE STUDY OF PERISTOMAL INFECTIONS AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY OVER A FOUR-YEAR PERIOD

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INTRODUCTION: Incidence of peristomal infections following percutaneous endoscopic gastrotomy in the community is not well known. Data on subsequent site infections and the organisms responsible is limited. Despite the use of prophylactic antibiotics, the incidence of peristomal infections is significant and result in substantial morbidity in patients with PEGs.
AIMS & METHODS: We aim to evaluate the prevalence of peristomal infection in our local community over a four year period after their PEG placement. Other objectives were to characterise the microbiology from wound site swabs and to identify any correlation between peristomal infection and patient characteristics. Our study also looked at incidence of subsequent peristomal infection rates in the community prospectively over a 4-year period.
Patients aged 16 and over who have had percutaneous endoscopic gastrostomies placed at Derriford hospital, Plymouth, UK during years 2008 to 2012 were included in the study period. Patients with venting gastrostomies and those who had their gastrostomies placed while undergoing treatment for Head & Neck cancer were not included in this study. All patients had their PEGs placed according to British Society of Gastroenterology guidelines with pre-procedure prophylactic antibiotics. Community enteral feed dieticians followed all patients at clinically appropriate intervals in the community following discharge from hospital. They recorded incidence of infections and various other complications over the four-year period. Endoscopy reports, clinical case records, and microbiological investigation results were also reviewed. Excel and Stata 10 were used for data collection and analysis.
RESULTS: 341 patients underwent percutaneous endoscopic gastrostomy during the study period. 110 patients (31%) needed treatment for an insertion site infection. The median time from PEG insertion to first wound site infection was 85 days (14, 363). Mixed skin commensals (42.7%) followed by Staphylococcus aureus (29%) were most frequently isolated from gastrostomy wound site swab. Only one patient had Methicillin resistant staphylococcus aureus isolated. The spectrum of organisms for subsequent peristomal infection was similar to those causing the first infection. The majority of infections resolved with appropriate treatment. Indications for PEG insertion, age, sex and residence did not correlate with peristomal infection. Two patients needed replacement with new PEG tubes in view of infection. Both of them needed their PEG tubes replaced thrice further. No specific organisms were associated with the removal and replacement of PEG tubes.
CONCLUSION: Our rates of peristomal infection are similar to previous studies[1]. Although staphylococcus aureus was frequently isolated from insertion site, the prevalence of MRSA was much lower in our cohort[2]. The time from PEG insertion to initial infection was also much longer[2].
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Disclosure of Interest: None declared

P0561 RESTORATION OF BOWEL CONTINUITY CAN REDUCE THE RISK OF CHRONIC CHOLESTASIS IN PATIENTS WITH A SHORT BOWEL

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INTRODUCTION: Patients with a short bowel and on home parenteral nutrition (HPN) have an increased risk of chronic cholestasis. This is may be due to recurrent sepsis, reduced bile flow with biliary stasis or associated with HPN. Restoration of bowel continuity can result in HPN requirements being reduced or stopped. This study aims to determine the effect of restoration of bowel continuity on the risk of chronic cholestasis (CC).
AIMS & METHODS: A retrospective review of patients with short bowel due to mesenteric infarction from 2000-2010. Chronic cholestasis (CC) was defined as two of bilirubin, alkaline phosphatase and gamma-glutamyl transferase being 1.5 times the upper limit of normal for more than 6 months.
RESULTS: Number of patients with data on liver functions was 101 (55 females, median age 54 years). Fifteen (54%) of 28 patients with a jejunostomy had CC while 4 (25%) of 16 patients who had a primary anastomosis and 11(19%) of 57 patients who had a delayed anastomosis had CC. Univariate analysis showed restoration of bowel continuity reduced the risk of chronic cholestasis

($p = 0.002$). Of 11 patients with delayed anastomosis and CC, 3 had resolution of CC, 3 patients died and 5 had continuing CC.
CONCLUSION: Restoration of bowel continuity can reduce the risk of chronic cholestasis in patients with a short bowel.
Disclosure of Interest: None declared

MONDAY, OCTOBER 20, 2014 9:00–17:00
THE IMMUNE SYSTEM: A DRIVING FORCE IN DIGESTIVE HEALTH AND DISEASE I – POSTER EXHIBITION – HALL XL

P0562 FACTORS RELATED TO LYMPH NODE METASTASIS AMONG ADDITIONAL SURGICAL RESECTION AFTER NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Indication of endoscopic resection for early gastric cancer (EGC) has been determined by the analysis of node-negative cancer using a large database of surgically resected EGC patients. Pathological assessment of tumor depth and lymphovascular infiltration among surgically resected specimens are likely to be underestimated compared to that of endoscopically resected specimens because the section interval is thick (five and two millimeters, respectively). The aim of this study was to clarify the related factors for lymph node metastasis (LNM) among additional gastrectomy in EGC patients who were judged as having a non-curative endoscopic submucosal dissection (ESD).
AIMS & METHODS: Clinical and pathological records of 455 patients who underwent gastrectomy with lymph node dissection for a non-curative ESD during September 2002 to December 2013 were retrospectively studied. Patients with (1) multiple synchronous or metachronous non-curative lesions, (2) recurrent lesions, (3) histological special type, (4) remnant stomach and (5) insufficient pathological data of preceding ESD were excluded. Main histological type (differentiated-type (D-type) or undifferentiated-type (UD-type)), lesion diameter ($\leq$2cm or 2cm$<$), tumor depth (mucosa (pT1a) or submucosa (pT1b)), lymphovascular infiltration, vertical tumor margin (VM) and ulcerative finding (UL) were examined.
RESULTS: A total of 359 patients (male/female: 287/72) with a median age of 70 year were enrolled. Additional gastrectomy was performed a median of 70 days after ESD. Main histologic type were D-type/UD-type 301/58, lesion diameter were $\leq$2cm/2cm$<$ 109/250, tumor depth pT1a/pT1b 82/277, lymphovascular infiltration was positive in 177, VM positive or indefinite was observed in 76, and UL was positive in 91 patients. LNM was found in 32 patients (9%). Univariate analysis revealed that tumor depth (OR: 4.8, 95%CI: 1.1-20.4) and lymphovascular infiltration (OR: 11.7, 95%CI: 3.5-39.1) were significant related factors for LNM. Multivariate analysis revealed that lymphovascular inflitration was an independent related factor for LNM (OR: 9.78, 95%CI: 2.76-34.59). LNM was found in 29 patients (16.4%) among 177 patients with positive lymphovascular infiltration. In contrast, LNM was found only 3 patients (1.6%) among 182 patients with negative lymphovascular infiltration.
CONCLUSION: Lymphovascular inflitration was an independent related factor for LNM among additional gastrectomy after non-curative ESD. Detailed search of lymphovascular infiltration is the most important factor in the pathological evaluation of endoscopically resected specimens.
Disclosure of Interest: None declared

P0563 METFORMIN INHIBITS NUCLEAR FACTOR KAPPAB SIGNALING AND ENDOPLASMIC RETICULUM STRESS IN GASTRIC EPITHELIAL CELLS, AND AMELIORATED ETHANOL INDUCED GASTRITIS IN MICE

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INTRODUCTION: Metformin has been recently reported to provide anti-inflammatory or antitumor activity in colitic and colitic tumor animal models through inhibition of nuclear factor kappaB (NF-κB) signaling. There is no evidence of metformin induced attenuation of gastric mucosal inflammation by alcohol.
AIMS & METHODS: The aim of this study is to investigate the effect of metformin on NF-κB signaling and endoplasmic reticulum (ER) stress in human gastric epithelial cells in vitro and on ethanol-induced acute murine gastritis in vivo. Human gastric epithelial MKN-45 cell lines were pretreated with metformin and then stimulated with tumor necrosis factor-α (TNF-α). Interleukin-8 (IL-8) expression was determined by real-time RT-PCR. NF-κB DNA-binding activity in the nuclear extracts was assessed by electrophoretic mobility shift assay (EMSA). The molecular marker of ER stress, including CHOP and XBP1 was evaluated using PCR. In the ethanol-induced acute gastritis model, mice were given absolute ethanol (50 mg/kg, 250 mg/kg) by oral gavage with or without metformin. Using the extracted gastric tissue, macroscopic assessment, histological evaluation and immunohistochemical staining for phospho-IκB kinase (IKK) was performed.
RESULTS: Metformin significantly inhibited the upregulated expression of IL-8 in MKN-45 cells stimulated with TNF-α in a dose dependent manner. Pretreatment of MKN-45 cells with metformin decreased activity of NF-κB in TNF- α -stimulated cells. CHOP and XBP1 mRNA expression was enhanced in the presence of TNF-α, and it was dampened by pretreatment of metformin. Administration of metformin significantly attenuated the severity of ethanol-induced acute murine gastritis, as assessed by macroscopic and histological evaluation of gastric mucosal damage.
CONCLUSION: These results indicate that metformin inhibits NF-κB activation and ER stress in gastric epithelial cells and that it ameliorates experimental murine gastritis. These results suggest that metformin is a potential gastroprotective agent.
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Disclosure of Interest: None declared

P0564 RESTING-STATE FMRI IN PATIENTS WITH NON-SPECIFIC DIGESTIVE TRACT DISEASES

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INTRODUCTION: The purpose of the study was to assess the differences in brain activity during resting-state fMRI (rs-fMRI) in patients with non-specific digestive tract diseases (Functional Dyspepsia-FD, Inflammatory Bowel Diseases-IBD and Irritable Bowel Syndrome-IBS) in comparison to healthy group.
AIMS & METHODS: Twelve patients (FD, IBS, IBD) and eleven in control group were included into the study.
The functional and anatomical images were acquired with a 3T Achieva TX Scanner (Philips Healthcare) with the use of the 8-channel head coil. To evaluate and exclude subjects with brain pathology standard T1 and T2 sequences were applied. No contrast agent was administered. For functional imaging a $T2^*$ Gradient Echo-Planar Imaging sequence was used. The rs-fMRI analyses were performed with the use of the standard preprocessing. Afterwards an Independent Component Analysis was applied resulting in maps of the Default Mode Network for each of the participants. Those were further compared across the groups. The following psychological tests were applied: STAI, EAS, EPQ-R, CISS, BPCQ.
RESULTS: Compared to patients with non-specific digestive tract diseases the healthy controls' DMN comprised additional areas in right hemisphere involving the Medial Frontal Gyrus and Cingulate Gyrus. The DMN network of the patients involved additional area in the medial frontal area. See table for detailed stereotactic coordinates and Z-scores.
Table 1 Significant additional brain regions of the Default Mode Network of the healthy controls compared with patients with non-specific digestive disorders

	Anatomical region	x	y	z	Z	No. of voxels
healthy > patients	Medial Frontal Gyrus	0	66	9	4.16	9
	Cingulate Gyrus	12	24	30	4.25	5
	Cingulate Gyrus	-9	0	36	4.08	6
patients > healthy	Superior Frontal Gyrus	-15	63	6	4.06	8

Results of the 2nd level between-group analysis, $p < 0.05$ FDR corrected, x, y, z are MNI coordinates of the most significant center of the activation within the activated cluster. Z = Z-value, BA = Brodmann
CONCLUSION: Our study showed that the DMNs of the patients and the control altered in the involvement of the medial structures of the prefrontal cortex (Medial Frontal Gyrus and Superior Frontal Gyrus) as well as the dorsal anterior cingulated cortex (the Cingulate Gyrus). Combined with the psychological results, the rs-fMRI indicates differences regarding emotional self-control. Further studies are required to establish clinical significance of those findings.
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Disclosure of Interest: None declared

P0565 MEDIUM-TERM EFFICACY OF SACRAL NERVE STIMULATION FOR IRRITABLE BOWEL SYNDROME

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INTRODUCTION: In a recent randomized, controlled, crossover study we concluded that sacral nerve stimulation (SNS) is an effective treatment for severe IBS.[1]
AIMS & METHODS: In the present study, we aimed at evaluating the medium-term results of SNS in the same group of patients.
Our criteria for permanent SNS were at least 30% reduction in IBS-specific symptom score (GSRS-IBS questionnaire) during the percutaneous nerve evaluation (PNE) test. Primary endpoint was change in the IBS-specific symptom score. Secondary endpoint was change in the IBS-specific quality of life score.
RESULTS: Forty-three selected patients with severe diarrhoea predominant or mixed IBS underwent a PNE test at our tertiary centre. Among these, 31 (76%, as 2 tests were inconclusive) qualified for permanent SNS and 26 (60%) were actually implanted. Of patients receiving permanent SNS 22 (85%) were eligible for the present study. At follow-up after median 42 months (range; 12-60) the median IBS-specific symptom score (26; range 13 to 64) remained significantly lower than at baseline (62, range 45 to 80) ($P < 0.0001$). The effect was observed in all IBS symptom clusters. Also, the median IBS-specific quality of life score remained significantly improved at follow-up (52, range 26 to 162) compared to baseline (134, range 82 to 180) ($p = 0.0001$). The effect was observed in all IBS quality of life domains. Therapeutic success was maintained in 18 patients (82%) of whom 5 had had the stimulator for 5 years.
CONCLUSION: The positive effect of SNS for selected patients with severe IBS is maintained at medium-term (1-5 years) follow-up.
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Disclosure of Interest: J. Fassov: None declared, L. Lundby Lecture fee(s) from: Medtronic Inc, S. Laurberg Other: Previously member of Medtronic Inćs medical advisory board, S. Buntzen Lecture fee(s) from: Medtronic Inc, K. Krogh: None declared

P0567 PREVALENCE AND SEVERITY OF IRRITABLE BOWEL SYNDROME IN MORBID OBESITY

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INTRODUCTION: The relationship between irritable bowel syndrome (IBS) and obesity has been poorly investigated. Only few recent reports have suggested an interesting correlation between obesity and IBS (1,2).
AIMS & METHODS: We aimed to determine the prevalence and severity of IBS and associated co-morbidities in a prospective cohort of obese patients. Ninety morbid obese patients (BMI 40.9±4.3 kg/m^2) were included prospectively before gastric bypass. The diagnosis of IBS and each subtype (predominance of constipation, diarrhea, alternant or undetermined) was performed according to the Rome III criteria using a Bristol scale for stool consistency. Patients were also asked for IBS related co-morbidities including chronic fatigue, migraine, low back pain, gastroesophageal reflux (GER), genitourinary problems and dyspepsia. Patients had to complete a set of questionnaires at the same time to assess the severity of IBS (IBS Severity Score), gastroesophageal reflux (Reflux Qol), psychological factors including anxiety and depression scale (HAD), fatigue (Fatigue Impact Scale), and quality of life (SF-12).
RESULTS: Among 90 obese patients, 26 of them (28.8%) fulfilled the Rome III criteria for IBS (IBS-D, n = 11, IBS-C, n = 9, IBS-A, n = 1, IBS-U n = 5). Obese patients with or without IBS were similar in age (41.7±13.1 vs 41.5±12.0 years $p = 0.9$), sex (69% vs 65% of females, $p = 0.3$) and BMI (40.9±3.9 vs 41.1 kg/m^2 $p = 0.8$). Obese patients with IBS reported significantly higher prevalence of GER (84% vs 25.9%, $p < 0.001$), migraines (75 % vs 25% $p = 0.01$), low back pain (80% vs 57% $p = 0.03$), genitourinary problems (19% vs 5% $p = 0.03$), chronic fatigue (80% vs 43% $p = 0.001$) and dyspepsia (69% vs 32% $p = 0.001$). Obese patients with IBS had significant higher score of fatigue (33±35 vs 63±39, $p = 0.0009$), anxiety (7.0±3.3 vs 10.4±3.8 $p = 0.0001$), depression (4.9±3.4 vs 6.8±4.1 $p = 0.03$), severity of IBS (58±55 vs 165±100 $p = 0.0001$), and poorer quality of life (39.1±4.7±36.0±5.4, $p = 0.01$) than those without IBS. Obese patients having both IBS and GER had significant higher IBS severity scores than those without GER (171.4±106 vs 95±42, $p = 0.05$). BMI did not correlated with IBS severity whatever the presence of Rome III criteria. In a logistic regression model including BMI, anxiety, depression, fatigue and GER score, only anxiety was significantly and independently associated with the presence of IBS (RR 1.25 CI 95% 1.1-1.51).
CONCLUSION: A relatively high 28.8% prevalence of IBS was found in obese patients. The severity of IBS was not correlated with BMI. However, anxiety was independently associated with IBS in obese patients suggesting that psychological factors are key features of IBS whatever the presence of obesity.
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Disclosure of Interest: None declared

P0568 CHRONIC INTESTINAL PSEUDO-OBSTRUCTION (CIPO): A MULTI-LEVEL NEUROMUSCULAR-BASED DIAGNOSTIC APPROACH

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INTRODUCTION: Chronic intestinal pseudo-obstruction (CIPO) is a failure of gut motility leading to recurrent episodes of intestinal sub-occlusion with no demonstrable mechanical reason. CIPO diagnosis and management is often very difficult because of the lack of standardized approach in relation to underlying causes.
AIMS & METHODS: We report our approach to diagnosis of CIPO patients with the aim to identify possible underlying neurological causes by using a multi-level investigation. Forty-nine CIPO patients (M: 15; age range: 19-63 yrs; F: 34; age range: 16-61 yrs) performed first-level exams including laboratory tests, neurological assessment and electromyography. Three patients did not comply to the diagnostic protocol and were excluded. Second-level examinations included muscle/skin biopsy and/or biochemical/molecular assays based on previous results. MR imaging and spectroscopy were performed if mitochondrial encephalomyopathy was suspected. Biochemical/molecular tests included thymidine phosphorylase activity and a-galactosidase enzyme assay as well as gene analysis of mitochondrial disorders; transthyretin or enteric smooth muscle actin genes were also performed. Full-thickness gut biopsies were obtained only in cases undergoing either elective or emergency surgery (because of intestinal sub-occlusion).
RESULTS: At the end of the complete diagnostic work up 46 out of 49 patients (94%) were thoroughly investigated. Three groups of CIPO patients were identified: A) n = 11 had mitochondrial diseases; specifically n = 6 had mitochondrial encephalomyopathy proved by genetic analysis (4 MNGIE, 1 MERRF, 1 POLG) and other n = 5 had a likely mitochondrial encephalomyopathy, although not yet confirmed by genetic analysis; B) n = 21 had a neuromuscular non-mitochondrial diseases; specifically n = 16 had neuropathy, in particular n = 3 polyneuropathy (1 associated with lymphoma, 1 Hu-related autoantibody, 1 idiopathic polyneuropathy), n = 12 small fiber neuropathy demonstrated by skin biopsy, n = 1 enteric neuropathy; finally, n = 5 had myopathy, in particular n = 1 myofibrillar myopathy and n = 4 an undefined myopathy; C) n = 14 had an idiopathic CIPO with no underlying neurological causes including abnormalities of the intrinsic or extrinsic innervation of the gut, as indicated by full thickness analysis and/or intestinal manometry.
CONCLUSION: After an accurate neurological evaluation and tests, only a third of CIPO are actually 'idiopathic'. Mitochondrial disorders should be always sought in patients with CIPO, while skin biopsy is suggested as an aid to unravel a 'small fiber' disorder, a peripheral neuropathy affecting also the autonomic nerve component. Taken together our data suggest that a thorough neurological evaluation and tests represent an important part in the management of patients with CIPO.
Disclosure of Interest: None declared

P0569 THE SAME DAY SPLIT CLINIC – A PRESCRIPTION FOR EFFICIENCY IN THE GASTROENTEROLOGY OUTPATIENT CLINIC

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INTRODUCTION: Worldwide, healthcare providers are striving to balance escalating costs with the patient's expectation of efficient access to specialist opinion, rapid investigation and treatment. Over the past 65 years, the NHS gastroenterology outpatient journey has remained unchanged. Patients are assessed at the first visit, followed by one or more hospital visits for gastrointestinal investigations and a return hospital attendance for final assessment. The same day split clinic has been designed, wherever possible, to condense the journey from months to hours.
AIMS & METHODS: Over a period of three months, each gastroenterology referral letter was previewed in advance of the outpatient appointment. Each patient was triaged as "solution" or "complex". For the "solution" cohort, investigations were predicted and scheduled for the same day as the outpatient attendance. Patients were asked to attend the clinic starved and told to expect one or more same day gastrointestinal investigations. On the appointment day, "solution" patients attended the same day split clinic for: 1) an initial specialist assessment, 2) scheduled investigation(s), 3) a return to the specialist clinic for a summative assessment & management plan.
RESULTS: Of 174 referrals, 95 patients were triaged from the referral letter as "Solution" patients, and 81 attended the split clinic (7 did not arrive, 4 postponed, 3 direct to surveillance colonoscopy). In those who attended, 46 same day tests were performed (14 upper endoscopies, 11 sigmoidoscopies, 5 barium swallows, 6 Eso Capsule endoscopies, 5 ultrasound scans, 1 electrogastrogram, 2 CT abdomen and 2 CT colonoscopy). Twenty-seven patients (34%) were discharged, and twenty-two (27 %) were discharged after a single follow up telephone consultation. Overall, 49 patients designated as "Solution" patients (60%) required only a single hospital visit. Sixteen patients (17%) were re-designated as "Complex" requiring further tests and 3 (3%) were referred elsewhere. Overall, 95 (46 same day tests and 49 return to follow up clinic in old system) return hospital visits were avoided. The visits were reduced by 40% and the follow up appointments were down by 60%.

CONCLUSION: Analytical triage of GP referral letters allows identification & triage of most "solution" patients. This facilitates pre-emptive investigation planning and scheduling which, in turn, supports a same day split clinic designed to condense months of investigation and follow up into a few hours. The well planned same day split clinic meets the patient's expectation for an efficient journey and a quick diagnosis. The inconvenience of numerous hospital attendances is minimized, whilst appointment capacity is freed up.
Disclosure of Interest: None declared

P0570 DEVELOPING A EUROPEAN CLINICAL RESEARCH NETWORK FOR PAEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

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INTRODUCTION: Paediatric European Digestive Diseases Clinical Research Network (**PEDDCReN)** was established in April 2013. The need for this initiative was identified by ENPR-EMA (The European Network of Paediatric Research at the European Medicines Agency). The Project is supported by LINKS funding from the UEG (United European Gastroenterology) and is led by the British, Irish and Dutch Societies of Gastroenterology in collaboration with ESPGHAN and ENPR-EMA.
AIMS & METHODS: The aim of PEDDCReN is to support the development of large studies in paediatric patients in the speciality of Gastroenterology, Hepatology and Nutrition (GHN).
We report the preliminary results of an online survey as a first step of PEDDCReN, identifying investigators' resources, expertise and interest in studies in this area in the UK, Ireland and the Netherlands.
The survey was designed by the steering group of PEDDCReN and utilised the web based system REDCap. It takes 5 minutes to complete with 1 respondent per hospital. To date the survey has had responses from paediatric gastroenterologists in the UK, Ireland and the Netherlands as members of BSG, BSPGHAN, Irish and Dutch Gastroenterology Societies. As a result of PEDDCReN promotions in UEG & ESPGHAN newsletters one centre from Italy, Germany, Serbia and Poland has also responded.
RESULTS: After six months 25 units (including 53 investigators) had replied representing children's services with a median of 211 beds (range 15-800). 10 were stand alone children's hospitals, 11 were children's hospitals co-located with adult hospitals, 2 were smaller children's units in adult hospitals and one was a neonatal unit. 76% of responding units had neonatal ICUs on site with almost all of these carrying out neonatal surgery. All wished to be part of PEDDCReN and were happy for contact details to be passed on to both industry and non-industry investigators. The survey identified each unit's interest in recruiting into a range of GI and liver diseases (eg 88% wished to recruit for IBD studies whereas only 24% for infant diarrhoea). Less than 33% would also recruit to liver studies including infective hepatitis. Of the respondents 60% have been a principle investigator (in their hospital) and 40% had been chief investigators for their country. 68% were willing to take on phase I or II studies but only 36% had done any in the last 3 years. 64% had a clinical research facility available on site and 68% have access to research nurses. Sites were also asked whether they currently followed up any patients with rare GI or liver diseases such as congenital enteropathy (12/25), congenital transport defect (7/25), polyposis syndromes (17/25), chronic intestinal pseudo-obstruction (15/25).
CONCLUSION: This shows the ability of PEDDCReN to identify interest, expertise and resources in 3 countries. This will shortly be extended to the rest of Europe. The potential for investigators and industry to utilise this network to support the development of large scale clinical trials and rare diseases studies within this speciality is a major benefit.
Disclosure of Interest: None declared

P0571 THE EFFICACY OF RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN IN PATIENTS WITH SEPSIS AND DISSEMINATED INTRAVASCULAR COAGULATION IN THE GASTROENTEROLOGY FIELD

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INTRODUCTION: Inpatients with digestive disease often have coexisting serious infections. Some of them result in disseminated intravascular coagulation (DIC). Recently, recombinant human soluble thrombomodulin (rTM) was approved and has been used in clinical practice for DIC treatment in Japan. However, there are few studies to evaluate the efficacy of rTM for DIC in the gastroenterology field. The purpose of this study is to make a comparison between rTM-treated patients and patients treated other agents, and to evaluate the efficacy of rTM.
AIMS & METHODS: The purpose of this study is to make a comparison between rTM-treated patients and patients treated other agents, and to evaluate the efficacy of rTM. Fifty-three inpatients at our department with sepsis-induced DIC between January 2009 and February 2014 were retrospectively analyzed. The patients were classified into the rTM treatment group (n = 25), and conventional treatment group (rTM was not used) as the control group (n = 28). Diagnosis of DIC was made according to the criteria of acute DIC of the Japan Association of Acute Medicine (JAAM). Platelet count, prothrombin time-international normalized ratio (PT-INR), levels of fibrin/fibrinogen degradation products (FDP), C-reactive protein (CRP), DIC scores based on JAAM criteria were measured on days 0,3, and 7 to evaluate therapeutic results. Furthermore, DIC resolution rate were assessed 3 and 7 days after the start of DIC treatment.
RESULTS: Before treatment, DIC scores based on JAAM criteria were 5±0.95 in the rTM group, and 5.9±1.3 in the control group ($p < 0.05$), respectively. However, there were no significant differences between two groups regarding age, sex, and causative disease of DIC. The duration of rTM administration was 3.6±1.44 days (range 1 to 7 days). As shown in the table, significant intra-group improvement was observed in all parameters except for FDP in both groups. However, there were no significant inter-group differences in comparison of all parameters. Result from the repeated measures analysis of variance, significant improvements were seen in the DIC scores in the rTM treated group ($p = 0.001$).

		Day0	Day3	Day7
Platelet count ($10^4/\mu L$)	rTM	11.1±6.5	10.5±4.7	17.9±9.0*
	control	10.6±6.9	8.4±5.7	14.9±8.7**
PT-INR	rTM	1.39±0.32	1.18±0.16**	1.21±0.22**
	control	1.43±0.32	1.22±0.3**	1.2±0.19**
FDP (μg/ml)	rTM	32.3±19.4	19.8±24.5	17.6±13.7
	control	37.4±34.1	24.9±14.5	22.2±13.0
CRP (mg/dL)	rTM	14.1±8.8	9.7±5.4*	6.6±5.6**
	control	14.5±7.6	12.2±6.1	7.5±5.2**
DIC score	rTM	5±0.95	3.1±1.8**	2.0±1.7**
	control	5.9±1.3	4.5±1.9**	3.2±2.3**
DIC resolution rate (%)	rTM		48	68
	control		28.6	50

Data are shown with Mean±SD *$p < 0.05$ vs Day0, **$p < 0.01$ vs. Day0

CONCLUSION: These results suggest that rTM would be the useful medicine for treatment DIC in the gastroenterology field.
Disclosure of Interest: None declared

P0572 THE EFFECT OF ACUTE SLIGHTLY INCREASED INTRA ABDOMINAL PRESSURE ON INTESTINAL PERMEABILITY AND OXIDATIVE STRESS IN A RAT MODEL

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INTRODUCTION: The harm of Intra-abdominal hypertension (IAH) on critically ill patients has gained great attention. However, there are still 60% under-IAH patients in critical care units, whose intra abdominal pressure (IAP) runs slightly higher, at 5 to 7 mmHg. Among the frequently IAH-affected organ systems, the intestine is initially influenced. Nevertheless, the adverse effect of transient exposure to slightly raised IAPs on intestinal mucosa remains unclear.
AIMS & METHODS: To study the acute effects of different grade nitrogen pneumoperitoneum on colon mucosa, male Sprague- Dawley rats were assigned to six groups with different IAPs (baseline, 4mmHg, 8mmHg, 12mmHg, 16mmHg, 20mmHg, n = 6 per group). During the 90 minutes' exposure, we dynamically monitored the heart rate and noninvasive hemodynamic paramaters. After decompression slowly, the arterial blood gas analyses were conducted. Then the structural injury to the colon mucosa was confirmed by light microscopy. The colon permeability was revealed by expression and localization of tight junction proteins (claudin 5 and occludin), combined with the absorption of fluorescein isothiocyanate dextran (FD-4, with another proportion of rats, n = 6 per group). The pro-oxidant–antioxidant balance of the colon was determined by the levels of malondialdehyde (MDA), glutathione peroxidase (GSH-Px), catalase (CAT) and serum super oxide dismutase (SOD).
RESULTS: IAPs greater than 12 mmHg significantly disturbed the colonic integrity, expression of tight junction protein, mucosal permeability to FD-4 and the pro-oxidant–antioxidant balance. Interestingly, slight elevation of IAPs not reaching the level of IAH also showed a similar undesirable effect. In 8mmHg group, mild hyponatremia, hypocalcemia and hypoxemia occurred, accompanied with the reduction of blood pressure and abdominal perfusion pressure. What's more, mild microscopically inflammatory infiltration and increase of MDA were also detected in under-IAH groups. 8mmHg-IAP markedly inhibited the expression of claudin 5 and occludin, though no significant differences were found in permeability to FD-4 between control and 8mmHg groups.
CONCLUSION: Acute exposure to slightly raised IAPs may bring adverse effects on intestinal permeability and pro-oxidant–antioxidant balance. Accordingly, we concluded that for critically ill patients, IAPs should be monitored dynamically and intervened as soon as possible to avoid the intestinal mucosal injury and the subsequent gut- derived sepsis.
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Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00

POSTER PLUS VIDEO II – POSTER EXHIBITION – HALL XL

P0573 USE OF A NOVEL SELF-EXPANDING METAL STENT TO ALLOW FOR ENDOSCOPIC DRAINAGE AND NECROSECTOMY OF PANCREATIC FLUID COLLECTIONS

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INTRODUCTION: Post-inflammatory peri-pancreatic fluid collections are frequent sequelae of severe acute pancreatitis. Collections are at risk of suppurative infection complicated by pancreatic necrosis. Over the last decade there has been an increasing emphasis on minimally invasive drainage procedures, including EUS-guided cyst-gastrostomy, and these approaches seem to be associated with lower morbidity and mortality. Access to the necrosis cavity has however been severely limited by having to maintain the tract with small diameter plastic stents. Recently, a novel flanged fully covered self-expanding metal stent (FCSEMS; NAGI stent, Taewoong Medical, Korea) has been developed to allow for better drainage of infected necrosis and easier endoscopic access into the cavity. Setting: A non-randomised prospective multicentre phase II study to determine the safety and efficacy of FCSEMS endoscopic cyst- gastrostomy in the management of complex/infected pancreatic fluid collections.
AIMS & METHODS: Patients were included if they had evidence of a pancreatic fluid collection which was deemed to be amenable for EUS- guided drainage after discussion at a HPB multidisciplinary meeting. Patients selected for EUS-guided drainage had cross sectional imaging (MR or CT) performed within 2 weeks of the procedure and then an EUS assessment was made of the necrotic component. The collection was punctured using a cystotome and the FCSEMS inserted over a guidewire with fluoroscopic control. Repeat procedures were performed as necessary.
RESULTS: A total of 11 patients (8 male, 3 female) were included in the study. Median age was 57.3 years. The aetiology of the collection was gallstones in 6 patients, idiopathic in 3, ischaemic in 1 and drug-induced in 1. Ten patients had evidence of at least 30% necrosis within the collection. Mean diameter of the collection was 15cm and EUS-guided puncture was initially performed in all patients. The tract was dilated with a balloon in 6 patients. Stent insertion was either with a 20mm (7 patients) or 30mm (4 patients) length FCSEMS. Ten patients underwent endoscopic necrosectomy, with a median of 3 procedures (range 1-10). Significant reduction in the size of collection was achieved in all patients. Adverse events included stent migration in 3 (2 spontaneously and 1 during necrosectomy). Two patients died of complications of severe acute pancreatitis.
CONCLUSION: FCSEMS insertion is feasible and safe for drainage of pancreatic fluid collections. It allows repeated through the stent necrosectomy procedures and appears to be a major advance in the management of infected pancreatic necrosis.
Disclosure of Interest: None declared

P0574 "LUCKY LOOP": A VARIANT OF AN ENDOLOOP + CLIP WOUND CLOSURE TECHNIQUE AFTER COLONIC DEFIANT POLYP REMOVAL

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INTRODUCTION: This report describes a variant of an iatrogenic wound closure technique after endoscopic mucosal
resection (EMR) or endoscopic submucosal dissection (ESD). After removal of defiant polyps without signs of perforation or important bleeding, iatrogenic wounds are generally not closed as second intention healing is expected. In the past patients were often hospitalized after those procedures for 2-3 days, but when discharged a 6.5% prevalence of delayed bleeding persists(1). The combined technique of endoloop plus clip or clip alone to close iatrogenic wounds or perforations during operative endoscopies is a well established practice. Clips plus endoloop technique have been coined King Closure(2) or "clutching rose stems" techniques(3).
AIMS & METHODS: We propose "a tobacco-pouch" suture technique for wounds that are a maximum of 4 cm diameter, anchoring a single endoloop with 5-6 long type clips cirumferencially to the wound edge perimeter and closing the loop using a single double channel endoscope. A hemoclip short type is placed over the plastic tube that tightens the loop to fix the suture at the end of the procedure.
Sixteen (8 ESD and 12 EMR) patients underwent endoscopic removal of polyps >25 mm <40 mm between June and December 2013. All the iatrogenic wounds were closed with the technique described in the video. The mean time to perform the procedure was 8 min (range 6-13 min). High definition endoscopes PCF-H180AL and GF-H180J (OLYMPUS, Tokyo, Japan) with an external artificial second channel, a 30 mm diameter endoloop (PolyLoop®, OLYMPUS, Tokyo, Japan) and Clips HX-610-090L and HX-610-135S (EZ-Clip®, OLYMPUS, Tokyo, Japan) were used. Carbon dioxide insufflation was used during all of the procedures. The patients were examined three, seven and thirty days after the procedure.
RESULTS: All the patients were discharged 2 hours after the endoscopic procedure was completed and none had any post procedural complications (fever, delayed bleeding, perforation or abdominal pain).
CONCLUSION: These results demonstrate that when this closure is utilized patients can be safely discharged from the hospital 2-3 hours after endoscopic removal of a polyp. The technique is quick, (it was coined "Lucky Loop" in honor of Luky Luke the fast solitary gunslinger cartoon character created by Maurice De Bevere) easy and economic and can be also used in cases of large gastrointestinal perforations or in patients that can't stop double or triple antiplatelet therapy.
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Disclosure of Interest: None declared

P0575 PERFORMANCE CHARACTERISTICS OF COLORECTAL FULL SPECTRUM ENDOSCOPY (FUSE) – PROSPECTIVE, PARALLEL, RANDOMIZED STUDY

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INTRODUCTION: Full Spectrum Endoscopy (FUSE) provides a 330° field of view, thereby potentially allowing the endoscopists to see more anatomy in comparison to standard forward viewing endoscopes (FVE). Recent data has already shown that FUSE is feasible to significantly reduce adenoma miss rates.
AIMS & METHODS: The aim of this prospective, parallel, randomized study was to assess the performance characteristics of FUSE in comparison to FVE. Patients were randomly assigned to undergo colonoscopy with FUSE (Group A) or FVE (Group B) after a previous sample size calculation. Performance characteristics including time to cecum, withdrawal time, total examination time, medication, patient and endoscopists' satisfaction, and polyp detection rates were recorded.
RESULTS: 57 patients were included (male 52%; mean age 56 years, Range 21–88 years). Time to cecum (minutes, mean ± SD) was 4.05 ± 0.6 minutes for FUSE and 5.48 ± 0.6 for FVE ($P < 0.05$). Withdrawal times were 12 ± 4.4 minutes and 15 ± 4.5 minutes for FUSE and FVE, respectively. Total examination time was 16.5 ± 4.4 minutes in the FUSE group and 20.1 ± 4.5 minutes in the FVE group. Sedation was less required in the FUSE group as compared to FVE (mean propofol dosage, 170 mg vs. 230 mg). Significantly more patients needed analgesia in the FVE group (meperidine; $p = 0.01$). Patient and endoscopists satisfaction were high throughout the cases and not different between both groups. Per patient polyp detection rates were 37% and 18% for FUSE and FVE, respectively.
CONCLUSION: Advancement times of the scope to the cecum and withdrawal times were faster with the FUSE scope as compared to standard FVE. Satisfaction rates of patients and endoscopists were similar in both groups while patients needed more sedation and analgesia in the FVE group. Although more polyps were found in the FUSE group the study was not powered to compare adenoma detection rates between both groups.
Disclosure of Interest: None declared

P0576 DEVELOPMENT AND VALIDATION OF A SIMPLE CLASSIFICATION SYSTEM FOR IN VIVO DIAGNOSIS OF COLORECTAL POLYPS USING VIRTUAL CHROMOENDOSCOPY – THE VISIBLE STUDY

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INTRODUCTION: Although the diagnostic performance of virtual chromoendoscopy (VCE) has already been reported, validated classification systems allowing both experienced and inexperienced endoscopists to apply VCE have not been established.
AIMS & METHODS: To develop and validate a simple classification system for differentiating hyperplasic and adenomatous colorectal lesions by using VCE.
In the first phase, the capacity of experienced endoscopists to predict the histology of colorectal polyps was assessed. In the second phase, a simplified classification was developed allowing histologic prediction. Thirdly, the validity of the classification was evaluated among inexperienced raters, including medical students and GI fellows. Last, a pilot clinical evaluation was performed during real-time colonoscopy. The study was performed in a multicenter, international setting.
RESULTS: A simple classification system for differentiating hyperplasic and adenomatous colorectal lesions by using VCE was developed and validated. Diagnosis was made in 78% to 89% (mean 82.5%) of polyps with high confidence. Sensitivity and specificity ranged from 95% to 98% and 78% to 100%, respectively. During real-time colonoscopy, diagnosis was made with high-confidence in 84% of polyps with sensitivity of 91%, specificity of 85%, and accuracy of 93%. Positive and negative predictive values were 93% and 93%, respectively.

CONCLUSION: We developed and validated for the first time a simple classification system for differentiating hyperplasic and adenomatous colorectal lesions by using VCE during real-time colonoscopy.
Disclosure of Interest: None declared

P0577 THE OBSERVATION OF SECOND-GENERATION AUTOFLUORESCENCE IMAGING (AFI) HELPS EASILY TO DETECT OF FLAT COLON NEOPLASIA FOR NON-EXPERT ENDOSCOPISTS

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INTRODUCTION: We reported about the features of observation for colon polyps by using the AFI system 1). Namely, hyperplastic lesion is shown as dark green color similar to surrounding mucosa. In contrast, most of the neoplastic lesion is changed to magenta color at the localized tumor area. And also, this strength of change is suggested to correlate with the histological grading. In this study, we examined the benefits of using this system to detect the colon neoplasia for beginner endoscopists.
AIMS & METHODS: Two studies were used to clarify for the usefulness by second-generation AFI observation. One method used four pictures (white light conventional image (WHL), indigo carmine dye sprayed image (CE), NBI and AFI). Another method used short movies, which recorded WHL and AFI within about one minute, respectively. At first study, twenty-four cases (flat type intramucosal lesion 22 cases and depressed submucosal invasive cancer; 2 cases) were retrospectively reviewed. In contrast, thirty cases (sessile serrated (SS) lesion; 12 cases, intramucosal (IM) lesion; 13 cases and submucosal invasive cancer (SM); 5 cases) were reviewed at second study. These pictures and videos were shown to a group of 5 beginner endoscopists (non-experienced for using AFI system) and a group of 4 expert endoscopists (experienced more than 1000 cases). The used scope is CF: FH260AZI with second generation Lucera Elite system (Olympus Medical Systems, Tokyo, Japan).
RESULTS: At first study, the visualization score was defined as follows: the worst visualization was scored as 0 and the best as 10. And to evaluate the visualization of colon neoplasia, we calculated the average visual analog scale (VAS) scores for each groups. The mean AFI visualization score; 8.9 was significantly higher than that of WHL; 6.5, CE; 8.2 and NBI; 7.1 by non-experienced group. And there was difference in average visualization scores between AFI; 7.5 and another modalities (WHL; 4.8, CE; 7.2 and NBI; 5.8) by experienced group. At second study, the strength changing to the magenta color from dark green with excitation light was evaluated by 10-point VAS. In non-experienced group, the score of SS lesion, IM lesion and SM lesion were 2.3, 5.2 and 7.8, respectively. In contrast SS lesion, IM lesion and SM lesion were 2.4, 5.7 and 7.8 in experienced group, respectively. It was shown almost same as VAS scores between non-experienced and experienced as result.
CONCLUSION: AFI provided significantly better visualization to detect and differentiate non-neoplastic lesion and neoplastic lesion for beginner endoscopists. It suggested that it is not difficult to diagnose the indication of endoscopic treatment for neoplastic changes within intramucosal layer using AFI system for non-experienced endoscopist. It was also expected to detect flat elevated lesion more easily by non-experienced endoscopists.
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Disclosure of Interest: None declared

P0578 THE ACCURACY OF REAL-TIME PROBE BASED CONFOCAL LASER ENDOMICROSCOPY FOR DIFFERENTIATION OF COLORECTAL POLYPS DURING COLONOSCOPY

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INTRODUCTION: Reliable real-time differentiation between neoplastic and non-neoplastic colorectal polyps during colonoscopy may guide treatment decisions and reduce the need for post hoc histologic evaluation of resected polyps. In the hands of experts, probe based confocal laser endomicroscopy (pCLE) has been suggested to be a highly accurate technique for this. Previous studies have shown a short learning curve for offline interpretation of pCLE images of colorectal polyps. It is however not known whether colonoscopists starting to use this technique can also accurately differentiate colorectal polyps during routine colonoscopy by using real time pCLE to directly evaluate images.
AIMS & METHODS: The primary aim was to determine the diagnostic accuracy of real-time pCLE for the differentiation of colorectal polyps during the first 50 pCLE cases of two endoscopists routinely performing colonoscopy. The secondary aim was to compare the sensitivity for diagnosing neoplasia small polyps ($\leq$5 mm) in this study with a sensitivity threshold of $\geq$90% that is required for selective polypectomy or 'resect and discard' strategies. We included patients of 45 years or older undergoing colonoscopy for screening, surveillance or diagnostic work-up between August 2012 and April 2014. After a training to obtain and interpret pCLE images two senior endoscopists performed 50 pCLE procedures each. Intravenous fluorescein was used as contrast agent. All polyps were resected endoscopically and histologic diagnosis by an expert pathologist was used as reference. Primary outcome was the diagnostic accuracy, defined as the percentage of polyps for which pCLE correctly differentiated between non-adenomatous, adenomatous and carcinomatous polyps.
RESULTS: The overall diagnostic accuracy of real time pCLE for colorectal polyps was 75% and was not different between the endoscopists (74% vs. 76%, p = 0.81). Accuracy remained stable when comparing the first 25 procedures with the last 25 procedures of both endoscopists (respectively 76% vs. 72%, p = 0.75 and 76% vs. 76%, p = 1.00). According to the size of the polyps, accuracy was non-significantly different (67% for 68 polyps $\leq$5 mm, 86% for 21 polyps $\leq$10 mm and 89% for 18 polyps $>$10 mm; p = 0.08). Sensitivity for detecting neoplasia in polyps $\leq$5 mm was 65% (59% for right sided polyps and 73% for left sided polyps).
CONCLUSION: The diagnostic accuracy of two endoscopists starting to use real time pCLE for colorectal polyps was 75% and remained stable during the first 50 procedures. Sensitivity for detecting neoplasia in small polyps was below the required 90% and suggests that real-time pCLE cannot be used to guide follow-up decisions and that histologic evaluation of removed polyps is still required.
Disclosure of Interest: None declared

P0579 NOVEL COMPUTER-AIDED DIAGNOSIS SYSTEM FOR COLORECTAL LESIONS USING ENDOCYTOSCOPY

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INTRODUCTION: Endocytoscopy (EC) enables observation of nuclei at 450-fold magnification during gastrointestinal endoscopy, thus allowing precise prediction of lesion pathology, however it requires training and experience.[1,2]
AIMS & METHODS: The aim of the present study was to develop and evaluate a computer-aided diagnosis (CAD) system for EC imaging of colorectal lesions. The proposed CAD system comprised image acquisition, nuclear segmentation, feature extraction, and classification into three pathological groups (non-neoplastic, adenoma, and cancer). The classification algorithm was programmed based on six features of nuclei that were significantly relevant to pathological classification by multivariate analysis: area (p = 0.009), standard deviation of area (P $<$ 0.001), circularity (P $<$ 0.001), circularity of the top 20 nuclei (P $<$ 0.001), shortest diameter (P $<$ 0.001), and longest diameter (P $<$ 0.001). To validate this CAD system, we conducted a pilot study using test sets of EC images from 176 small colorectal polyps (132 neoplastic lesions and 44 non-neoplastic lesions, all $\leq$10mm). The performance of the CAD system for prediction of neoplastic change was compared with diagnoses by two expert endoscopists and two trainee endoscopists. The average time for diagnosis and intra-observer agreement (using 20 EC images at a 4-week interval) were also measured and compared among the three groups.
RESULTS: The CAD system automatically output the pathological prediction of all subject images immediately on their input. The CAD system provided a sensitivity of 92.0% and an accuracy of 89.2% which were comparable with those provided by the experts (p = 0.868 and 0.256, respectively) and significantly higher than those provided by the trainees (P $<$ 0.001 and 0.002, respectively). The CAD system achieved a feasible specificity of 79.5%, which was not significantly different from that achieved by the experts and trainees (p = 0.081 and 0.728, respectively). The CAD system also enabled instant diagnosis which took only 0.3 seconds for each lesion with perfect reproducibility (Kappa = 1). (See Table)

	Computer-aided diagnosis (CAD)	Experts	Trainees	P value (CAD vs experts)	P value (CAD vs trainees)
Sensitivitiy, %	92.0	92.7	81.8	0.868	$<$0.001
Specificity, %	79.5	91.0	75.6	0.081	0.728
Accuracy, %	89.2	92.3	80.4	0.256	0.002
Time for diagnosis, seconds	0.3	4.5	16.0	$<$0.001	$<$0.001
Intra-observer agreement	Almost perfect (Kappa = 1)	Substantial (Kappa = 0.79)	Substantial (Kappa = 0.71)	NA	NA

CONCLUSION: This fully automated CAD system provides excellent sensitivity and accuracy with acceptable specificity, ultra-rapidness, and perfect objectivity. Thus, it can be a powerful tool for decision support during screening colonoscopy.(This study was registered as UMIN000012797 and supported by JSPS KAKENHI Grant Number 25860564.)
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Disclosure of Interest: None declared

P0580 TRANS-ANAL SUBMUCOSAL ENDOSCOPIC RESECTION (TASER): A NEW ENDO-SURGICAL APPROACH TO THE RESECTION OF BENIGN GIANT RECTAL LESIONS

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INTRODUCTION: Trans-anal surgical (TEMS/TAMIS) and advanced endoscopic resection (ESD, P-EMR) procedures have the potential to provide complete and successful eradication of giant rectal polyps. Both approaches however have limitations in terms of practicality and safety. We describe a new endo-surgery technique called Trans-Anal Submucosal Endoscopic Resection (TASER) which combines the advantages of both the endoscopic and transanal surgical approach.
AIMS & METHODS: The GelPoint Path trans-anal access port allows simultaneous passage of an endoscope and two laparoscopic retractors. Working with the endoscopic image the laparoscopic retractors (Johen 33mm forceps) allow dynamic tissue retraction to facilitate endoscopic dissection (Flush knife –BT) or snare placement (Olympus snare master/spiral snare). All procedures were performed under general anesthesia and with patients in the lithotomy position.
RESULTS: Eleven patients (mean age 55 years, 3 male/8 female) underwent TASER for 11 lesions, distributed from the lower rectum to the recto-sigmoid junction and with a median size of 85mm, range 40-180mm. Polyp morphology was (3/11 flat (Paris 2a), 4/11 sessile (Paris 1s) and 4/11 mixed type (Paris 2a+1s). In all cases a circumferential mucosal incision was made and histology confirmed free lateral margins in all cases. 10/11 rectal polyps were adenomatous and one had a small focus of moderate differentiated adenocarcinoma (incomplete local excision).
Complete endoscopic excision in a single session was achieved in 10/11 cases (91%). Median completion time of the procedure was 215min, range 120-480min. Tissue retraction was used in every case and resection was completed by ESD alone (4/11), ESD + EMR (4/11) ESD + EMR + trans-anal surgical excision (3/11). Intra-procedural bleeding occurred in 8 cases, controlled with hemostatic clips and Coagrasper (Olympus); surgical suturing was required in one case (1/8). Prophylactic clips (2/11) and surgical sutures (1/11) were placed to treat deep muscle injury. There were no perforations and no delayed bleeding episodes. Patients were discharged the day following TASER in all cases. Surveillance at 3-6 months revealed no recurrence in 6 cases, whereas in four cases the follow up procedure is still pending. The malignant polyp case was referred to surgery with a good clinical outcome (T3, N0, M0).
CONCLUSION: TASER appears to be a safe and efficient approach providing an optimal platform for resection of large rectal lesions. In our experience it provides the optimal platform for the minimally-invasive management of these high risk lesions.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
LIVER & BILIARY II – POSTER EXHIBITION – HALL XL

P0581 EVALUATION OF FERRITIN >1000 CUTOFF POINT TO DIAGNOSE LIVER IRON OVERLOAD

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INTRODUCTION: Ferritin > 1000 has been associated with high grade fibrosis in hemochromatosis and in liver iron overload disorders.
AIMS & METHODS: To establish the nosologic characteristics of ferritin >1000 ng/ml to diagnose high liver iron overload (hepatic iron index > 1.9) (HIO) and for the diagnosis of significant iron overload in liver (> 60 micromol Fe/g) (SIO).
Cohort of consecutive patients studied by MRI for quantification of liver iron concentration (LIC). Variables: age, sex, ferritin and LIC. We calculate the mean and standard deviation for quantitative variables and absolute and relative frequencies for qualitative variables.
The relationship between ferritin and LIC is analyzed using a simple linear regression model.
To establish the nosological characteristics of ferritin we calculated the sensitivity (S), specificity (Sp), positive predictive value (PPV) and negative (NPV) with their 95% CI.
RESULTS: Total number of patients was 538 (449 men), with a mean age of 53.6 (SD 13.4). Mean ferritin value was 804.5 (SD 655.2). 56 patients (10.4%) had HIO and 125 (23.2%) had (SIO). Mean LIC in patients with ferritin > 1000 was 55.9 micromol Fe /g. The PPV for HIO is 27.1% (19.9 to 35.8) and NPV of 94.3% (91.6 to 96.1). With our prevalence of 10.4%, the expected results by chance alone would have been: PPV = 10.7% (5 to 21.5) and NPV = 89.6 (86.6 to 92), close to the values obtained with ferritin > 1000. To diagnose SIO, PPV of ferritin >1000 is 50% (41.1 to 58.9) and NPV of 84.3% (80.5 to 87.5). In this case, the expected results by chance would have been: PPV 24.6% (17.7 to 33.1) and NPV 77.1% (72.9 to 80.9).
CONCLUSION: Ferritin > 1000 has a low value for the diagnosis of HIO or for SIO.
Disclosure of Interest: None declared

P0582 DIAGNOSTIC ALGORITHM FOR HIGH LIVER IRON OVERLOAD. WHEN IS MRI INDICATED?

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INTRODUCTION: HIO is considered if the Hepatic iron index > 1.9 (estimated by MRI).
AIMS & METHODS: To develop and validate a diagnostic algorithm for high iron overload (HIO) based on laboratory and genetic variables.
We collected a retrospective cohort with all consecutive patients between 2001-2008 studied by Magnetic Resonance Imaging (MRI) to determine liver iron concentration (LIC). This cohort served as the derivation set. We analyzed all variables using univariate statistics with the MRI acting as the gold standard. We studied the best combination of the diagnostics variables to build the algorithm.
We validated the algorithm in a prospective cohort, collecting all patients referred to our hospital for study of iron metabolism alteration since 2009 onwards. We estimate the sensibility, specificity and predictive values with 95% CI.
RESULTS: *Retrospective cohort*: 242 patients (198 men/44 women), mean age 52,4 (SD 13.3). Thirty six of them had HIO. Nearly half of the patients (117/242 = 48.4%) had both Transferrin saturation index (TSI) and Ferritin elevated and 28 (11.5%) were C282Y homozygous. The final algorithm was as follows: We consider a patient as having HIO with the simultaneous occurrence of TSI and Ferritin elevated and C282Y homozygosis. HIO is discarded if TSI or Ferritin are within normal values. The rest should be studied by MRI.
Prospective cohort: 177 patients (148 men/29 women), mean age 56 (SD 13.9). The nosological characteristics of the algorithm in this validation study are:
CONCLUSION: MRI is not necessary in 77% of the patients for HIO diagnosis. MRI is indicated inpatients not C282Y homozygous with raised TSI and Ferritin.
Disclosure of Interest: None declared

P0583 LIVER IRON CONCENTRATION (LIC) IN PATIENTS REFERRED FOR HYPERFERRITINEMIA (HF) TO A SECONDARY HOSPITAL: ANALYSIS OF THE DIFFERENT GROUPS ACCORDING TO HFE MUTATIONS AND TRANSFERRIN SATURATION INDEX (TSI)

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INTRODUCTION: Olynyk et al (1) analyzed in Australia in 2009 the LIC by MRI of 52 consecutive patients who were referred for HF to a tertiary hospital. They described three different groups according to HFE mutations and TSI (A Group: no predisposing mutations (PM) for Hereditary Hemochromatosis (HH) and TSI > 45 %, B Group: PM for HH: C282Y/C282Y; C282Y/H63D, and TSI > 45 %; C Group: no PM for HH and normal TSI). They concluded that LIC in B Group was significantly higher than in A and C groups. In the Basque Country, predisposing mutations differ, with relevance of the H63D/H63D mutation (2).
AIMS & METHODS: To study the relevance of HFE mutations and TSI in determining LIC of HF patients attending the outpatient clinic at a secondary hospital.
Prospective study of 132 consecutive patients with HF. January to December 2010. In 120 HFE study was available. In 79 LIC was obtained by MR. In 71 patients values of HFE mutations, TSI, and LIC by MR were available. The LIC was measured in µmol / g (normal ≤ 36 µmol /g) by MR (Alústiza et al method (3)).
RESULTS: mean age: 55.68 ± 14.26 (23-83), 55 men and 16 women (77.5 %, 22.5 %). The mean age for men was 53.07 ± 13.61; 64.63 ± 13.14 in women. The mean LIC by MR in men was 35.66 ± 36.85; 38.81 ± 29.75 in women. Patients in A Group: 21, 14 with normal LIC, 7 raised LIC; B Group: 19-H63D/H63D; C282Y/H63D-, 11 normal LIC, 8 raised LIC; C Group: 31 patients, 23 normal LIC, 8 raised LIC. The mean LIC in A Group: 38.80 ± 45.18 (5-210), B group: 48.96 ± 37.51 (15-160), C group: 28.12 ± 18.85 (5-75). We compared the LIC mean values of the 3 groups using ANOVA, with no significant differences.
CONCLUSION: In our study, the LIC in different groups of patients referred for HF to a secondary hospital, with different predisposition to HH (PM, raised TSI), are similar. The different HFE mutations and TSI values do not appear to be relevant in the LIC of these patients.
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Disclosure of Interest: None declared

P0584 GLUCAGON-LIKE PEPTIDE-1 (GLP-1) ANALOGUE, LIRAGLUTIDE, INHIBITS OXIDATIVE STRESS AND INFLAMMATORY RESPONSE IN THE LIVER OF RATS WITH DIET INDUCED NON-ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Liraglutide, a glucagon-like peptide-1 (GLP-1) analogue, has been demonstrated to reduce hepatic steatosis. However, the mechanisms of the lipid-lowering effect of liraglutide in the liver remains unclear. The aim of the present study was to investigate the beneficial effect of liraglutide on diet induced non-alcoholic fatty liver disease (NAFLD) and the underlying mechanisms in rats.
AIMS & METHODS: NAFLD was induced by in Sprague-Dawley rats by feeding a high fat and high cholesterol (HFHC) diet. Liraglutide (0.6 mg/kg body weight/day) was injected intraperatoneally to the rats subjected to HFHC diet 4 weeks before sacrificing. Body and liver weight, fasting blood glucose (FBG), fasting insulin, serum aminotransferase (ALT) and lipid accumulation in the liver were determined. Markers of oxidative stress, such as malondialdehyde (MDA), free fatty acid (FFAs), superoxide dismutase (SOD), and pro-inflammatory cytokine tumor necrosis factor-a (TNF-a) were detected with RIA or ELISA kits. Serum and hepatic adiponectin were measured. The expression of JNK-1 and phosphorylated JNK1 were examined with Western blot.
RESULTS: Liraglutide improved insulin resistance, decreased hepatic steatosis and reversed liver dysfunction. The hepatic levels of MDA, FFAs, TNF-a were significantly decreased. While, the SOD and adiponectin levels in the liver were significantly elevated by liraglutide treatment. Administration of liraglutide also inhibited the expression of JNK-1 and phosphorylated JNK-1.
CONCLUSION: Liraglutide exerted anti-oxidative and anti-inflammatory effects in the liver and consequently reverse hepatic steatosis and insulin resistance. Such effects might be mediated by the elevation of adiponectin levels and the inactivation of JNK1.
Disclosure of Interest: None declared

P0585 SHORT CHAIN C6-CERAMIDE LIPOSOMAL UPTAKE AFFECTS INFLAMMATION, PROLIFERATION, FIBROSIS AND OXIDATIVE STRESS IN MCD-INDUCED NASH IN VIVO

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INTRODUCTION: Ceramides are members of the sphingolipid family and are an integral part of the lipid bilayer of cell membranes. Ceramides exert biological effects through cellular proliferation, differentiation and cell death. The role of changes in endogenous ceramides to the pathogenesis of NAFLD to NASH is sparse. In this study the effect of exogenous liposomes containing short chain C6-Ceramide (Lip-C6) was evaluated in a NASH model and in vitro in primary human Hepatic Stellate Cells (hHSC) as possible Lip-C6 target.
AIMS & METHODS: NASH was induced by feeding mice for 9 weeks a methionine-and choline-deficient (MCD) diet, or control diet (CD), followed by a single tail-vein injection of Lip-C6. The effect of Lip-C6-treatment was investigated by measuring ALT/AST, histology, Q-PCR and protein analysis. Possible changes in hepatic ceramide magnitude/species specificity and sphingosines were measured by employing untargeted LC-MS/MS lipidomics. The effect of Lip-C6 on primary hHSC proliferation, cytotoxicity and signaling pathways was investigated.
RESULTS: MCD-Lip-C6 treatment did not exacerbate MCD-induced NASH when analyzing ALT/AST, steatosis, lobular inflammation, ballooning, apoptosis and fibrosis. Protein analysis showed that Lip-C6-treatment affects the endogenous antioxidant system KEAP1-Nrf2-NQO1 in MCD-fed mice. MCD-fed mice showed a reduction in p-JNK, cleaved caspase-3/PARP, the mRNA stabilizing protein ELAV1/HuR and its downstream target phosphorylated p62 when compared to CD-fed mice which were not affected by Lip-C6-treatment. Exogenous liposomal short chain ceramide C6 treatment does not affect inflammation markers TNFalpha and NFKB signalling pathway. A strong phosphorylation of AMPK was induced in Lip-C6-treated MCD-fed indicating a stimulation of energy producing catabolic pathways. Of particular note, Lip-C6-treatment reverses the significant decreases in phosphatidylcholines (PC) and phosphatidylethanolamines (PE) species and rearranges the significant increases in specific sphingolipid species in MCD-fed mice. Moreover, Lip-C6-Rhodamine was taken up by primary hHSC and Lip-C6-treatment inhibits proliferation and cytotoxicity in a concentration-dependent manner.
CONCLUSION: These results demonstrate that a single injection of short chain C6-ceramide liposomes does not exacerbate inflammation, apoptosis, proliferation and oxidative stress in MCD-induced NASH, possibly by restoring changes in membrane lipid content induced by NASH.
Disclosure of Interest: F. Zanieri: no conflict of interest to declare, L. Longato: no conflict of interest to declare, S. Omenetti: no conflict of interest to declare, S. Galastri: no conflict of interest to declare, S. Madiai: no conflict of interest to declare, T. V. Luong: no conflict of interest to declare, T. Fox: no conflict of interest to declare, S. S. S. Velandy: no conflict of interest to declare, M. Kester Directorship(s) for: Penn State Research Foundation has licensed ceramide nanotechnology to Keystone Nano, Inc. (PA, USA) and M. K. is cofounder and Chief Medical Officer of Keystone Nano, M. Pinzani: no conflict of interest to declare, K. Rombouts: no conflict of interest to declare

P0586 APOC3 (−455T > C) POLYMORPHISM CONFERS SUSCEPTIBILITY TO NONALCOHOLIC FATTY LIVER DISEASE IN A HAN CHINESE POPULATION

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INTRODUCTION: Genetic variation in apolipoprotein C3 (*APOC3*) was reported to be associated with nonalcoholic fatty liver disease (NAFLD), but its role in Chinese population is not well understood.
AIMS & METHODS: To investigate the association between the apolipoprotein C3 (*APOC3*, -455T > C) polymorphism and nonalcoholic fatty liver disease (NAFLD), we recruited 300 NAFLD patients and 300 healthy controls to a cohort representing Han Chinese at The First Affiliated Hospital, Sun Yat-sen University, from January to December 2012. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and DNA sequencing were used to genotype the *APOC3* (-455T > C) variants.
RESULTS: After adjusting for age, gender, and BMI, TC and CC genotypes were found to increase the susceptibility to NAFLD compared to that of the TT genotype, with odds ratios (ORs) of 1.94 (95% CI, 1.26-2.98) and 3.01 (95% CI, 1.76-5.16), respectively. Further stratification analysis indicated that the CC genotype was more susceptible to insulin resistance (IR) than the TT genotype, with OR of 2.59 (95% CI, 1.26-5.30). The CC genotype also was associated with a much higher risk of hypertension, hypertriglyceridemia, and low levels of high-density lipoprotein cholesterol ($P < 0.05$). No association was found between the *APOC3* (-455T > C) polymorphism and body-mass index, level of fasting plasma glucose, serum uric acid, total cholesterol, and low-density lipoprotein cholesterol ($P > 0.05$).
CONCLUSION: *APOC3* (-455T > C) genetic variation is involved in the susceptibility to develop NAFLD, IR, and some metabolic syndrome disorders in the Han Chinese population.
Disclosure of Interest: None declared

P0587 SERUM ADIPOKINES IN PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE, IS THERE A ROLE FOR PREDICTING THE SEVERITY OF LIVER DISEASE?

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INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD) is considered to be among the most common liver diseases world-wide. NAFLD encompasses a broad spectrum of pathological conditions ranging from simple steatosis (SS) to steatohepatitis (NASH), fibrosis and finally even cirrhosis. Adiponectin (A) has been associated with inhibition of fibrogenesis and liver protection while leptin (L) contributes to fibrogenesis in various chronic liver diseases, notably in NASH.
AIMS & METHODS: To determine the validity of serum adipokines including leptin, adiponectin, and A/L ratio to act as a potential markers for NAFLD and to discriminate NASH from SS.
Patients and methods: Eighty four patients who have bright liver on abdominal ultrasonography and 28 healthy individuals served as control group. Serum Leptin and Adiponectin were estimated by ELISA technique. Liver biopsy was done for 46 patients and according to histopathological examination they were divided into 21 patients with SS and 25 patients with NASH.
RESULTS: The serum concentration of adiponectin was significantly lower in NASH than SS group ($P < 0.001$). There was no significant difference between serum concentration of leptin in both groups ($p = 0.4$). A/L ratio in NASH group was significantly lower than SS group ($P < 0.001$). Adiponectin was negatively correlated with BMI, total cholesterol and LDL-C in both groups. A/L ratio in NASH group was significantly positively correlated with adiponectin ($P < 0.001$) while it was significantly negatively correlated with leptin ($P < 0.001$). In SS group A/L ratio was significantly negatively correlated with leptin ($r = -0.863$, $P < 0.001$).
CONCLUSION: In patients with NAFLD, the serum adiponectin and A/L ratio can discriminate simple steatosis from NASH and predict the severity of liver injury.
Disclosure of Interest: None declared

P0588 MYOSIN LIGHT CHAIN KINASE INVOLVED IN INTESTINAL BARRIER FUNCTION CHANGE OF MICE WITH NAFLD

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INTRODUCTION: Myosin Light Chain Kinase (MLCK) plays a central role in the mechanisms of barrier dysfunction, and some studies showed nonalcoholic fatty liver disease (NAFLD) had intestinal barrier function change. The present study aimed to identify whether MLCK was involved in the pathogenesis of nonalcoholic fatty liver disease (NAFLD).
AIMS & METHODS: The NAFLD mice model was established by giving high-fat diet (HFD) and NASH was induced by lipopolysaccharide (LPS) administration. Mice received MLCK inhibitor ML-7 by intraperitoneal injection. The level

of ALT, AST was assessed. The degree of liver steatosis was observed by HE stain. Intestinal mucosal tight junction was observed by electron microscope, and the occludin protein was stained by immunofluorescence.
RESULTS: MLCK expression increased in NAFLD and NASH groups vs control group. ALT and AST elevated in the NAFLD and NASH group, which could be reduced by MLCK inhibitor ML-7 (Table.1, *P<0.05 vs NAFLD group, ** P<0.05 vs NASH group). The liver pathology showed no significant change after ML-7 administration. The intestinal tight junctions occludin protein were seemed to be ameliorated by ML-7,but there were no significant difference.

U/L	Control	NAFLD	NAFLD+ML-7	NASH	NASH+ML-7
ALT	20.33±0.843	20.00±2.014	13.80±0.663	31.70±3.208*	18.80±1.597**
AST	46.67±2.704	44.00±2.075	37.60±2.349	117.6±12.23*	73.10±5.382**

CONCLUSION: MLCK inhibitor ML-7 could protect liver function via improving the intestinal barrier of NAFLD mice.
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Disclosure of Interest: None declared

P0589 EPITHELIAL MYOSIN LIGHT CHAIN KINASE-DEPENDENT BARRIER DYSFUNCTION INVOLVED IN INTESTINAL BARRIER FUNCTION CHANGE OF MICE WITH NAFLD

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INTRODUCTION: Myosin Light Chain Kinase (MLCK) plays a central role in the mechanisms of barrier dysfunction, and a lot of studies showed the intestinal barrier permeability increased in nonalcoholic fatty liver disease (NAFLD).
AIMS & METHODS: The research aimed to identify whether MLCK was a regulator in the intestinal barrier permeability change of nonalcoholic fatty liver disease (NAFLD). The NAFLD mice model was established by giving high-fat diet (HFD) and NASH was induced by lipopolysaccharide (LPS) administration. Mice received MLCK inhibitor ML-7 by intraperitoneal injection. The intestinal mucosal tight junction was observed by electron microscope, and the LPS concentration of portal vein was detectedd by ELISA.
RESULTS:
MLCK expression increased significantli in fatty liver (NAFLD) and NASH, which could be blocked by ML-7. The intestinal epithelial tight junction of NASH were broader compared with control group, which could be improved by MLCK inhibitor ML-7 (Table 1). The LPS in portal vein of NASH mice was higher, suggesting the intestinal barrier permeability dysfunction. After MLCK was blocked by ML-7, the LPS in portal vein decreased significantly.

nm	Control	NAFLD	NAFLD+ML-7	NASH	NASH+ML-7
TJ	14.90±0.329	19.80±1.197*	19.20±0.997*	26.6±1.200*	14.90±0.666#

Table 1: The tight junction of intestinal epithelial of different groups.
CONCLUSION: The intestinal barrier function was restored by specifically inhibiting MLCK, suggesting that MLCK activity was responsible for the change of barrier function in NAFLD.
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Disclosure of Interest: None declared

P0590 ABACAVIR AND DIDANOSINE ENHANCE ACETAMINOPHEN-INDUCED HEPATOTOXICITY THROUGH GSH DEPLETION

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INTRODUCTION: Liver disease is a leading cause of mortality among HIV-infected patients and has been related in some cases to combined Antiretroviral Therapy (cART). Little is known about the acute effects of nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) on hepatic cells, although the purine analogue abacavir (ABC) has been reported to induce an acute mitotoxic effect *in vitro*. Since acetaminophen (APAP), a well-known hepatotoxic drug, is commonly prescribed to HIV-infected patients and also interferes with mitochondria, we hypothesised that its combination with antiretrovirals can specifically exacerbate the hepatotoxic effects of the latter drugs.
AIMS & METHODS: To analyse the acute mitochondrial effects of clinically relevant concentrations of the purine analogues ABC and didanosine (ddI), to assess their impact on mitochondrial function and the viability of hepatic cells, and to explore potential synergisms with APAP and other hepatotoxic drugs. Several parameters of mitochondrial function (oxygen consumption, mitochondrial membrane potential -$\Delta\psi_m$-, reactive oxygen species –ROS- production, intracellular ATP levels, GSH levels) and cellular viability were assessed in non-HIV-infected Hep3B and hepatocyte-like HepaRG cells treated (1-48h) with the purine analogues ABC and ddI. Further experiments were performed in the presence of sub-damaging concentrations of different hepatotoxic stimuli (APAP, the antiretroviral drugs ritonavir and nevirapine, and ethanol). Data were reported as mean+/-SEM, and their statistical significance versus vehicle was analyzed by one-way ANOVA. Correlations were analysed using Spearman's correlation coefficient.
RESULTS: Clinical concentrations of purine analogues produced an immediate and significant decrease in mitochondrial function, evident in a concentration-dependent inhibition of O_2 consumption, increased ROS production, and a reduction of $\Delta\psi_m$ and intracellular ATP levels. This mitochondrial dysfunction did not compromise cell survival, as the aforementioned parameters returned to previous values after 24h treatment. However, co-administration of these drugs with APAP concentrations below those considered toxic in hepatic cellular models exacerbated the deleterious effects of both treatments on mitochondrial function and cellular viability, thus decreasing intracellular GSH concentrations. Such effect was not observed with the other hepatotoxic stimuli evaluated. Interestingly, a significant positive correlation was detected between GSH levels and cell viability.
CONCLUSION: The combination of ABC or ddI with low concentrations of APAP significantly effects GSH concentrations in a way that increases the risk of APAP-mediated liver injury. Our findings are of considerable relevance given that APAP is currently prescribed to patients taking NRTI and that HIV infection itself has been reported to undermine intracellular GSH levels.
Disclosure of Interest: None declared

P0591 THE NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR EFAVIRENZ MODIFIES THE INFLAMMATORY RESPONSE OF HEPATIC CELLS

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INTRODUCTION: Efavirenz (EFV) is the most widely used drug in the treatment of HIV-infection, but has recently been associated with oxidative stress, mitochondrial dysfunction and endoplasmic reticulum stress in hepatocytes. As mitochondrial damage and ER-stress are frequently related to inflammatory disease, we have evaluated the effects of EFV on the cytokine/chemokine expression pattern of hepatic cells. In addition, we have explored the possible involvement of the redox-sensitive transcription factor nuclear factor-kappaB (NF-kB) and NLRP3 inflammasome, both of which trigger signalling pathways implicated in hepatic inflammation and liver injury.
AIMS & METHODS: Non-HIV-infected Hep3B cells were treated with clinically-employed concentrations of EFV (10 and 25μM). Inflammation-related gene expression was studied with Real time PCR. Activation of NF-kB was confirmed by Western blot. An electrophoretic mobility shift assay (EMSA) was carried out to determine the binding of NF-kB to promoters of some of the genes whose expression was found to be up-regulated. Chemokine secretion was evaluated in culture supernatant samples using an immunoassay kit. Data ($n \geq 3$) were analysed with one-way ANOVA followed by a Newman-Keuls test. *$p<0.05$, **$p<0.01$, ***$p<0.001$ (vs control).
RESULTS: EFV induced mRNA expression of the inflammatory mediators TNFα, IL-6, PAI-1, TXNIP and NLP3 in a significant and concentration-dependent manner. Furthermore, EFV reduced IkBa protein levels, thus increasing NF-kB translocation to the nucleus. The EMSA assay demonstrated that trans-activation of PAI-1 was mediated by interaction of NF-kB with a consensus sequence located within the PAI-1 promoter. Nevertheless, EFV also significantly reduced the production and secretion of IL-8 and IP-10, chemokines involved in the progression of liver injury.
CONCLUSION: Due to its inhibitory effects on mitochondrial function, EFV promotes a pro-inflammatory response through NF-kB- and NLRP3-dependent pathways. Interestingly, EFV also reduced the secretion of IL-8 and IP-10, thus playing a dual role in regulating the inflammatory response. In the context of lifelong use of EFV, these effects could accumulate and exacerbate the liver toxicity induced by other stimuli such as other antiretroviral drugs, co-infections (hepatitis B and/or C) or co-morbidities associated with HIV infection.
Disclosure of Interest: None declared

P0592 LIVER FUNCTION AND ELASTICITY MONITORING DURING RHEUMATOID ARTHRITIS DISEASE MODIFYING TREATMENT

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INTRODUCTION: Rheumatoid arthritis (RA) requires early intervention with disease modifying drugs (DMARDs) in order to prevent disease progression and disability [1]. Liver safety issues may delay or limit DMARDs administration [2].
AIMS & METHODS: Aim: to assess liver function tests and liver elasticity during first year of RA DMARDs treatment in everyday clinical practice.
Methods: 20 consecutive rheumatologists' out-patients (16 females) aged from 26 to 56 (mean 47.7) were enrolled in a prospective cohort study. All had newly diagnosed established seropositive RA according to ACR/EULAR 2010 criteria. Viral hepatitides being preliminarily excluded, anthropometry, serum ALT, AST, GGTP, bilirubine levels, were registered as safety measures by 2, 4, 12, 24, 36, 48 week. Liver ultrasound elastography (FibroScan, Echosens, France) was performed twice: at enrollment and end of study visit. RA disease activity was assessed by DAS28 index by 12, 24, 26 and 48 week. All patients were administered oral methotrexate 10-25 mg weekly or leflunomide 20 mg daily as DMARDs. Ibuprophen up to 1200 mg per 24 hours was allowed as on demand rescue treatment. Rescue medication consumption was registered by tablets count. All patients received advices on smoking cessation, diet optimization, physical exercises and daily activies adjusted to body mass index and comorbidities.
RESULTS: All patients had comorbidities by DMARDs initiation. The most frequent were arterial hypertension (11 pts.), dyslipidemia (20 pts.), obesity (5 pts.), high fasting glucose (7 pts.), type 2 diabetes mellitus (5 pts.). In 13 subjects metabolic syndrome (MS) was diagnosed. Non-alcocholic steatohepatitis (NASH) was diagnosed in 7 patients, while normal liver elasticity was found in only 1 subject.
DMARDs administration during 1 year resulted in DAS28 20% reduction in all subjects, 50% DAS28 reduction was registered in 16 subjects, and 70% response was found in 7 subjects. Liver elasticity has increased in 1 person with Type 2 diabetes mellitus. There had been 7 liver test worsening episodes during 1 year study. All liver test increases were seen in obese subjects with glucose metabolism disorders. No difference between methotrexate and leflunomide groups was found.
CONCLUSION: NASH had been frequent in RA patients before DMARDs were started. All liver test abnormalities during DMARDs administration were likely to be NASH related. The data support the hypothesis that conventional RA treatment is safe and does not cause liver lesions.
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Disclosure of Interest: None declared

P0593 OSTEOPOROSIS AND BONE FRACTURES IN ALCOHOLIC LIVER DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Excessive alcohol consumption is an well-established risk factor for osteoporosis and bone fractures. However, moderate amount of alcohol ingestion is known to be associated with higher bone mineral density (BMD). Osteodystrophy is a frequently overlooked complication in patients with chronic liver disease, which could result in serious outcome. However, the exact prevalence or mechanism of osteodystrophy in patients with alcoholic liver diseases (ALD) have not been described.
AIMS & METHODS: The aim of this study was to evaluate the current evidence on osteoporosis and bone fractures in ALD. Case-control or cohort studies were identified from databases (Pubmed, EM-BASE, and the Cochrane Library). The searching keywords were 'alcoholic liver diseases', 'osteoporosis', or 'bone fractures' using Boolean operators. The prevalence of any fractures or osteoporosis, and BMD score were extracted and analyzed using risk ratios (RRs) and standardized mean difference (SMD). A random effect model was applied based on Higgins I^2 tests. Publication bias was evaluated using a funnel plot, Egger's test, trim and fill, and the rank correlation test.
RESULTS: In total, 16 studies performed between 1986 and 2011 were identified and analyzed. Overall, ALD showed an RR of 1.944 (95% CI: 1.354-2.791, $P < 0.001$) for the development of bone fractures. However, ALD showed an RR of 0.849 (95% CI: 0.523-1.38, $P = 0.509$) for the development of osteoporosis. BMD was not statistically different between ALD and control group, although lower trend in patients with ALD (SMD in femur BMD: -0.192, 95% CI: -0.48-0.096, $P = 0.191$) (SMD in spine BMD: -0.429, 95% CI: -0.925-0.067, $P = 0.09$). Subgroup analysis showed consistent results. Publication bias was only detected in the analysis of bone fractures.
CONCLUSION: Current publications indicate significant association between bone fractures and ALD, however insignificant association between osteoporosis and ALD. Due to the qualitative and quantitative heterogeneity among studies, further researches using homogenous population with common validated measurement of BMD and risk factors are needed to elucidate the mechanism of bone fractures in ALD.
Disclosure of Interest: None declared

P0594 IS SQSTM1/P62 A DEFENCE AGAINST EFV-INDUCED HEPATOTOXICITY?

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INTRODUCTION: Sequestome 1/p62 is a multifunctional protein known to be involved in autophagy, during which it acts as a substrate carrier and becomes degraded. It has also been reported that p62 plays important roles in other cellular events, including oxidative stress responses, proteostasis, inflammation and cell survival, while, interestingly, it is implicated in several liver diseases, such as non-alcoholic steatohepatitis. The non-nucleoside reverse transcriptase inhibitor Efavirenz (EFV) is widely employed in combined antiretroviral therapy to treat HIV1 infection, and, though generally considered safe, has been associated with hepatotoxic events. Although the underlying mechanisms of the deleterious hepatic effects of EFV are still unclear, evidence points to altered lipid metabolism, mitochondrial dysfunction/mitophagy and endoplasmic reticulum stress in human hepatocytes.
AIMS & METHODS: To analyse the implication of p62 in EFV-induced toxicity in hepatocytes. The human hepatoma line Hep3B and cells lacking functional mitochondria (Hep3B rho-zero obtained through pharmacological interruption of mtDNA replication) were exposed to clinically relevant concentrations (10 and 25μM) of EFV for 4, 8, 24 and 48h. Key experiments were carried out with pharmacological inducers of oxidative stress (rotenone) or endoplasmic reticulum stress (thapsigargin). Quantitative PCR was performed to analyse p62 gene expression. Western Blot was employed to measure LC3 II (a marker of autophagy induction) and p62 protein levels and translocation to the nucleus of the transcription factors NF-kB and Nrf2, which have been reported to regulate p62 expression and to be involved in ER/oxidative stress and autophagy.
RESULTS: EFV clearly enhanced the protein expression of LC3 II (Microtubule-associated protein 1A/1B-light chain 3), but no reduction of p62 levels was observed. Conversely, both mRNA and protein expression of p62 were increased in EFV-treated cells in a concentration- and time-dependent manner. Western blot studies demonstrated that EFV promoted translocation of NF-κB, but not of Nrf2, to the nucleus. Moreover, the increase in p62 protein level triggered by EFV in wild type hepatocytes was less pronounced in rho-zero cells and completely absent in rotenone.
CONCLUSION: Despite inducing autophagy, clinical concentrations of EFV increase p62 expression, an effect that maybe related to NF-kB translocation to the nucleus. The results obtained in rho-0 cells suggest that overexpression of p62 is a defence mechanism against the mitochondrial and ER dysfunction triggered by EFV.
Disclosure of Interest: None declared

P0595 THE INCIDENCE RATE OF ALCOHOLIC FATTY LIVER RELATED TO ALCOHOL CONSUMPTION: A 4-YEAR RETROSPECTIVE COHORT STUDY

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INTRODUCTION: Alcohol consumption is one of the most well-known common causes of fatty liver. There is a lack of studies on incidence rate of alcoholic fatty liver related to alcohol consumption. We conducted a retrospective cohort study design to examine the relationship between alcohol consumption and alcoholic fatty liver among healthy Koreans.
AIMS & METHODS: A healthy cohort of 29,281 individuals, who had participated in a medical health check-up program in 2008, was followed up until 2012. Alcoholic fatty liver was diagnosed and defined based on both ultrasonographic finding and serum AST/ALT ratio ≥ 2. Alcohol consumption was divided into four groups (non-drinker, $<$20g/d in Female & $<$40g/d in Male, 20-40g/d in F & 40-60g/d in M, $>$40g/d in F & $>$60g/d in M). Cox proportional hazard model was used to determine if alcoholic fatty liver was associated with baseline alcohol consumption level.
RESULTS: During 100,233 person-years of follow-up, 4,889 cases of alcoholic fatty liver was diagnosed between 2009 and 2012. After adjusted for sex, age, interaction effect between sex and alcohol consumption level, the Hazard ratios (HRs) for incidence rates of alcoholic fatty liver increased according to the baseline alcohol consumption levels (HR: 0.926, 95% CI 0.827-1.038, HR: 3.257, 95%CI 2.323-4.565, HR: 3.728, 95%CI 2.238-6.213), compared to the non-drinker.
CONCLUSION: Alcoholic consumption was associated with an increased rate of alcoholic fatty liver. In female, incidence of alcoholic fatty liver was higher than the male. In addition, obesity was independent risk factors for incidence of alcoholic fatty liver.
Disclosure of Interest: None declared

P0596 UNIVERSAL SCREENING FOR ALCOHOL MISUSE IN ACUTE MEDICAL ADMISSIONS IS ACHIEVABLE AND IDENTIFIES PATIENTS AT HIGH RISK OF LIVER DISEASE

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INTRODUCTION: Many people who die from Alcohol Related Liver Disease (ARLD) have a history of recurrent hospital admissions. These episodes may represent missed opportunities for intervention. Universal screening of medical patients has been advised but little is known of the feasibility of this or its efficiency at detecting high risk cases. In 2011, we introduced a 7-day Alcohol Specialist Nursing Service (ASNS) coupled with universal screening of medical patients using a novel electronic data capture system. We now present our data on the feasibility of unselected screening and the resulting alcohol profiles of over 28,000 medical admissions in a major acute hospital serving a catchment population of 650,000.
AIMS & METHODS: From July 2011 to December 2012, all admissions via the Acute Medical Unit (AMU) were screened using the VitalPAC clinical observation system with a VitalPAC Alcohol Assesment Score (VPAAS) based on the Paddington Alcohol Test. At-risk patients (VPAAS of 6 or more) were referred to the ASNS and an Alcohol Use Disorders Identification Test (AUDIT) performed. Data analysis was performed on patient demographics, unit consumption, diagnosis, mortality and previous Emergency Department (ED) attendances and admissions.
RESULTS: There were 29,361 admissions of whom 28,098 (96%) completed VPAAS alcohol screening. Mean AMU population age was 67.4 years, 52.3% female. Of 1,123 high risk cases, 770 were seen by the ASNS and 636 defined as dependent (AUDIT >20). Compared to the general AMU cohort, the at-risk group had more ED attendances (7.8 vs 2.9) and hospital admissions (4.8 vs 3.1) in the previous 3 years and a lower age of death (58.3 vs 81.5). Dependent women had fewer recurrent attendances and admissions than men but had a higher mortality rate and lower age of death (52.2 vs 62.4). The maximum AUDIT score of 40 was recorded in 41% of cases seen by the ASNS and this subgroup had a mean age of death of 52.7 with 6.2 admissions and 10.8 ED attendances previously. The most frequent primary diagnoses in those with a VPAAS of 6+ were liver disease, mental health disorders and GI bleeding.
CONCLUSION: Our analysis of over 28,000 admissions demonstrates that screening of all medical patients for alcohol misuse is achievable. We successfully identified a cohort of high risk patients with recurrent admissions and ED attendances, high unit consumption and an elevated risk of liver disease and early death. This cohort can be targeted with interventions to reduce the burden of alcohol related harm.
Disclosure of Interest: P. Meredith: None declared, P. Schmidt Consultancy for: Unpaid research advisor to The Learning Clinic, who created & licenced VitalPAC, S. Atkins: None declared, P. Greengross Consultancy for: Part-time Medical Director of The Learning Clinic, who created & licenced VitalPAC, G. Westwood: None declared, R. Aspinall: None declared

P0597 CHEMOPROPHYLAXIS IN PORTUGUESE MILITARY PERSONNEL. SHALL MEFLOQUINE BE CONSIDERED A SAFE DRUG FOR THE LIVER?

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INTRODUCTION: Mefloquine is a drug administered in the chemoprophylaxis of malaria (*Plasmodium falcipurum*). The arising migration to malaria endemic areas has contributed to the increase of mefloquine prescription. This drug has a low potential hepatotoxicity induction, with only two reported cases of acute hepatitis.
AIMS & METHODS: Observational and analytical study. The military personnel who took part in NATO Operation Ocean Shield, on board Portuguese Navy Frigate D. Francisco de Almeida in 2011, having port visits of malaria endemic regions, such as Djibouti, were suggested to perform chemoprophylaxis (mefloquine 250mg / week), starting a week before entering Djibouti territorial waters and finishing 12 weeks after departure. A survey was conducted on the 11th week of prophylaxis, in order to assess the degree of adherence and adverse effects. Serum analyses before and after the mission were cumulatively conducted at the home port.
RESULTS: 85 military personnel participated in this study, showing no disease or chronic medication, reduced alcohol consumption, no remarkable pre-deployment blood analysis issues and that had completed the full course of chemoprophylaxis. 75% of the side effects were the gastroenterological related (29% upper abdominal pain, 24% diarrhea, 22% heartburn). Two weeks after the end of the deployment, analytical blood analysis of the military personnel revealed liver enzymes changes in 14% of the cases (mean values: AST 67 IU/ L, ALT 82 IU/L, gamma GT 98 IU/L, alkaline phosphatase174 UI/L). There were no changes in bilirubin values. Six weeks after chemoprophylaxis, an analytical reassessment was performed revealing that changes only persisted in two individuals, in who the presence of hepatic steatosis was found, on completion of further ecographic investigation.
CONCLUSION: Whereas a significant proportion of individuals had an increase in liver enzymes levels, the theoretical potential for liver injury is not to be discharged when planning prophylaxis, particularly when in synergy with other factors such as medication, alcohol consumption, and liver disease.
Disclosure of Interest: None declared

P0598 IS ALCOHOLIC FATTY LIVER DISEASE ASSOCIATED WITH THE METABOLIC SYNDROME?

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INTRODUCTION: Accumulating evidence supports an association between nonalcoholic fatty liver disease (NAFLD) and metabolic syndrome (MetS). However, there still are not enough studies to date showing association between alcoholic fatty liver disease (AFLD) and metabolic abnormalities.
AIMS & METHODS: We conducted this study to investigate whether AFLD is associated with the MetS and its components. A total of 52303 subjects (63.1% men, and 36.9% women) were included in this cross-sectional study. The presence of fatty liver was assessed using standard ultrasound criteria. The term ''significant alcohol consumption'' was defined as weekly alcohol consumption exceeding 210 g in men and 140 g in women for the previous 2 years. The presence of metabolic abnormalities were compared according to the fatty liver status and its etiology. Logistic regression model was performed to assess the odds ratios (ORs)
RESULTS: The prevalence of NAFLD and AFLD was 29.1% and 4.6%, respectively. The MetS was more prevalent in AFLD (31%) and NAFLD (23.2%) than in control group (3.6%, $p<0.001$). All metabolic components of AFLD group, including waist circumference, blood pressure, serum triglyceride, high density lipoprotein, and fasting blood glucose were statistically worse or more severe than those of NAFLD group ($P<0.001$). After adjusting for other multiple covariates, the ORs (95% confidence interval [CI]) for MetS was higher in the AFLD (3.86; 3.44-4.34) than NAFLD group (2.89; 2.68-3.12).
CONCLUSION: MetS and its components are associated with both NAFLD and AFLD. However, AFLD has a higher risk of MetS than NAFLD. Further prospective studies are needed to investigate the effects of AFLD on the development of MetS.
Disclosure of Interest: None declared

P0599 THE BETA-BLOCKERS HAVE A BENEFICIAL OR A HARMFUL EFFECT IN PATIENTS WITH CIRRHOSIS AND PORTAL HYPERTENSION?

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INTRODUCTION: The possible harmful effect of non-selective beta-blockers for the treatment of portal hypertensive-related complications (esophageal varices and advanced ascites) in patients with cirrhosis has been suggested by few recent studies.
AIMS & METHODS: Thus, the aim of the study was to determine the risk of mortality in patients with cirrhosis and portal hypertension taking non-selective beta-blocker therapy for the prevention of variceal hemorrhage.
We performed a retrospective analysis of 3215 patients admitted with cirrhosis and portal hypertension to Institute of Gastroenterology and Hepatology Iasi from 2009-2013. There were considered two groups: patients with varices only (1436 cases) and those with both varices and ascites (1779 cases) (Table).
RESULTS: The primary outcome measure for this study was the in-hospital mortality by any cause. Overall, the mortality was 102/1851 (5.51%) for the patients in treatment with beta-blockers and significantly higher for patients not taking beta-blockers 189/1364 (13.85%) ($p < 0.01$).
When we assessed the correlation between the beta-blockers use and mortality in each sub cohort we obtained similar results (Table); In the sub cohort with varices only, the mortality was 4.62% (40/864) for the patients taking beta-blockers and 11.19% (64/572) in the group without treatment ($p<0.05$). In the sub cohort with varices and ascites the mortality was 6.28% (62/987) for the patients taking beta-blockers and 15.78 (125/792) in the group without treatment ($p<0.01$)
We evaluated several parameters for correlation with the in-hospital mortality. Multivariable regression analysis revealed that Child-Pugh score was associated with increased mortality, while the use of beta-blockers was associated with reduced mortality. The other parameters which were evaluated (hemoglobin, platelets, bilirubin, INR, creatinine) didn't influenced significantly the mortality.

	Beta-blockers therapy		
	Yes	No	P-value
Varices only	N = 864	N = 572	
Mortality	4.62%	11.19%	<0.05
Varices and ascites	N = 987	N = 792	
Mortality	6.28%	15.78%	<0.01
All patients	1851	1364	
Overall mortality	5.51%	13.85%	<0.01

CONCLUSION: In a very large cohort of cirrhotic patients with portal hypertension, the mortality was significantly lower in patients treated with non-selective beta-blockers than in those not taking beta-blockers. These data confirm that the use of non-selective beta-blockers provides a significant survival benefit in patients with cirrhosis and portal hypertension. Thus, we recommend the use of non-selective beta-blockers in patients with portal hypertension and its complications.
Disclosure of Interest: None declared

P0600 EVALUATION OF THE RELATIONSHIP BETWEEN THE CHRONIC LIVER DISEASE QUESTIONNAIRE AND THE EQ-5D INDEX IN HEPATIC ENCEPHALOPATHY PATIENTS TREATED WITH RIFAXIMIN-A

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INTRODUCTION: Estimation of health-related utility is a vital component of the evaluation of the relative cost-effectiveness of healthcare interventions. The correlation between different measures of quality of life and health-related utility in hepatic encephalopathy (HE) has not been explored.
AIMS & METHODS: The aim of this study was to characterize for the first time the relationship between scores for the Chronic Liver Disease Questionnaire (CLDQ) and health-related utility as measured by the EQ-5D index in patients with HE. Data were available from a phase three trial of rifaximin-α in patients with recurrent HE. CLDQ and SF-36 scores were recorded at monthly visits. EQ-5D scores were derived from the SF-36 using a recognized mapping technique. Generalized, linear, mixed modelling methods were used to examine for any association in order to allow for repeated measures.
RESULTS: 202 of the 299 trial patients, with 920 corresponding observations, were included in this analysis, having excluded those with missing values at baseline. The average age of the cohort was 57 years, and 133 (66%) were males, with an average baseline MELD score of 13.8 units. The average time since diagnosis of HE was 23 months. The model had an r-squared value of 0.827, indicating a strong relationship between EQ-5D index and CLDQ. The model equation was EQ-5D = -0.010 + 0.136*CLDQ. Other potential covariates, such as age and sex, were tested but were not significant (at 0.05).
CONCLUSION: This is the first time that a direct association between the EQ-5D index and the CLDQ score has been reported. The r-squared value of this association suggests that liver-related morbidity may explain the majority of differences in health-related utility in these subjects.
Disclosure of Interest: E. Berni Consultancy for: Norgine, C. Bannister Consultancy for: Norgine, C. Poole Consultancy for: Norgine, P. Conway Other: Employee of Norgine, K. Nanuwa Other: Employee of Norgine, C. Currie Consultancy for: Norgine

P0601 OUTCOMES OF SECONDARY PROPHYLAXIS FOR GASTRIC VARICEAL BLEED WITH BETA BLOCKER AFTER GASTRIC VARICEAL OBTURATION FOR GASTRIC VARICEAL BLEEDING

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INTRODUCTION: Gastric variceal obturation therapy using Histoacryl for the gastric variceal bleeding is the most appropriate treatment. However, the secondary prophylactic efficacy of beta blocker after gastric variccal obturation therapy has not been established. We wanted to evaluate the secondary prophylactic efficacy of beta blocker after gastric variceal obturation therapy. We conducted this study from January 2011 to January 2014.
AIMS & METHODS: We enrolled 100 consecutive patients, with gastric variceal bleeding who received gastric variceal obturation therapy using Histoacryl. Gastric variceal obturation therapy was continued until gastric variceal eradication. Among these 100 patients 48 patients underwent only gastric variceal obturation therapy (Group I) and 52 patients along with gasstric variceal obturation therapy did receive beta blocker therapy (Group II). We gave Carvedalolo 12.5 to 25 mg daily doses. In all patients, the desired heart rate was achieved. The rate of rebleeding free overall survival was observed in two groups by Kaplan-Meyer analysis.
RESULTS: This is ongoing study, we are reporting the interim results. The mean follow-up period was 24 months. During follow-up period, rebleeding occurred in 10 patients (20%) in group 1 and 20 patients (40%) in group 11 respectively.15 patients died in group 1 and 25 patients in group 11 over 2 years period, which was statistically significant at p = 0.05. The mean rebleeding free survival times were 70 and 40.months, respectively, and were statistically significant (p = 0.05). The mean overall survival time were 60 versus 40 months, respectively, and were significant differences between two groups (p = 0.001).
CONCLUSION: The beta blocker adding therapy after gastric variceal obturation therapy using Histoacryl for first gastric variceal bleeding could decrease rebleeding and mortality, as compared with gastric variceal obturation therapy alone. Further prospective large-scale studies are needed to confirm or refute our observation.
Disclosure of Interest: None declared

P0602 SPLEEN STIFFNESS AS A PREDICTOR OF DECOMPENSATION IN LIVER CIRRHOSIS

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INTRODUCTION: Noninvasive assessment of chronic liver disease is of major importance. Spleen stiffness measurement (SSM) was proposed as a surrogate noninvasive marker for prediction of large esophageal varices (LEV) or clinically significant portal hypertension (CSPH). It was recently hypothesised that SSM may predict clinical decompensation (CD) during follow up in cirrhotic patients.
AIMS & METHODS: The aim of this study was to evaluate SSM as a predictor of decompensation in patients with cirrhosis.
Fifty-two consecutive compensated cirrhotic patients due to viral (HCV and/or HBV) or alcoholic aetiology were included. They were mainly men (27; 52%) with a mean age of 55.9 years. 25 patients (48%) had large (grade 2 and 3) oesophageal varices at inclusion. All patients underwent liver and spleen stiffness measurement at baseline as previously described, abdominal ultrasound and liver function was assessed by usual biochemical tests. Modified SSM (mSSM) was also calculated from each spleen elastogram using an alternate calculation algorithm so that an extension of the scale (up to 150 kPa) could be obtained. Clinical decompensation was defined as the occurrence of one of the following: variceal bleeding, development of ascites, hepatic encephalopathy (HE), jaundice (total bilirubin > 3 mg/dl), infection, spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), hepatocellular carcinoma (HCC) or death or liver transplantation.
RESULTS: During the median follow-up period of 13 months (range 4-28), 23 patients (44%) decompensated. Most frequent cause of CD was ascites (7 patients, 30.4%), followed by infection/SBP (6 patients, 26.1%), variceal bleeding (4 patients, 17.4%), HE and HCC (3 patients, 13.05% in each group). 14 patients (26.4%) had more than one episode of decompensation and 3 (5.6%) died during the follow-up.
In multivariate analysis baseline values of mSSM (HR = 1.085; p = 0.01), albumin (HR = 0.17; p = 0.02) and total bilirubin (HR = 1.642; p = 0.05) were the only variables associated with CD in the follow-up, overcoming LSM, SSM and MELD.
CONCLUSION: Although conducted in a small heterogeneous population of cirrhotic patients for a limited period of time, the findings of this study supports the conclusion that modified SS measurement by transient elastography together with simple biological parameters (Albumin and Bilirubin) may have an important clinical relevance by selecting patients with high risk of decompensation.
Disclosure of Interest: None declared

P0603 SMALL BOWEL CAPSULE ENDOSCOPY AS A TOOL TO DIAGNOSE PORTAL HYPERTENSIVE ENTEROPATHY IN CIRRHOTICS: THE EDINBURGH EXPERIENCE

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INTRODUCTION: Portal hypertensive enteropathy (PHE) remains difficult to diagnose in patients with cirrhosis and portal hypertension. Small bowel capsule endoscopy (SBCE) would be ideal in this situation but it is rarely performed
AIMS & METHODS: We aimed to determine the prevalence of PHE using SBCE in a cirrhotic patient population from our centre
Methods. This was a retrospective study using the SBCE data base of our unit. We searched through 1,477 patients that had SBCE between 2005 and 2013. Patients with cirrhosis who underwent SBCE were identified, data retrieved and abstracted. The Fischer's exact test or the chi square test were used to compare between groups. A two-tailed P value of <0.05 was considered statistically significant.
RESULTS: We identified 53 patients with cirrhosis who underwent SCBE. We used PillCam®SB (Given®Imaging Ltd, Israel) system on 36 patients and the MiroCam® capsule (IntroMedic Co, Korea) on 17 patients. Thirty patients were referred for iron deficiency anaemia, 15 for obscure gastrointestinal bleeding and 4 for other indications. Four data sets were not available for review at the time of the study, leaving 49 patients to be reviewed. Mean age was 61.19±14.54 years (M/F = 27/22). The most common aetiology for cirrhosis in our patients was alcoholic liver disease (15 patients) followed by NAFLD (9 patients) and hepatitis C (7 patients). Thirty three patients had evidence of portal hypertensive gastropathy (PHG) and 17 patients had evidence of oesophageal varices. In total, 29 patients had SCBE evidence of PHE (67%). 28/29 (96.5%) of patients with PHE had also evidence of PHG. 13/17 (76.4%) patients with oesophageal varices had also evidence of PHE. Mean gastric transit time was 54 ± 9 minutes and mean small bowel transit time was 204 ± 64 minutes. There were no statistically significant differences between the mean gastric transit times in cirrhotic patients with and without PHE (p = 0.235) or the small bowel transit time (p = 0.49). Our mean follow up was 58.0 ± 13.7 months. Twenty patients died during the follow up period. There was no correlation between the presence of PHE and aetiology of liver disease ($p = 0.4261$) or subsequent death ($p = 0.2145$).
CONCLUSION: The prevalence of PHE in our study was 67%. SBCE is a useful tool in evaluating PHE in cirrhotic patients irrespective of aetiology.
Disclosure of Interest: None declared

P0604

Parameter	HPS (n=14) X±SD (Range)	PPH (n=14) X±SD (Range)	Other (n=42) X±SD (Range)
CSV (mL)	75,96±20,68 (54,4-116,96)	84±20,94 (61-116,74)	86,69±18,81(46,78-132,2)
MAP (mm Hg)	88,43±8,94 (76,66-100)	83,38±4,39 (78,33-90)	93,8±7,5 (78,33-110)
CI	3,31±1,32 (2,05-6,26)	3,52±0,92 (2,7-4,10)	3,69±0,89 (1,97-5,74)
SVR	2421,46±878,65 (979,01-3900,43)	1992,76±420,35 (1595,28-2321,15)	2129,18±533,9 (1347,72-3865,03)
NT-proBNP (pg/mL)	1264,64±2188,45 (88,78-6052,5)	1323,39±2028,7 (127,52-5849,1)	607,93±1149,73 (11,31-5849,1)
PRA (μg/ml/h)	4,41±5,85 (0,1-16,8)	12,66±20,26 (0,6-57,6)	6,21±11,28 (0,1-57,6)
NA (nmol/L)	5,97±4,18 (1,46-11,51)	586,29±1532,21 (0,3-4061)	149,90±759,51 (0,3- 4061)

P0604 THE SENSITIVITY AND SPECIFICITY OF INHIBITORY CONTROL TEST IN THE DIAGNOSIS OF MINIMAL HEPATIC ENCEPHALOPATHY: A META-ANALYSIS

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INTRODUCTION: Minimal hepatic encephalopathy (MHE) is a complication of liver cirrhosis that does not show symptoms of overt hepatic encephalopathy (OHE). This state reflects alterations in cognitive function, but clinically exhibit a normal mental status examination. Patients with MHE have been shown to have higher rates of automobile accidents, it predicts the development of OHE, and is associated with poor survival.
Diagnosis of MHE is difficult, as the absence of clinical evidence of encephalopathy is key to its diagnosis. Neuropsychological testing, specifically the Psychometric Hepatic Encephalopathy Score (PHES), is accepted as a reference standard in the diagnosis of MHE. Newer computer-assisted techniques, such as the Inhibitory Control Test (ICT), have been studied to improve the detection of MHE. ICT is a simple computer-based test, consisting of presentation of several letters at 500-millisecond intervals. The ease of performing the test in the outpatient setting may make it a good test for detecting MHE.
AIMS & METHODS: This study aims to determine the sensitivity and specificity of Inhibitory Control Test in diagnosing minimal hepatic encephalopathy. COCHRANE and MEDLINE were searched for articles published between January 2003 to October 2013. Studies that compared ICT with psychometric tests in cirrhotics were included. Data analysis was performed using the validated application Meta-Disc version 1.4 (Universidad Complutense, Madrid, Spain). The DerSimonian-Laird random effects method was used to produce summary estimates of sensitivity, specificity, likelihood ratios (LR), and diagnostic odds ratio (DOR).
RESULTS: The search strategy identified 133 studies. Based on pre-stated criteria, three studies were included in the final review. There were 235 patients with liver cirrhosis and a matched control group that underwent both psychometric testing and ICT. Pooled data showed that the ICT had a sensitivity of 88% ($I^2 = 0\%$), specificity of 72% ($I^2 = 69.2\%$), and DOR was 21.2 (95% CI: 8.08–55.24). A symmetrical sROC depicted an area under the receiver operator curve (AUC) of 0.89 (standard error 0.03).
CONCLUSION: Inhibitory Control Test is a good tool to exclude cirrhotic patients without minimal hepatic encephalopathy. It is effective in discriminating patients with MHE from those without MHE and therefore has potential as a screening test. However, more high-quality studies are needed to establish test accurarcy.
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Disclosure of Interest: None declared

P0605 SYSTEMIC HEMODYNAMICS IN PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS AND HEPATOPULMONARY SYNDROME OR PORTOPULMONARY HYPERTENSION

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INTRODUCTION: There is a lack in knowledge about the correlation of systemic circulation parameters and the degree of liver failure with respect to the presence of hepatopulmonary syndrome (HPS) and portopulmonary hypertension (PPH).
AIMS & METHODS: The aim of this study was to evaluate the changes in the systemic circulation by using non-invasive diagnostic approach in the patients fulfilling the criteria for HPS and PPS. The study sample included 70 patients with alcoholic liver cirrhosis;22 patients with grade A, 24 patients with grade B, and 24 patients with grade C according to the Child-Pugh clinical score. Systemic circulation measurements included: heart rate (HR), mean arterial pressure (MAP), cardiac index (CI), systemic vascular resistance (SVRI) and cardiac stroke volume (CSV)[1]. Neurohumoral parameters included: NT-proBNP, noradrenalin (NA) and plasma renin activity (PRA). HPS was diagnosed if the presence of impaired arterial oxygenation ($PaO_2 < 80$mmHg and alveolar-arterial oxygen gradient $\geq$15mmHg; for patients older than 64 years $PaO_2 \leq 70$ mmHg, and A-a gradient $\geq$20 mmHg) and pulmonary vascular abnormalities were found. PPH was characterized by increased mean pulmonary artery pressure >25 mmHg at rest and if the diameter of the main pulmonary artery is $\geq$29 mm with concomitant segmental artery–to-bronchus ratio $>$ 1:1 at least in three out of four pulmonary lobes, or the ratio of the main pulmonary artery diameter to the aortic diameter >1.
RESULTS: HPS and PPH were found in 28 (40%) patients. Patients with HPS were mostly patients from group B (57.2%) and C (42.8%) with respect to the degree of liver failure, while all patients with PPH were patients with advanced liver failure. When correlating systemic hemodynamic and neurohumoral parameters in relation to the presence of HPS and PPS no significant difference was found. (Table 1).
CONCLUSION: The combined application of the Doppler and contrast echocardiography is a simple, non-invasive and reproducible method that enables the diagnosis of both HPS and PPH. Systemic hemodynamic parameters remained unchanged among patients with HPS and PPS.
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Disclosure of Interest: None declared

P0606 DO COAGULATION AND PLATELET FUNCTION DISORDERS INFLUENCE THE PREVALENCE OF VARICEAL BLEEDING IN PATIENTS WITH LIVER CIRRHOSIS?

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INTRODUCTION: Bleeding from gastro-esophageal varices is a life-threatening condition and occurs in approximately one third of patients with liver cirrhosis during their lifetime. On the other hand patients with history of variceal bleeding have 70% risk of recurrent bleeding within the next year since the first episode. Coagulation disorders in patients with liver cirrhosis are complex, and their role in variceal bleeding remains unclear. Previous studies have shown that the results of standard laboratory tests such as prothrombin time (PT) and activated partial thromboplastin time (APTT) provide a narrow measure of procoagulant system only and do not predict bleeding in cirrhotic patients. Thromboelastometry has been used for decades for intraoperative transfusion guidance and it can show defects in multiple components of hemostasis. Multiplate® impedance platelet aggregometry (IPA) allows rapid evaluation of platelet aggregation in whole blood.
AIMS & METHODS: The aim of our study was to compare the character of coagulation disorders in patients with liver cirrhosis and a history of variceal bleeding with non-bleeding cirrhotic patients. We compared standard laboratory clotting tests, thromboleastometry (ROTEM® thromboelastometer) and IPA parameters of cirrhotic patients with medium-large varices who have never bled (non-bleeding group) with patients with a history of variceal bleeding at least 3 weeks before (bleeding group). The following thromboelastometry parameters were measured: clotting time (CT), clot formation time (CFT), maximum clot firmness (MCF) and the clot amplitude at 5, 10 and 15 minutes in three tests with specific activators to evaluate the extrinsic (EXTEM) and intrinsic (INTEM) systems, and the clotting factors alone after platelet inactivation (FIBTEM). In addition, IPA was performed with ADP as an activator and aggregation was quantified as area under the curve (AUO).
RESULTS: Blood was sampled from 44 patients (23- non-bleeding group, 21-bleeding group). Baseline characteristics of the bleeding and non-bleeding groups were comparable apart from a more prolonged PT in the bleeding group [15,8 (14,1 - 17,3) *vs* 14,3 (13,5-16,0), $p = 0.045$]. The severity of liver disease according to Child–Pough score was comparable in both groups [8,00 points (8,0-10,0) – non-bleeding group *vs* 9,0 (8,0-10,0) – bleeding group, $p = 0.889$]; 5 patients – class A, 23 patients - class B, 16 patients - class C. In FIBTEM there was significantly lower amplitude at 15 minutes in the bleeding group compared with non-bleeding group [12.0 (9,5-14,5) *vs* 15.0 (11,0-19,0), $p = 0.049$]. The

other results of thromboelastometry and aggregometry parameters did not differ significantly between both groups, which suggest a compensatory role of platelets in EXTEM and INTEM tests. The compensatory role of platelets is also supported by the results of IPA in which we demonstrated higher value of AUO in bleeding group in comparsion with non-bleeding group [273.0 (99,0-557,0) *vs* 189.00 (132,0-640,0), NS].
CONCLUSION: Despite prolonged PT in bleeding group, the patients with liver cirrhosis with and without history of variceal bleeding have similar efficiency of blood clotting, which may suggest compensatory role of platelets in these patients.
Disclosure of Interest: None declared

P0607 REAL WORLD EXPERIENCE OF RIFAXIMIN FOR HEPATIC ENCEPHALOPATHY - EFFECTIVE MAINTENANCE OF REMISSION AND REDUCTION OF HOSPITAL ADMISSIONS IN A LARGE SECONDARY CARE PATIENT COHORT

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INTRODUCTION: Rifaximin has been shown to maintain remission of chronic hepatic encephalopathy (HE) and reduce hospital admissions (Bass et al 2010). However, the literature mainly reflects tertiary centres and could include referral bias. Therefore, we examined the ''real world'' utility of rifaximin in a large secondary care acute hospital, serving a population of 650,000.
AIMS & METHODS: All patients with cirrhosis and chronic HE who were commenced on rifaximin between May 2010 and November 2012 were identified from a departmental database and pharmacy records. Analysis included formal review of casenotes, pathology, hospital admission statistics and calculation of MELD, UKELD and Child's-Pugh scores. Data were analysed for the 6 months prior to rifaximin usage and at 3, 6 and 12 months later.
RESULTS: The study population comprised 42 patients, 62% male, mean age 59 years. Cirrhosis aetiology was alcohol 55%, NASH 24%, autoimmune 10%, HCV 5%, miscellaneous 6%. At initiation, 24% of patients were using alcohol and 19% took quinolone secondary prophylaxis against spontaneous bacterial peritonitis. Mean baseline prognostic scores were Child's-Pugh 9.4 (SD 2.1), MELD 15.0 (SD 7.9), UKELD 51.2 (SD 5.1). Survival at 3, 6 and 12 months post-rifaximin was 78%, 67% and 62% respectively. There was a significant reduction in Child's-Pugh scores at 3 and 6 months ($p<0.01$) but not 12 months and no significant change in MELD or UKELD. Comparing the 6 months pre/post rifaximin, hospitalisation days fell from 233 to 143, a mean of 5.6 per patient, representing a saving of €1,829 in healthcare tariff costs. The number of admission episodes fell from 25 to 11.
CONCLUSION: In an unselected ''real world'' cohort of patients with chronic hepatic encephalopathy, rifaximin was associated with fewer readmission spells and a reduction in bed days with potential savings in healthcare utilisation costs. The efficacy of rifaximin for the maintenance of remission in patients with chronic HE can be demonstrated in a secondary care environment.
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Disclosure of Interest: H. Preedy: None declared, A. Fowell: None declared, R. Aspinall Consultancy for: RA has received consultancy fees from Norgine UK

P0608 NON-INVASIVE PORTAL HYPERTENSION AND OESOPHAGEAL VARICES EVALUATION BY LIVER AND SPLEEN TRANSIENT ELASTOGRAPHY IN PATIENTS WITH CHRONIC LIVER DISEASE

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INTRODUCTION: Liver transient elastography (TE) can predict liver fibrosis with high specificity and sensitivity. However, there is only limited data if TE could predict clinically significant portal hypertension or presence of oesophageal varices.
AIMS & METHODS: The aim of our study was to assess correlation between liver and spleen transient elastography, hepatic venous pressure gradient (HVPG) and presence of oesophageal varices. In this prospective study the correlations of liver and spleen TE with HPVG and presence of oesophageal varices were assessed in 78 chronic liver disease patients (50 patients had chronic hepatitis C). Spleen TE was feasible in 72 of them. TE was measured at the same day before HPVG measurement. Interquartile range/median $<20\%$ and success rate $>60\%$ were considered as good quality criteria during TE both for spleen and liver investigations. Endoscopy was performed in one week period after TE was done. Oesophageal varices were classified into 0 - III grades (according Baveno consensus). Patients were categorised into those with and without oesophageal varices. HPVG was measured using catheter occlusion technique by experienced radiologist. Patients were classified in to $>=12$mmHg (clinically significant portal hypertension), and <12mmHg HPVG groups. Cut-off values were established by ROC analysis.
RESULTS: Strong correlation of liver stiffness R – 0.74 ($p<0.01$) and moderate correlation of spleen stiffness R – 0.52 ($p< 0.01$) with HVPG were established. To determine the patients with HVPG $>=12$mmHg, liver TE cut-off value 18.5kPa had sensitivity 0.91 and specificity 0.74; spleen TE cut-off value 57.0 kPa had sensitivity 0.75 and specificity 0.77. Area under the ROC curve was 0.90 for liver TE and 0.83 for spleen TE.
Strong correlation of liver stiffness R – 0.61 ($p<0.01$) and moderate correlation of spleen stiffness R – 0.48 ($p< 0.01$) with oesophageal varices grade were established. To predict the presence of oesophageal varices liver TE cut-off value 21.5kPa had sensitivity 0.86 and specificity 0.83; spleen TE cut-off value 57.0 kPa had sensitivity 0.73 and specificity 0.75. Area under the ROC curve was 0.86 for liver TE and 0.76 for spleen TE.
CONCLUSION: Liver transient elastography strongly correlates and spleen TE moderately correlates with HVPG and oesophageal varices grade. Liver TE accurately predicts significant portal hypertension and oesophageal varices in patients with chronic liver disease and is more sensitive and specific than spleen TE. Therefore liver transient elastography could be reproducible outpatient screening tool for portal hypertension or oesophageal varices.
Disclosure of Interest: None declared

P0609 NUTRITIONAL EVALUATION OF THE CIRRHOTIC PATIENT WITHOUT ASCITES: IS THERE A ROLE FOR ANTHROPOMETRIC PARAMETERS?

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INTRODUCTION: Malnutrition due to chronic liver disease is common and its assessment is difficult. The anthropometric parameters, often used in clinical practice, have limited use in the nutritional evaluation of cirrhotic patients mainly those with ascites/edema. Some studies demonstrate that Maastricht Nutritional Index (MI) is the best assessment in early stages of the disease, however the best method of nutritional evaluation in cirrhotic patients remains controversial.
AIMS & METHODS: Aim: To determinate the role for anthropometric parameters in the nutritional evaluation of cirrhotic patients without ascites and compare it with the MI.
Patients and Methods: Prospective study of cirrhotic outpatients without ascites (diagnosis based on histological evidence and/or high clinic/ biochemical /imagiological suspicion). Exclusion criteria: enteric nutrition, amputation, malabsorption syndrome, chronic pancreatitis, inflammatory bowel disease, chronic kidney disease, acquired immunodeficiency syndrome, neuromuscular diseases and oncologic advanced disease. Included patients where classified according Child-Pugh Score; weight (kg), height (cm) and body mass index (BMI) were evaluated; and based in MI they were stratified in mild (>0-3), moderate (>3-6) and severe (>6) impaired nutritional status.
RESULTS: 50 cirrhotic patients were included in the study, 84% (n = 42) had alcoholic cirrhosis, the mean age was 58+/-11.4 years and 60% were male (n = 30). Concerning cirrhosis severity: 88% (n = 44) were Child-Pugh A and 12% (n = 6) Child-Pugh B. 8% (n = 4) had a BMI $<18.5\%$, regardless of age, gender or etiology. MI detected malnourishment/malnutrition in 38% (n = 19) of patients: 24% (n = 12) mild and 14% (n = 7) moderate impaired nutritional status. In MI evaluation no statistically difference was found between etiology, gender and age. No association between malnutrition and disease severity (Child-Pugh Score) was found with both methods.
CONCLUSION: In this study anthropometric parameters underestimate malnutrition in cirrhotic patients when compared with the Maastricht Nutritional Index, which detected malnutrition in early stages of hepatic disease.
Disclosure of Interest: None declared

P0610 EFFICACY OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT FOR THE PREVENTION OF VARICEAL REBLEEDING IN CIRRHOTIC PATIENTS WITH PORTAL VEIN THROMBOSIS

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INTRODUCTION: Although several studies have elucidated the beneficial effects of TIPS on PVT in patients with cirrhosis[1, 2, 3] in short term, it is regrettable that the long term effects of TIPS in cirrhotic patients with PVT is not very clear, especially in patients with a history of oesophageal and gastric varices bleeding, therefore the aim of this retrospective study was to evaluate the feasibility, safety, and efficacy of TIPS for the prevention of variceal rebleeding in cirrhotic patients with PVT.
AIMS & METHODS: ***Aim*** The aim of this study was to evaluate the efficacy of TIPS for the prevention of variceal rebleeding in cirrhotic patients with PVT retrospectively.
Methods Forty consecutive cirrhotic patients with a history of variceal bleeding were referred for TIPS between August 2008 and December 2013. All patients were diagnosed with non-malignant PVT, including 37 partial PVT and 3 portal cavernoma. Patients were followed until last clinical evaluation, diagnosis of hepatocellular carcinoma, liver transplantation, or death.
RESULTS: TIPS were successfully placed in 85% of patients (34/40), 86.5% (32/37) in patients with partial PVT and 66.7% (2/3) with portal cavernoma, without complication or TIPS-related mortality. Patients with successful TIPS were followed up for a mean of 12.9 months (range1-37 months) and portosystemic pressure gradient (PSG) was reduced from a mean 21.6 ±4.0 to 14.4± 5.2mm Hg after TIPS placement, the decreasing amplitude of PSG reached 29.4% ± 5.0% from baseline. The 1- and 2-year cumulative variceal rebleeding rates were 11.8% and 48.5% in the success group and 16.7% and 37.5% in the failure group, respectively ($p=0.438$). The only independent predictor for variceal rebleeding in the success group was TIPS shunt flow velocity. The cumulative rate of TIPS dysfunction at 1-and 2-year was 11.8% and 31.4%. Hepatic

encephalopathy occurred in 44.1% (15/34) of patients, and all of them happened within the first year after TIPS. The 1- and 2-year cumulative survival rates were 80.1% and 49.9% in the success group and 100% and 75.0% in the failure group, respectively ($p = 0.471$).
CONCLUSION: TIPS placement is safe, feasible and has a fairly high success rate to prevent variceal rebleeding in cirrhotic patients with PVT. Moreover, TIPS can highly decrease the risk of variceal rebleeding because of the reduction of PSG, and the only independent predictor for variceal rebleeding was TIPS shunt flow velocity. We suggest TIPS should be considered a viable treatment option for cirrhotic patients with PVT, especially in patients with a high risk of variceal rebleeding.
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Disclosure of Interest: None declared

P0611 CO-LOCALIZATION OF HBX AND COXIII PROMOTES HL-7702 CELL PROLIFERATION THROUGH CROSSTALK AND SYNERGY OF COX-2 AND B-CATENIN SIGNAL PATHWAYS

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INTRODUCTION: Hepatocellular carcinoma (HCC) is one of the most common malignant diseases, and HBx leads to the development of HBV-associated HCC. Our recent studies have revealed that HBx can interact with the inner mitochondrial membrane protein, COXIII, by yeast two-hybrid system, mating experiment and coimmunoprecipitation.
AIMS & METHODS: To futher explore the co-localizaiton of HBx and COXIII in HL-7702 cell and to investigate the molecular mechanism of HBx in HL-7702 cell proliferation. A HL-7702 cell line stably expressing the HBx gene by lentivirus vectors were constructed. Confocal microscopy was utilized to assess the interaction between HBx protein and COXIII. The functional relevance of HBx protein–COXIII interaction was investigated in cell cultures.
RESULTS: Our studies first demonstrated that HBx co-localized with the inner mitochondrial protein, COXIII, in HL-7702 cells, causing the up-regulation of COXIII protein expression as well as COX activity. HBx elevated the generation of mitochondrial ROS and ROS was necessary for it to activate the expression of COX-2. Moreover, HBx promoted cell proliferation through COX-2/β-catenin signaling pathways.
CONCLUSION: Collectively, the major finding of this study is that the co-localization of HBx and COXIII leads to the changes of mitochondrial biogenesis and morphology. Besides, COX-2 and β-catenin signal pathways stimulated by mitochondrial ROS have crosstalk and synergy in the oncogenesis of HBV-associated HCC.
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Disclosure of Interest: None declared

P0612 RISK FACTORS ASSOCIATED WITH MORTALITY IN HEPATITIS E RELATED ACUTE LIVER FAILURE DURING PREGNANCY

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INTRODUCTION: HEV infection is fatal during pregnancy. The mortality rate in pregnant women with ALF is 15-20%, which is associated with an altered status of hormones and difference in immune response.
AIMS & METHODS: Aim of the study is to determine biochemical and haemotological factors associated with mortality in Hepatitis E related acute liver failure during pregnancy. A total of 73 consecutive ALF pregnant patients with HEV infection were recruited in the study during July 2008 to August 2013 and patients were followed up until death or complete recovery. Patients with viral co-infections and with history of pre-existing liver disease were excluded. Biochemical and pathological parameters included detailed liver function tests (AST, ALT, alkaline phosphatase and total serum bilirubin), total proteins, prothrombin time and complete haemogram. All the cases were screened for hepatitis virus markers by ELISA. ROC curve was drawn to predict cut-off level of serum albumin in ALF pregnant patients.
RESULTS: The mean maternal age and gestational at delivery were 25.32 $\pm$3.62years and 29.53$\pm$4.62 weeks respectively. Forty six out of 73 (63.01%) ALF pregnant patients were non survived and twenty seven out of 73 (36.98%) were survived. HEV was found to be the commonest cause of ALF in pregnancy. It was found that in univariate logistic regression analysis AST, ALP, bilirubin, prothrombin time, total protein and albumin were the statistically significant factors between survival and non-survival group. A multivariate logistic regression analysis was performed using significant independent variables, and it was found that variables that independently predicted mortality were serum alkaline phosphatase (OR = 5.21, 95% CI = 1.27-21.42; $p < 0.05$), prothrombin time (OR = 6.47, 95% CI = 1.69–24.77; $p < 0.01$), serum albumin (OR = 7.85, 95% CI = 1.73-35.55; $p = 0.01$) and serum total protein (OR = 3.88; 95% CI = 1.01–14.94; $p < 0.05$). A receiver operating characteristic curve was drawn for serum albumin. The area under the curve was 0.643. The serum albumin level of $\leq$2.1g/dl was found to be the cut-off for ALF pregnancy patients with 67% sensitivity and 63% specificity.
CONCLUSION: Serum albumin, serum total protein, serum alkaline phosphatase and prothrombin time were significant independent risk factors associated with mortality in ALF pregnant patients.
Disclosure of Interest: None declared

P0613 FAVORABLE ANTIVIRAL EFFECT OF NUCLEOSIDE ANALOGUES REDUCES HEPATOCELLULAR CARCINOMA DEVELOPMENT IN HIGH RISK PATIENTS WITH CHRONIC HEPATITIS B VIRUS INFECTION

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INTRODUCTION: Chronic hepatitis B virus (HBV) infection leads to cirrhosis and hepatocellular carcinoma (HCC). Recently, HCC risk scales enable us to estimate the risk of developing HBV related HCC (REACH-B score, Lancet Oncol 2011;12:568). The objective of this study was to evaluate the on-treatment predictive factors of nucleoside analogues (NAs) to reduce HBV related HCC development for the high risk patients of chronic HBV infection in Japan, where genotype C is the most prevalent.
AIMS & METHODS: This study was retrospective cohort study including the patients treated with NAs for at least 12 months. The patients were applied into REACH-B score and risk scores were generated based on sex, age, serum ALT concentration, HBeAg status, and serum HBV DNA level. The favorable responses of NAs were defined as each of these cases, (1)decrease in serum ALT levels to within the normal range by 24 weeks, (2)decrease in HBV DNA less than 4.0 log copies/mL by 24 weeks, (3) achievement of HBeAg seroconversion or (4)decrease in HBsAg less than 100 IU/mL. We compared the incidence of HCC between favorable responder and poor responder.
RESULTS: A total of 76 Japanese patients with nucleoside-naïve chronic HBV infection were included. Thirty two patients were started with lamivudine, 44 patients were started with entecavir. Mean treatment duration was 1387 days (range 374-4360). Mean pre-treatment HBV DNA and ALT levels were 7.14 log copies/mL and 282 IU/L, respectively. The mean age was 50.0$\pm$11.9 years and 47 (61.8%) patients were male. Forty (52.6%) patients were HBeAg positive, 18 patients (23.7%) had clinical evidence of liver cirrhosis. Genotype C was the most prevalent (43 of 48, 89.6%). Nine patients developed HCC during follow-up. All 9 patients were from the group whose REACH-B scores were 11 points or more (52 patients, defined as high risk patients, in this study). Of the high risk patients, those who had achieved HBeAg seroconversion reduced HCC development significantly ($p = 0.0478$). The cumulative HCC incidence rates at 5-year were 4.7% and 40.0% for the patients who achieved HBeAg seroconversion (favorable responder) and those who did not (poor responder), respectively.
CONCLUSION: The high risk patients still have the risk of developing HCC. NAs can reduce HCC development for the high risk patients with chronic HBV infection (Hepatology 2013;58:98). From our study, favorable antiviral effect (for example, achievement of HBeAg seroconversion) of NAs may reduce HCC development in the high risk patients with chronic HBV infection.
Disclosure of Interest: None declared

P0614 PREVIOUS INTERFERON THERAPY DOES NOT LEAD TO A BETTER VIROLOGICAL RESPONSE IN PATIENTS TREATED WITH ENTECAVIR: A COHORT STUDY

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INTRODUCTION: Entecavir (ETV) is a potent inhibitor of HBV replication.
AIMS & METHODS: The aim of the study was to explore if previous interferon (IFN) therapy might influence response to Entecavir in chronic hepatitis B.
A retrospective cohort study was performed, including all subjects who received ETV for chronic hepatitis B, in the south-Eastern Romania. We assessed viral response, HBeAg loss and seroconversion, HBsAg loss and seroconversion, biochemical response. Comparison of categorical data was performed by c^2-test or Fisher's exact were applicable.

RESULTS: 533 patients were followed for a median period of 24 months. The cohort was 64% male, 23% HBeAg-positive, 23% IFN-pretreated, 17% Lamivudine-pretreated, 8% cirrhotics. At baseline, the median hepatitis B virus DNA was 5.95 (interquartile range = 1.08-9.97) log10 IU/ml. At week 48, 71% of the patients (32% HBeAg-positive; 82% HBeAg-negative) achieved a virological response and 91% (78% HBeAg-positive; 95% HBeAg-negative) of those with elevated baseline alanine aminotransferase showed a biochemical response. Thirty-two per cent (39/123) of the HBeAg-positive patients lost HBeAg and 23% (28/123) achieved seroconversion to anti-HBe. Positive predictive factors for virologic response are: low score of fibrosis (p-0.006), low level of HBV DNA (p-0.003). Negative predictive factors for virologic response are: HBe antigen positive status (OR odds ratio 0.15, 95%CI confidence interval 0.07-0.30; p-value < 0.001), prior IFN therapy. (OR 0.45, 95% CI 0.24-0.86; p-value 0.015). Baseline level of ALT, age, sex, previous Lamivudine therapy had no impact on virologic response. Virological breaktrough was found in 0.8% of patients. Seven patients (1.31%) showed clearance of hepatitis B surface antigen.
CONCLUSION: ETV maintained and even increased the high initial response rate (from 71% to 90.6%). Low score of fibrosis, low level of HBV DNA, HBe antigen negative status, absence of prior interferon therapy predict a good virologic response. Lamivudine-resistant patients usually respond well to ETV, but 15.62% are non-responders, suspect of Entecavir resistance.

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Disclosure of Interest: None declared

P0615 BENEFITS OF LONGER DURATION NUCLEOS(T)IDE ANALOGUES THERAPY IN PATIENTS WITH CHRONIC HEPATITIS B: A NATIONWIDE COHORT STUDY

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INTRODUCTION: Nucleos(t)ide analogues (NUCs) therapy reduced the risk of hepatitis B virus (HBV) disease progression. However, whether NUCs long-term therapy is more effective than short-term therapy remains controversial.
AIMS & METHODS: We conducted a nationwide cohort study based on Taiwan's National Health Insurance Research Database (NHIRD) between October 1, 2003 and December 31, 2011. Among the CHB patients, we used propensity scores to match 8,631 patients with NUCs therapy for at least 1.5 years (long-term therapy cohort) with 8,631 patients with NUCs therapy for at least 90 days, but less than 1.5 years (short-term therapy cohort). Major outcomes, including liver decompensation, hepatic failure, or overall mortality, between the 1.5 and 3 years after date of starting NUCs therapy were analyzed. Cumulative incidences and multivariable analyses were calculated after adjusting for competing mortality.
RESULTS: Compared with short-term therapy cohort, long-term therapy cohort had significantly lower risk of liver decompensation (1.05%; 95% confidence interval [CI], 0.81-1.30% vs. 2.13%; 95%CI, 1.82-2.45%; $P < 0.001$), hepatic failure (0.35%; 95% CI, 0.21-0.49% vs. 0.63%; 95% CI, 0.46-0.80%; p = 0.008), and overall mortality (1.67%; 1.37-1.98% vs. 2.44%; 95% CI, 2.10-2.77%; P < 0.001). After adjusting for competing mortality and other confounders, long-term therapy was associated with a reduced risk of liver decompensation (adjusted hazard ratio, aHR: 0.47; 95%CI, 0.36-0.62, P < 0.001), hepatic failure (aHR: 0.53; 95%CI, 0.33-0.86, p = 0.01) and overall mortality (aHR: 0.67; 95% CI, 0.53-0.84, p = 0.001).
CONCLUSION: NUCs long-term therapy was associated with reduced risks of liver decompensation, hepatic failure and overall mortality in CHB patients.

Disclosure of Interest: None declared

P0616 THE INACTIVE HBV-CARRIER PROFILE: THE LONG-TERM OUTCOME

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INTRODUCTION: The inactive HBV profile is one of the aspects of natural history of chronic hepatitis B (HVB). We aimed to define epidemiological, clinical and virological features of inactive HVB-carriers and to evaluate their long-term outcome
AIMS & METHODS: It's a monocentric and descriptive study including 575 chronic HVB-carriers - over 18 years old- followed since 1998. The inactive HBV profile was defined by normal serum aminotransferases, HBeAg-negative state and DNA levels < 2000 IU/ml. We excluded patients with HIV and/or HCV co-infection and alcohol consumers. HBV-reactivation was defined by an HVB DNA load up to 2000 IU/ml. All clinical, biological and serological data were collected. Serum HBV DNA levels were measured using real-time PCR quantification assays. Liver biopsy was indicated according to international recommendations
RESULTS: Of 575 considered patients, the inactive HVB-carriers represented 49.7% (n = 286). Mean age was 35.5 years old [18-63], male gender was prominent (sex-ratio = 1.93). Mean time of follow-up was 6 years [1- 15]. The most probable ways of HVB transmission were unprotected sexual practices and unsafe tooth-care (respectively 57 % and 34.5%). Ultrasonography found an heterogeneous hepatic parenchyma in 12% and steatosis in 4%. Liver biopsy was indicated in 6 patients: fibrosis was less than F2 according to Metavir score. HVB-reactivation was reported in 2 patients (0.01%) which indicates antiviral treatement. Spontaneous HBsAg loss was achieved in 5 patients. No case of hepatocellularcarcinoma was reported.
CONCLUSION: Our "real-life" experience confirms that the inactive HVB profile is associated to less complications and better long-term outcome.

Disclosure of Interest: None declared

P0617 ANTIVIRAL EFFICACY OF ENTECAVIR VERSUS ENTECAVIR PLUS ADEFOVIR FOR HEPATITIS B VIRUS RTA181V/T MUTANTS ALONE

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INTRODUCTION: Hepatitis B virus (HBV) rtA181V/T mutants developed by long-term nucleos(t)ide analogues therapy are known to confer cross-resistance for other nucleos(t)ide analogues, except entecavir (ETV). Although ETV has primarily been used as rescue therapy for rtA181V/T mutants, some studies have reported that rtA181V/T mutants could induce cross-resistance to ETV. In practice, a clinical investigation reported that rtA181V/T mutants might confer HBV DNA persistence, and showed an association with incomplete response, despite rescue therapy with ETV.
AIMS & METHODS: The aim of this study was to investigate antiviral efficacy of ETV alone and in combination with adefovir (ADV) as rescue therapy for HBV rtA181V/T mutants alone. A total of 30 patients who received ETV (1.0 mg/day) monotherapy or ETV plus ADV (10 mg/day) therapy over 48 weeks against HBV rtA181V/T mutants only without other concomitant mutation between April 2008 and October 2011 were enrolled. The subjects were divided into the ETV group ($n = 16$) and the ETV + ADV group ($n = 14$). Virological, biochemical, and serological response after 48 weeks of rescue therapy were investigated retrospectively.
RESULTS: No significant difference in baseline characteristics, including serum HBV DNA levels (4.8 ± 1.7 vs. $4.1 \pm 1.8 \log_{10}$IU/mL) and the rate of HBeAg positivity (93.8 vs. 100%) was observed between the two groups ($p > 0.05$). Virological response at 48 weeks showed complete virological response (serum HBV DNA < 20 IU/mL) (62.5 vs. 42.9%), partial virological response (6.3 vs. 28.6%), non-response (25.0 vs. 28.6%), and virological breakthrough (6.3 vs. 0%), respectively. No statistical significance was observed in virological response ($p = 0.278$). No significant difference in mean reduction of serum HBV DNA and biochemical response rates was observed between both groups, respectively (4.3 ± 2.9 vs. $4.1 \pm 1.8 \log_{10}$IU/mL; $p = 0.294$, 88.9 vs. 100%; $p = 1.000$). In addition, no significant difference in HBeAg loss or seroconversion was observed between the two groups (26.7 vs. 28.6%; $p = 1.000$).
CONCLUSION: As rescue therapy for HBV rtA181V/T mutants alone, ETV monotherapy was clinically as effective as ETV plus ADV therapy.

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Disclosure of Interest: None declared

P0618 HEPATOCELLULAR CARCINOMA IN CHRONIC HEPATITIS B PATIENTS UNDER ANTIVIRAL TREATMENT - RISK FACTORS AND THE PERFORMANCE OF A VALIDATED PREDICTIVE RISK SCORE

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INTRODUCTION: Antiviral therapy reduces but does not eliminate the risk of hepatocellular carcinoma (HCC) in chronic hepatitis B patients with or without cirrhosis. Retrospective or prospective observational cohort studies that provide HCC data for patients mainly treated with tenofovir are lacking.
AIMS & METHODS: We performed a single-center retrospective cohort study of 120 patients with chronic hepatitis B (age, 47±14; 83 male), 20% (n = 24) with clinical cirrhosis, who were treated with tenofovir 300mg daily (n = 85; 72%) or entecavir 0.5/1mg daily (n = 33; 28%) for at least 12 months. Patients co-infected with hepatitis C virus or human imunodeficiency virus were excluded. Univariate and multivariate analysis of risk factors associated with HCC development were performed. Accuracy of a recent validated HCC-risk score (REACH-B) was assessed.

RESULTS: Our population was mainly caucasian (n = 80; 67%) and african (n = 37; 31%). The most common serological profile was AgHBe negative (n = 82; 73%). 69 patients (60%) were treatment-naïve. Alcohol abuse was reported in 14 patients (12%). The rates of biochemical, total and partial virological response were: 96.5%, 89.2% and 8.3%. The mean time under antiviral therapy was 41±19 months. After a 82±54 months of follow-up, 9 patients (7.6%) developed HCC. The 1 and 3-year cumulative incidence of HCC was 2.7% and 11.1%. Patients who developed HCC were older ($p < 0.001$), alcoholics ($p < 0.05$), cirrhotic at baseline ($p < 0.05$; OR = 15.469; 95%CI: 3.454-69.272) and displayed a higher REACH-B score at baseline ($p < 0.05$). On an univariate analysis, a REACH-B baseline score ≥ 8 predicted relatively well HCC occurrence ($p = 0.071$; OR = 6.352; 95%CI: 0.754-53.486) however, a score ≥ 12 points predicted better ($p < 0.05$; OR = 10.595; 95%CI: 2.275-49.338). Gender, ethnic origin, AgHBe status, baseline viremia, previous treatment and time under antiviral therapy were not associated with HCC occurrence. Through logistic regression, multivariate analysis identified as risk factors associated with HCC occurrence: cirrhosis at baseline ($p = 0.016$; OR 7.975; 95%CI: 1.464-43.432) and REACH-B score baseline ≥ 12 ($p = 0.015$; OR 7.603; 95%CI: 1.480-39.070). The 1 and 3-year cumulative incidence of HCC in patients with REACH-B score baseline ≥ 8 was 7.4% and 16.8%, while a score ≥ 12 confered a risk of 12.6% and 42.7%, respectively. By Kaplan-Maier analysis, excluding alcohol abusers, patients who scored ≥ 8 points in REACH-B had a significantly higher risk of developing HCC ($p = 0.029$) compared with those with < 8 points. At baseline, the REACH-B score performed well, with a AUC of 0.811 (95%CI: 0.668-0.954). A cut-off score of ≥ 8 (at baseline) yielded 87.5% sensitivity, 47.6% specificity, 11.5% positive predictive value (PPV) and 98% negative predictive value (NPV).

CONCLUSION: Even with long periods under antiviral therapy, the occurrence of hepatocellular carcinoma in patients with chronic hepatitis B remains a problem. In our cohort, HCC mostly occured in older (≥ 50 y/o) and alcohol consuming patients, probably with an underlying cirrhotic liver. The performance of REACH-B score (with a cut-off ≥ 8) in non-alcoholic patients seems to perform well in predicting the risk of developing HCC.

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P0619 REACTIVATION OF HEPATITIS B VIRUS IN HBSAG-NEGATIVE HBCAB-POSITIVE PATIENTS WITH PSORIASIS UNDERGOING IMMUNOSUPPRESSIVE THERAPY

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INTRODUCTION: Viral hepatitis reactivation has been widely reported in patients undergoing immunosuppressive therapy; however, few data are available on the risk of HBV reactivation in patients with psoriasis receiving immunosuppressive drugs.

AIMS & METHODS: We conducted a retrospective study to value the effect of immunosuppressive therapy on HBV infection in psoriatic patients.

The study included all consecutive psoriatic patients who attended an Italian tertiary referral hospital from 2008 to 2012. A total of 412 patients were consecutively enrolled. We evaluated: HBV markers, type of immunosuppressive treatment and the occurrence of HBV reactivation. Reactivation was defined as reappearance of HBsAg, increase in HBV-DNA at least 1 log in comparison to basal level, in association with or without increase of aminotransferase levels. The observational period ranged from the beginning of immunosuppressive treatment to 6 months after the end of therapy.

RESULTS: A total of 225/412 (54.6%) patients with psoriasis and receiving immunosuppressive therapy (cyclosporine or methotrexate, and/or biological drugs, such as adalimumab, infliximab, etanercept, golimumab, ustekinumab) were tested for markers of HBV infection. We identified 23/225 subjects (10.2%) with isolated HBcAb positivity and 36/225 (16%) with HBcAb/HBsAb positivity. No patient was HBsAg positive. No patient underwent preemptive therapy with Lamivudine or other antiviral drugs. No patient showed episodes of HBV reactivation.

CONCLUSION: In dermatological setting the immunosuppressive therapy, in HBcAb+ and HBcAb+/HBsAb+ patients, seems to be safe regardless to the type of treatment schedule.

Disclosure of Interest: None declared

P0620 SPANISH MULTICENTRE STUDY PIBHE: PREVALENCE OF HEPATITIS B VIRUS INFECTION AND IMMUNIZATION IN HEMODIALYSIS PATIENTS

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INTRODUCTION: The estimated prevalence for chronic hepatitis B virus (HBV) infection is 0-10 % in hemodialysis patients, with wide variations geographically and between units in the same country. The estimated prevalence in Spain was 3.1 % in 2003. Immunization in the vaccinated patients is 40-70 % compared to 97% of the general population.

AIMS & METHODS: National multicenter cohort study, approved by the Ethics and Clinical Investigation Committee of the coordinating center, conducted between January 2013 and January 2014. The aim of this study was to determine the prevalence of HBV in hemodialysis patients in Spain and their situation regarding immunization. A case report form was sent to all the hemodialysis units of Spain to collect information about the patients after informed consent. The data were included in a central database.

RESULTS: One hundred and forty two hemodialysis units participated (104 hospitals, 38 satellite centers). Of the 13,845 patients included, 125 were HBV-positive, resulting in a prevalence of 0.9%. A third of the centers had a HBV-positive patient. The mean age was 66.6 (20-98) in the HBV-negative patients and 45.5 years old in HBV-positive patients (26-72).

In HBV-positive patients, 17.3 % were coinfected with hepatitis C and/or human immunodeficiency viruses. 70 % of patients had positive antiHBe. 82% had a viral load below 2,000 IU/ml. The AST and ALT levels were 18.3 ± 10.5 IU / ml and 14.5 ± 9 IU / ml, respectively. 8.7 % had undergone a liver biopsy; 32% had received antiviral treatment; 37.5 % were candidates for renal transplantation and 65.2 % were followed for Gastroenterology.

In HBV-negative patients, 33.6 % had not been vaccinated; 14.2% had positive anti-HBc. Fourteen different vaccination schedules were used. The immune response stood at 66.4 %. The levels of anti-HBs after vaccination were 10-99 mIU/ml in 29.5 %, 100-999 mIU/ml in 23.9% and equal to or greater than 1000 mIU/ml in 8.4%. More than a half (56.7%) had received a vaccination course; 22.6 %, two cycles; 0.6%, three cycles; and 9.5%, an annual booster. The most likely to achieve an immune response was achieved with four doses of 40 mcg of adjuvanted vaccine (OR 4.9), for the same age and number of revaccination cycles and boosters. Age and dose and adjuvant vaccine usage influenced the immune response and the title of antiHBs reached ($p < 0.05$). 81.1 % of researchers agreed that the questionnaire had helped them to assess the management of HBV infection that performed on their patients.

CONCLUSION: Prevalence of chronic HBV infection in hemodialysis in Spain is low, and so are the rates of immunization against HBV. The vaccination schedules are diverse and have been correlated with the immune response. It would be necessary to formalize the most effective schedule in increasing immunization in these patients.

Disclosure of Interest: None declared

P0621 REACTIVATION OF HBV INFECTION IN HBSAG NEGATIVE ONCOHAEMATOLOGICAL PATIENTS TREATED WITH CHEMOTHERAPY CONTAINING OR NOT RITUXIMAB

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INTRODUCTION: Routine prophylaxis for hepatitis B reactivation is recommended for oncohaematological HBsAg+ subjects undergoing immunosuppressive therapy, due the risk of reactivation. In particular, HBV reactivation occurs more frequent in patients receiving Rituximab. Nonetheless,the incidence in those receiving Rituximab-free therapy needs to be better investigated

AIMS & METHODS: This study evaluates the effects of chemotherapy with or without Rituximab in patients HBsAg negative/HBcAb positive with Non-Hodgkin Lymphoma (NHL) or Hodgkin Lymphoma (HL).

123 patients (21 with NHL and 102 with HL) were consecutively enrolled. We evaluated HBV markers, treatment schedule and occurrence of HBV reactivation (reappearance of HBsAg, increase in HBV-DNA at least 1 log in comparison to basal level with or without increase of aminotransferase levels during therapy and 6 months after the end of therapy).

RESULTS: 46 patients (M/F 24/22, median age 49 yrs, range 21-74 yrs), 33 with isolated HBcAb and 13 with HBcAb/HBsAb positivity, were observed. Six/46 were treated with therapeutic schedule containing Rituximab. Five/6 received successfully preemptive therapy with Lamivudine. HBV reactivation was observed in the only patient (HBcAb/HBsAb positive) treated with R-CHOP without Lamivudine prophylaxis. None of the other 40 patients treated with cytotoxic chemotherapy without Rituximab (ABVD-VEBEP) and without receiving preemptive therapy, showed HBV reactivation.

CONCLUSION: HBV reactivation is mainly related to the type of therapy. Our data revealed that patients with ''occult HBV infection'' receiving chemotherapy with Rituximab, in absence of prophylactic therapy, may be at high risk of reactivation. Otherwise, prophylaxis is not mandatory in patients HBcAb positive with or without HbsAb positivity undergoing Rituximab-free schedule. This results suggest that preemptive therapy will be tailored to the cytotoxic chemotherapeutic schedule.

Disclosure of Interest: None declared

P0622 HEPATITIS B SEROLOGIC MARKERS AFTER 14 YEARS OF UNIVERSAL NEW-BORN VACCINATION

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INTRODUCTION: The burden of hepatitis B infection around the world is very high. In Portugal, hepatitis B vaccination was part of the National Vaccination Programme, with vaccination of all adolescents, since 1995, extended to all newborns in the year 2000. The aim of the present study was to evaluate how it affected serological markers of hepatitis B in the general population and in high-risk groups.
AIMS & METHODS: Prevalence of HBs Ag was evaluated in a sample of three groups: adult general population (GP): 989 individuals, prison population (PP): 784, and drug-users (DU): 18305. Prevalence of HBsAg, HBsAb, HBcAb, and ALT and AST serum levels were determined in the general population.
RESULTS: Prevalence of HBsAg was GP: 12/989(1.2%); PP: 32/784 (4.1%) and DU: 927/18305 (5.0%). In the GP, the prevalence of HBsAg negative, HBsAb positive with HBcAb negative (suggesting effective previous vaccination) was: 315/989 (31.8%), with mean age: 38.8 years. Furthermore two thirds of the individuals aged less than 30 years had the latter pattern. Prevalence of HBcAb positive was 107/989 (11%): in 29 (2.9%) cases isolated, and in 75 (7.5%) associating with HBsAb positive, the latter suggesting past infection.
CONCLUSION: Prevalence of HBs Ag was higher in the risk populations, although no major differences were found. There is evidence of effective vaccination status in the younger population. Emphasis on continuing universal hepatitis B programmes is of utmost importance.
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Disclosure of Interest: None declared

P0623 IL28B POLYMORPHISM CORRELATES WITH ACTIVE HEPATITIS IN HBEAG-POSITIVE CHRONIC HEPATITIS B PATIENTS

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INTRODUCTION: In recent studies, polymorphisms near the IL28B gene are strongly associated with spontaneous and treatment-induced viral clearance in chronic hepatitis C patients. However, the role of IL28B in the prediction of treatment outcome in chronic hepatitis B (CHB) patients and association with the natural course of CHB is currently debated. This study aimed to determine the relationship between IL-28B polymorphisms and hepatitis activity in CHB.
AIMS & METHODS: 190 treatment-naïve CHB patients were identified and IL28B related SNPs were determined by pyrosequencing method. Active hepatitis in patients without liver cirrhosis was defined as persistent ALT $>$ 2 x upper limit of normal (ULN) for over 3 months or a peak ALT level $>$ 5x ULN. In patients with liver cirrhosis, active hepatitis was defined as persistent ALT$>$ ULN for over 3 months.
RESULTS: 143 patients were enrolled and 41(38%) had active hepatitis. rs12979860 CC and rs8099917 TT were 87%. and the two SNPs were found to be in strong linkage disequilibrium (D'$=1.0$, $r^2=0.9082$). The IL28B SNP rs12979860 minor allele "T" and rs8099917 minor allele "G" were correlated with active hepatitis in patients with HBeAg positve CHB ($p=0.029$). On the contrary, in HBeAg negative CHB there was no relationship between IL28B SNPs and active hepatitis.
CONCLUSION: We could find that host immune response related to IL28B polymorphism considering viral factor like genotype plays an important role in active hepatitis in HBeAg positive CHB patients.
Disclosure of Interest: None declared

P0624 TREATMENT OF HEPATITIS C IN PRISON IN FRANCE IN 2011-2012: MORE PATIENTS TREATED IN FEWER MEDICAL JAILHOUSE UNITS: RESULTS OF NATIONAL PRACTICE SURVEY

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INTRODUCTION: In France inmates' health care was done by public hospitals since 1994. Access to antiviral treatment was normally equal as people outside. Treatment of hepatitis C was until 2011 dual therapy (peg-interferon and ribavirin); in 2011, two direct antiviral agents (AAD), telaprevir INCIVO* and boceprevir VICTRELIS*, were available in triple therapy. National 2005 study of practices had demonstrated that at time of dual therapy, only 14 % of inmates with hepatitis C were treated. Recent national health institute studies (PRI2DE and PREVACAR) did not allow to answer the question of percentage of inmates treated for hepatitis C. Did arrival of triple therapy increase or decrease patients' percentage treated in prison?
AIMS & METHODS: Our objective was to study in national survey, in retrospective vision (since compassionate use of AAD in January 2011) and prospective vision over 2011 and 2012, number of patients treated by dual therapy and triple therapy in MJU. It was postal and/or mail survey.
RESULTS: On December 31th 2013, 77 MJU over 182 participated and were already analyzed: they took care of 38998 inmates; hepatitis screening was systematically proposed in 100 % of MJU; 30290 serology C were annually realized in 2011 and 31580 in 2012; 2012 rate was 4.5 % positivity (677 patients). Followed patients were 1579 in 2011 and 1717 in 2012; 49 % of MJU had regular hepatology consultation (one per month to two per week) and 33 % regular infectious diseases consultation; to evaluate liver fibrosis 227 FIBROSCAN* and 511 FIBROTEST / FIBROMETRE were realized in 2012 but only 2 liver biopsy. In 2011, 301 patients were treated (19 % of patients with serology C positive) and in 2012, 497 patients (29 %). Triple therapy constituted 12 % of treatment in 2011 and 39 % in 2012 (telaprevir 80/72 %, boceprevir 20/28 % in 2011/2012); 42 % of the MJU introduced no treatment in 2011 (77 % any triple therapy) and 56 % in 2012 (66 % any triple therapy).
CONCLUSION: These results allowed following conclusions: 1/ frequent positive patients VHC in jailhouses, 2/ good screening and diagnosis and using widely not invasive methods of fibrosis 3/ but very different practices for hepatitis treatment between few MJU treating a lot of patients and a lot of MJU treating none. Compared with national study of 2005, percentage of treated patients was doubled but percentage of MJU involved decreases in 45 %. A score of care of people infected by hepatitis C will be calculated from answers to items screening, specialized consultation, treatments 2011 and treatments 2012.
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P0625 SAFETY COMPARISON OF 12- AND 24-WEEK TREATMENTS IN HCV GENOTYPE 1-INFECTED PATIENTS WITH CIRRHOSIS: RESULTS FROM TURQUOISE-II

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INTRODUCTION: Interferon-containing protease inhibitor regimens have been associated with a high rate of serious adverse events (AEs) in patients with cirrhosis.[1] We report the safety of the 3 direct-acting antiviral (3D) regimen of ABT-450 (identified by AbbVie and Enanta) co-dosed with ritonavir (r), ombitasvir (formerly ABT-267) and dasabuvir (formerly ABT-333) with ribavirin (RBV) in the treatment of 380 HCV genotype 1-infected patients with cirrhosis.
AIMS & METHODS: Patients were randomized to receive the 3D+RBV regimen for 12 (N$=208$) or 24 weeks (N$=172$). Key eligibility criteria included: Child-Pugh A cirrhosis, platelet count $\geq$60.000 cells/mm3, serum albumin $\geq$2.8 g/dL, and total bilirubin <3 mg/dL. Treatment-emergent AEs from the time of study drug administration until 30 days after last dose for all patients who received $\geq$1 dose of study drug are reported.
RESULTS: The percentage of patients experiencing any AE, severe, or serious AEs were similar in both arms. AEs were mostly mild or moderate in severity. The most common AEs in the 12- and 24-wk arms respectively, were fatigue (32.7% vs. 46.5%), headache (27.9% vs. 30.8%), and nausea (17.8% vs. 20.3%). Four (1.1%) patients experienced AEs consistent with hepatic decompensation but were considered unrelated to study drugs. Five of 380 (1.3%) patients experienced serious AEs that were assessed by the investigator to have reasonable possibility of being related to the 3D regimen. All patients who modified RBV dose for any reason, 4 patients who received erythropoietin, and 2 patients who received a transfusion all achieved SVR12.

Treatment-Emergent AEs, n (%)	12-Wk 3D+RBV (N$=208$)	24-Wk 3D+RBV (N$=172$)
Any AE	191 (91.8)	156 (90.7)
Severe AE	14 (6.7)	13 (7.6)
Serious AE	13 (6.3)	8 (4.7)
AE Leading to Study Discontinuation	4 (1.9)	4 (2.3)
AE Leading to RBV Dose Reduction	17 (8.2)	22 (12.8)
Death	0[a]	0

[a]One patient died due to non-treatment emergent AEs that began 80 days after the last dose of study drug.

CONCLUSION: The 3D+RBV regimens were generally well tolerated, with no clinically significant differences in safety profiles based on treatment duration. AEs reported in this study of 380 patients with cirrhosis were generally consistent with those demonstrated for the 3D+RBV regimen in previous studies of patients without cirrhosis.

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P0626 STUDY ON IL28B SNP RS12979860 AND SNP RS8099917 GENOTYPING AND TREATMENT RESPONSE WITH PEGYLATED INTERFERON AND RIBAVIRIN IN EGYPTIAN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

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INTRODUCTION: Hepatitis C virus (HCV) infection is a common universal problem especially in the Arab world. A single nucleotide polymorphism near the IL28B gene on chromosome 19 coding for interferon-lambda-3 is associated with an approximately 2-fold difference in SVR rates among patients of different ethnicities.

AIMS & METHODS: The aim was to assess the value of IL28B SNP rs12979860 and SNP rs8099917 as a predictor of virological response to Pegylated interferon plus ribavirin in treatment of Egyptian patients with chronic hepatitis C virus infection. Our study included 604 HCV infected Egyptian patients with genotype 4. All patients received pegylated Interferon 2a and 2b plus ribavirin. We divided our cases according to their response to treatment into two groups: group I (344 patients) responded to treatment and group II (260) non responder patients. Analysis of both IL28 rs8099917 and IL28rs12979860 by real time PCR technique were done to all patients.

RESULTS: TT genotype of IL28 rs8099917 was associated with a higher response rate to treatment than other genotypes. TT genotype was present in 53.2% of responders Vs 17.7% of non responders ($P<0.001$) while GG genotype was present in 6.4% of responders Vs 37.7% of non responders ($P<0.001$). T allele was present in 73.4% of responders Vs 40 % in non responders while G allele were present in 26.6% of respnders Vs 60% in non responders ($P<0.001$). The response rate was lower in patients with T allele compared to those with C allele of IL28 rs12979860 and CC genotype were present in 47.4% of responders Vs 5% of non responders and TT genotype were present in 6.1% of responders Vs 33.1 % of non responders ($P<0.001$). The C allele was present in 70.6% of responders Vs 36% of non responders while T allele was present in 29.4% of responders Vs 64% of non responders ($P < 0.001$).

CONCLUSION: *IL28B* polymorphisms are strong predictors of virological response in chronic hepatitis C with genotype 4 and analysis of IL-28B genotype might be used to guide treatment for these patients.

Disclosure of Interest: None declared

P0627 IMPACT OF HEPATITIS C VIRUS ON ALLOGRAFT SURVIVAL AFTER RENAL TRANSPLANTATION

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INTRODUCTION: The long-term impact of hepatitis C virus (HCV) infection on kidney allograft survival remains controversial. Some studies found a significant deleterious effect of HCV infection on allograft survival and also higher mortality in this group of patients.

AIMS & METHODS: In this retrospective, single-center study, we aimed to compare the differences in kidney allograft survival over a long-term follow-up period between non-infected vs infected patients. Study population (HCV infected patients) was selected from a kidney transplant center database (1985 - 2013) and compared to a random sample extracted from the same database. Groups were compared using Chi-square test, student-T test, Mann-Whitney U test and survival methods (Kaplan-Meier) when appropriate. Statistical analyses were carried using SPSS 20.0 IBM@ (Chicago, IL, United States).

RESULTS: We identified 34 patients with HCV infection and the random sample population was 80 patients. The mean follow-up period, for both groups, was 132 months (range: 67-290). There was no statistical differences between groups regarding age, gender, ethnic origin, previous dialytic support (or kind of dialytic support) or primary kidney disease. HCV infected patients remained longer on dialysis waiting-time period (median: 60 months; $P^{25/75}$: 48/132) and were younger at transplantation timing (37±12 y/o). Imunossupressive regimens using calcineurin inhibitors (75% vs 40%; $p < 0.05$) and azathioprine (44% vs 16%; $p< 0.05$) were more frequently applied on HCV infected patients. On the other hand, there was a significant lesser use of tacrolimus (28% vs 55%; $p < 0.05$). Regarding hospitalization (69% vs 65%), septic complications (35% vs 43%), primary allograft disfunction (31% vs 26%), new-onset diabetes after transplant (4% vs 13%) or malignancy, there were no significant differences between groups. A higher frequency of *major* cardiovascular events was detected on HCV infected group (32% vs 9%; $p < 0.05$). The global rate of allograft loss was significantly higher among HCV group (50% vs 20%; $p < 0.05$). The 1, 5 and 10 year-allograft survival rate in HCV group was 94.1%, 78.1% and 66.9%; for the sample group: 94.9%, 89.1% and 80.4%. Using a survival model (Kaplan-Meier), there was no statistical difference (log rank test: $p=0.154$) in allograft survival between HCV positive and negative patients. In order to isolate the effect of HCV on allograft survival we used a Cox regression model, showing that HCV infection, althought negatively impacted on allograft survival (HR: 1.657; IC95%: 0.817-3.364; $p=0.162$), that effect had no statistical significance.

CONCLUSION: Our findings suggest that, whilst HCV may play an ominous effect on allograft survival of renal transplants, its global effect is minor. Hence, in light of our findings, renal transplantation in HCV infected patients seem to foretell similar allograft survival as that in general population.

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P0628 ASSOCIATIONS OF REACTIVE OXYGEN SPECIES AND IRON METABOLISMS WITH DEVELOPMENT OF HEPATOCELLULAR CARCINOMA AFTER PEGYLATED INTERFERON THERAPY IN JAPANESE PATIENTS WITH CHRONIC HEPATITIS C

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INTRODUCTION: Chronic hepatitis C (CHC) may induce reactive oxygen species (ROS) and excessive iron deposition in the liver.

AIMS & METHODS: The present study was planned to clarify the impact of surplus ROS and iron deposition on virological response to the therapy with pegylated interferon plus ribavirin and development of hepatocellular carcinoma (HCC) thereafter for CHC patients. A total of 210 CHC patients who received combination therapy of pegylated interferon and ribavirin are enrolled. Liver histology was evaluated for all the patients before the therapy. Hepatic ROS was assessed with immunohistochemical staining of 8-hydroxy-2-deoxyguanosine (8-OHdG). Hepatic iron deposition was assessed by Prussian blue staining. Factors associated with hepatic 8-OHdG levels were analyzed by stepwise logistic regression analysis. Proportional hazard models were utilized to identify patient characteristics associated with HCC development after interferon therapy.

RESULTS: Severe hepatic iron deposition was significantly associated with high level of 8OHdG in stepwise logistic regression analysis ($p <0.0001$). Interferon therapy resulted in sustained virological responses (SVR) in 104 patients. Hepatic 8OHdG was significantly associated with SVR in univariate analysis for the patients with HCV genotype 1, without statistical significance in multivariate analysis. Hepatic iron deposition showed no significant associations with SVR for the patients with HCV genotypes 1 or 2. During the follow-up after interferon therapy (median period of 4.6 year), HCC development was observed in 14 patients (16%). Heavy alcohol drinking, low platelet counts, non-SVR and high levels of hepatic 8OHdG had significant associations with HCC development ($p=0.0276$, 0.0102, 0.0067, and 0.0003, respectively).

CONCLUSION: Hepatic 8OHdG level was useful in prediction of HCC development after interferon therapy for CHC patients.

Disclosure of Interest: None declared

P0629 HCV AND HBV PREVALENCE IN THE POPULATION: LARGE DISPARITY BETWEEN HEPATITIS C IN THE GENERAL POPULATION, COMPARING WITH HIGH RISK GROUPS

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INTRODUCTION: The burden of hepatitis B and C infections around the world is high. With the upcoming very effective treatments for hepatitis C and the rather effective treatments for hepatitis B, there is urge to identify these patients and estimate their prevalence in each country.

AIMS & METHODS: Hepatitis B and C prevalence was evaluated in a sample of three groups: adult general population (GP): 989 individuals, prison population (PP): 784, and drug-users (DU): 19832. HBsAg, HBsAb, HBcAb, anti-HCV (Cobas, Roche), ALT and AST were done. In the general population, anti-HCV positive individuals were tested for HCV PCR.

RESULTS: Prevalence of Anti-HCV was: GP: 5/989 (0.5%); PP: 147/784 (18.8%) and DU: 11862/19839 (59.8%). Prevalence of HBsAg was GP: 12/989(1.2%); PP: 32/784 (4.1%) and DU: 927/18305 (5.0%). Interestingly, among individuals that were anti- HCV positive in the GP, only 20% were HCV PCR positive. In Portugal, adult GP is estimated about 8 600 000

individuals, PP are about 14 000, and DU are about 30 000. So, according to the percentages found, it is expected that we have about 69 000 individuals with anti-HCV, and it is expected that 105 000 are HBs Ag positive. It is possible that the prevalence of HCV PCR positive individuals is much lower in the general asymptomatic population. Even assuming a 50% prevalence of HCV RNA positive among anti-HCV positive patients, it would result in about 34 500 individuals with active infection and potentially needing treatment. Prevalence of elevated aminotransferases among patients with either hepatitis B or C in the GP was not different from those with negative markers (17.6% vs. 8.1%, p = n.s.).
CONCLUSION: Hepatitis C showed high disparity in prevalence according to the risk groups, with low prevalence on the general population and very high in risk groups. Differently, the prevalence of hepatitis B showed a more homogeneous pattern of distribution. These results suggest that screening for hepatitis C in the general population is not cost-effective, but risk groups such as drug-users or people in prisons should be regularly screened.
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P0630 THE MITOGEN-ACTIVATED PROTEIN KINASE ERK5 IS INVOLVED IN HEPATOCELLULAR CARCINOMA CELL PROLIFERATION IN VITRO AND IN VIVO

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INTRODUCTION: Despite great progress in the diagnosis and management of hepatocellular carcinoma (HCC), the molecular mechanisms underlying the tumor development and progression remain poorly understood, overall limiting the patients' outcome. ERK5 is a member of the MAPK family and has been implicated in fundamental biologic processes relevant for tumor development.
AIMS & METHODS: The aim of this study is to evaluate the relevance of this pathway ERK5 in HCC biology.
Huh-7 and HepG2 were cultured by standard methods. ERK5 was silenced by siRNA transfection or with shRNA and lentiviral vectors. The specific ERK5 inhibitor XMD8-92 was also used. *In vivo* development of HCC was evaluated using the Huh-7 xenograft model in athymic nude mice.
RESULTS: *In vitro* experiments demonstrated that ERK5 silencing or specific inhibition, using an inhibitor called XMD8-92, causes growth arrest of HCC cells, affecting in particular the G1/S transition. This phenotype was associated with an increase in p27Kip protein expression a critical negative regulator of cell cycle progression typically expressed in G0/G1 arrested cells. Additionaly knock down of ERK5 activity induces a marked inhibition of c-Rel expression, a member of NFkβ family required for the normal proliferative regeneration of hepatocytes. In a mouse model of HCC xenograft, administration of XMD8-92 significantly decreased tumor volume This reduction is associated with a reduced proliferation, as observed by Brdu incorporation assay. Moreover XMD8-92-treated xenografts the expression of c-Jun, a proto-oncogene essential for cell proliferation, was reduced compared to control samples. Finally as already observed *in vitro*, XMD8-92 treatment induced a strong decrease of c-Rel transcription factor expression.
CONCLUSION: This study disclose a strong regulation of cell proliferation in HCC, affecting the biological activity of different oncogenic targets. Affecting this pathway could be considered a novel and effective approach for the treatment of HCC.
Disclosure of Interest: None declared

P0631 HEAT SHOCK FACTOR 1 (HSF1) INVOLVEMENT IN TUMOUR RECURRENCE AFTER RADIOFREQUENCY ABLATION IN AN ANIMAL MODEL OF SECONDARY LIVER CANCER

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INTRODUCTION: Heat shock factor 1 (HSF1), is the master regulator of genes encoding molecular chaperones and is involved in cellular processes such as stress response, cell differentiation and carcinogenesis. Recent studies identified a HSF1-regulated transcriptional program specific to high malignancy and distinct from the classical HSF1-induced heat shock response. We investigated the expression of HSF1 during tumour formation and after Radiofrequency Ablation (RFA) in vivo. In vitro experiments were employed to mimic radiofrequency ablation and to analyse the effect of shRNA-HSF1-nanoliposomes as a possible adjuvant thermo-sensitizing therapy in combination with radiofrequency ablation (RFA) in metastatic liver cancer.
AIMS & METHODS: Colon carcinoma CT26 cells, expressing HSF1, HSP70 and HSP90, were used to assess shRNA-HSF1-nanoliposomal uptake, toxicity/efficiency by employing immunofluorescence, Q-PCR and protein analysis. In vitro sub-lethal heat experiments were performed to mimic radiofrequency ablation, and this by using different time points/temperatures. An orthotopic murine model of coloncarcinoma cancer - liver metastasis was used to analyse HSF1 expression during tumour formation. Radiofrequency ablation (RFA) in small animals was optimized to investigate the HSF1-induced-and related signalling pathways in the treatment of liver metastasis.
RESULTS: shRNA-HSF1-nanoliposomes were taken up by 99% of cells without inducing cytotoxicity. Sub-lethal heat treatment of 45 and 50 degrees Celsius induced p-ERK, p-AKT and HSF1-related proteins at different timepoints investigated and this coincided with a nuclear to cytosolic shift of HSF1, HSP70/90, AKT and ERK. Apoptosis was only significantly induced after 10 days post-heat treatment. In vivo, tumours highly expressed HSF1, HSP70/90, AURBK and p-ERK and p-AKT. Radiofrequency-ablated tumours showed an increase in HSF1 and HSP70/90 protein expression after 6 and 10 days post-RFA, suggesting the involvement of HSF1 during the process of tumour recurrence.
CONCLUSION: This study demonstrates that HSF1 is highly expressed in CRC liver metastasis and suggest its possible involvement in tumour recurrence after employing radiofrequency ablation.
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P0632 BASIC FIBROBLAST GROWTH FACTOR MEDIATES ACQUIRED RESISTANCE TO SORAFENIB IN HEPATOMA CELLS

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INTRODUCTION: Sorafenib is a multikinase inhibitor used to treat patients with hepatocellular carcinoma (HCC). The main obstacle to efficient cancer treatment with this agent is the acquired drug resistance that develops in many patients. We aimed to determine whether sorafenib-treated hepatoma cells release soluble factors that cause sorafenib resistance.
AIMS & METHODS: HepG2 cells were incubated with sorafenib for 24 hours. The culture medium was rinsed, the cells were maintained for 24 more hours, and cytokines released into the medium were analysed by enzyme-linked immunosorbent assay. The culture medium was transferred to the newly seeded HepG2 cells, which were then maintained with a different concentration of sorafenib for 2 to 48 hours. Cell growth and apoptosis in sorafenib-treated cells were analysed by MTT and annexin V assay. Cell signalling was analysed by western blotting.
RESULTS: The level of basic fibroblast growth factor (FGF-2) in the culture medium of sorafenib-treated cells was increased to 1.8-fold that of the controls (14.3 vs. 7.7 pg/mL, respectively; $p < 0.05$), while other growth factors such as transforming growth factor beta and insulin growth factor were unchanged. When the cells were maintained in the culture medium of sorafenib-treated cells, the cell numbers were increased by 1.35-fold ($p < 0.05$), and the levels of phosphorylated Akt, extracellular signal-regulated kinases 1/2, and nuclear factor kappa B were increased by 2.5- to 4.0-fold. The annexin V assay showed that the effect of sorafenib on cell apoptosis was inhibited in the cells maintained in the medium of sorafenib-treated cells (apoptotic rates after sorafenib treatment in control cells vs. cells maintained in the medium of sorafenib-treated cells: 76.5% vs. 17.7%, respectively; $p < 0.05$), which was rescued by pretreatment with the FGF receptor inhibitor PD173074.
CONCLUSION: FGF-2 might be an essential mediator of acquired resistance to sorafenib. Combination treatment with sorafenib and FGF-2 inhibitor may be effectively used to treat patients with HCC in the future.
Disclosure of Interest: None declared

P0633 HEPATOMA CELLS CAN BE REVERTED TO ORIGINAL NORMAL CELLS BY SINGLE SMALL RNA

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INTRODUCTION: The human ncRNA gene *RGM249* regulates the extent of differentiation of undifferentiated cancer cells. Because shRNA for *RGM249* induced the upregulation of hsa-miR-520d that converted 293FT cells to hiPSCs, we attempted to perform the functional analysis to examine the anti-cancer effects of it on an undifferentiated hepatoma cell.
AIMS & METHODS: To identify the crucial factors underlying this process, we investigated the effects of lentivirally inducing miR-520d expression in HLF cells (520d-HLF) *in vitro*. To clarify the underlying mechanism, we performed gene expression analysis, cell cycle analysis, cell sorting, metabolomic analysis, migration assay and DNA methylation assay in transfectants. Subsequently, we evaluated tumor formation in a xenograft model using 520d-HLF.
RESULTS: 520d-HLF cells or the cells sorted by both alkaline phosphatase and GFP were Oct4 and Nanog positive within 24 h, showed p53 upregulation and hTERT downregulation, and mostly lost their migration abilities. Cell cycle analysis revealed homogeneous growth and metabolomic analysis showed that the TCA cycle was not elevated. Methylation level in transfectants decreased to the similar level to that in hiPSC. After lentiviral infection, the cells were intraperitoneally injected into mice, resulting in benign teratomas (6%), the absence of tumors (87%) or differentiation into benign liver tissues (7%) at the injection site after 1 month.
CONCLUSION: We are the first to demonstrate the loss of malignant properties in cancer cells *in vivo* through the expression of a single microRNA (miRNA). This miRNA successfully converted 293FT and hepatoma cells to hiPSC-like

cells partly or mainly via both stemness- and demethylation-mediated process. The regulation of malignancy by miR-520d appears to be through the conversion of cancer cells to normal stem cells, maintaining p53 upregulation.
Disclosure of Interest: None declared

P0634 MATRINE INDUCED MITOCHONDRIAL-DEPENDENT APOPTOSIS AND AUTOPHAGY IN HEPATOMA CELLS

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INTRODUCTION: Matrine is an active component monomer that is extracted from Sophora flavescens. Our previous study found that matrine could induce cell apoptosis, and dramatically increase the generation of autophagosomes in hepatocellular carcinoma cell lines. Autophagy, a self-defense mechanism, has been found to be associated with drug resistance in hepatocellular carcinoma (HCC) therapy. However, the effect and exact mechanisms of matrine-induced autophagy and apoptosis in therapy of HCC are still not very clear.
AIMS & METHODS: Our study was aimed to investigate the role and related mechanisms of matrine-induced apoptosis and autophagy in hepatoma cells HepG2 and Bel_{7402}.
Cell apoptosis was detected by flow cytometry analysis (Annexin V–FITC/PI double-staining assay), JC-1 probe, the activity and activating cleavages of caspase-3, -8, and -9. MTT assay and colony forming assay were used to assess the effect of matrine on viability and proliferation of HCC cells. Autophagic flux in HCC cells was analyzed using the expression of LC3BI/II and p62/SQSTM1, GFP-LC3 transfection and LysoTracker staining, and transmission electron microscopy. Moreover, regarding to the associated mechanisms, Genechip technique was used to find matrine-induced autophagic related gene.
RESULTS: 1. Matrine at different concentrations could inhibit the viability and proliferation of HepG2 and Bel_{7402} cells, and induce apoptosis in a concentration-dependent manner ($p < 0.05$).
2. Matrine could induce the decrease of mitochondrial membrane potential (MMP) and up-regulation of cytochrome-c expression. After treated with matrine, the expression of pro-caspase decreased and the cleaved caspase-8,-9,-3 increased.
3. The turnover of LC3BI/IIratio, the increasing number of GFP-LC3 positive cells ($P < 0.05$) and the formation of phagophores, autophagosomes, autolysosomes observed by transmission electron microscopy, implied that autophagy was induced in matrine-treated HCC cells.
4. Genechip results showed that the level of lamp-1 elevated at 7.4 times. The result was further proved by the detection of Realtime PCR and western blot. Immunofluorescence results showed that Lamp-1 colocalized with lysosomes in HepG2 cells, and localized at the autolysosomes after autophagy was induced.
CONCLUSION: 1. Matrine has the inhibitory effect of HCC celllines HepG2 and Bel7402,and could induce apoptotic cell death via mitochondrial mediated caspase dependent way.
2. Matrine could induce autophagy in HepG2 and Bel_{7402} cells, and lamp-1 is related to the formation of autolysosomes, and possibly involved in matrine-induced autophagy.
Disclosure of Interest: None declared

P0635 EXPRESSION OF FERRITIN LIGHT CHAIN IN HEPATIC OVAL CELLS IS A USEFUL BIOMARKER OF HEPATOCELLULAR CARCINOMA DEVELOPMENT

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INTRODUCTION: Hepatic oval cells are unique bipotential progenitor cells that differentiate into both bile duct cells and hepatocytes. Although it has been widely recognised that oval cell-derived hepatocytes are possible progenitors of hepatocellular carcinoma (HCC), the functional properties of these cells are unclear.
AIMS & METHODS: To investigate the protein expression profile in oval cell-derived hepatocytes, we compared proteomes from lysates from normal hepatocytes and oval cell-derived hepatocytes using two-dimensional (2D) gel sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and matrix-assisted laser desorption ionization time-of-flight tandem mass spectrometry (MALDI-TOF/TOF MS). Hepatocytes were isolated from normal rat livers by the collagenase perfusion method, while oval cell-derived hepatocytes were obtained from cultured rat oval WB-F344 cells or rat littermates treated with 2-acetamidofluorene plus partial hepatectomy. To verify the results of 2D SDS-PAGE, the protein expression levels of ferritin light chain (FLC) in human liver tissue samples (33 patients without HCC and 28 with HCC) were examined by western blotting and immunohistochemical analysis.
RESULTS: Two-dimensional SDS-PAGE showed 11 major protein spots that changed in abundance between normal hepatocytes and oval cell-derived hepatocytes. Three of these differently expressed protein spots were analysed by MALDI-TOF/TOF MS. The level of FLC expression was significantly higher in oval cell-derived hepatocytes (7- to 10-fold, $p < 0.05$). Western blotting of human liver tissue samples showed that the levels of FLC expression were 4- to 8-fold higher in patients with than without HCC. Immunohistochemical analysis showed that hepatocellular FLC was strongly expressed in 21 of 28 patients with HCC, while strong expression of FLC was detected in 12 of 33 patients without HCC ($p < 0.05$).
CONCLUSION: Several proteins, including FLC, are distinctly overexpressed in oval cell-derived hepatocytes. FLC expression is increased in human liver tissues adjacent to HCC, indicating that FLC might be a useful biomarker for identification of the development of HCC.
Disclosure of Interest: None declared

P0636 RNA BINDING PROTEIN NOVA1 PROMOTES TUMOR GROWTH IN VIVO AND ITS POTENTIAL MECHANISM AS AN ONCOGENE MAY DUE TO ITS INTERACTION WITH GABAARΓ2

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INTRODUCTION: Our previous study discovered the expression of Nova1 in hepatocellular carcinoma and proved that high expression of Nova1 is associated with poor prognosis of HCC. Recent research proved that Nova1 regulates the alternative splicing of GABAA receptor $\gamma 2$(GABAAR$\gamma 2$) pre-mRNA in central nervous system. Moreover, the theory that the GABAergic system is involved in HCC progression has also been illustrated before. However, the expression of GABAAR$\gamma 2$ and its relations with Nova1 in hepatocellular carcinoma remain elusive.
AIMS & METHODS: The aim of this study is to explore the potential mechanism of Nova1 as an oncogene for HCC. To make clear the existence of interactions between Nova1 and GABAAR$\gamma 2$ in HCC and their relations with tumorigenesis. Immunohistochemical staining were used to identify the protein expression level of GABAAR$\gamma 2$ in HCC and its paired non-tumor tissue. Its relations with clinicopathologic features were calculated. The HCC tumor xenografts animal models were established. The tumor size was estimated and then removed for western blot analysis. For double immunofluorescence staining, the slides were incubated with DyLight 448 Affinipure Rabbit Anti-Goat IgG and DyLight 594 Affinipure Goat Anti-Rabbit IgG and analyzed via the microscope. The cell-lysated proteins were precleared with 2 μg anti-Nova1 or anti-GABA AR$\gamma 2$ antibodies and then incubated with protein G-agarose and antibodies. The precipitates were analyzed by western blotting.
RESULTS: The expression level of $GABA_AR\gamma 2$ positive cell in the cancerous tissue was lower than para-cancerous tissues. Univariate analysis and multivariate Cox analysis showed that intratumoral Nova1 was significantly associated with OS and TTR. Patients with higher intratumoral $GABA_AR\gamma 2$ had longer OS rate and TTR time. In vivo test, our results showed that, the volume of the xenotrans in the over-expression group surpassed that in the control group, and the volume of the xenotrans in the knockdown group far smaller than its control group. Immunohistochemical staining and Western blot showed down-regulation of Nova1 accompanied with increased expression of GABAAR$\gamma 2$ and GABA. Up-regulation of Nova1 resulted decreased expression of $GABA_AR\gamma 2$ and GABA. Furthermore, the localizations of GABA and $GABA_AR\gamma 2$ were visualized under microscopy. The SMMC-7721 cells expressing the GABA and $GABA_AR\gamma 2$ protein exhibited fluorenscence concentrated in the cytoplasm, and also in the nucleus. Co-localization of Nova1 and $GABA_AR\gamma 2$ proteins in the cytoplasm was evidenced by overlapping fluorescence signals in Huh7 cell. Co-IP results showed that Nova1 was easily detected through anti-Nova1 antibody in the $GABA_AR\gamma 2$-immunoprecipitates. Reciprocal co-IP experiments using anti-Nova1 antibody indicated the existence of $GABA_AR\gamma 2$, as confirmed by immunoblotting.
CONCLUSION: Nova1 not only interacts with $GABA_AR\gamma 2$ in CNS but also in the peripheral HCC tumor tissue. It is hypothesized that ectopic expression of Nova1 may down regulate the expression of GABAAR$\gamma 2$, and decrease the influx of cl- and tumor cells membrane potential diffences, thus leading to the proliferation of HCC.
Disclosure of Interest: None declared

P0637 EPIGENETIC SILENCING OF THE TUMOR SUPPRESSOR MICRORNA-122 DURING HEPATOCARCINOGENESIS FROM NONALCOHOLIC STEATOHEPATITIS

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INTRODUCTION: Nonalcoholic steatohepatitis (NASH) has emerged as a common cause of chronic liver disease and virus-independent hepatocellular carcinoma (HCC) in patients with obesity, diabetes and metabolic syndrome. However, little is known about the pathogenesis of HCC derived from NASH.
AIMS & METHODS: To reveal the molecular mechanism underlying hepatocarcinogenesis from NASH, microRNA (miRNA) expression profiles were analyzed. HCCs and non-tumor liver tissues from STAM mice, an animal model developing HCC from NASH, and tissue specimens obtained from primary HCC patients were used in this study. MiRNA expression profiles were analyzed by microarray and quantitative RT-PCR. To investigate the regulatory mechanism of miRNAs, DNA methylation assay and chromatin immunoprecipitation (ChIP) assay were performed in liver cancer cells treated with the DNA methylation inhibitor 5-aza-2'-deoxycytidine (5-Aza-CdR).
RESULTS: Histopathological images of the liver in STAM mice at the ages of 6, 8, 12, 18 weeks showed findings compatible with fatty liver, NASH, liver cirrhosis (LC), and HCC, respectively. *MiR-122* expression in non-tumor LC at the age of 18 weeks was significantly lower than that in LC at the age of 12 weeks. *MiR-122* expression was further decreased in HCCs compared with non-tumor LC at

the age of 18 weeks. *MiR-122* expression was also decreased in clinical HCC samples. Treatment of liver cancer cells with 5-Aza-CdR reactivated *miR-122* expression with decreased cell proliferation and down-regulation of its target, CyclinG1. The results of ChIP assay indicated that 5-Aza-CdR activated *miR-122* expression by enhancing binding of peroxisome proliferator activated receptor-gamma (PPAR-γ) to the *miR-122* promoter region.
CONCLUSION: These findings indicate that epigenetic silencing of the tumor suppressor *miR-122* plays a critical role during hepatocarcinogenesis from NASH. DNA methylation inhibitors such as 5-Aza-CdR may have clinical promise for the prevention and treatment of HCC derived from NASH.
Disclosure of Interest: None declared

P0639 PLASMA CYCLASE-ASSOCIATED PROTEIN 2 IS A NOVEL BIOMARKER IN EARLY STAGE AND ALPHA-FETOPROTEIN NEGATIVE HEPATOCELLULAR CARCINOMA PATIENTS

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INTRODUCTION: Hepatocellular carcinoma (HCC) is the third leading cause of cancer related deaths worldwide, early detection of HCC is critical to monitor disease progression, selection of therapeutic options and post-surgery surveillance. Alpha-fetoprotein (AFP) is traditionally an indispensible marker for the diagnosis of HCC, since 33.3% of small HCC patients are AFP negative, it is crucial to discover new sensitive marker to compensate the negative AFP in HCC diagnosis and surveillance. Cyclase-associated protein 2 (CAP2) has recently been proposed to be a candidate biomarker for detection of early HCC.
AIMS & METHODS: We aim to evaluate the sensitivity and specificity of CAP2 as a biomarker for HCC patients with special attention to those at early stage and AFP negative. The CAP2 and AFP plasma levels were analyzed by enzyme-linked-immunosorbent assay in 86 HCC, 59 cirrhotic patients, and 30 normal individuals.
RESULTS: The results showed that both CAP2 and AFP plasma levels in HCC patients were significantly elevated when compared to cirrhosis. CAP2 level correlates well with HCC patient's histological grade, clinical stage and tumor size; but not with patient's age, gender, hepatitis B virus infection status and plasma AFP level. CAP2 had better sensitivity (82.6%) as compared to AFP (59.3%) alone for general HCC patients, and in early stage of HCC patients (78.6% vs 40.4%). In addition, CAP2 is able to complementary to AFP to predict 82.9% of HCC in AFP negative patients.
CONCLUSION: We concluded that CAP2 is a promising biomarker for the prediction of HCC in both AFP negative and early stages of HCC patients.
Disclosure of Interest: None declared

P0640 USEFULNESS OF CONTRAST-ENHANCED SONOGRAPHY (CEUS) IN THE SURVIVAL OF PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCCC) SUBMITTED TO NON-SURGICAL TREATMENTS

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INTRODUCTION: CEUS is an ultrasound technique with a good diagnostic agreement with spiral CT in the evaluation of efficacy of non-surgical treatments of HCC. The early evaluation of these treatments with CEUS may allow to obtain a more complete necrosis of the tumoural nodules.
AIMS & METHODS: We evaluated if CEUS is able to affect the outcome of these patients. 181 cirrhotic with HCC (M/F:112/69; mean age 71 yrs; Child A/B: 151/30), treated from 1/1999 to 12/2012 with non-surgical treatments for unresectable lesions: 116 with RFTA; 44 with combined treatment of RFTA and TACE and 21 with PEI; solitary nodule:132 pts; 2-3 hcc:32; multinodular HCC:17 cases. All patients underwent to spiral CT one month after the procedure; the first 66 patients (treated before January 2002), didn't perform CEUS, (group-A); 115 patients were submitted to CEUS (after January 2002) 24 hours after the treatments (group-B). We correlated the following variables with the survival (S) and the disease-free-survival (DFS): number and diameter of HCCs; AFP values; type of treatment; aetiology and class of Child; the early evaluation of the treatment with CEUS. Statistics was performed with chi-square and Kaplan-Meyer curves (SPSS release-18)
RESULTS: Mean follow-up of 181 pts: 52 months (group-A: 41,4; group-B: 60,2). During the follow-up 52/66(78,8%) pts in group-A and 49/115(42,6%) pts in group-B died. Recurrence was found: group-A:45/56(80.3%) pts, group-B:73/115 (63.47%) pts. The patterns of recurrence were: new lesions away from the treated nodules: group-A: 23 cases; group-B: 47 cases; local tumour regrowth: group-A: 22 pts; group-B:26 pts. At multivariate analysis the number and diameter of the nodules, sex, and type of the treatment weren't statistically correlated with S and DFS. Value of AFP and Child class were correlated with S (S:p = 0.001), the early evaluation of the efficacy of the treatment with CEUS and the association CEUS-AFP were statistically correlated (CEUS: DFS: p = 0.042);(CEUS and AFP: DFS: p = 0.036)
CONCLUSION: The early evaluation of the efficacy of the non-surgical treatments of HCC with CEUS lets to obtain a more complete necrosis of the tumour and to reduce the recurrence for local regrowth of the HCC achieving a higher percentage of disease-free survival
Disclosure of Interest: None declared

P0641 CUMULATIVE OPERATOR VOLUME IN RELATION TO TUMOR RECURRENCE AFTER RADIOFREQUENCY ABLATION FOR HEPATOCELLULAR CARCINOMA

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INTRODUCTION: Radiofrequency ablation (RFA) is the main minimal-invasive curative therapy for hepatocellular carcinoma (HCC). However, the recurrence rate remains unsatisfactory.
AIMS & METHODS: We aim to investigate the role of cumulative operator volume on HCC recurrence after RFA. We conducted a retrospective cohort study based on Taiwan's National Health Institute Research Database (NHIRD). We identified 52,096 patients with newly diagnosed HCC between 2004 and 2011. Among them, 5,890 received radiofrequency ablation (RFA) as their first therapy for HCC. Patients were categorized into five quintiles according the physicians experience (RFA volume). Patients in the lowest and highest RFA volume quintiles were 1:1 matched by propensity score. Cumulative incidences of HCC recurrence was analyzed.
RESULTS: Patients in the highest RFA volume quintile had significantly lower 5-year HCC recurrence cumulative incidence (65.8%; 95% CI: 59.5-72.1%) compared to the risk for lowest RFA volume quintile (71.4%; 95% CI: 66.2-76.5%) ($P < 0.05$). On multivariate analyses, the highest RFA volume was an independent protective factor for HCC recurrence (HR = 0.80; 95% CI: 0.67-0.97). Multivarate stratified analyses confirmed the association between higher RFA volume and lower HCC recurrence risk in nearly all subgroups.
CONCLUSION: More RFA experience was associated with reduced risk of HCC recurrence.
Disclosure of Interest: None declared

P0642 INCIDENTAL HEPATOCELLULAR CARCINOMA: RISK FACTORS AND LONG-TERM OUTCOME AFTER LIVER TRANSPLANTATION

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INTRODUCTION: Orthotopic liver transplantation (OLT) currently represents the treatment of choice for early hepatocellular carcinoma (HCC). Preoperatively known HCC (pkHCC) is diagnosed via imaging methods prior to OLT or HCC, denoted as incidental HCC (iHCC), is found postoperatively in the liver explant.
AIMS & METHODS: The aim of our study was a comprehensive analysis of post-transplant survival of patients with iHCC and identification of risk factors of iHCC occurrence in cirrhotic liver.
We retrospectively reviewed 33 adult cirrhotic patients with incidentally found HCC comparing them with 606 tumor-free adult cirrhotic patients with end-stage liver disease (group Ci) who underwent OLT in our center between January 1995 and August 2012. Within the same period, a total of 84 patients were transplanted for pkHCC. We compared post-transplant survival of iHCC, Ci group and pkHCC patients. In the group of cirrhotic patients (Ci + iHCC) we searched for risk factors of iHCC occurrence.
RESULTS: There was no difference in sex, MELD score and time spent on the waiting list in either group.
In the multivariate analysis we identified the age > 57 years (OR 3.37, 95% confidence interval (CI) 1.75-8.14, $P < .001$), HCV or alcoholic liver disease (ALD) (OR 3.89, 95% CI 1.42-10.7, $P < .001$) and alpha-fetoprotein (AFP) level > 6.4 μg/l (OR 6.65, 95% CI 2.82-15.7, $p = .002$) to be independent predictors of iHCC occurrence. Either 1-, 3- and 5-year overall survival (OS) or 1-, 3- and 5-year recurrence-free survival (RFS) differed in iHCC patients compared with Ci group (iHCC: OS 79%, 72% and 68%, respectively; RFS 79%, 72% and 63%, respectively, vs. Ci group: OS = RFS 93%, 94% and 87%, respectively; $P < .001$).
CONCLUSION: We conclude that the survival of iHCC patients is worse than in tumor-free cirrhotic patients, but comparable with survival of pkHCC patients. Independent risk factors for iHCC occurrence in cirrhotic liver are age, HCV or ALD etiology of liver cirrhosis and AFP level.
Disclosure of Interest: None declared

P0643 SINGLE-STEP BALLOON-OCCLUDED PERCUTANEOUS RADIO-FREQUENCY THERMAL ABLATION (RFA) PLUS TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION (TACE) FOR TREATMENT OF "COMPLEX" UNRESECTABLE HEPATOCELLULAR CARCINOMA

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INTRODUCTION: To evaluate the feasibility, safety and efficacy of single-step balloon-occluded-RFA followed by TACE in patients with "complex" unresectable HCC, previously not suitable to RFA alone due to their localization.
AIMS & METHODS: 63 consecutive patients with at least one HCC lesion (mean diameter 4.35±1.8cm), adjacent to the diaphragm (25 lesions), proximal to the hepatic veins (17), portal vein (19), glisson's capsule (34), cholecistis (6) and/or located on the intra-abdominal free surface (5), considered as "complex" for their unfavourable location, and not suitable for RFA alone, were enrolled in our single-center multidisciplinary pilot study. The treatment was composed of RFA (single 2-cm or 3-cm monopolar needle insertion) during occlusion of the feeding artery followed by superselective TACE (conventional-TACE or with DC-BEAD). Adverse events and intra/periprocedural complications were clinically assessed. Tumor response was evaluated on 1-month, 6 months and 1 year follow-up multiphasic CT based on mRECIST criteria.
RESULTS: Technical success was achievied in all patients. 7 patients (11.2%) experienced intra and periprocedural complications, such as fistuale (2), bleeding (3), cholecistitis (1) and ascites (1), that resolved spontaneously. A mean total treated diameter (necrotic diameter plus circonferential peripheral lipiodol uptake for conventional TACE; mean necrotic diameter for TACE with DC-Bead) of 4.96±2.37 was obtained. Based on mRECIST criteria, on 1- and 3-months follow up CT, a tumor response was obtained in all patients, with a complete response achieved in 31 out of 63 patients (49.2%), a partial response in 38.1% (24 patients: residual tumor $< 30\%$ in 14 patients, $> 30\% > < 50\%$ in 6 patients, $> 50\%$ in 4 patients), and no response in 3 patients, without any progressive disease. 5 patients were lost to follow up. 18 out of 27 patients (66.6%) that underwent a CT-scan on 6-months follow up maintained a complete response.
CONCLUSION: Balloon-occluded-RFA plus TACE seems to be a safe and effective therapy for the treatment of "complex" HCC, allowing to obtain a high complete local response rate, without complications, also in patients not suitable to RFA alone.
Disclosure of Interest: None declared

P0644 COMPARISON OF CLINICAL PRESENTATIONS AND OUTCOME OF HEPATOCELLULAR CARCINOMA BETWEEN HEPATITIS C AND NONALCOHOLIC FATTY LIVER CIRRHOSIS: A SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Hepatocellular carcinoma (HCC) is the most common primary liver tumor, and represents the third leading cause of cancer death worldwide [1, 2]. Chronic hepatitis C cirrhosis is one of the leading risk factors for HCC but increasing cases are seen in nonalcoholic fatty liver disease (NAFLD).
AIMS & METHODS: The aim of the study was to compare demographics, treatments and survival among hepatitis C virus (HCV/HCC) and NAFLD (NAFLD/HCC) cohort of patients. Data were collected from medical electronic case notes, imaging reports and reports from HCC multidisciplinary meetings.
RESULTS: Among 289 patients, 210 patients (73%) had underlying HCV/HCC and 79 patients (27%) had NAFLD/HCC. The median age at diagnosis was significantly higher in NAFLD/HCC patient cohorts ($p < 0.001$). The majority (more than 80%) were male. Body mass index (BMI) was significantly higher in NAFLD/HCC than HCV/HCC ($p < 0.001$). The majority of the patients in NAFLD. HCC were Caucasian (96%), whilst the HCV/HCC cohort was significantly more ethnically diverse ($p < 0.001$). Diabetes mellitus was more common in NAFLD/HCC patients ($p < 0.001$). The median alpha fetoprotein level in HCV/HCC patients were 33.0 compared to 14.1 in NAFLD/HCC although it did not reach the statistical significance ($p = 0.100$). The size of HCC and the numbers of HCC were similar between the two groups. Majority of patients in HCV/HCC and NAFLD/HCC were Barcelona stage A (51% vs 48%) and stage B (28% vs 39%). Treatment modalities such as radiofrequency ablation (RFA), trans arterial chemoembolization (TACE) or sorafenib used in both groups of patients were similar. Overall survival between the two groups did not differ significantly ($p = 0.122$), however we have found that HCV/HCC patients were more likely to be transplanted ($p = 0.003$).
Among 298 patients, 61 patients (29%) from HCV/HCC cohort and 11 patients (14%) from NAFLD/HCC were transplanted. The only significance factors were BMI ($p = 0.013$) and presence of underlying diabetes mellitus ($p = 0.002$) which were more common in NAFLD/HCC patients. 15% were treated with RFA and 18% received TACE therapy prior to liver transplantation (LT) in HCV/HCC compared to 18% and 9% in NAFLD/HCC respectively. Tacrolimus and Mycophenolate Mofetil were two most common immunosuppression regimes used post LT. Post transplant survival appeared to be slightly worsen in HCV/HCC patients compared to NAFLD/HCC, although it did not reach statistical significance ($p = 0.113$). Post LT freedom from recurrence of HCC among the two cohort was similar ($p = 0.848$).
CONCLUSION: Despite the NAFLD/HCC being older and with higher metabolic risk factors, a significant proportion could undergo active therapy. Furthermore, patients with NAFLD/HCC selected for transplantation seemed to have better long term outcomes, possibly due to stricter selection for transplantation as well as variations in tumor biology between the two groups.
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Disclosure of Interest: None declared

P0645 HIGH ALPHA-FETOPROTEIN LEVELS AND PRESENCE OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION CAN PREDICT THE OCCURRENCE OF HEPATOCELULLAR CARCINOMA IN CIRRHOTIC PATIENTS

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INTRODUCTION: The international guidelines strongly recommend the screening of hepatocellular carcinoma (HCC) in cirrhotic patients by ultrasound every 6 months ± tumor markers (such as alfa feto protein – AFP), but because of the large number of patients and often limited resources some biomarkers for prioritizing patients for screening would be very helpful.
AIMS & METHODS: Our aim was to assess the HCC occurrence according to AFP values, presence of clinically significant portal hypertension (HVPG ≥ 10 mmHg), Child-Pugh score, MELD score, liver stiffness values assessed by Transient Elastography (TE), and liver disease etiology (viral vs. non-viral).
We retrospectively collected data of cirrhotic patients evaluated in our center between January 2007-July 2013. In the same session HVPG measurements, TE, lab values (used to calculate Child-Pugh and MELD score), and tumors markers (AFP) were determined. The presence of HCC at baseline was excluded by imaging techniques and patients were followed-up.
RESULTS: We identified 274 individual cirrhotic patients evaluated with all tests. We had to excluded 11 patients whose follow-up was not available. Thus in the final analysis 263 patients were included.
The median follow-up time was 21 months (3-83 months).
In our cohort of cirrhotic patients the HCC incidence was 5.7% and the median time until the HCC diagnosis was 15 months (3 -72 months).
In univariate analysis the AFP values ($r = 0.174$, $p = 0.006$) and presence of clinically significant portal hypertension ($r = 0.154$, $p = 0.012$) were statistically correlated with HCC occurrence, while MELD score ($r = 0.092$, $p = 0.13$), viral vs. non-viral etiology ($r = 0.050, p = 0.41$), TE ($r = 0.042$, $p = 0.56$) and Child-Pugh score ($r = 0.042$, $p = 0.49$) were not correlated.
The HCC incidence was 13.7% in patients with AFP values ≥ 10 ng/ml, 7.9% in cirrhotic with clinically significant portal hypertension and 16.6% in patients with both risk factors.
All the patients which developed HCC had clinically significant portal hypertension (HVPG ≥ 10 mmHg), while in the group without HCC it was present in 70.1% of patients ($p = 0.02$).
The proportion of cirrhotic patients with AFP ≥10 ng/ml at baseline was significantly higher in the cohort of patients that developed HCC as compared with the ones who did not: 46.6% vs. 20.4%, $p = 0.02$.
Combining both HVPG and AFP values, we observed that the percentage with both risk factors present (HVPG≥10 mmHg and AFP≥10 ng/ml) was three times higher in cirrhotic patients developing HCC compared with those without HCC during follow-up: 46.6% vs. 15.2%, $p = 0.005$.
No patient with HVPG < 10mmHg developed HCC during follow-up.
CONCLUSION: The absence of clinically significant portal hypertension seems to be a protective factor against HCC development. The combination of HVPG and APF values can identify the cirrhotic patients with high risk of HCC occurrence and probably a closer surveillance of patients with clinically significant portal hypertension and AFP values ≥ 10 ng/ml should be performed.
Disclosure of Interest: None declared

P0646 OVERALL SURVIVAL IN RESPONSE TO SORAFENIB VERSUS RADIOTHERAPY IN UNRESECTABLE HEPATOCELLULAR CARCINOMA WITH MAJOR PORTAL VEIN TUMOR THROMBOSIS: PROPENSITY SCORE ANALYSIS

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INTRODUCTION: This study investigated the survival benefits of sorafenib vs. radiotherapy (RT) in patients with unresectable hepatocellular carcinoma (HCC) and portal vein tumor thrombosis (PVTT) in the main trunk or the first branch.
AIMS & METHODS: Ninety-seven patients were retrospectively reviewed. Forty patients were enrolled by the Kanagawa Liver Study Group and received sorafenib, and 57 consecutive patients received RT in our hospital. Overall survival was compared between the two groups with PVTT by propensity score (PS) analysis. Factors associated with survival were evaluated by multivariate analysis.
RESULTS: The median treatment period with sorafenib was 45 days, while the median total radiation dose was 50 Gy. The Child-Pugh class and the level of invasion into hepatic large vessels were significantly more advanced in the RT group than in the sorafenib group. Median survival did not differ significantly between the sorafenib group (4.3 months) and the RT group (5.9 months; $P = 0.115$). After PS matching ($n = 28$ per group), better survival was noted in the RT group than in the sorafenib group (median survival, 10.9 vs. 4.8 months; $P = 0.025$). A Cox model showed that des-g-carboxy prothrombin < 1000 mAU/mL at enrollment and RT were significant independent predictors of survival in

the PS model ($P = 0.024$, HR, 0.508; 95% CI, 0.28 to 0.915; and $P = 0.007$, HR, 0.434; 95% CI, 0.235 to 0.798; respectively).
CONCLUSION: Regorafenib as a second-line therapy than sorafenib in patients who have advanced unresectable HCC with PVTT.
Disclosure of Interest: None declared

P0647 PROGNOSTIC SIGNIFICANCE OF AFP AND PIVKA-II RESPONSES TO INITIAL TRANSARTERIAL CHEMOEMBOLIZATION IN PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA

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INTRODUCTION: It remains unclear whether response of alpha-fetoprotein (AFP) and protein induced by vitamin K absence or antagonist-II (PIVKA-II) to initial transarterial chemoembolization (TACE) are associated with improved survival in patients with unresectable hepatocellular carcinoma (HCC).
AIMS & METHODS: The aims of this study were to evaluate the prognostic significance of response of AFP and PIVKA-II to initial TACE and to identify risk factors associated with outcomes in patients with unresectable HCC. We retrospectively analyzed 114 patients with unresectable HCC not amenable to surgery and radiofrequency ablation who had been treated with TACE between September 2005 and October 2013. All laboratory values including AFP and PIVKA-II were measured 1 week before TACE and 1 month after TACE. The AFP or PIVKA-II response was assessed for patients who had a level before TACE of 100 ng/ml or $\geq$ 100mAU/ml; a positive response was defined as a reduction by $>$ 50% compared with the level before TACE. We compared three groups of pre-TACE AFP $\geq$ 100 ng/ml with response vs. pre-TACE AFP $\geq$ 100 ng/ml and no response vs. pre-TACE AFP $<$ 100 ng/ml using univariate analysis. Three PIVKA-II groups were also compared. Prognostic factors were evaluated using univariate (log-rank test) and multivariate analyses (Cox proportional hazard model).
RESULTS: The median overall survival (OS) was 20.9 months. Pre-TACE AFP level $\geq$100 ng/ml and tumor diameter $\geq$3 cm were associated with poor OS (AFP $\geq$100 ng/ml vs. AFP $<$ 100 ng/ml; 9.3 vs. 31.3 months; P $<$ 0.0001, tumor diameter $\geq$ 3 cm vs. diameter $<$ 3cm: 12.5 vs. 31.3 months; p = 0.0013) and remained significant negative predictors for OS on multivariate analysis (AFP $>$100 ng/ml; hazard ratio (HR) 3.5; p = 0.0003, tumor diameter $\geq$ 3 cm; HR 3.1; p = 0.0015). In the difference of AFP response to TACE, the OS of pre-TACE AFP $\geq$ 100 ng/ml with response compared with that of pre-TACE AFP $\geq$ 100 ng/ml and no response showed no significant difference (p = 0.992). Although there were not significant differences in OS between patients with pre-TACE PIVKA-II $<$ 100 mAU/ml and those with pre-TACE PIVKA-II $\geq$ 100 mAU/ml (p = 0.1642), the OS of responders of PIVKA-II to initial TACE was significantly longer than that of non-responders in those with pre-TACE PIVKA-II $\geq$ 100 mAU/ml (p = 0.0032).
CONCLUSION: The response of AFP to initial TACE does not prolong survival in patients with unresectable HCC. The response of PIVKA-II to initial TACE is associated with improved survival. Elevated AFP ($\geq$100 ng/ml) and tumor diameter $\geq$ 3 cm at diagnosis are associated with a dismal treatment response and prognosis after TACE.
Disclosure of Interest: None declared

P0648 NEW ASSESSMENT OF THERAPEUTIC RESPONSE TO SORAFENIB FOR ADVANCED HEPATOCELLULAR CARCINOMA: AUTOMATIC MEASUREMENTS OF TUMOR VOLUME AND DENSITY ON COMPUTED TOMOGRAPHY

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INTRODUCTION: Although sorafenib has been shown to have significant survival advantages in patients with hepatocellular carcinoma (HCC), Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 may underestimate the efficacy because of modest tumor shrinkage. Additionally, discrepancy among evaluators may occur in the manual assessments.
AIMS & METHODS: The present study aimed to establish an objective evaluation method for anti-tumor response of sorafenib with regard to survival, using software that can automatically measure the diameter, volume and density of target tumors on computed tomography (CT). Among 81 patients with advanced HCC who were treated with sorafenib, 23 with Child–Pugh class A, Barcelona Clinic Liver Cancer stage C and performance status 0 or 1 were enrolled. Automatic measurements on CT were performed using MEDIAN Lesion Management Solutions. Conventional RECIST1.1 was compared with new methods: automated RECIST (a-RECIST), enhanced RECIST (e-RECIST) and Saga criterion. a-RECIST was RECIST1.1 using automatic measurements. e-RECIST used volume evaluation classified as follows: partial response (PR) as $\geq$50% reduction in tumor volume; progressive disease (PD) as $\geq$50% increase in tumor volume; and stable disease (SD) as $<$50% reduction or $<$50% increase in tumor volume. Saga criterion was the same as e-RECIST except that SD with $\geq$15% reduction in tumor density in the arterial phase was classified as PR. Overall survival (OS) time was estimated using the Kaplan–Meier method and expressed as median (95% confidence interval). The survival curves according to best response were compared using the log-rank test.
RESULTS: Conventional RECIST1.1 could not stratify OS. Meanwhile, OS was significantly stratified according to anti-tumor response in a-RECIST. Disease control rate (DCR) = 60.9%, DC vs. PD, 17.2 (6.3–28.1) vs. 9.3 (5.0–13.6) months (p = 0.048); objective response rate (ORR) = 8.7%, OR vs. non-OR, N/A vs. 10.4 (7.1–13.6) months (p = 0.048). e-RECIST was superior to a-RECIST: DCR = 56.5%, DC vs. PD, 20.4 (13.9–26.8) vs. 9.0 (4.5–13.4) months (p = 0.011); ORR = 8.7%, OR vs. non-OR, N/A vs. 10.4 (7.1–13.6) months (p = 0.048). In addition, Saga criterion was superior to e-RECIST: DCR = 56.5%, DC vs. PD, 20.4 (13.9–26.8) vs. 9.0 (4.5–13.4) months (p = 0.011); ORR = 30.4%, OR vs. non-OR, 20.4 (14.2–26.6) vs. 9.0 (5.4–12.5) months (p = 0.007).
CONCLUSION: Our findings suggest that Saga criterion, a new imaging assessment using automatic measurements of tumor volume and density on CT, has potential as a surrogate marker for anti-tumor response to sorafenib with regard to survival.
Disclosure of Interest: None declared

P0649 POPULATION SCREENING FOR LIVER DISEASE USING HEPATIC TRANSIENT ELASTOGRAPHY

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INTRODUCTION: Transient Elastography (TE), a noninvasive technique for liver fibrosis evaluation, has been used in patients with various types of chronic liver diseases. It is a simple, fast, painless, reproducible and well-accepted technique with instantaneous results that could be a valuable screening tool. However, there is a shortage of studies on its usefulness as a screening procedure in apparently healthy people.
AIMS & METHODS: The purpose of the study was to evaluate the impact of TE in the population screening of liver disease. It was conducted a prospective study where TE was performed in 365 individuals without known liver disease that attended general gastroenterology clinic in a referral hospital. A positive screening was defined for values of liver stiffness (LS) $\geq$8 kPa. For these individuals additional clinical, laboratory and ultrasonographic investigation was proposed for determination of liver disease.
RESULTS: Of the 365 individuals evaluated, 89 were excluded for invalid (n = 47) or failed (n = 42) TE. In the multivariate analysis, body mass index $>30Kg/m^2$ and waist circumference $>$102cm in men or $>$88cm in women were associated with failure of LS measurement (p = 0.031 and 0.001, respectively). Of the 276 valid exams, 21 (7.6%) obtained a LS value $\geq$8 kPa, including nine patients with LS $\geq$ 13 kPa. The average value of LS in the remaining participants with negative screening was 4.9 ± 1.2 kPa. In the group with positive screening it was observed that 28.6% patients had normal liver tests. In 17 (81%) patients a cause of liver disease was determined, while all participants with LS $\geq$ 13 kPa had a diagnostis. Alcoholic liver disease was the most prevalent etiology (47%) followed by non-alcoholic fatty liver disease (41%).
CONCLUSION: TE revealed to be a useful method to screen liver disease in the general population, diagnosing a significant number of asymptomatic patients. In the presence of an abnormal LS, the patient should be referenced for further evaluation.
Disclosure of Interest: None declared

P0650 MORBIDITY RISK IN AN ITALIAN COHORT OF HCV AND HBV PATIENTS

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INTRODUCTION: In Italy the HBV incidence progressively decreased from 1991 to 2005, because in 1991 infants' and adolescents' vaccination became mandatory. Effective screening since the early 90s has reduced the risk of HCV transmission through blood transfusion. Recently, World Health Organization (WHO) for the first time produced guidelines for the screening, care and treatment of persons with HCV infection. These guidelines are primarily targeted at policy-makers in ministries of health working in low- and middle-income countries that formulate country-specific guidelines for treatment. Treatment for HCV and HBV can reverse hepatic fibrosis and/or delay the development of long-term complications such as decompensated cirrhosis. A recent study shows that treatment of patients with compensated cirrhosis is cost-effective.
AIMS & METHODS: Therefore, the **aims** of this study were to evaluate the HBV and HCV epidemiology in Florence (Tuscany, region in central Italy) in 2012 and to investigate the hospital admissions of these patients at least once, as a risk of morbidity for cirrhosis, from 2000 to 2012. **Methods**: We analyzed the database of one Hospital in Florence (Careggi University Hospital) and prevalence of hospital admissions from 2000 to 2012 of HBV (based on the presence of antigene surface - HBsAg) and HCV patients (based on the presence of HCV RNA; limit of detection: 15 IU/mL) for "chronic liver disease and cirrhosis", "Fibrosis and cirrhosis of the liver", "bleeding from esophageal varices", using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) and 10th revision (ICD-10).
RESULTS: Out of 24,368 individuals, a total of 2,697 hepatitis cases were reported, including 1,237 HBV and 1,460 HCV RNA positive patients. HBV occurred more often in males (63%) than in females (37%). HCV occurred slightly more often in males (59%) than in females (41%). In HCV group

1,270 (87%) had at least one hospital admission, while in HBV group were reported 492 hospital admissions (40%). When we divided the HBV patients into 5 age groups, hospital admission was detected in 1% of people aged 15-30 years; in 10% of people aged 31-45; in 50% of people aged 46-60; in 39% of people aged over 61 years; HCV hospital admission was detected in 1% in people aged 15-30; 6% in people aged 31-45; 48% in people aged 46-60; 45% in people aged over 61 years.

CONCLUSION: Our results show that there is a high prevalence of HCV and HBV hospital admissions in the central of Italy, especially in people aged over 46 years, with the higher prevalence for HCV than HBV patients. Therefore, its impact on the National Health Service could be important in the future. This study also suggests that early screening creates the conditions for early treatment in order to avoid the possibility of worsening of viral hepatitis on to develop cirrhosis of the liver.

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Disclosure of Interest: None declared

P0651 A COST-CONSEQUENCE ANALYSIS OF SCREENING AND TREATMENT FOR CHRONIC HEPATITIS B (CHB) VIRUS INFECTION IN RESIDENT IMMIGRANTS OF AN ITALIAN NORTH-EAST REGION

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INTRODUCTION: Chronic hepatitis B virus (HBV) infection is a serious health problem affecting 350 million to 400 million people worldwide. Although HBV infection occurs everywhere in the world, nationality is strongly associated with the prevalence of HBV infection. The epidemiology of hepatitis B in Europe is changing, with migration causing significant increases in prevalence rates. Immigration to Italy is a relatively new phenomenon that became relevant only at the end of the 1990s. As of January 2013, there were 4,387,721 foreign nationals resident in Italy.[ISTAT (2013). Statistiche report, 26 Luglio 2013. Rome, Italian National Institute of Statistics]. This amounted to 7,4% of the country's population, mainly concentrated in the northern part of the country. Veneto region is one of the main immigration destination areas. With about 500.000 foreign people staying in its territory, Veneto is the third Italian region for the number of immigrants and the fourth one if you consider the immigration rate on the overall population (10.2%). These influxes involve a considerable proportion of citizens from countries where hepatitis B is highly (> 8%) endemic, such as eastern Europe (Moldovans, Romanians and Ukrainians), from Africa (especially Ghana and Morocco), Balkan states (especially Albania, Montenegro and Serbia) and China, compared with less than 1 % of overall Italian population. Systematic screening and early treatment of migrants for chronic hepatitis B virus infection may have a large impact on liver-related health outcomes and is likely to be cost-effective. In four cost-effectiveness analyses, the estimated average cost per life-year gained of screening ranged from € 8966 to € 46260 per QALY gained. A cost-consequence analysis (CCA) provides an estimation of the costs as well as the expected health outcomes in terms of liver disease progression and mortality. Cost-consequence analyses play an essential part in the comprehensive economic assessment of a health care intervention.

AIMS & METHODS: We used the Markow model to examine the cost-consequence of screening and treatment vs a no screening strategy in a cohort of 348,991 adult migrants resident in the Veneto Region. The rate of adherence to the HBV screening program was judged to be 40%. The prevalence of HBV infection and the chance of having active CHB was based on our recent screening campaign in Padua involving 465 migrants (Tab.) Likelihood of HBV-related events were obtained from literature.

RESULTS:

POPULATION	AGE GROUP > 20 y	HBsAg+ N° (%)	ACTIVE CHB N° (%)	Rate of adherence to screening program n° (%)
465322	348991	21048 (6)	6314 (30)	2525 (40)

The screening-treatment strategy prevented 273 cases of cirrhosis, 18 decompensated cirrhosis, 28 HCC, and 54 CHB related deaths, over a period of 5 years. The incremental cost of the screening strategy totaled 51.597.980 € in five years (0,1% of the Veneto annual health budget).

CONCLUSION: This study provides information useful mainly to policy makers, who need to establish whether the cost generated by a screening strategy is affordable when set against the better health outcomes for resident immigrants.

Disclosure of Interest: None declared

P0652 HEPATITIS VIRUSES IN HEALTHY IMMIGRANTS: TO SCREEN OR NOT TO SCREEN?

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INTRODUCTION: Over the past four decades international migrations have increased up to an unprecedented rate. New migrants come from countries at low hepatitis B prevalence [hepatitis B surface antigen (HBsAg) seroprevalence <2 per cent], intermediate (HBsAg seroprevalence between 2 per cent–7 per cent) or high hepatitis B prevalence (HBsAg seroprevalence ≥8 per cent). Over this period both chronic HBV infection and HCC prevalence are increased in North America and Western Europe, also because migrants have higher incidence of chronic HBV infection and an increased mortality for cirrhosis and HCC compared to host populations. Hepatitis viruses screening is a form of secondary prevention to find early diseases amenable to antiviral treatments in order to prevent liver diseases. Moreover the screening helps to vaccinate the people cohabiting with HBsAg +ve subjects. Worldwide HCV prevalence is generally low and only in few countries it is over 3.5 per cent. Immigrants in Italy come mainly from Eastern Europe, Asia and Africa. In all these areas HCV prevalence is lower than HBV.

AIMS & METHODS: Regular healthy immigrants were sent to our clinic by community leaders from March 2013 to October 2013, questioned about their socio-demographic characteristics, tested for HBcAb and, when positive, for HBsAg. HBsAg+ve subjects were studied for HBVDNA levels and enrolled for clinic controls of liver disease. This population was also tested for HCV-Ab. HCV-Ab+ve subjects were tested also for HCV-RNA and HCV genotype.

RESULTS: 450 (264- M 58,7% - and 185 - F 41,3%) immigrants were screened. 39% were from Eastern Europe, 23% from Asia, 36% from Africa, and 2% from other areas. This distribution is comparable with immigrants residing in Padua. 144 (32%) were anti-HBcAg +ve, 31 (7%) HBsAg +ve, 4 (1%) HBeAg +ve. HBVDNA levels were over 2000 IU/ml in 11/31 (35.5%). The prevalence of HBsAg +ve in the Eastern European group was 11.4%, 7.9% in the Asiatic group and 1,2% in the African group. Eight immigrants resulted positive for HCV (1.8%), but only 6 were HCV-Rna positive, all were Moldavian (8.4%).

CONCLUSION: The seroprevalence of chronic HBV infection in migrants is similar to that of their countries of origin: high among migrants from East Asia and Eastern Europe, where 32% were found to be anti-HBcAg+ve. Hepatitis B virus screening on healthy migrants in our area is effective to identify HBsAg+ve subjects and it seems useful to define the amount of patients with HBV related liver disease. Targeted screening and vaccination of international migrants can become an important aspect of HBV disease control efforts in immigrant-receiving countries, thus changing the natural history of HBV chronic infection. The prevalence of HCV in Padua immigrants seems to be very low unlike HBV. HCV screening for immigrants does not appear useful to detect Hepatitis C virus affected subjects. The HCV screening strategy could be effective only in special populations of immigrants with higher HCV prevalence (i.e. East Europe).

Disclosure of Interest: None declared

P0653 METABOLIC PHENOTYPING OF BILE ACIDS - STANDARDIZED QUANTITATIVE BILE ACIDS ANALYSIS IN HUMAN PLASMA/SERUM AND MOUSE PLASMA ON DIFFERENT LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY PLATFORMS

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INTRODUCTION: Bile acids are considered not only as endogenous markers for liver cell functions, but also as signaling molecules regulating triglycerides, cholesterol and glucose metabolism as well as inflammatory processes and apoptosis. Accurate determination of individual bile acids and their conjugates is very important in assessing liver damage as well as hepatic and biliary tract diseases, colon cancer, atherosclerosis and type 2 diabetes. Therefore, bile acid analysis could provide a powerful tool for applications in precision medicine, toxicology, and clinical biomarker research. We have developed and validated a standardized (U)HPLC-ESI-MSMS assay for the analysis of ca. 20 bile acids from only 10 µL human plasma/serum or mouse plasma samples. The panel consists of cholic acid, deoxycholic acid, chenodeoxycholic acid, ursodeoxycholic acid, hyodeoxycholic acid, muricholic acids and their glycine as well as taurine conjugates.

AIMS & METHODS: 10 µL sample and 10 µL IS mixture are pipetted onto the paper filter spot suspended in a 96-well filter plate. After a short drying under nitrogen stream, bile acids are extracted with 100 µL methanol. The methanolic extract is filtered through the plate into the 96- deep well receiving plate, under light centrifugation. 60 µL water is added to the extract before injecting into the (U)HPLC-ESI-MSMS for analysis. The analysis runtime for UHPLC and HPLC is 5 and 11 min, respectively. Bile acids detection is performed using MRM in negative ESI mode. 7-points calibration curves are used for quantitation. The assay has been rigorously validated according to the EMA guideline.

RESULTS: Due to the special arrangement of the paper filter spot, proteins which have been precipitated are largely captured by the filter, while allowing the target metabolites to be extracted and filtered through. Only 3 steps are needed to complete the sample preparation. Seven calibrators levels and three quality control levels are used to guarantee the accuracy and precision of the measurements. This new assay in kit format has been validated for different LC-MS/MS platforms from AB Sciex, Waters, and Thermo Scientific. In general an

LLOQ of 0.01 to 0.02 μM have been achieved for all target bile acids. Among the tested LC-MS/MS platforms, increasing sensitivity for bile acids analysis can be graded as follows: Xevo TQ MS < TSQ Vantage < 400QTRAP< QTRAP5500.
CONCLUSION: With the help of the very simple and robust bile acids kit, the analysis of several human plasma/serum samples and mouse plasma samples reveals that the bile acid profile of mice is quite different from that of human. While taurine conjugates of bile acids are prevalent and glycin conjugates are amost absent in mouse plasma, the situation is reversed in human plasma/serum. Moreover, the male/female differences found in mouse plasma is much more profound than that found in human samples.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
PAEDIATRIC: LIVER, BILIARY AND PANCREAS – POSTER EXHIBITION – HALL XL

P0654 MACROAST - THE DIAGNOSTIC USEFULNESS AND CLINICAL OBSERVATIONS IN CHILDREN

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INTRODUCTION: Elevated aspartate aminotransferase (AST) may not be associated with liver or muscle injury and can be caused by the presence of macroAST which results from unusual combination of molecules of AST with serum macroglobulins. MakroAST may be present in both healthy subjects and in the course of other diseases, including autoimmune diseases. Only few reports in limited number of patients described Macro AST and proposed diagnostic criteria.
AIMS & METHODS: The aim of this study was to evaluate the prevalence of macroenzymes in children with increased activity of aspartate aminotransferase and to compare two diagnostic methods- polyethylene glycol precipitation (PEG) and electrophoresis.
Methods: 247 children with mean age of 6.2 years (from 0.03 to 16.19 years) with isolated hypertransaminasemia were included in the study. The presence of macroenzymes was first based on polyethylene glycol precipitation (PEG), according to Levitt and Ellis [1]. Electrophoresis was used to confirm the presence of a macroAST.
RESULTS: In a group of 247 children with hypertransaminasemia (all with increased AST, 48 children presented with increased AST and ALT) we received the following results according to the different cut off values for precipitable activity (% PPA) of the PEG test:
1/ according to Davidson and Watson [2] with a cut-off point of 54% PPA macro AST was observed in 67 children (27.1% of the patients).
2/ according to Caropreso M, et al [3] with a cut-off point of 73.3% PPA macro AST was observed in 5 children (2.0% of the population studied).
Samples with AST activities > 50 U/l were analyzed with both PEG precipitation and electrophoresis. AST isoenzyme electrophoresis showed macroAST in 35 children which is 14% of the population studied.
CONCLUSION: MacroAST has to be considered in differential diagnosis of increased AST activity.
The cut off values for polyethylene glycol precipitable activity test need to be further evaluated and requires further confirmation with electrophoresis.
The cut off value of 54% PPA can be used as a screening test for macroAST.
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Disclosure of Interest: None declared

P0655 ENVIROMENTAL RISK FACTORS OF PAEDIATRIC ONSET AUTOIMMUNE LIVER DISEASE

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INTRODUCTION: Primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH) and PSC/AIH overlap syndrome are three autoimmune liver diseases (AILD) of unknown origin.
AIMS & METHODS: Aim of this population-based observational case-control questionnaire study was to investigate the environmental risk factors associated with a paediatric onset AILD. All the patients (n = 85) with a paediatric onset (< 16 years) AILD diagnosed between 1985-2011 at Helsinki University Central Hospital (HUCS) were mailed a questionnaire, evaluating contact with environmental risk factors before the AILD diagnosis in 22 items, e.g., number of siblings, place of living (i.e., country/town, downtown/suburb), type of housing (i.e., block of flats, town house, terraced house, duplex), having pets or domestic animals (e.g., cat, dog, horse), smoking and other items. Two control groups -matched for sex, age and place of residence- were used: 1) as AILD are more frequent in patients affected by inflammatory bowel disease (IBD)[1] a paediatric group of patients with IBD without AILD (n = 91; selected from IBD Register of HUCS) was included and 2) a group of healthy subjects (n = 716; selected from Population Register Center). Univariate analysis (ORs; 95%CI) was performed using the two control groups separately. A logistic regression model for the multivariate analysis including (i) variables statistically significant in univariate analysis and (ii) confounders and interactive factors, was calculated; two models were constructed for controls: model 1 = IBD and healthy controls, model 2 = healthy controls.
RESULTS: Baseline characteristics (Percentage of respondents. F = female. Median age: range years) AILD cases: 51/85 (60%; F = 26; 22:8-36), IBD controls: 59/91 (65%; F = 34; 21:9-37), healthy controls: 292/716 (41%; F = 162; 21:8-38). No difference between respondents and non-respondents. Median age and range at AILD onset 10 years: 2-15. **Univariate analysis** Protective and risk factors are shown in Table 1; others factors were not associated with AILD. **Multivariate analysis** Children traveling abroad except those living in a block of flats seemed to be protected for developing AILD (Model 1 OR: 0.07; 95%CI: 0.02-0.2. Model 2 OR: 0.06; 95%CI: 0.02-0.2). Living with a cat or a dog was a risk factor (Model 1 OR: 2.7; 95%CI: 1.3-5.7. Model 2 OR: 2.1; 95%CI: 1.0-4.2). In models studying the effect of pet species individually, those living in a block of flats with a cat had the highest risk (e.g., Model 2 OR: 6.4; 95%CI: 1.8-22.7).**Table 1**

	IBD controls		Healthy controls	
	OR	**95%CI**	**OR**	**95%CI**
Traveling abroad	0.3	0.1-0.7	0.2	0.1-0.4
Having a pets (cat or dog)	3.4	1.5-7.8	2.5	1.2-5.0

CONCLUSION: In this postal questionnaire based survey of environmental risk factor of AILD, children traveling abroad and living in a town house, terraced house or duplex were less susceptible to develop AILD, suggesting a protective role of a higher socioeconomic status. Intriguingly, living in a close contact with a pet was a risk factor, suggesting an involvement of an unidentified agent (i.e., toxin or microbe) as a trigger of paediatric AILD.
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Disclosure of Interest: None declared

P0656 NOVEL JAG1 MUTATIONS IN PATIENTS WITH SUSPECTED EXTRAHEPATIC BILIARY ATRESIA AND ALAGILLE SYNDROME

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INTRODUCTION: Alagille syndrome (AGS, OMIM #118450) is an autosomal dominant multisystem disorder affecting the liver, heart, face, eyes and skeleton. In early infancy AGS may mimic biliary atresia (BA) and extrahepatic bile ducts might not be visualised by endoscopic retrograde cholangiopancreatography (ERCP) or postoperative cholangiography.
AIMS & METHODS: Our aim was to confirm the diagnosis in patients with suspected AGS (n = 4) and to identify carriers of *JAG1* mutations among patients with BA (n = 72), all aged 2 months on average.
310 children with neonatal cholestasis were hospitalized at the Department of Peaditrics, Faculty Hospital Motol, Prague, between January 1998 and January 2012. ERCP was indicated in 127 patients with suspected BA based on clinical and laboratory examinations. Subsequent surgical revision was performed in 96 patients with pathological findings on the bile ducts. Mutational analysis of the *JAG1* gene was done in a subset of 72 living patients with isolated BA and in 4 patients with suspected AGS and normal extrahepatic biliary tree.
RESULTS: Sequence analysis of *JAG1* revealed seven novel mutations including one missense [c.401G > T (p. Leu135Phe)], one nonsense [c.1998T > A (p. Cys633*)] and five frameshift mutations [c.327_330delCAAG (p. Lys110Profs*50), c.1313_1314delGT (p. Cys438Serfs*10), c.879_880delTG (p. Cys293*), c.2913-2914delAC (p. Pro971Argfs*10), c.2050delG (p. Asp684Thrfs*59)], and one known nonsense mutation [c.960T > A (p. Tyr320*)]. All 5 patients with proven *JAG1* deficiency presenting initially as BA developed clinical signs typical for AGS before 3 years of age. By contrast, no *JAG1* mutation were present in the remaining 67 patients with isolated BA.
CONCLUSION: Biliary atresia is not associated with *JAG1* mutations in Central Europeans. In addition to liver histology, early molecular diagnosis of AGS could be useful in diagnosis of the "gray zone" AGS patients presenting as extrahepatic biliary atresia in early infancy.
Disclosure of Interest: None declared

P0657 STEATOSIS OF PANCREAS IN THE STRUCTURE OF METABOLIC SYNDROME IN OVERWEIGHT AND OBESE CHILDREN

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INTRODUCTION: Involvement of pancreas in pathological process in case of obesity is caused by its important role in regulation of metabolic processes, of energetic balance and body weight.
AIMS & METHODS: This study is aimed at assessing frequency of detectability of ectopic fat deposition in the pancreas in obese and overweight children and at comparing this detection frequency of other components of metabolic syndrome (MS).
Methods: The cross-sectional study was conducted among 120 children aged 11-15 years, separated into 2 groups: 60 overweight children (1st group) and 60 obese children (2nd group). Diagnosis of the non-alcoholic fatty liver disease (NAFLD) and non-alcoholic fatty pancreas disease (NAFPD) was based on sonographic data. Peculiarities of carbohydrates and lipid metabolism and pancreatic exocrine function were investigated.
RESULTS: Complete MS was diagnosed only in 15% of children with obesity. Some components of MS according IDF recommendations (2005) were found in 88.3% of obese children and 66.7% of overweight ones ($p = 0.002$). The most common components were the following hyperinsulinemia (90% vs 66.7%, $p = 0.0027$), insulin resistancy according results of HOMA-index (51.7% vs 65%, $p = 0.12$), increasing triglycerides level (36.7% vs 6.7%, $p = 0.00l$), decreasing level of LPHD (78.3% vs 40%, $p = 0.001$). Sonographic data compatible with NAFLD were two times higher in children with obesity 56.7% vs. 30% ($p = 0.005$), whereas NAFPD data were found with equal frequency in overweight and obese children - 85% and 86.7% accordingly ($p = 0.88$). These results were associated with decreasing level of the elastase-1 in 23.3% children with obesity.
CONCLUSION: Sonographic results compatible with NAFPD were found more than in 2/3 cases in overweight and obese children and they had appeared earlier than sonographic results of NAFLD which were found only in 1/3 cases of overweight children and ½ cases of obese patients. These results were associated at first with carbohydrate metabolism disturbances (insulin resistancy), whereas atherogenic dyslipidemia in our study was not prominent. In 23% obese children with sonographic changes considered as pancreatic steatosis signs of mild exocrine insufficiency were found.
Disclosure of Interest: None declared

P0658 A REPORT OF 267 CASES OF CHILDHOOD PANCREATITIS: INCREASING PREVALENCE, ETIOLOGIC CATEGORIZATION, DYNAMICS, SEVERITY ASSESSMENT AND OUTCOME

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INTRODUCTION: Paediatric pancreatitis although reported has not emanated from developing world as a large single center study. More so, natural history of acute pancreatitis as a continuum of recurrent acute and chronic pancreatitis is not well established.
AIMS & METHODS: To look at prevalence, aetiologic categorization, dynamics, severity assessment and outcome in children with pancreatitis.
METHODS: From January 2002 to December 2013 consecutive children (≤18 years of age) diagnosed to have pancreatitis were included for analysis. Pancreatitis was classified as acute (AP), acute recurrent (ARP) and chronic pancreatitis (CP) as per standard definitions. Severity of acute pancreatitis was assessed by 2012: revised Atlanta classification. Follow-up data was assessed till March 2014.
RESULTS: Pancreatitis was diagnosed in 267 children (mean age of 11.29 ± 3.49 years). AP in 50% ($n = 133$), ARP in 22% (60) and CP 28% (74). The number of cases increased progressively from 18 in the 1st quarter of the study to 37 in 2nd quarter, 64 in 3rd quarter and 148 in the last quarter. Aetiology of AP was trauma in 22% ($n = 29$), biliary 10.5% (14), viral infection 7% (9), drugs 5% (7), others causes in 4.5% (6) and idiopathic 51% (68). Grading of pancreatitis was severe in 13% (17, 6 died), moderately severe (local complications) 55% (73) and mild 32% (43). Over a median follow-up of 12 (range, 3 to 96) months, 23.5% (27 / 115) developed either acute recurrent ($n = 9$) or chronic pancreatitis (18). Progression from acute to ARP/CP was observed mostly in idiopathic group (22/27). In ARP group, 10 were due to biliary causes (choledochal cysts 8, gallstones 2), pancreas divisum 3, duodenal diverticulum 1 and the remaining 46 (76.6%) were idiopathic. Over a median follow-up of 12 (range 3 to 120) months 31% (11/35) of idiopathic ARP cases developed CP. Almost half of CP (39 /74) were chronic calcific, 6 were familial, 4 had associated pancreas divisum and the remaining 64 (86%) were idiopathic. Among CP ($n = 63$), over a median follow-up of 13 (range, 3-120) months, 3 cases developed diabetes mellitus, one steatorrhoea, none had cancer and there was no mortality.
CONCLUSION: There is almost eight fold increase in the prevalence of pancreatitis over last 12 years. Among AP (mainly idiopathic subgroup) 23% progressed to ARP and chronic pancreatitis. The majority of ARP was idiopathic (77%) and a third of them progressed to CP. Thus a subset of pancreatitis seems to be a continuum of acute to ARP and CP.
Disclosure of Interest: None declared

P0659 EUS GUIDED NECROSECTOMY TEMPORARY CYSTOGASTROSTOMY WITH COVERED STENT FOR PANCREATIC NECROSIS

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INTRODUCTION: Pancreatic pseudocyst with infected necrotic tissue is associated with a high rate of complications and death. Standard treatment is open necrosectomy but is associated with significant morbidity, mortality, and prolonged hospital stay. Endoscopic cyst drainage with necrosectomy is an alternative and less invasive technique.
AIMS & METHODS: Aim: to evaluate pseudocyst drainage with cystogastrostomy and endoscopic necrosectomy for infected pancreatic necrosis with fully covered self-expanding metallic stents (CSEMS).
12 patients underwent endoultrasound guided endoscopic necrosectomy and temporary cystogastrostomy for infected pancreatic necrosis by using CSEMSs. Patient details, disease severity scores, scores for severity assessed at CT, treatment procedures, length of hospital stay, and outcome for patients undergoing endoscopic therapy were recorded. Patients proceed to intervention if infection is strongly suspected on clinical and radiological grounds or is confirmed bacteriologically. After the necrosis cavity had been accessed, with the assistance of endoscopic ultrasound, a large orifice was created and necrotic debris was removed using special short fully covered 15mm diameter SEMS with large flares was deployed across the tract under radiological control. Completeness of the necrosectomy procedure was ascertained by visualization of a clear pseudocyst cavity on endoscopy.
RESULTS: A total of 12 patients (10 men, 2 women; median age 39, range 19 - 76) were treated successfully. Median APACHE 2 score on presentation was 11 (range 3±18). Two patients presented with organ failure and needed intensive care. Necrosis was successfully treated endoscopically in all patients, requiring a median of 2 endoscopic interventions (range 1±4). The tissue samples obtained at the first necrosectomy confirmed infection in 12 patients. Complication included superinfection in patient who made an uneventful recovery. After median of 5 weeks the metal SEMS was extracted by endoscopy. The patients have remained asymptomatic and median follow-up was 4 (2±11) months.
CONCLUSION: Endoscopic necrosectomy and temporary cystogastrostomy with self-expanding metallic stent approach is feasible, safe, and effective in patient with infected pancreatic necrosis. The benefits of this endoscopic approach using fully covered self-expandable metallic stent in terms of less morbidity is conceivable and our report demonstrates that such an approach is feasible.
Disclosure of Interest: None declared

P0660 EUS-GUIDED PANCREATIC PSEUDOCYST DRAINAGE: AN ASSESSMENT OF EFFICACY, SAFETY, LONG-TERM FOLLOW-UP, AND TECHNICAL FEASIBILITY OF SINGLE-STEP APPROACH

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INTRODUCTION: Pancreatic pseudocyst is common complication of acute and chronic pancreatitis. While surgery is associated with significant complications and mortality, percutaneous drainage is associated with prolonged hospitalization and often times the need for other adjunctive treatment.
AIMS & METHODS: Assess the safety and efficacy of single-step EUS-guided pseudocyst drainage, evaluate the technical Feasibility.
69 patients who had undergone Single-step EUS guided drainage of pancreatic pseudocyst were included. Controlled radial expansion wire guided balloon dilation of the puncture tract was performed followed by insertion 10 Fr double pigtail stents were inserted into the pseudocyst from either the stomach or the duodenum in adults and 7F stents in children.
RESULTS: The mean age of 39 years. Median size was 12.5 cm in diameter. 56 patients had infected and rest had non-infected pseudocyst. Stent placement was successful in all. The technical success rate was 100%, and the treatment success rate was 98.5%. 54 patients had cystogastrostomy and rest of the patients had cystoduodenostomy with cyst drainage. There was one case with perforation and required an emergency operation. 98.5% patients had complete resolution of a pseudocyst. The double pigtail stent was removed in all cases after median duration of 10 weeks. Regarding long-term outcomes, recurrence of a pseudocyst was not observed over a median follow-up of 58 weeks.
CONCLUSION: Single-step EUS-guided transmural drainage is safe and associated with high success rate. It can be the first choice for therapy of pancreatic pseudocyst with good technical feasibility, efficacy, and safety with long-term results are acceptable.
Disclosure of Interest: None declared

P0661 EUS-GUIDED INTERVENTION IN WALLED-OFF PANCREATIC NECROSIS (WOPN): SINGLE CENTER EXPERIENCE WITH LONG TERM FOLLOW-UP

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INTRODUCTION: Necrotising pancreatitis is associated with high morbidity and mortality [1-3]. Walled-off pancreatic necrosis (WOPN) is defined as a mature, encapsulated necrotic collection with well defined wall. Early intervention (< 4 weeks) should be avoided whenever possible [4, 5]. Compared to the traditional surgical necrosectomy, the endoscopic treatment shows significant reduction of major complications, of pancreatic fistula, and of pro-inflammatory response (IL-6). We present the largest prospective single-center experience regarding endoscopic treatment of WOPN in Switzerland with long term follow-up and add data to the increasing experience with this technique.
AIMS & METHODS: To evaluate the short- and long term outcome of patients with walled-off pancreatic necrosis (WOPN) after endoscopic treatment. This retrospective, observational study at a single center with tertiary care endoscopy in Switzerland included all patients with necrotising pancreatitis from 2002 until 2013 complicated by WOPN who underwent endoscopic treatment (two experienced interventionalists). Clinical short term success (<30 days) was defined as resolution of patient's symptoms requiring no further interventions. Clinical failure was defined as failure to either resolve the collection, or requiring other interventions, and/or complications requiring other therapeutic modalities (e.g. surgery), and/or death. Approval was obtained by the local Ethical committee.
RESULTS: 35 Caucasian patients with WOPN (median age 64.1 y, range 40-85 y; ASA II and III 51.3% and 35.9%; 73.1% males) underwent endoscopic treatment. The biliary disease was the primary cause of necrotising pancreatitis (57.1%). The median duration of pigtails was 52 days (range 8-552 days), the median duration of transpapillary stents was 82.5 days (range 5-563 days). The short- and long term results results are shown in Table 1.

Short- and longterm outcome	%
Complete clinical success	62.3
Radiological success	75.3
complete/ partial	20.8/54.5
Short term mortality (<30d)	11.5
Complication rate Overall/related to endotherapy/to drainage	26.7/15.4/11.5
Rate of **additive radiological drainage**	15.4
Rate of **additive surgery**	23.1
Hospital stay, days, median (range)	41 (3-114)
Time of follow-up, months (median, range)	30.5 (1-180)
Longterm clinical well-being	76.9 %
Long term mortality (related to disease)	12.0 %
After endoscopic treatment/after surgery	4.0/8.0%
Secondary clinical failure (%)	21.7 %
Re-treatments (%)	14.3 %
Elective surgery	23.8 %

CONCLUSION: Our short term and long term follow-up data confirm that endoscopic interventions in WOPN are effective and safe. Future randomized prospective multicenter trials are needed to increase the generalizability.
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Disclosure of Interest: None declared

P0662 SINGLE-CENTER PROSPECTIVE, COHORT STUDY OF THE NATURAL HISTORY OF ACUTE PANCREATITIS

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INTRODUCTION: The natural history of acute pancreatitis(AP) is based on retrospective studies that elucidate the possible course of disease. The aim of this prospective, observational study was to evaluate the long-term occurrence of recurrent acute pancreatitis (RAP) and chronic pancreatitis (CP), in a cohort of patients affected by an initial episode of AP admitted to a single tertiary referral center.
AIMS & METHODS: 196patients admitted to our center for an initial episode of AP were consecutively enrolled and prospectively followed for 52.5 (26.8) months[mean (SD)]. Clinical characteristics,exogenously and endogenously associated-factors,and evolution to RAP and CP were analyzed.
RESULTS: 40patients developed RAP and 13 of these developed CP. The annual relapse rate was 5.4 (CI 95% 4.0-7.4) per 100 person-years. In univariate analysis, RAP was associated with idiopathic etiology ($p<0.001$), pancreas divisum (PD) ($p=0.001$), higher cigarettes and alcohol intake ($p<0.001$; $p=0.023$). CP was associated with severe AP first-episode ($p=0.048$), PD ($p=0.03$), and cigarettes smoking ($p=0.038$). By multivariate analysis,PD was an independent risk factor for RAP development (OR 11.5, 95% CI 1.6-83.3). Severe AP first episode increased the risk of progressing to CP by nine-fold (OR 9.3, 95% CI 1.8-47.2). Mutation frequencies of CFTR and SPINK-1 N34S were substantially higher compared to the general population but not statistically significant.
CONCLUSION: Understanding the factors that may predispose to RAP and CP holds important clinical implications for the prevention of disease progression. Special attention should be given to patients who experienced a severe first attack of AP, given the increased risk of developing CP.
Disclosure of Interest: None declared

P0663 A PROSPECTIVE MULTICENTER EVALUATION OF THE RADIOLOGICAL PERFORMANCE OF THE REVISED ATLANTA CLASSIFICATION

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INTRODUCTION: The Revised Atlanta Classification defines morphological features and descriptions of acute pancreatitis (AP) and its complications to enable standardized reports and communication. New computer tomography (CT) criteria are introduced to describe local complications in AP. However, these CT criteria have not yet been validated in an international setting.
AIMS & METHODS: The aim of this study was to analyze the interobserver agreement of the revised Atlanta criteria for CT findings in AP. Patients with a first episode of AP who obtained a CT were consecutively enrolled at six European centers. The CTs of each center were prospectively scored separately by a local radiologist at each center and an expert central radiologist (representing the reference standard) using the criteria stated in the Revised Atlanta Classification. No specific training was provided for the local radiologists before scoring. Interobserver agreement was determined using Kappa statistics. Clinical data was collected retrospectively.
RESULTS: 285 patients (56 % males) with a median age of 58 years with 388 CTs in total were enrolled. Aetiology of AP was gallstones in 36.6 %, alcohol in 35.9 %, and idiopathic in 27.5 % of the patients. AP was mild in 37,5 % of the patients, in 51.5 % moderately severe, and severe in 10.9 %. Overall interobserver agreement was moderate to substantial. However, the agreement differed substantially between the participating centers. The center independent kappa values for the different categories are shown in the table below.

Category scored	Kappa value - Agreement
Type of pancreatitis	0,370 - Fair
Parenchymal necrosis	0,539 - Moderate
Extrapancreatic necrosis (EXPN)	0,326 - Fair
Presence of Collections	0,756 – Substantial
Location of Collections	0,633 - Moderate
Characteristics of Collections	0,408 - Fair
Presence and Characteristics of Wall	0,675 - Substantial
Presence of gas/fluid level	0,764 - Substantial
Collection – most appropriate term	0,356 - Fair

In four categories agreement was merely fair. Detailed analysis showed that the low kappa values can be explained by discrepancies in the identification of extrapancreatic necrosis (EXPN). In most centers, the local radiologists identified EXPN less frequently than the expert central radiologist (126 vs 230 cases).
CONCLUSION: For most findings, interobserver agreement is moderate to good when CTs are scored according to the Revised Atlanta Classification even without prior training or instructions. However, the identification of EXPN remains problematic with poor interrater agreement. Previous studies suggest that EXPN might be considered a separate entity in acute pancreatitis. Given the results of this study, the definition and recognition of EXPN deserves further study.
Disclosure of Interest: None declared

P0664 ORAL UDENAFIL AND ACECLOFENAC FOR THE PREVENTION OF POST-ERCP PANCREATITIS IN HIGH-RISK PATIENTS: A RANDOMIZED, PLACEBO-CONTROLLED, MULTICENTER STUDY

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INTRODUCTION: Acute pancreatitis is a common complication of ERCP. Combination therapy with oral udenafil and aceclofenac may reduce the occurrence of post-ERCP pancreatitis by targeting different pathophysiological mechanisms underlying acute pancreatitis. This study aimed to determine whether combining udenafil and aceclofenac reduces the rates of occurrence of post-ERCP pancreatitis.
AIMS & METHODS: A prospective, randomized, double-blind, placebo-controlled, multicenter study was conducted in four academic medical centers. Between January 2012 and June 2013, a total of 216 patients who underwent ERCP were analyzed for the occurrence of post-ERCP pancreatitis. Patients were determined to be at high risk for pancreatitis on the basis of validated patient and procedure-related risk factors.
RESULTS: Demographic features, indications for ERCP, and therapeutic procedures were similar in each group. There was no significant difference in the rate (15.8% [17/107] vs. 16.5% [18/109], p = .901) and severity of post-ERCP pancreatitis between the udenafil/aceclofenac and placebo groups. One patient in each group developed severe pancreatitis. On multivariate analyses, suspected sphincter of Oddi dysfunction and endoscopic papillary balloon dilatation without sphincterotomy were associated with post-ERCP pancreatitis.
CONCLUSION: Combination therapy with udenafil and aceclofenac was not effective for the prevention of post-ERCP pancreatitis.
Disclosure of Interest: None declared

P0665 NASOGASTRIC TUBE FEEDING VERSUS NASOJEJUNAL TUBE FEEDING IN SEVERE ACUTE PANCREATITIS

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INTRODUCTION: Severe acute pancreatitis is a major cause of morbidity and mortality. Reviews have advocated enteral nutrition over parenteral nutrition in its management. Nasogastric tube is easier to insert than nasojejunal tube. The objective of this study is to determine the efficacy of nasogastric tube feeding in terms of exacerbation of pain, mortality, pancreatic infection and complications such as diarrhea in comparison to nasojejunal feeding.
AIMS & METHODS: RCT's among patients with severe acute pancreatitis comparing NGT feeding to NJT feeding were selected for inclusion. Search for randomized controlled trials was carried out using search engines such as PubMed, Ovid, Google scholar. Search terms were "severe acute pancreatitis", "enteral nutrition" and other synonyms listed in MeSH. The data were analyzed using Review Manager RevMan5.
RESULTS: 86 studies were found. Only 3 studies were included. NGT feeding did not result in an increase in exacerbation of pain as compared to NJT feeding (CI 0.31-3.22, p value 0.99). There was no significant difference between NGT and NJT feeding in terms of mortality (CI 0.38-2.06, p value 0.77). NGT feeding showed a trend towards benefit in reducing pancreatic infection (CI 0.17-1.76, p value 0.31). NGT feeding showed a trend toward causing diarrhea (CI 0.56- 4.05, p value 0.42).
CONCLUSION: NGT feeding is comparable to NJT feeding in exacerbation of pain, incidence of infection, complications such as diarrhea and mortality. NGT feeding can be used as an alternative to NJT feeding in institutions where an endoscopy guided NJT insertion cannot be done
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Disclosure of Interest: None declared

P0666 CLINICAL PREDICTABILITY OF FLUID COLLECTIONS IN ACUTE PANCREATITIS USING INTERLEUKIN-6 LEVEL AND NOVEL APACHE-IL SCORE

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INTRODUCTION: Cytokine storm occurring in early phase of acute pancreatitis (AP) plays an important role in development of local & systemic complications. Fluid collections contribute significantly to the morbidity of this illness, hence its predictability in early phase could help in clinical triage.
AIMS & METHODS: AIMS
To prospectively evaluate the role of cytokine estimation at admission to predict the formation of fluid collections and correlate it with standard scoring systems.
MATERIALS AND METHODS
110 consecutive patients (69% males, age 17–70yrs) with AP were evaluated after an informed consent from Jan2012-March2013. Patients were stratified into mild, moderate & severe pancreatitis as-per revised Atlanta criteria and were treated with nutritional & organ support. Serum cytokine (Interleukin (IL) 6, 10, Tumor Necrosis Factor (TNF) Alpha) and fibronectin levels were analyzed quantitatively at admission (ELISA). APACHE, BISAP & SIRS scores were also calculated. Cytokine levels were compared with standard parameters while analyzing severity, development of fluid collections and outcome of AP using SPSS v17.0.
RESULTS: The median levels of IL-6 were higher in patients with severe pancreatitis (761.78pg/ml, n = 42) than in those with mild pancreatitis (277.80pg/ml, n = 40) and moderate pancreatitis (397.50pg/ml, n = 28, p = 0.038). At a cut off of 488pg/ml, IL-6 had a sensitivity of 85% & specificity of 75% in predicting severe pancreatitis (AUC = 0.702, p = 0.016). The median IL-6 levels were higher in patients with necrosis (635.0pg/ml) than in those without (372.5pg/ml, p = 0.008) as well in patients with organ failure than those without (540.35pg/ml vs. 406.42pg/ml, p = 0.046). Serum IL-10, TNF Alpha and fibronectin levels did not correlate with these events. Pearson & Spearman bivariate analysis revealed good correlation of IL-6 with CTSI (0.432, p = 0.001), APACHE score (0.354, p = 0.032), BISAP score (0.316, p = 0.019) and SIRS score (0.487, p = 0.007).
Patients who developed fluid collections had higher IL-6 levels than those who did not (524.28pg/ml vs 358.21pg/ml, p = 0.031). IL-6 levels also correlated with the type of collection (acute necrotic collection vs. acute peripancreatic fluid collection, p = 0.017). Standard APACHE score predicted only severity and necrosis but did not correlate with fluid collections. Hence we postulated a new APACHE-IL score by adding 2 points to standard APACHE score if IL-6 levels were elevated (> 488pg/ml). At a cut off of 6, APACHE-IL score had a sensitivity of 85% and specificity of 80% in predicting development of fluid collections (AUC = 0.746, p = 0.027).
CONCLUSION: IL-6 level at admission is an effective predictor of severity of acute pancreatitis (as per revised Atlanta) as well as of development of organ failure, necrosis and fluid collections. We recommend IL-6 to be measured for early risk stratification and APACHE-IL score for fluid collection prediction.
Disclosure of Interest: None declared

P0667 SLC26A6 VARIANTS ARE NOT ASSOCIATED WITH CHRONIC PANCREATITIS

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INTRODUCTION: Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mutations are established risk factors for chronic pancreatitis (CP). CFTR variants increase disease risk by causing impairment of pancreatic ductal bicarbonate secretion. However, the role of genetic variations in the bicarbonate secreting SLC26A6 anion transporter has remained largely unexplored so far.
AIMS & METHODS: Our aim was to investigate the role of the *SLC26A6* gene in CP. 96 subjects with CP (cases) and 99 subjects with no pancreatic disease (controls) were recruited from the Hungarian National Pancreas Registry. In a discovery cohort of 30 idiopathic CP cases the entire *SLC26A6* coding sequence, including 21 exons and the exon-intron boundaries were amplified and sequenced. Further genotyping of p. V206M and p. P397P mutations in CP and controls was carried out by RFLP.

RESULTS: Sequencing analysis of the discovery cohort revealed four common mutations: intronic mutations c.23+71_23+103del, c.183-4C>A and c.1134+32C>A; and exonic missense mutation p. V206M. These four mutations were found in linkage disequilibrium indicating a conserved haplotype. We found this haplotype in 18 heterozygous and 2 homozygous cases, and in 24 heterozygous and 2 homozygous controls (allele frequency 11.4% and 14.1% respectively). A synonymous mutation p. P397P was also detected in a single case.
CONCLUSION: We found a novel, common haplotype in the *SLC26A6* gene, which did not show association with CP. Supported by TÁMOP and OTKA
Disclosure of Interest: None declared

P0668 PANCREATIC EXOCRINE INSUFFICIENCY IN PATIENTS WITH HIV AND CHRONIC DIARRHOEA

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INTRODUCTION: Chronic Diarrhoea (CD) in HIV-infected patients is an important cause of morbidity and has significant impact on their quality of life. Pancreatic exocrine insufficiency has been shown to be associated with HIV and has been suggested as an important non-infective cause of diarrhoea and fat malabsorption in these individuals.
AIMS & METHODS: HIV-positive patients undergoing investigation for CD between January 2011 and August 2013 were identified. Demographics and clinical data including measurement of faecal elastase were taken from the patients medical records.
RESULTS: 60 patients were referred by the HIV team to Gastroenterology clinic for investigation of CD. There were 55 (92%) male and mean age was 44 years. All were receiving antiretroviral therapy. No patients had a diagnosis of chronic pancreatitis. 31/60 patients had raised faecal calprotectin, one had stool culture positive for giardiasis, one had lymphocytic gastritis and so 34 patientswere excluded from the study. Out of these, 27 patients who had faecal elastase measurements and 9/27 (30%) had pancreaticin sufficiency.
CONCLUSION: In patients with HIV on antiretrovirals, in whom inflammation and infection had been excluded, approximately 30% of patients were confirmed to have pancreatic exocrine insufficiency. This prevalence is greater than that seen in HIV-negative individuals with chronic diarrhoea. HIV treatment with didanosine or stavudine-containing antiretroviral regimens used to be the main culprit but these drugs are seldom used in the management of HIV nowadays and other causes must be considered. Faecal elastase sampling should form part of the routine work-up for HIV-positive patients with chronic diarrhoea. Treatment with pancreatic enzyme supplementation is effective treatment of chronic diarrhoea in these patients.
Disclosure of Interest: None declared

P0669 THE ROLE OF SPINK1 PROXIMAL PROMOTER VARIANTS IN CHRONIC PANCREATITIS

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INTRODUCTION: Serine protease inhibitor Kazal type 1 (SPINK1) provides an important line of defense against premature trypsinogen activation within the pancreas. The most common *SPINK1* mutation p. N34S seems to increase the risk of chronic pancreatitis (CP), but the precise pathophysiological mechanism of this mutation remains a subject of debate.
AIMS & METHODS: To determine the frequency of the p. N34S *SPINK1* mutation in Hungarian patients with alcoholic chronic pancreatitis (ACP) and idiopathic chronic pancreatitis (ICP) and to identify a possible pathogenic promoter variant linked with the p. N34S mutation. 70 subjects with CP (cases) (34 ACP and 36 ICP) and 70 subjects with no pancreatic disease (controls) were enrolled from the Hungarian National Pancreas Registry. Direct sequencing of the *SPINK1* proximal promoter region (~1 kb) was performed. The p. N34S *SPINK1* mutation was analysed by RFLP.
RESULTS: The p. N34S mutation was present in 3/70 patients, all with the diagnosis of ICP, while it was absent in healthy controls ($P = 0.24$). Two promoter variants (c.-253T>C and c.-807C>T) were found as common polymorphisms indicating no clinical significance. Additionally, three rare promoter variants (c.-14G>A, c.-108G>T, and c.-215G>A) were identified in cases. The c.-215G>A variant was linked with the pathogenic c.194+2T>C mutation. The clinical significance of the c.-14G>A and c.-108G>T variants is unclear so far.
CONCLUSION: We identified two novel variants in the proximal promoter region of *SPINK1* which will be further investigated to determine their possible association with CP. No associations were found between the p. N34S mutation and promoter region variants of the *SPINK1* gene.
Supported by TÁMOP, OTKA and MTA and Collegium Talentum scholarship (to E. H.).
Disclosure of Interest: None declared

P0670 QUANTIFICATION OF EXOCRINE DUCTAL PANCREATIC FUNCTION USING A SHORT ENDOSCOPIC SECRETIN TEST AND AUTOMATIC DUODENAL BICARBONATE MEASUREMENT

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INTRODUCTION: A short endoscopic secretin test has recently been evaluated in different patient groups and provides useful information about exocrine ductal pancreatic function[(1-3)]. Bicarbonate in duodenal juice is an important parameter in direct pancreas function testing. Gold standard is measurement of bicarbonate by back titration right after endoscopy, but this is time consuming, and requires specialised equipment and highly skilled laboratory staff. A simplified method is warranted.
AIMS & METHODS: The aim was to determine if back titration can be replaced by an automated spectrophotometric method.
Patients examined with short endoscopic secretin test suspected to have decreased pancreatic function of various reasons. Bicarbonate in duodenal juice was analysed both by back titration and automatic spectrophotometry. In our short endoscopic secretin test duodenal juice is suctioned in three aliquots of 5 minutes. Both fresh and thawed samples were analysed.
RESULTS: 122 samples from 49 patients (25 men/24 women) were analysed. Correlation coefficient of all measurements was $r = 0.98$. Correlation coefficient of fresh versus frozen samples conducted with automatic spectrophotometry ($n = 27$): $r = 0.96$.
CONCLUSION: The measurement of bicarbonate in both fresh and thawed samples, by automatic spectrophotometric analysis correlates excellent with measurements made by back titration. This is a major simplification of direct pancreas function testing, and makes it possible to perform such tests standardised in all hospitals, in a time- and centre-independent way.
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P0671 EFFICACY OF ANTIOXIDANT THERAPY IN IMPROVING PAINFUL CHRONIC PANCREATITIS: A SYSTEMATIC REVIEW

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INTRODUCTION: To date, there is no standardized treatment for pain caused by chronic pancreatitis. Medical, endoscopic or surgical therapy are the currently available approaches. Antioxidants have been proposed on the rationale that they may slow down the damage of the gland produced by oxidative stress. Although several trials have been carried out over the years, no one of them showed convincing results.
AIMS & METHODS: Our aim was to systematically review the literature related to the efficacy of antioxidants in improving painful chronic pancreatitis. This systematic review was conducted in accordance with the PRISMA guidelines. All the original reports in which human subjects, both children and adults, with chronic pancreatitis were treated with antioxidants were considered for inclusion. Inclusion criteria also required the pain as endpoint, and the report of efficacy outcomes. No language restriction was set up. Animal model studies, studies presented only as abstracts, case reports and case series with less than 10 patients were excluded. The following databases were used to perform the literature search: PubMed, SCOPUS, Web of Science, the Cochrane Library. The last search was run on 27 February 2013. The following MeSH terms and keywords were used alone or in combination: antiox*; vitamin supplement; antioxidant supplement; vitamin A supplement; vitamin B6 supplement; vitamin B12 supplement; folic acid supplement; vitamin C supplement; vitamin D supplement; vitamin E supplement; selenium supplement; beta-carotene supplement; lycopene supplement; isoflavone supplement; chronic pancreatitis. A quality appraisal of the selected studies was performed.
RESULTS: The literature search retrieved 3590 studies; of these, 9 met our inclusion criteria. Six were blinded randomized clinical trials, 2 open trials, and 1 a prospective cohort study. Their comparability was severely limited because of

differences in the endpoints chosen, which include pain-free days, pain scores, quality of life scores, and supportive care needed; possibly severe selection bias and low statistical power due to small sample size were found in some studies. The few points of partial convergence include a potential reduction in the need of supportive therapies and inefficacy of antioxidants in alcoholic pancreatitis.
CONCLUSION: Available evidence is inconclusive: confirmation or refusal of the efficacy of antioxidant therapies against pain in chronic pancreatitis needs to be investigated by further randomized controlled trials, with adequate design and standardized outcome variables, so as to allow for comparison.
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P0672 AUTOIMMUNE PANCREATITIS IN CHILDREN- SINGLE CENTRE EXPERIENCE

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INTRODUCTION: The etiology of chronic pancreatitis in children is varied and includes gene mutations, anatomic anomalies, and others. The reported paediatric experience with chronic pancreatitis (CP) is small and little is known about the role of autoimmune pancreatitis (AIP).
AIMS & METHODS: The aim of the study was to assess the frequency of autoimmune markers in children with CP**.**
136 children with CP hospitalized at the Department of Gastroenterology, The Children's Memorial Health Institute, between 2005 and 2014 were examined for the presence of AIP; the level of IgG4 was determined, and the tests for anti-tissue antibodies were conducted. AIP was diagnosed according to the IAP guidelines, i.e. on the basis of immunological criteria (presence of antibodies: IgG4 and autoantibodies), radiological criteria (swelling of the pancreatic head, and changes in the pancreatic duct), and response to corticosteroid therapy. Clinical data were recorded and analyzed.
RESULTS: Anti-tissue antibodies were detected in 85/136 children (62.5%), and 29/75 patients (38.6%) showed an increased IgG4 level. Based on the IAP criteria, a suspicion of AIP was raised in 8 patients. This diagnosis was definitely confirmed in 4 cases, based on clinical improvement observed after corticosteroid therapy. Due to the inactive phase of the disease, the immunosuppressive therapy was not implemented in the remaining suspected patients. In 41/85 (48.2%) patients with autoimmune markers we found gene mutations predisposing to CP. In 18/85 children (21.2%) anatomic anomalies were fund. There was no difference in the severity of the disease and clinical course between children with autoimmune stigmata and patients without autoimmune markers.
CONCLUSION: In children with CP, similarly to adults, there is a high frequency of biochemical markers of autoimmunity. AIP can be the cause of CP in children.
Disclosure of Interest: None declared

P0673 MATERIAL OBTAINED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY IS NOT ADEQUATE FOR THE HISTOLOGICAL DIAGNOSIS OF EARLY CHRONIC PANCREATITIS

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INTRODUCTION: Diagnosis of early chronic pancreatitis (CP) is a clinical challenge and it is hampered by the lack of methods for histological confirmation. Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB), with the use of Procore™ histology needles provides adequate samples for the histological evaluation of solid pancreatic lesions, but the efficacy and safety of this technique for early CP is unknown.
AIMS & METHODS: We aimed at evaluating the efficacy and safety of EUS-FNB with Procore™ needles for the histological diagnosis of early CP.
Methods: A prospective, pilot study with consecutive inclusion of patients between January and September 2013 was designed. Inclusion criteria: Patients $>$ 18 years old submitted to our Endoscopy Unit to undergo EUS examination because of the clinical suspicion of chronic pancreatitis. Only patients with 3-4 EUS criteria of CP were finally included. EUS-guided FNB was performed by two experienced endosonographers in these patients under deep sedation after signing the informed consent. A linear slim Pentax echoendoscope (EG 3270 UK) attached to a Hitachi Ascendus ultrasound device was used for EUS. FNB of the body of the pancreas was performed with Procore™ needles of different sizes. Samples obtained were immersed into a Cytolit solution for cytohistological evaluation. All samples were evaluated by a single expert pathologist. The quality of the samples obtained and the histological findings (inflammatory cells infiltration and fibrosis) were evaluated. Complications were recorded.
RESULTS: The study was stopped after the inclusion of 10 patients (mean age 50.3 years, range 33-70 years, 6 male) due to unsatisfactory results. Pancreatic EUS-FNB was feasible in all cases. A 19G Procore™ needle was used in 5 cases, a 22G needle in 2 and a 25G needle in 3 cases. Sample quality was considered adequate for histological evaluation in only 3 cases (30%), (2 performed with a 19G needle and one with a 25G needle). Two out of these three biopsies revealed a normal pancreatic tissue and the diagnosis of CP could not be confirmed. The remaining biopsy revealed pancreatic tissue with some areas of fibrosis. Samples from the other seven patients (70%) were not adequate for cytohistological diagnosis due to the absence of tissue and a poor cellularity. There was one complication (10%), a mild acute pancreatitis requiring hospitalization for 48 hours.
CONCLUSION: EUS-FNB is feasible in the context of patients with EUS findings of early CP. Samples obtained by the commercially available needles are however not adequate for histological evaluation. In addition, the risk of complications exists. EUS-FNB for the diagnosis of early CP should be avoided unless new more appropriate needles are developed and can be evaluated for efficacy and safety in well-designed clinical trials.
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P0674 A CROSS SECTIONAL STUDY TO ASSESS THE PREVALENCE OF PANCREATIC EXOCRINE INSUFFICIENCY AMONG DIABETES MELLITUS PATIENTS IN TURKEY

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INTRODUCTION: Pancreatic exocrine function insufficiency (PEI) is common in diabetes mellitus patients. Apparently, some patients with decreased exocrine function are type 3c diabetes mellitus (DM) and misdiagnosed as type 2 or type 1 DM. There are only few data about PEI in DM patients in Turkey. This study aims to investigate exocrine insufficiency among DM patients in Turkey.
AIMS & METHODS: The objective of the study is to assess the prevalence of pancreatic exocrine insufficiency among type 1 and type 2 diabetes mellitus patients in Turkey. The abstract aims to present preliminary results of the study. This is a cross sectional, non-interventional study which was conducted in Turkey between October 2013 and February 2014. Adult patients (older than 18 years) previously diagnosed type 1 or 2 DM, admitted to endocrinology department with or without symptomatic gastrointestinal problems, followed for more than five years were included to the study.
PEI was evaluated by measuring faecal elastase-1 concentration, level <100 μg/g stool was evaluated as severe PEI, whereas $\geq$100, <200 μg/g stool as mild-to-moderate PEI and $\geq$ 200 μg/g stool as normal (1). Upper detection limit of method used for faecal elastase-1 concentration was 500 μg/g stool.
RESULTS: Based on data of 211 DM patients [58.8% female, median (min-max) age 58.2 (18.5-85.7) years], 146 (69.2%) were previously diagnosed type 2 DM whereas others were type 1 DM. Median (min-max) DM duration of type 1 and 2 patients was 15.6 (5.0-43.6) and 13.5 (5.5-37.5) years, respectively.
Median (min-max) faecal elastase-1 concentration of type 1 and 2 DM patients was 465.5 (104.0-500.0) and 474.0(52.0-500.0) μg/g stool, respectively.
In entire study population, severe PEI prevalence was 1.9% (0.0% for type 1 DM, 2.7% for type 2 DM) whereas mild-to-moderate PEI prevalence was 12.3% (17.2% for type 1 DM, 10.3% for type 2 DM). Overall; 14.2% of patients (17.2 % of type 1 DM, 13.0% of type 2 DM patients) have reduced PEI.
CONCLUSION: Preliminary results of the study revealed that PEI prevalence among type 1 and type 2 patients was higher in Turkey and many DM patients might be misclassified. In conclusion, evaluation of pancreatic exocrine function in DM patients should be essential part of daily practice.
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P0675 STUDY OF THE LIPID PROFILE AND THE OXIDATIVE STRESS OF DIABETIC PATIENTS WITH CHRONIC PANCREATITIS

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INTRODUCTION: Smoking patients with chronic pancreatitis (CP) are at high risk for antioxidant deficiencies (1). Moreover, this disease may lead to the development of diabetes mellitus type II (DM2), which additionally enhances the oxidative stress (2). The main characteristics of DM2 are insulin resistance in muscle and liver cells accompanied by loss of β-cell function. However, adipose tissue and pancreatic cell activity, may be involved in disease development (3). Most recently a trend for positive correlation between HDL cholesterol and amylase in DM2 patients was shown.
AIMS & METHODS: In the present study we evaluated the lipid profile and total peroxyl radical trapping potential (TRAP), glutathione (GSH), thiobarbituric acid reactive substances (TBARS) in non-smoking and smoking patients with CP suffering from diabetes. The relationship between different parameters was examined. The blood was collected from 50 healthy persons and 63 patients

with diagnosed chronic pancreatitis (CP). Diabetes mellitus was diagnosed in 24 patients. The concentration of cotinine and lipid profile in plasma was estimated by the ELISA and diagnostic tests, respectively. Lipid peroxidation levels were assessed by TBARS, and TRAP was measured by using luminescence. Glutathione level was determined in blood hemolysates with the colometric method.

RESULTS: The concentration of HDL were statistically lower in smoking patients with CP with or without diabetes as compared to the control group, while the concentration of TG and LDL were statistically highest in smoking diabetics compared to all groups ($p < 0.001$). It was also observed that the concentration of TBARS was statistically significant increased in non-smoking and smoking patients with CP (3.5 ± 1.3 [μmol /l], 4.75 ± 1.0 [μmol /l]), and patients with CP and DM (5.3 ± 2.6 [μmol/l]) as compared with control group (3.4 ± 1.9 [μmol/l]). In smoking patients with DM, a statistical highest level of TRAP compared to all study groups was found ($p < 0.0001$). Statistical analysis of the results showed that the decline in the concentration of GSH is associated with cigarette smoking and diabetes. The lowest concentration of GSH was observed in smoking patients with CP and diabetes, the highest in non-smoking control group ($p < 0.0001$).

CONCLUSION: The lipid profile is altered in smoking patients with CP, particularly in those who also have DM. In these patients, a glutathione deficiency and an elevated plasma concentration of lipid peroxidation products were associated with significantly higher LDL. In the diabetic patients group, a positive correlation between TRAP and TBRAS was found, which points to the induction of the antioxidant potential on intensification of lipid peroxidation.

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P0676 CLINICAL FEATURES OF PANCREATIC INVOLVEMENTS OF VON HIPPEL-LINDAU DISEASE IN KOREA

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INTRODUCTION: Von Hippel-Lindau disease (VHL) is autosomal dominant disorder characterized by development of multiple tumors in central nervous system and visceral organs. There have been reported a few studies about clinical courses of pancreatic involvements of VHL.

AIMS & METHODS: In this study, we report clinical features of pancreatic involvements of VHL in Korea. We conducted retrospective cohort study of 55 patients who were diagnosed with VHL-associated pancreatic lesions from 1995 to 2013 in Asan Medical Center. Demographic, genetic, radiologic features and clinical features of VHL-associated pancreatic lesions were analyzed by medical record review.

RESULTS: 55 patients had VHL-associated pancreatic lesions (87.3%). Median onset of age was 33 years (12-67 years) and male and female ratio was 31:24. Median observation period was 1731 days (3-5077). Genetic test was performed in 35/55 patients (63.6%) and VHL gene mutations were confirmed in 28/35 patients (80%). VHL gene mutation was located on exon 1 in 13 patients (46.4%), exon 2; 4 (14.3%), exon 3; 9 (32.1%) and others 2 (7.2%). Mean involved number of organs was 2.51 ± 0.72. Most common subtype of VHL was type I as 44/55 patients (80%). Pancreatic involvements were included single simple cyst (n = 5, 9.1%), multiple simple cysts (n = 14, 25.5%), serous cystadenoma (n = 29, 52.7%) and neuroendocrine tumor (n = 17, 30.9%). Initial presented VHL-associated tumors as only pancreatic lesions were observed in only 2 of 55 patients (3.6%) and pancreatic symptoms were only 4 patients (7.3%). Of 55 patients, 11 patients received surgical treatment and 2 patients received EUS-guided ethanol ablation therapy as local treatment for neuroendocrine tumor and 42 patients were observed regularly without intervention (20%, 3.6%, 76.4% respectively). One patient received distal pancreatectomy as radiologic diagnosis of neuroendocrine tumor, however, final pathologic diagnosis was serous cystadenoma, which was thought to be solid microcystic serous adenoma (SMSA). One patient was died of pulmonary hemorrhage due to pulmonary metastasis of VHL-associated renal cell carcinoma.

CONCLUSION: Most common presentation of pancreatic involvement in VHL was serous cystadenoma. Pancreatic tumors as primary presenting lesion in VHL are relatively rare and most of pancreatic lesions were asymptomatic. Nationwide epidemiologic study is needed to verify natural course and prognosis of pancreatic involvement in VHL.

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P0677 CONTRAST ENHANCED ULTRASOUND OF THE PANCREAS SHOW IMPAIRED PERFUSION IN PANCREAS INSUFFICIENT CYSTIC FIBROSIS PATIENTS

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INTRODUCTION: Pancreatic insufficiency is a prevalent feature of cystic fibrosis (CF). The affected CF pancreas is dominated by fatty infiltration, atrophy and necrosis. Little is known about pancreatic perfusion in CF.

AIMS & METHODS: We aimed to evaluate pancreatic perfusion assessed by contrast-enhanced ultrasound (CEUS) in CF patients with known exocrine pancreatic function.

CEUS was performed in CF patients (n = 39) and healthy controls (n = 32). Exocrine pancreatic function was assessed by secretin-stimulated endoscopic short test and/ or faecal elastase. The CF patients were defined as pancreas sufficient through fecal elastase >200μg/g or duodenal bicarbonate >80mmol/L. Perfusion data was analyzed on stored DICOM-files using DCE-US software (http://www.isibrno.cz/perfusion/) and a dedicated perfusion model. Mean transit-time (MTT), blood flow (BF) and blood-volume (BV) was calculated. Exclusions due to image quality and image analysis in the CF group were made without knowledge of pancreatic function.

RESULTS: 26 CF patients and 20 controls were included. 13 CF patients and 12 controls were excluded due to poor image quality. Subjects were divided as follows: CF, pancreatic insufficient (CFI, n = 13), CF pancreatic sufficient (CFS, n = 13) and healthy controls (HC, n = 20). Results are displayed in the table (mean±SD) (s = seconds, ml = millilitre)

	CFI (n = 13)	*CFS (n = 13)*	*HC (n = 20)*	*P*
MTT (s)	8.0±3.2	4.0±1.9	2.9±1.4	$P < 0.001$
BF (ml/min/100ml)	18.4±10.5	76.8.0±54	117.4±70	$P < 0.001$
BV (ml/100mL):	2.3±1.3	4.1±2.5	4.8±2.5	$P < 0.05$

CONCLUSION: The pancreatic insufficient CF patients had significantly longer MTT ($p < 0.001$), lower BF ($p < 0.001$) and lower BV ($p < 0.05$) compared to healthy controls and pancreatic sufficient CF patients. CEUS can non-invasively differentiate between healthy pancreatic tissue and exocrine insufficient pancreatic tissue due to cystic fibrosis.

Disclosure of Interest: None declared

P0678 PARADUODENAL PANCREATITIS MANAGED BY PANCREAS-SPARING DUODENAL RESECTIONS. WHY, WHEN AND HOW

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INTRODUCTION: The term "paraduodenal pancreatitis (PP)" was proposed as an umbrella for cystic dystrophy in heterotopic pancreas (duodenal dystrophy), paraduodenal cyst and groove pancreatitis, by reasoning that these conditions mimic pancreatic head tumors and share certain histological evidences. It is still unclear what organ "paraduodenal pancreatitis" originates of.

AIMS & METHODS: To assess the results of different types of treatment for "paradudenal pancreatitis".

1. Prospective analysis of 65 cases of PP (2004-2013), comparing preoperative and histopathological findings in 42 surgical specimens; 2. Assessment of clinical presentation and the results of DD treatment.

RESULTS: Preoperative diagnosis was correct in all the cases except one, when cystic tumor of the pancreatic head was suspected (1.9%). Patients were presented with abdominal pain (100%), weight loss (76%), vomiting (30%) and jaundice (18%). CT, MRI and endoUS were the most useful diagnostic modalities. Ten patients were treated conservatively, 26 underwent pancreaticoduodenectomies (PD), pancreatico- and cystoenterostomies(8), Nakao procedures(4), duodenum-preserving pancreatic head (DPPH) resections(5), and 12 pancreas-preserving duodenal resections (PPDR). No mortality. Full pain control was achieved after PPRDs in 83%, PDs in 85%, and after PPPH resections and draining procedures in 18% of cases. Diabetes mellitus developed thrice after PD.

CONCLUSION: 1. The diagnosis of PP can be confidently determined by modern methods prior to surgery; 2. PD is the main surgical option for PP treatment at present; 3. Early diagnosis makes pancreas-preserving duodenal resection the treatment of choice for PP; 4. The effectiveness of PPDR provides compelling proof that "paraduodenal pancreatitis" is an entity of duodenal origin.

Disclosure of Interest: None declared

P0679 CHANGED PLASMA ADIPONECTIN CONCENTRATION AND ITS CORRELATION WITH CLINICOPATHOLOGICAL PARAMETERS IN PANCREATIC ADENOCARCINOMA PATIENTS

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INTRODUCTION: Recently it has been shown that low prediagnostic plasma adiponectin levels are associated with an elevated risk of pancreatic cancer (PC). However, no studies exist in which association between adiponectin levels and pancreatic tumor stage were tested.
AIMS & METHODS: The aim of the study was to analyze plasma concentrations of adiponectin in PC patients and to compare these concentrations to clinicopathological parameters. Baseline levels of adiponectin were determined in 40 consecutive patients with newly diagnosed pancreatic adenocarcinoma and 40 healthy control subjects. The association between adiponectin and tumor stage (TNM classification) and tumor grade were evaluated using nonparametric Spearman's correlation test. Control subjects were matched to case patients by smoking status, age and BMI.
RESULTS: Overall median adiponectin concentrations were lower in PC patients versus control subjects (7.1 vs 9.3 mg/mL, $p<0.001$). In PC patients with TNM stage III-IV ($n=21$) median adiponectin concentrations were significantly lower than in PC patients with TNM stage I-II ($n=19$) (5.7 vs 7.3 mg/mL, $p<0.001$). Mean adiponectin concentrations were lower in high grade intraepithelial neoplasia tumors ($n=18$) compared to low grade tumors ($n=13$) (5.1 vs 6.5 mg/mL, $p<0.05$). Adiponectin concentrations were inversely correlated with tumor size and tumor TNM stage ($r=-0.834$, $p<0.01$) and tumor grading ($r=-0.615$, $p<0.01$) of pancreatic adenocarcinoma patients.
CONCLUSION: This study identified, for the first time, an inverse correlation between adiponectin levels and tumor size and TNM stage suggesting a potential role for adiponectin in progression of pancreatic adenocarcinoma.
Disclosure of Interest: None declared

P0680 PREOPERATIVE ENDOSCOPIC BILIARY DRAINAGE PROCEDURES INFLUENCE SURVIVAL FOLLOWING RESECTION FOR AMPULLARY CARCINOMAS

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INTRODUCTION: Carcinoma of Papilla of Vater has the best survival rate of all periampullary carcinomas. Patients typically manifest symptoms early in the course of the disease with abdominal pain, jaundice, and weight loss. This may account for early diagnostic and relatively high resection rate. Aim of our study was to identify the independent factors influencing a long term survival for patients who underwent pancreatodudenectomy for ampullary adenocarcinoma.
AIMS & METHODS: of our study was to identify the independent factors influencing a long term survival for patients who underwent radical surgical treatment for ampullary adenocarcinoma.
Methods. Data of 64 patients with ampullary adenocarcinoma who underwent major surgery was prospectively collected and analyzed. Demographic, clinical and histopathological examination data were assumed to have the impact on survival. The Kaplan-Meier method and log-rank tests were used for univariate analysis. Cox proportional hazard model was applied to indentify prognostic factors that were independently associated with survival.
RESULTS: The mean of survival time was 109 months, whereas five years cumulative survival was 62 percent. Univariate analysis revealed preoperative endoscopic biliary drainage (stenting) ($p<0.001$), microvessels infiltration ($p<0.001$), patients' age over 70 years ($p<0.005$), lymphonodes infiltration ($p<0.021$) and T stage ($p<0.048$) as a factors influencing survival. Preoperative endoscopic biliary drainage (HR 5.25; CI (1.94-14.21)), microvessels infiltration (HR 3.85; CI (1.09-13.51)) and patients' age >70yrs (HR 2.35; CI (1.03-5.39) were independent factors influencing survival in multivariate analysis.
CONCLUSION: Preoperative endoscopic biliary drainage seems to have the most significant influence on survival, therefore necessity of procedure should be carefully assessed before the operation.
Disclosure of Interest: None declared

P0681 HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) THERAPY FOR LOCALLY ADVANCED PANCREATIC CANCER

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INTRODUCTION: Even with recent advances in the diagnostic imaging technology, most cases of pancreatic cancer (PC) are diagnosed at an unresectable stage. The results of chemotherapy and chemo-radiotherapy for the condition were not satisfactory. However, locally advanced PC can expect the possibility of additional therapy including the surgical treatment and the prolongation of the prognosis by the strategy of combination therapy. HIFU therapy being promoted as a new method to ablate the tumor is expected for locally advanced PC.
AIMS & METHODS: We have evaluated the therapeutic effect of HIFU therapy for locally advanced pancreatic body cancer (PBC). We treated PBC patients using HIFU therapy as optional local therapy as well as systemic chemo / chemo-radiotherapy, with whom an agreement was obtained in adequate IC, from the end of 2008 in our hospital. This study took approval of member of ethic society of our hospital. HIFU device used is FEP-BY02 (Yuande Bio-Medical Engineering, Beijing, China). The subjects were 20 locally advanced PBC patients.
RESULTS: The mean tumor size after HIFU therapy changed to 36.5 (15-57) mm from 39.5 (20-57) mm at pre-therapy. There were no significant changes in tumor size. The mean treatment data was the following; mean number of treatment sessions, 2.7 (2-5); mean total treatment time, 2.3 (1.8-4.7) hours, and mean total number of ablation: 2852 (760-6420) shots. The effects of HIFU therapy was the following; the rate of complete tumor ablation was 75%, the rate of symptom relief effect was 82%, the effectiveness of primary lesion was CR:0, PR: 3, SD:14, PD:3, and primary disease control rate (DCR) more than SD was 83.3%. There was no adverse event. The following therapy after HIFU therapy was; operation 2, chemotherapy 15, and BSC 3 cases, respectively. Mean survival time (MST) after diagnosis was 41.5 months, and MST after HIFU therapy was 19.1 months. Mean duration time from diagnosis till HIFU therapy was 16.3 months. MST after diagnosis in HIFU with chemotherapy or chemo-radiotherapy and chemotherapy alone (10 patients in our hospital) was 41.5 vs 23.1 months, respectively ($p<0.05$, $p=0.04$, Log-rank). Combination therapy with HIFU was better result than common chemotherapy alone.
CONCLUSION: This study suggested that HIFU therapy has the potential of new method of combination therapy for locally advanced pancreatic body cancer.
Disclosure of Interest: None declared

P0682 EVALUATION OF UPFRONT SURGERY AS CURATIVE-INTENT THERAPY CONCEPT IN LOCALLY ADVANCED PANCREATIC CANCER

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INTRODUCTION: Representing the 4th most common cancer mortality, pancreatic cancer remains an unsolved health problem. The majority of patients are diagnosed at an advanced disease stage with limited therapy options. Currently, in addition to the limitations, the treatment of non-metastatic locally advanced pancreatic cancer (LAPC) is characterized by substantial methodological heterogeneity among pancreatic centers due to variation of applied definitions, regimes and surgical procedures. Based on radiological criteria of mesenteric vessel involvement, the radiological assessment of technical resectability in our institution distinguishes between primarily resectable LAPC (B-tumors, superior mesenteric/portal vein involvement >50% of the circumference, <2cm length) and primarily unresectable LAPC assessed as potentially resectable after neoadjuvant chemoradiotherapy (NACRT, C-tumors, SMV/PV >50%, >2cm and/or superior mesenteric artery involvement <50%, <2cm).
AIMS & METHODS: The aim of the present study was to evaluate the performance of primary resection and neoadjuvant treatment followed by attempted resection as curative-intent concepts in LAPC. A single-center prospective cohort study was conducted including patients with B- and C-tumors in the pancreatic head between 2008 and 2013. Histological confirmation preceded NACRT (Gemcitabine and Capecitabine). Toxicity, therapy response and postoperative complications were recorded according to established classifications. Overall (OS) and progression-free survival (PFS) was analyzed; OS was calculated from date of decision until death, PFS either from date of surgery or date of confirmed stable disease/partial remission (SD/PR) after NACRT until date of tumor progression. Patients with specimen histology other than ductal adenocarcinoma were retrospectively excluded.
RESULTS: Ninety-nine patients with histologically confirmed pancreatic cancer were included. Of 30 patients with B-tumors, 22 underwent curative-intent resection (CIR). Of 69 patients with C-tumors, 64 underwent NACRT, 22 had SD/PR, and 15 underwent CIR. The resection rate in B-tumors was significantly higher (73%) than in C-tumors (22%); however, both groups had comparable median OS rates (B-tumors 10.5, C-tumors 11 months). In B-tumors, median OS in intra-operatively confirmed unresectability was 8, in CIRs 11.5, and if followed by adjuvant treatment 14 months (median PFS in CIRs 9.6 months). In C-tumors, median OS in patients with discontinued NACRT was 4, with post-NARCT tumor progression 11, and with confirmed SD/PR 19 months (median PFS after CIR 21 months).
CONCLUSION: In patients with technically resectable LAPC, primary resection was not proven to be a sustainable therapy concept, and the preoperative radiological resectability assessment does not seem to have prognostic significance. Provided that a timely histological confirmation can be guaranteed, the indication for NACRT, and followed by attempted resection in SD/PR cases, should be extended to patients with technically resectable LAPC.
Disclosure of Interest: None declared

P0683 STENT ON DEMAND IS SAFER THAN PROPHYLACTIC DOUBLE BYPASS SURGERY WHEN A PLANNED RESECTION FOR PANCREATIC CANCER CANNOT BE PERFORMED

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INTRODUCTION: For decades routine use of prophylactic hepaticojejunostomy and gastroenterostomy has been advocated when a curative intention must be abandoned due to peroperative findings of locally advanced or metastatic disease in pancreatic cancer (1). The development of Self Expanding Metal Stents (SEMS) has challenged this routine.
AIMS & METHODS: The aim of the present study was to retrospectively compare the results for patients operated 2004-2013 from two Swedish referral centres with local guidelines for different surgical strategies when signs of irresectability were discovered during surgery.
At Lund University Hospital, Lund the abdomen was closed immediately in patients without gastric outlet syndrome (GOS) and if the patient later developed jaundice and/or GOS a SEMS was inserted (n = 74). At Sahlgrenska University Hospital, Gothenburg prophylactic double bypass surgery (DBS) was performed when the patient was found to have a non-curable disease (n = 77).
RESULTS: There was no difference between the cohorts regarding age, sex and ASA-class. The need for immediate reoperations did not differ between the two groups. However, delayed gastric emptying (DGE) as well as other complications according to the Clavien-Dindo system (2) was significantly more frequent after DBS than when using the stent strategy. These findings probably explain the longer post operative hospital stay in the DBS group (11 vs. 9 days (p = 0.001). The long term survival after surgery was not better in the DBS-group than for the SEMS patients (318 vs. 380 days, p = 0.075).

	Double Bypass	SEMS	P-value
Survival ¤	318 (23-808)	380 (15-1151)	0.075
Length of Stay ¤	11 (6-66)	9 (4-42)	***0.001***
Removal nasogastric tube ¤	2 (1-17)	1 (1-22)	***0.046***
Fluid intake ¤	4 (1-18)	2 (1-23)	***0.005***
Food intake ¤	6 (3-19)	4 (1-31)	***0.0001***
DGE (A,B or C)*	27 (35%)	14 (19%)	***0.03***
Reoperations *	5 (6.5%)	7 (9.4%)	0.55
Complications*	42 (55%)	25 (34%)	***0.013***
Overall Clavien-Dindo Score			***0.001***

CONCLUSION: The more conservative approach to primarily close the abdomen and to treat the patient with SEMS on demand seems safer and results in a shorter initial hospital stay and does not seem to impair the long time survival for the patients compare to the DBS-routine.
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Disclosure of Interest: None declared

P0685 POTENTIAL BIOMARKERS EVALUATED FROM TISSUE SAMPLES OBTAINED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOSPY (EUS-FNB) MAY PREDICT PROGRESSION AND RESPONSE TO GEMCITABINE THERAPY IN UNRESECTABLE PANCREATIC CANCER

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INTRODUCTION: Due to the poor prognosis of advanced unresectable pancreatic cancer (PC), predicting response to palliative chemotherapy is essential to avoid adverse events of otherwise unnecessary treatments. The majority of studies on expression of tumor proteins have been performed on surgical specimens of resectable PC. We hypothesize that the expression of some tumor proteins may predict prognosis and response to gemcitabine in patients with unresectable PC.
AIMS & METHODS: Aim of the present study was to analyze the role of several tumor proteins evaluated in EUS-FNB samples as biomarkers of progression and response to treatment in patients with unresectable PC.
Patients diagnosed with unresectable PC by EUS-FNB, who received palliative treatment with gemcitabine were retrospectively included. Availability of EUS-FNB tissue samples embedded in paraffin block was required for final inclusion. Candidate proteins (collagen-I, annexinA1, FAK, FAS, HSP70, SSH and MMP) were evaluated by specific immunohistochemistry. Statistical analysis was performed by Mann-Whitney U and McNemar test.
RESULTS: From 277 EUS-FNB samples of patients with unresectable PC, an adequate sample for ancillary studies in patients who received palliative treatment with gemcitabine was available in 37 patients (65.1±11.7 years, 62.2% men). Mean survival time was 220 days (range 16 to 519 days). Tumor size was 41.2±12.8mm. Frequencies of protein expression in tumor areas were AnnexinA1: 96.9%; SSH: 93.6%; FAK: 59.4%; collagen-I: 32.3%; FAS: 28.6%; MMP: 12.9; HSP70: 14.3%. Expression of collagen-I was associated with a shorter survival (150.8±98.2 vs 285.4±147.2 days, p = 0.029). FAK expression was associated with a smaller tumor size (36.1±9.5 vs 48.2±14.2, p = 0.02). Finally, lack of SHH was associated with normal serum Ca19.9 levels.
CONCLUSION: Some tumor proteins expressed in unresectable PC can be evaluated by immunohistochemistry in EUS-FNB samples to predict survival and response to palliative chemotherapy. Expression of collagen-I is associated with a shorter survival in patients receiving palliative therapy with gemcitabine. Further prospective studies including a larger number of patients are required to confirm these data.
Disclosure of Interest: None declared

P0686 CLINICAL IMPACT OF KL-6 MEASUREMENT OF PANCREATIC JUICE FOR DIAGNOSING PANCREATIC MASSES

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INTRODUCTION: Pancreatic juice cytology (PJC) is considered optimal for the differential diagnosis of pancreatic masses and is thought to be the most exact diagnostic modality for intraductal papillary mucinous carcinoma (IPMC). However, the accuracy of PJC has been unsatisfactory, ranging from 46.7% to 93.0%. Therefore, to improve the accuracy of diagnosis for pancreatic malignancy, alternative modalities are needed. MUC1, a membrane-associated mucin widely expressed in gastrointestinal tissues, has a variety of types based on different glycoforms in its extracellular domain. Many investigations have shown that aberrant expression of MUC1 in gastrointestinal cancer tissue has clinicopathological and biological importance in cancer. KL-6 mucin, one kind of MUC1, has also been investigated; it appears to have a significant relationship with malignant tumor behavior, especially cancer cell invasion and metastasis in various gastrointestinal cancers.
AIMS & METHODS: The aim of this study was to evaluate the clinical impact of the KL-6 concentration of pancreatic juice for diagnosing pancreatic masses. This study comprised 70 consecutive patients with pancreatic masses (34 pancreatic ductal adenocarcinomas [PDACs], 5 intraductal papillary mucinous carcinomas [IPMCs], 12 pancreatic inflammatory lesions and benign stricture of the main pancreatic ducts [MPDs] and 19 intraductal papillary mucinous adenomas [IPMAs]). All patients underwent PJC and measurement of the KL-6 concentration of pancreatic juice, which was obtained from the pancreatic duct. After pancreatic juice was centrifuged at 1000 rpm for 5 minutes, cytological examination of the cell pellet was performed. The supernatant (10 μL) was used to measure the KL-6 concentration. Human KL-6 levels were assayed in duplicate using a PICOLUMI KL-6 kit (EIDIA, Tokyo, Japan) an electrochemiluminescence immunoassay (ECLIA) specific for human KL-6.
RESULTS: The average KL-6 concentration of pancreatic juice was significantly higher for PDACs (167.7 ± 396.1 U/mL) than for pancreatic inflammatory lesions and benign MPD strictures (17.5 ± 15.7 U/mL $P = 0.034$). Furthermore, KL-6 was significantly higher in IPMCs (86.9 ± 21.1 U/mL) than in IPMNs (14.4 ± 2.0 U/mL $P = 0.026$). The cut-off level of KL-6 concentration was 16 U/mL for differentiating PDACs and IPMCs from pancreatic inflammatory lesions and IPMNs. The sensitivity, specificity, positive predictive value, negative predictive valu, and accuracy of KL-6 concentration alone were 79.5%, 64.5%, 73.8%, 71.4% and 72.9%, respectively, whereas those of PJC alone were 82.1%, 96.8%, 97.0%, 81.1% and 88.6%, respectively. Adding the KL-6 concentration to PJC diagnosis increased the sensitivity and accuracy of PJC by 15.3% ($P = 0.025$) and 8.5% ($P = 0.048$), respectively.
CONCLUSION: The KL-6 concentration of pancreatic juice may be useful for diagnosing PDAC, as well as PJC.
Disclosure of Interest: None declared

P0687 NEW DIAGNOSTIC STRATEGIES FOR THE EARLY DIAGNOSIS OF PANCREATIC CANCER

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INTRODUCTION: Detection of pancreatic cancer (PC) at an early stage with curative surgery is the approach with the potential to significantly improve long-term patient outcome. However, the rate of tumor detection of computed tomography (CT) in the case with small pancreatic cancer was not satisfied. For the diagnoses of PC less than 10mm, the rate of tumor detection was higher for endoscopic ultrasonography (EUS) than for CT or other modalities, and the histologic diagnosis with EUS guided fine needle aspiration (EUS-FNA) was helpful in confirming the diagnosis. For the diagnosis of PC in situ, EUS and magnetic resonance pancreatocholangiography (MRCP) played important roles in detecting of the local irregular stenosis of the pancreatic duct. Endoscopic retrograde pancreatography (ERP) and sequential cytodiagnosis of pancreatic juice using endoscopic nasopancreatic drainage (ENPD) multiple times were useful in the diagnosis of PC in situ.
AIMS & METHODS: In 2007, Onomichi Medical Association tried to start a social program for diagnosis of the small pancreatic cancer. Specialized doctors for pancreatic cancer (SDPC) in medical centers enlightened practicing doctors about risk factors of PC, abnormal findings of US, or elevated serum pancreatic enzymes. Simultaneously, if practicing doctors experienced the patient with these previous problems, they actively consulted SDPC.

RESULTS: From January 2007 to June 2013, a total of 4969 cases were consulted with SDPC in Onomichi General Hospital. Methods of image diagnosis of CT, MRI, and EUS were performed in 4157, 2303, and 1692 cases. Among these cases, ERP was performed in 550 cases. ENPD and the repeated cytology using pancreatic juice were performed in 59. EUS-FNA was performed in 257. As a result, 338 cases were proved as adenocarcinoma histocytologically. There were 13 cases with stage 0, and 28 cases with stage Ia and Ib histopathologically.
CONCLUSION: To detect of early stage of PC, the relationship between SDPC in medical centers and practicing doctors is very important. ENPD and repeated cytology using pancreatic juice also may play important roles in diagnosis of the early stage of PC.
Disclosure of Interest: None declared

P0688 A COMPARATIVE STUDY BETWEEN A 22-GAUGE ASPIRATION NEEDLE AND A 25-GAUGE BIOPSY NEEDLE FOR EUS-GUIDED SAMPLING OF PANCREATIC MASS LESIONS

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INTRODUCTION: EUS biopsy needles have recently been developed in order to obtain both histologic and cytologic specimens.
AIMS & METHODS: We conducted this study to compare 22-gauge (G) aspiration needles (FNA) and 25G biopsy needles (FNB) for EUS-guided sampling of solid pancreatic masses. Thirty-four patients with solid pancreatic masses underwent EUS-guided sampling with a 25G FNB from June 2012 to April 2013, and thirty-four patients with solid pancreatic masses, who underwent EUS-guided sampling with a 22G FNA from June 2011 to May 2012, served as the historical control group. EUS-guided sampling was performed using the standard technique without an on-site cytopathologist.
RESULTS: The diagnostic rates of cytology were 97.1% (33/34) with 22G FNA needles and 85.3% (29/34) with 25G FNB needles ($P=0.197$). The diagnostic rates of histology were 23.5% (8/34) with 22G FNA needles and 41.2% (14/34) with 25G FNB needles ($P=0.194$). There was no significant difference in the mean number of needle passes (5.09 vs 5.76, $P=0.089$) or needle malfunctions (2.9% vs 11.8%, $P=0.356$) between 22G FNA and 25G FNB needles, respectively. No complications were identified in either group.
CONCLUSION: The 25G FNB needle was not superior to the 22G FNA needle in the diagnostic yield of histology for EUS-guided sampling of pancreatic mass lesions, as the diagnostic yield, technical performance, and safety profiles were comparable between both of them.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00-17:00
ENDOSCOPY AND IMAGING II - POSTER EXHIBITION - HALL XL

P0689 EFFECTIVENESS OF ENDOSCOPIC MANAGEMENT FOR ANASTOMOTIC LEAKAGE AFTER GASTRECTOMY IN GASTRIC CANCER

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INTRODUCTION: Anastomotic leakage after gastrectomy is an important determinant of early and late morbidity and mortality. Various methods for postoperative leakage are used including conservative, endoscopic or surgical treatment.
AIMS & METHODS: We aimed to evaluate the effectiveness and safety of endoscopic intervention for the management of leakage after gastrectomy. We retrospectively reviewed 57 patients with anastomotic leakage after gastrectomy for gastric cancer that was treated with endoscopic interventions between December 2007 and March 2014. Clinical aspects of leakages and endoscopic managements, closure rates and treatment related complications were evaluated.
RESULTS: Anastomotic leakages were found at esophagojejunostomy (n = 26), duodenal stump (n = 14), gastroduodenostomy/gastrojejunostomy (n = 10), wedge resection (n = 3), esophagogastrostomy (n = 2) or jejunal stump (n = 2). Median size of leak was 8mm (range, 2 - 40mm). The leakages were treated by endoclips (n = 13), endoclips with detachable snare (n = 31) or stent (n = 13). Simultaneously, abscess around the leak was drained by external drains (n = 32). After endoscopic treatment, complete closure was achieved in 42 patients (73.7%) and partial closure in 13 patients (22.8%). In all patients with partial closure, final closure of leak was achieved by continuing conservative treatment. Among remaining two patients, one with failed endoscopic treatment went on to receive surgery and the other died due to septic shock during endoscopic treatment. Treatment related complication (esophageal fistula) occurred in one patient who was treated with stent. The complete closure rate of the leaks at duodenal or jejunal stump was significantly lower than that of leaks at other sites ($P=0.027$), whereas the size of leak and the method of endoscopic management were not associated with the complete closure rate.
CONCLUSION: Endoscopic management using clips or stent represents an effective and safe method for anastomotic leakage after gastrectomy in gastric cancer and it can be an easily available minimally-invasive option which may reduce leakage related mortality and morbidity.
Disclosure of Interest: None declared

P0691 RISK FACTORS OF DELAYED ULCER HEALING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Post-endoscopic submucosal dissection (ESD) iatrogenic ulcer is known to have specific histologic features and heal faster than peptic ulcer. However, some iatrogenic ulcers show delayed healing.
AIMS & METHODS: The aim of this study is to clarify risk factors of delayed ulcer healing after gastric ESD. For this, we reviewed medical records of patients who had ESD for gastric high-grade adenoma or early gastric cancer between January 2005 and February 2012. Delayed ulcer healing was defined as sustaining unhealed iatrogenic ulcer at 3 months after the ESD. To find potential risk factors we reviewed following parameters: age, sex, comorbidity that might influence mucosal healing, history of peptic ulcer, history of abnormalities, antiplatelet or NSAID usage, size of the specimen, location and histologic type of lesion, *Helicobacter pylori* status, and hot biopsy.
RESULTS: Among 2,140 subjects, 11 were excluded because of anticoagulation, 3 because of emergency for post-ESD bleeding, and 346 were excluded because of loss of 3 month follow-up endoscopy. Out of the total 1680 patients enrolled, 95 had delayed ulcer healing. In multivariate analysis, diabetes (OR 1.743; 95% CI: 1.017-2.989, $p=0.043$), coagulation abnormality (OR 3.195; 95% CI: 1.535-6.650, $p=0.002$), specimen size greater than 4cm (OR 2.999; 95% CI 1.603-5.611, $p=0.001$), and hot biopsy (OR 7.149; 95% CI 1.738-29.411, $p=0.006$) were revealed to be independent risk factors of delayed ulcer healing. Meanwhile, persistent *Helicobacter pylori* infection was not shown to be related to the delayed ulcer healing.
CONCLUSION: Patients those who undergo ESD for large gastric lesions and massive hemostasis, especially with diabetes or coagulation abnormalities, tend to have delayed healing of iatrogenic ulcer. For such patients initial dosage increment of PPI or addition of other anti-ulcer agents after ESD should be considered.
Disclosure of Interest: None declared

P0692 CHARACTERISTIC ENDOSCOPIC FINDINGS OF HELICOBACTER PYLORI-NEGATIVE EARLY GASTRIC UNDIFFERENTIATED ADENOCARCINOMA

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INTRODUCTION: *Helicobacter Pylori (HP)* negative gastric cancer is rare. Recently, we experienced *HP* negative early gastric cancer.
AIMS & METHODS: The purpose of this study is to evaluate the clinical characteristics of *HP*-negative Early Gastric Undifferentiated adenocarcinoma. We examined 35 cases (19 males and 16 females) with 36 lesions of Helicobacter Pylori (*H.pylori*)-negative Early gastric undifferentiated adenocarcinoma. All cases were treated by Endoscopic Submucosal Dissection. All cases had no history of *H.pylori* eradication, no inflammatory changes on the resected specimen, and no sign of atrophy on endoscopy, with negative results for pepsinogen and urea creath tests.
RESULTS: Of the 36 lesions, 35 were diagnosed as signet-ring cell carcinoma, with only 1 case of poorly differentiated adenocarcinoma. The mean lesion size was 7.4mm. The macroscopic type was 0-IIc in 30 (83%) lesions and 0-IIb in 6 lesions. 33 (92%) lesions showed pale lesion in color. The depth classification was intramucosal in 36 lesions. Of the 36 intramucosal lesions, 3 (8%) were limited to the proliferative of the mucosa, 22 (61) invaded from the proliferative zone to the upper side, and only 1 (2%) case invaded the lower mucosa. With respect to the background mucosa, 25 (69%) lesion originated from the fundic gland area, 5 (14%) originated from the intermediated zone, and 6 (17%) originated from the pyloric glands. The incidden of HP-N-UEG was 2.3% of all ESD cases.
CONCLUSION: *HP* negative early gatric cancer was rare. However, we experienced HP negative early gastric undifferentiated adenocarcinoma. These cases may have considerable relevance in the near future.
Disclosure of Interest: None declared

P0693 CHROMOENDOSCOPY WITH INDIGO CARMINE DYE ADDED TO ACETIC ACID FOR DELINEATING EARLY GASTRIC CANCERS IS USEFUL AND EASIER THAN MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING

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INTRODUCTION: Endoscopic submucosal dissection (ESD) was developed to improve the rate of en bloc resection for early gastric cancer (EGC). Although a clear diagnosis of EGC demarcation is important for proper treatment, demarcations are often obscure. To achieve a successful ESD outcome, it is very important to accurately determine the lateral extent of the tumor. The determination of EGC demarcation has traditionally been performed with conventional endoscopy and chromoendoscopy (CE) using indigo carmine dye. However, it is sometimes difficult to identify the margins of the tumors, especially those of superficial or flat-type tumors. Various techniques using magnifying endoscopy

(ME) have been developed to enhance images of EGC demarcations. Magnifying endoscopy with narrow band imaging (ME-NBI) has reportedly been useful in overcoming this problem but the use of ME–NBI is limited by the technical difficulties in manipulating the scopes. Therefore, easier methods are required that make it possible to accurately determine the lateral extent of these tumors. Chromoendoscopy with indigo carmine dye added to acetic acid (CE-IA) has recently been reported to improve the diagnostic yield in terms of recognizing the tumor borders in patients with EGC. Our purpose was to compare the diagnostic performance of CE-IA with that of ME-NBI and conventional ME (CME). We investigated three methods to determine which is more effective in enhancing the recognition of EGC demarcations.

AIMS & METHODS: The study group included 266 lesions of consecutive 259 patients with differentiated EGC who underwent ESD at Aichi Medical University Hospital between January 2006 and March 2014. The recognition of demarcations were evaluated using CME (n = 193), ME-NBI (n = 43) and CE-IA (n = 30). All observations were made on optimal foci and at the highest magnification ratios possible. For CE-IA, 20–30 mL of 1.5% acetic acid was sprinkled onto the lesion and 10-20 mL of 0.2% indigo carmine dye was similarly sprinkled 30-60 seconds later using a washing pipe. The recognition of demarcations between the lesion and the normal mucosa were classified as distinct or indistinct by observation of CME, ME-NBI and CE-IA.

RESULTS: The demarcations of the lesions were distinct in 64.8% (125/193) with CME, in 81.4% (35/43) with ME-NBI and in 90.0% (27/30) with CE-IA. ME-NBI and CE-IA clarified the demarcation in a significantly higher percentage compared with CME ($P < 0.05$). However, the determination rate of EGC demarcation did not differ between ME-NBI and CE-IA. The mean duration of determination procedure for demarcation with CE-IA was significantly shorter than that with ME-NBI (6.97±3.75 min vs. 8.57± 4.33 min, $P < 0.05$).

CONCLUSION: CE-IA and ME-NBI are useful in determining the lateral extent of EGCs. The mean duration of determination procedure for EGC demarcation was significantly reduced using CE-IA compared with ME-NBI. The demarcations of EGDs were recognized most easily using CE-IA.

Disclosure of Interest: None declared

P0694 CLINICOPATHOLOGICAL FACTORS INFLUENCE ACCURATE ASSESSMENT OF ENDOSCOPIC ULTRASONOGRAPHY FOR EARLY GASTRIC CANCER

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INTRODUCTION: The advent of endoscopic ultrasonography (EUS) has significantly improved the preoperative diagnosis and staging of gastric cancers. EUS is the most reliable nonsurgical method available for assessing primary tumor with a high diagnostic rate of accuracy in staging gastric cancer. This assessment is an important factor in choosing a proper treatment such as endoscopic resection or surgery. Especially in early gastric cancers (EGC), the size, gross appearance, histologic diagnosis, degree of differentiation, and depth of invasion are very important factors to be considered for therapeutic decision making. Endoscopic submucosal dissection (ESD) currently is widely accepted as a standard treatment strategy for EGC without any risk of lymph node metastasis because the ESD procedure facilitates en bloc resection even in patients with large or ulcerous lesions. Therefore, it has become more important in treatment planning to determine the depth of invasion accurately before treatment. The aim of this study was to evaluate the clinicopathological factors affecting the diagnostic accuracy of EUS and to compare the diagnostic accuracy evaluated by endoscopic findings with that by EUS in EGCs.

AIMS & METHODS: During the period from April 2009 to January 2014, 136 patients (94 men and 42 women; age range, 44-88 years; mean age, 72.1 years) with an endoscopic diagnosis of EGCs underwent EUS to define pretreatment staging. Diagnoses of invasion depth by EUS or endoscopic findings were divided into intramucosal (M) and submucosal invasion (SM). All patients underwent curative treatment by either ESD or standard surgical intervention, and all lesions were evaluated by histopathological examination. Both EUS-determined diagnosis and conventional endoscopy-determined diagnosis were compared with the final histopathological evaluation of resected specimens, and the impact of various clinicopathological parameters on diagnostic accuracy was analyzed.

RESULTS: The accuracy of invasion depth were 83.0 % for EUS and 74.5 % for conventional endoscopy, respectively. There was significant difference related with the accuracy of invasion depth between EUS and endoscopic findings ($p < 0.01$). The diagnostic accuracy of EUS for predicting tumor invasion depth was significantly affected by the tumor location and the tumor size. Lesions located in the posterior wall of the stomach larger than 3 cm were significantly associated with lower diagnostic accuracy in predicting the tumor invasion. These lesions had higher probability of overstaging estimated by EUS. However, no significant differences were found in histopathological differentiation, tumor gross appearance and ulceration. Unexpectedly, the observation time for EUS was the same as that for conventional endoscopy (6.8±3.1 minutes vs. 6.1±4.2 minutes).

CONCLUSION: EGCs larger than 3 cm located in the posterior wall of the stomach should be cautiously considered in the decision on treatment modality by pretreatment EUS staging. Moreover, observation time for EUS was so short that a sedation was not considered to be required during EUS investigation.

Disclosure of Interest: None declared

P0695 ADDITORY RISK FACTORS FOR PYLORIC STENOSIS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION, AND VARIOUS MANAGEMENTS

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INTRODUCTION: Endoscopic mucosal dissection (ESD) is useful method for local resection of early gastric neoplasia. [1,2] But, ESD can cause early and late complications commonly known as bleeding, perforation, and stricture formation. [3] In previous study, Coda S, et al., circumferential extent of a mucosal defect > 3/4 and longitudinal extent > 5 cm were each significantly related to the occurrence of post-ESD stenosis in both cardiac and pyloric resections. And endoscopic balloon dilatation can be an effective treatment of them. [4]

AIMS & METHODS: The aim of this study is to clarify the previous risk factors and determine the additory risk factor. And we report another management methods for pyloric stenosis after ESD. Retrospectively a total of 1621 early gastric neoplasia resected by ESD at a single institution between 2005 and 2012. Pyloric stenosis is defined when a 1 cm diameter endoscope could not passed through the pyloric ring.

RESULTS: Among 126 cases which resected from the pylorus, stenosis occurred in six cases. Significant differences were found between longitudinal diameter of resected specimen (≥5cm) and the others (<5cm) (odd ratio = 15.362, $p = 0.037$), circumferential mucosal defect over the half (≥270°) and the others (<270°) (odd ratio = 23.840, $p = 0.015$). Also the number of repeated ESD was significant different between the single lesion and the others (≥2 times) (odd ratio = 26.169, $p = 0.040$). Six patients of pyloric stenosis received endoscopic balloon dilatation for treatment of post-endoscopic resection stricture and 4 patients has improved symptoms. But two patients received an additional procedure for treatment of pyloric stenosis. One of them underwent subtotal gastrectomy and other was treated with metallic pyloric stent.

CONCLUSION: The risk factors of pyloric stenosis were the longitudinal diameter of resected specimen (>5cm) and circumferential mucosal defect over 75% of pyloric ring in this study. In addition, repeated ESD limited pylorus also caused pyloric stenosis. We thought the diameter of specimen and circumferential defect are important factors as previous study. [4] And this study revealed another risk factor: repeated procedure is additional risk factor of pyloric stenosis after ESD. In treatment of post-endoscopic resection stricture, balloon dilatation is effective treatment. But, according Coda S, et al., procedure is needed more than nine times on average. [4] Frequent the procedures decrease quality of life. Therefore more confident short-term treatment is needed. Pyloric stent is useful management of pyloric stricture. But it is too expensive and has complications like stent-migration. This is must be resolved first.

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Disclosure of Interest: None declared

P0696 ULTRA THIN ENDOSCOPE WITH NARROW BAND IMAGING (NBI) IN DIAGNOSTIC OF GLUTEN DEPENDENT AND INDEPENDENT SMALL INTESTINAL ATROPHY IN INFANT AND UP TO 36 MONTHS AGE CHILDREN

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INTRODUCTION: Using high-resolution endoscopy is sharply limited at this age. It remains unclear whether there are differences in the high-resolution endoscopic assessment of the small intestinal mucosal pit pattern at congenital intestinal atrophy (non gluten) and atrophy at a gluten sensitivity enteropathy.

AIMS & METHODS: Inclusion criteria were: child wasn't older 36 month and has low weight gain (WHO criteria) and non bloody diarrhea. Investigation performed with permission and control of the local ethic committee. We analyzed endoscopy results of 32 cases (13 girls).

Endoscopy: the EXERA III with an endoscope GIF - N180 4.9 mm in diameter was used Evaluation of duodenal mucosa was done with narrow band imaging (NBI, more brightly than in EXERA II light source) and for additional sign of atrophy water flow with addtion of semethicon was done too. Two biopsy specimens were taken minimally. The description of a biopsy was carried out by a standard technique with special orientation biopsies specimens, by two independent pathology experts. Four criteria were used for endoscopic and histological (HYS) intestinal atrophy assessment: definitely yes, probably yes, probably no, definitely no. The main group was divided on two subgroups: A - age up to 6 months (group of strictly non gluten enteropathy) and B - 6 - 36 months (probably gluten dependent enteropaty).

RESULTS: Age in group A (N = 17) was: mean – 2.9 (CI 95% = 2-4), median - 3.0 (CI 95% = 1-4). Frequency of the HYS definitely yes atrophy was in 5, probably yes- 1. Atrophy rate was 35% (Exact 95% C. I. (Fisher's) = 14.2-61.7). Frequency of the endoscopic definitely yes atrophy was in 6, probably yes- 2. Endoscopy sensitivity 0.67(CI 95% = 0.35 - 0,88, specificity 1,00 (CI 95% = 0.68 - 1,0), odds ratio (Fleiss)- 33(CI 95% = 1,6 - 151,23). If endoscopy negative, expected HYS negative will definitely to no atrophy.

Age in group B (N = 15) was: mean – 23,5 (CI 95% = 18,5-28,4), median - 21,0 (CI 95% = 17-33). Frequency of the HYS definitely yes atrophy was in 4, probably yes- 0. Atrophy rate was- 26,7% (Exact 95% C. I. (Fisher's) = 7,8-55,1), and not different significant from group A. Frequency of the endoscopic definitely yes - atrophy was in 4, probably yes - 1case. Sensitivity 0.8 (CI95% = 0.38 - 0,96; specificity 1,00 (CI95% = 0.72 - 1,00), odds ratio (Fleiss) 63 (2,22 - 313,23), and LR (Test = Negative) = 0.2.

CONCLUSION: In infant and up to 36 months age children with low weight gain and non bloody diarrhea small intestinal atrophy rates are from 14.2% to - 61.7%. We found no difference in the two groups (gluten associated or not) used to assess ultra thin with NBI endoscopy sensitivity, specificity, and it has value as a good standard for visual endoscopic evaluation of duodenal villi changes as a method for exclusive intestinal atrophy.

Disclosure of Interest: K. Marakhouski Other: "Olympus" CIS expert

P0697 PROSPECTIVE ASSESSMENT OF THE LEVEL OF TEMPORAL AROUSAL AND SAFETY OF NURSE-ADMINISTERED PROPOFOL SEDATION FOR ESOPHAGOGASTRODUODENOSCOPY

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INTRODUCTION: Propofol sedation is widely used, mainly in Europe and the US, not only as an induction agent for general anesthesia but also in the field of gastroenterological endoscopy. Especially in the US, the certified registered nurse anesthetists perform general and local anesthesia for many endoscopic procedures under anesthesia management, independently from doctors. However, quite a few states prohibit individuals other than anesthetists from performing propofol sedation from the safety aspect. Propofol sedation, which is "easy to give and wean off," by nurse-administered propofol sedation (NAPS) is quite meaningful, and could thereby reduce labor costs and charges for recovery rooms and curb medical expenses.

AIMS & METHODS: We prospectively examined the safety of propofol sedation at the time of esophagogastrodudenoscopy (EGD). Between July 2013 and January 2014, EGD was performed under NAPS in outpatients, and time to arousal and safety were prospectively assessed. Propofol was administered manually in a prespecified regimen, and, before the test and at 10 and 60 min after the test, the mean blood pressure, $Sp0_2$, grasping power of both hands, visual acuity of both eyes, Mini Mental State Examination (MMSE) score, and reflex nerve test were assessed and compared.

We hypothesized that "MMSE score recovers to the pretest value 60 min after the completion of EGD under propofol sedation." To prove this hypothesis, we tested non-inferiority of MMSE at 60 min after the test against that before the test. We calculated that 87 eligible patients were needed to obtain a significant difference, and estimated the number of patients to be included at 104, expecting 20% of the patients to be ineligible. Quantitive variables were evaluated by *t*-test, and the significance level of <0.05 was considered statistically significant.

RESULTS: 95 patients (mean age: 55.5 ± 14.9 years; male/female ratio: 37/58 cases; mean examination time: 315.6 ± 115.8 s; mean induction dose of propofol: 0.097 ± 0.019 mL/kg; and mean total dose: 0.129 ± 0.027 mL/kg) were included for analysis. All patients could be successfully sedated and opened their eyes immediately after the test. Before the test vs. 10 min after the test, the mean blood pressure (mmHg) was 95.19 ± 13.20 vs. 90.13 ± 12.34 ($p < 0.01$); grasping power of right hand (kg) was 27.7 ± 8.08 vs. 26.2 ± 8.49 ($p < 0.01$); grasping power of left hand (kg) was 26.4 ± 8.08 vs. 25.3 ± 8.22 ($p < 0.01$); and MMSE (points) was 27.3 ± 2.2 vs. 26.8 ± 2.4 ($p < 0.05$); all of which showed significant differences. Before the test vs. 60 min after the test, the mean blood pressure (mmHg) was 95.19 ± 13.20 vs. 91.80 ± 11.88 ($p < 0.01$), showing a significant decline. No occasional symptoms were observed in all patients.

CONCLUSION: EGD under NAPS was performed safely and all factors other than mean blood pressure returned to the pretest condition 60 min after the test. Blood pressure was also in an acceptable range as per discharge criteria, and the patients were considered to be allowed to be safely discharged from hospital after 60 min.

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Disclosure of Interest: None declared

P0698 DEVELOPMENT OF PROPOFOL SEDATION FOR THERAPEUTIC ENDOSCOPY UNDER DEEP SEDATION WITH SPONTANEOUS RESPIRATION

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INTRODUCTION: In recent years, propofol sedation has attracted attention for use during therapeutic endoscopy under deep sedation with spontaneous respiration. However, a standard protocol for propofol sedation has not yet been established.

AIMS & METHODS: Our aim was to establish a simple and safe protocol for propofol sedation during therapeutic endoscopy. This study retrospectively investigated 89 patients (67 male, 22 female; mean age 71.2 years) who underwent endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) of the esophagus and stomach under anaesthesia with 1.0% propofol. Patients were assigned to 1 of 5 groups (phases 1 – 5) each corresponding to a different dosing protocol. After beginning phase 1, when it was deemed that the dose of propofol was insufficient or excessive, the dose was adjusted and the next phase was begun in a different group of patients. In all phases, the initial dose of 1.0% propofol was administered after bolus injection of pethidine hydrochloride (0.5 mg/kg), and 1.0 mL of propofol was added every minute until anaesthesia to level 6 on the Ramsey Sedation Scale was achieved. Subsequently, continuous drip infusion was performed to maintain the depth of sedation. Induction and maintenance doses in each phase are shown in the table below. When the patient showed movement, a bolus injection of 1.0 mL propofol was repeated every minute until suitable sedation was obtained, and continuous drip infusion was increased to a dose of 5 mL/h. Oxygen saturation and blood pressure were monitored during all procedures. A BIS monitor was used at phase 5. Continuous drip infusion was stopped temporarily under the following conditions: SpO_2 <90%, BP <80 mm Hg, or BIS score <60 (5 seconds or more). Following recovery, the rate of continuous drip infusion was decreased to 5 mL/h. We calculated the dose of propofol at the time of induction and during the maintenance phase, the number of additional bolus injections, and the average total dose of propofol. The incidence of cardiorespiratory suppression was evaluated for each phase. The incidence of BIS below 60 was also evaluated in phase 5.

RESULTS: During induction, no cardiorespiratory suppression occurred in any of the phases. During the maintenance phase, circulatory suppression occurred more frequently in phases 1-4 than in phase 5. In contrast, no respiratory suppression occurred in any of the phases.

Table: Propofol dosing and the incidence of adverse events during each phase of study

CONCLUSION: This newly developed propofol anesthesia protocol (phase 5) could be safe for therapeutic endoscopy under deep sedation with spontaneous respiration.

Disclosure of Interest: None declared

P0699 MAGNIFICATION ENDOSCOPY WITH ACETIC ACID-ENHANCEMENT AND NARROW-BAND IMAGING FOR PREDICTING HISTOLOGIC CHARACTERISTICS OF GASTRIC MUCOSAL NEOPLASMS

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INTRODUCTION: Magnification endoscopy with narrow-band imaging (NBIME) that visualizes the capillary patterns of gastric surface structure is useful for predicting the histologic characteristics of superficial gastric neoplasms. NBIME with acetic acid-enhancement (A-NBIME) clearly visualize the microstructure pattern of gastric mucosal surface.

AIMS & METHODS: We performed a prospective study to compare the diagnostic reliability of white light endoscopy (WLE), NBIME, and A-NBIME for the histologic characteristics of gastric mucosal neoplasms. Consecutive 220 gastric neoplasms (49 adenomas, 144 differentiated adenocarcinomas, and 27 undifferentiated adenocarcinomas) were photographed with WLE, NBIME and A-NBIME.

Macroscopic patterns by WLE, capillary patterns by NBIME and microstructure patterns by A-NBIME were respectively classified into type M1/M2/M3, type C1/C2/C3/C4 and type S1/S2/S3, by referring to the previously reported

Table to abstract P0698

	Phase1 (n=27)	Phase 2 (n=11)	Phase 3 (n=7)	Phase 4 (n=14)	Phase 5 n=30)
Dose of initial bolus injection (mg/kg)	0.5	0.33	0.5	0.5	0.5
Dose of continuous drip infusion (mg/kg/h)	5	3.3	3.3	2.5	2.5
Average number of additional bolus injections at introductory phase	1.07 (0∼6)	4.0 (1∼13)	1.6 (0∼5)	3.8 (0∼7)	3.6 (0∼17)
Average number of increasing maintenance dose	0.7 (0∼5)	1.5 (0∼2)	1.3 (0∼5)	2.6 (1∼5)	1.9 (0∼7)
Average total dose (mL)	48.5(17∼109)	60.1 (24∼135)	49.6 (16∼133)	44.4 (12∼95)	52.1 (7.5∼170)
SpO_2 < 90%	0	0	0	0	0
Blood pressure < 80 mm Hg	11 (40.7%)	3 (27.3%)	3 (42.9%)	4 (28.6%)	3 (4.8%)
BIS score < 60 (>5 seconds)	NA	NA	NA	NA	1 (1.6%)

classifications as described below. Macroscopic pattern; Type M1: the protruded and whitish lesions with roundish edge and smooth or often nodular surface. Type M2: the irregular-shaped and depressed, flat, or elevated lesion in red or similar color to the surrounding mucosa. Type M3: the depressed and whitish lesions often with variously sized nodules on the lesion. Capillary pattern; Type C1: capillaries with homogenous diameters and distributions. Type C2: capillaries with heterogeneous diameters and irregular distributions. Type C3: capillaries grow in disorder with unclear mucosal microstructure. Type C4: capillaries are invisible or obviously decreased. Microstructure pattern; Type S1: glandular crypts present, homogeneously sized, shaped and arranged foveolae or grooves. Type S2: glandular crypts present, heterogeneous. Type S3: glandular crypts are absent or severely decreased.
Endoscopic images were independently reviewed by three expert endoscopists. Type M1/M2/M3 in WLE, type C1/C2/C3 in NBIME, and type S1/S2/S3 in A-NBIME were used as the indicator of adenoma/differentiated adenocarcinoma/undifferentiated adenocarcinoma, respectively. Type C4 in NBIME was excluded from the analysis of histologic diagnostic accuracy. The histologic diagnostic accuracy and interobserver diagnostic agreement was compared among modalities.
RESULTS: The kappa values of interobserver agreement for WLE, NBIME, and A-NBIME diagnosis were 0.33(0.31-0.36), 0.58(0.55-0.61), and 0.61(0.54-0.67), showing an insufficient diagnostic agreement for WLE and a statistically good diagnostic agreement for both NBIME and A-NBIME. Adenomas/differentiated adenocarcinomas/undifferentiated adenocarcinomas were statistically related to type M1/M2/M3 in WLE, type C1/C2/C3 in NBIME and type S1/S2/S3 in A-NBIME, respectively ($P<0.01$). Type C4 of capillary pattern by NBIME did not show a statistical correlation to the specific histologic characteristics. The diagnostic accuracy of WLE, NBIME, and A-NBIME were 79.0%, 74.1%, and 90.5%, showing statistical superiority of A-NBIME ($P<0.01$). No additional effect of NBIME to WLE.
CONCLUSION: A-NBIME is superior to WLE and NBIME in the predictive histological diagnosis of gastric mucosal neoplasms with good clinical feasibility.
Disclosure of Interest: None declared

P0700 HIGHEST POWER MAGNIFICATION IS SUPERIOR TO LOW POWER MAGNIFICATION FOR DELINEATION OF EARLY GASTRIC CANCERS USING NARROW BAND IMAGING

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INTRODUCTION: Curative endoscopic submucosal dissection (ESD) of early gastric cancers requires accurate determination of the horizontal extent of invasion. A number of studies have since reported superior diagnostic ability for magnifying endoscopy with narrow-band imaging (ME-NBI) over conventional endoscopy (CE) in delineating the lateral extent of early gastric neoplasias. However, there are few studies that have reported the actual magnifying ratio used when performing ME. The added benefits of ME-NBI over CE in terms of the difference in magnification level have yet to be elucidated.
AIMS & METHODS: The aim of this study was to investigate the improvement in diagnostic accuracy for tumor delineation obtained with different magnification levels of ME-NBI following CE. This study comprised a series of 161 consecutive early gastric cancers resected *en bloc* using ESD in 158 patients between July 2008 and June 2012. Each patient underwent sequential CE, LM-NBI and HM-NBI examinations during the same procedure as preoperative diagnostic examinations 1 to 2 weeks prior to ESD. On the day of the ESD procedure, or the preceding day, using HM-NBI we again identified the lesion margin, and made markings 3-5 mm outside the DL. After ESD with reference to the pathohistological findings, we identified the markings, and reconstructed the lateral extent of the cancer on the each endoscopic image (CE, LM-NBI, HM-NBI). The histologically determined cancer margins were used as the gold standard. The primary endpoint was the added benefit, as measured using the successful delineation rate, for the delineation of gastric cancer margins using CE+LM-NBI *vs* CE, and for CE+LM-NBI+HM-NBI *vs* CE+LM-NBI. We derived the successful delineation rate with 95% confidence intervals (CI) for early gastric cancers using each examination method, CE, CE+LM-NBI, and CE+LM-NBI+HM-NBI and used McNemar's test with Bonferroni's multiple comparison correction to calculate p values.
RESULTS: The clinical characteristics were as follows: average age 71 years; 116 males and 45 females; mean lesion diameter 19.2 mm (±14.4 mm, range 5-120 mm); and macroscopic type using the Paris classification type 0-I 4 lesions (2.5%), type 0-IIa 64 lesions (39.8%), type 0-IIb 38 lesions (23.6%), and type 0-IIc 55 lesions (34.2%). The location of the lesion was the upper part of the stomach in 46 cases (28.6%), middle part in 41 (25.5%), and lower part in 74 (46.0%). The successful delineation rates (95% CI) using CE, CE+LM-NBI and CE+LM-NBI+HM-NBI were 72.7 (68.5-79.9%), 88.9 (83.9-93.7%), and 98.1 (95.8-100%). The diagnostic accuracy improved significantly for CE+LM-NBI compared with CE ($P<0.001$) and for CE+LM-NBI+HM-NBI compared with CE+LM-NBI ($P<0.001$).
CONCLUSION: ME-NBI is an extremely useful modality for the delineation of the margins of early gastric cancers. HM-NBI is superior to LM-NBI in improving the successful delineation rate, following CE.
Disclosure of Interest: None declared

P0701 GASTRIC ATROPHY WAS A RISK FACTOR FOR THE PRESENCE OF MISSED SYNCHRONOUS LESION AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been widely accepted as a minimally invasive therapy for gastric adenoma or early gastric cancer (EGC). However, the risk of secondary gastric neoplasms developing during the surveillance period after ESD has become a important medical problem. In particular, there is a high possibility that ESD can miss synchronous gastric neoplasms compared with surgery.
AIMS & METHODS: In the present study, we aimed to investigate predictive factors associated with the presence of missed synchronous gastric neoplasms after ESD for gastric adenoma or EGC. We performed ESD in 370 patients with EGC or gastric adenoma from January 2008 through December 2012 at our institution. The patients with endoscopic surveillance interval less than 1 year, patients without curative resection, and patients with additional surgery were excluded from the study. Missed synchronous gastric neoplams were defined as any gastric neoplasms detected within one year after ESD, but initially unidentified. We compared clinical, endoscopic, and pathological factors between patients with missed synchronous gastric neoplasms and patients without missed synchronous gastric neoplasms.
RESULTS: Missed synchronous gastric neoplasms were found in 4.3% (16/370) of the patients. Among the 16 missed synchronous gastric neoplasms, three (18.8%) cases were carcinomas. In the univariate analysis, open-type gastric atrophy, gastric atrophy and intestinal metaplasia more than moderate degree were significantly associated with the presence of missed synchronous gastric neoplasms. In multivariate logistic regression analysis, only gastric atrophy more than moderate degree was the independent risk factor for the presence of missed synchronous gastric neoplasms (Exp (B) = 8.608, 95%CI: 1.036–45.549).
CONCLUSION: Gastric atrophy could be an independent risk factor for the presence of missed synchronous lesion after ESD. Careful endoscopic surveillance should be performed after ESD for patients with severe gastric atrophy.
Disclosure of Interest: None declared

P0702 EFFECT OF ELECTRICAL CURRENT MODE ON CLINICAL COURSE AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Several modes of electrical current are available for endoscopic submucosal dissection (ESD) of gastric epithelial tumor. There has been no data regarding whether the electrical current mode effects on clinical course after gastric ESD, including incidence of post ESD coagulation syndrome, ulcer healing rate.
AIMS & METHODS: AIM Clinical courses were surveyed according to the setting of two different dissecting mode: endocut or swift, to provide relating data on optimal adoption of mode for gastric ESD.
METHODS Among 286 consecutive sessions of gastric ESD, 200 lesions were surveyed after excluding cases: usage of endoknives other than IT2 knife, tumor with nearby scar, synchronous tumor, subepithelial tumor. Only one of endocut or swift mode was adopted for submucosal dissection in eaach session of ESD. All the procedure were performed using an electrosurgical unit, VIO 300D (ERBE, Germany). The ESD pathology, location of tumor, procedure and resection time, incidence of post ESD syndrome were assessed with demographic data. Patients with pyrexia (body temperature $>38.3\_C$) and upper abdominal pain or tenderness after ESD, with or without symptoms of peritoneal irritation were defined as having post ESD coagulation syndrome. Follow up endoscopy was performed at 3 months after the endoscopic therapy and rated as ulhealed if the ulcer was in A1 to H2 rated by Sakita-Miwa stage.
RESULTS: In total of 200 sessions, we applied endocut mode for 116 cases (58%) and swift mode at for 84 cases (42%). The demographic data between the two groups were not significantly different. Total of 16 post ESD coagulation syndromes were notified. Multivariate analysis revealed adoption of swift mode (OR 6.90, 95%CI: 1.83-25.92) and malignant pathology (OR 5.93, 95%CI: 1.46-24.02) was related post ESD coagulation syndrome. Ulcer healing rate judged at 3 months after ESD tended to be delayed for endocut mode, even though it was not statistically significant.
CONCLUSION: Mode of electrical current may be related to the incidence of post ESD coagulation syndrome or ulcer healing after gastric ESD. Randomized and controlled studies are warranted.
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Disclosure of Interest: None declared

P0703 TRANASAL VERSUS PERORAL PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: A PROSPECTIVE CASE CONTROL STUDY

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) is a challenge in patients with difficult oral intubation. Some cases of successful transnasal insertion of PEG were reported. But no any case control study was conducted to compare transnal and oral insertion of PEG.
AIMS & METHODS: This work is to investigate the difference between transnasal and peroral insertion of percutaneous endoscopic gastrostomy in clinical outcome. A prospective, case-control study was conducted to compare transnasal (T-PEG) and peroral (O-PEG) placement of a 20 Fr PEG tube in dysphagic patients without conscious sedation. Additional spraying lidocain solution and epinephrine solution to the nasal cavity and using ultrathin 5 mm endoscope (Olympus GIF-N-260) were applied to the T-PEG. The other premedication and procedure are same as conventional pull-method PEG. Neither the nasal cavity nor the oral cavity were decolonized in all patients. The success rate, operation time, occurrence of choking during PEG, nasal bleeding, stomal site infection, post-PEG complication were recorded and analyzed.
RESULTS: Thirty-nine insertions of T-PEG and thirty-eight insertions of O-PEG were attempted in 77 chronic dysphagic patients form home or nursing home. Mean age is (T-PEG vs O-PEG) 76.3±10.3 vs 79.5±6.9 years, male gender 67% vs 48%, operation time 14.6 ± 4.0 vs 11±3 minutes (p: 0.028), choking occurred in 3 vs 5 patients. One failed insertion and two nasal bleeding occurred in T-PEG. There are nine stomal site infection (8 pseudomonas aeruginosa infection including one systemic infection) in T-PEG and 14 stomal site infects (8 pseudomonas aeruginosa) in O-PEG ($p < 0.001$). One systemic infection of urinary tract, one buried bumper, and one soiling of stoma were observed respectively in T-PEG and O-PEG. No PEG related mortality occurred within 3 months after all PEG procedures.
CONCLUSION: Transnasal insertion is feasible in placing a 20 Fr PEG but it causes rare nasal bleeding rate and needs longer operation time. Stomal site infection is less but more dominant pseudomonas infection occurred in T-PEG. In conclusion, T-PEG is an alternative for patients who had difficulty in oral intubation. It needs more studies to concern the prophylaxis of pseudomonas infection.
Disclosure of Interest: None declared

P0704 PROPOFOL REQUIREMENTS FOR GASTROINTESTINAL ENDOSCOPY IN PATIENTS OLDER THAN 75 YEARS OLD

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INTRODUCTION: Numerous studies support the efficacy and safety of propofol in digestive endoscopy in which propofol is administered by non-anesthesiologist during endoscopic procedures. There is literature on the safety of sedation with propofol in elderly patients. However, there are no clear guidelines regarding the dose of propofol to be used in this group of patients in which comorbidity can make them more fragile, making the standard dose/kg of weight excessive to achieve a safe sedation.
AIMS & METHODS: The aims of this study were to establish the dose of propofol in patient ≥75 years compared with patients <75 years and to evaluate the safety of propofol when is administered by non-anesthesiologist. Between June 2012 and March 2014, we prospectively recorded all endoscopic procedures and safety data. Only diagnostic procedures were included for this study. We excluded: patients <18 years, not sedated by endoscopist, therapeutic and incomplete procedures, and also patients with two endoscopies performed on the same day. To reduce variability and determine whether the differences between the doses of propofol in both groups were related to age, all patients ≥75 years were matched on a 1:1 basis with the <75 years group in terms of weight, body mass index (BMI) and endoscopic procedure. All esophagogastroduodenoscopies (EGDs) and colonoscopies received an initial dose of propofol 0.5-1 mg/kg. Colonoscopies also received a fixed dose of 50 mcg of fentanyl. Subsequently, boluses of 10-20 mg propofol were administered to maintain an adequate level of sedation. Vital signs were recorded before, during and after the procedure. A statistical analysis was performed with the SPSS v20.0 program.
RESULTS: There were 439 diagnostic EGDs and 307 diagnostic colonoscopies performed in patients ≥75 years. When compared with patients <75 years, there were significant differences between groups in mean propofol dose, and mild adverse events. No serious adverse events occurred. Patients ≥75 years required significantly less propofol than patients <75 years, 72.99± 37.4mg vs. 120.54± 4.8mg for EGDs ($P < 0.001$) and 80.59±34mg vs 129.12± 55.9mg ($P < 0.001$) for colonoscopies (39.4% less in EGDs and 37.5% in colonoscopies). Table 1 shows the demographic, endoscopic procedures, propofol dose and adverse events in both groups.

Table 1. Demographic, endoscopic procedures, propofol dose and adverse events in both groups
Table to abstract P0704

	Age	Weight	ASA I/II/III (%)	EGD n	Colonoscopy n (%)	Propofol dose EGD / Colonoscopy	AE (%) Desaturation/ Bradycardia
≥75 years	81 ± 4	68.56 ± 12,4	17.3/70.3/12.4	439	307	72.99± 37.4/ 80.59±34	2.6/0.3
<75 years	51.3± 13	68.55 ± 12,4	62.8/34.9/2.3	439	307	120.54± 4.8**/ 129.12± 55.9**	0.8/0.3*

Data are presented as mean ± SD (range: 95% CI of the mean). Abbreviations: ASA (American Society of Anaesthesiology); EGD (Esophagogastroduodenoscopy). AE: adverse events. *$P < .005$; **$P < .001$
CONCLUSION: Propofol is safe when administered by non-anesthesiologists. Patients ≥75 years globally require almost 40% less propofol than patients <75 years. These results support the use of a lower dose of propofol in the elderly.
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Disclosure of Interest: None declared

P0705 CHANGES IN GASTRIC INTESTINAL METAPLASIA EXTENSION IN ANNUALLY FOLLOWED-UP PATIENTS: 1-YEAR RESULTS OF A STUDY PERFORMED BY MEANS OF NARROW BAND IMAGING WITH MAGNIFICATION ENDOSCOPY

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INTRODUCTION: Gastric Intestinal Metaplasia (GIM) is a precancerous condition potentially leading to gastric cancer. However, this occurs in a limited number of cases and, therefore, the need of endoscopic surveillance and follow-up is controversial. Moreover, there is no universal consensus regarding which patients should be better investigated and followed-up in the long-term period. Most of the experts among pathologists and gastroenterologists recommend to perform an upper endoscopy with multiple biopsies every three-year only in patients with extensive GIM, but no studies have validated the effectiveness of this protocol, so far.
AIMS & METHODS: Our aim was to investigate whether changes in extension and/or progression of GIM occur during a strict yearly endoscopic follow-up program. Between November 2011 and December 2013, we prospectively evaluated consecutive patients with an histologically defined diagnosis of GIM by means of Narrow Band Imaging with Magnification Endoscopy (NBI-ME) and multiples gastric biopsies (2 antrum +1 angulus +2 corpus). Helicobacter pylori infection was excluded. Patients with a GIM extension higher than 20% were offered to repeat the endoscopic examinations every year and, to date, 20 out of 121 accepted and were included in the follow-up program. Endoscopic examinations have been performed by experienced endoscopists (each of them with more than 1000 NBI-MEs performed). Biopsies were taken at sites suggestive for GIM based on NBI-ME appearance (i.e. presence of light blue crests on the surface of gastric mucosa) or randomly if no evident mucosal alterations were seen. Biopsies were assessed by two expert and blinded pathologists, who evaluated the percentage of extension of GIM at both times.
RESULTS: The median time between the two observations was 13 months (range 11-18). As shown in the Table, patients were divided in three categories, according to the changes in GIM extension, which was considered stable if there were tiny variations (0-5%) between the two observations, or raised/lowered otherwise. At 1-year, in all patients, the second evaluation confirmed the presence of GIM. In patients with worsened extension, the mean percentage of GIM increase was 20%, whereas the mean percentage of GIM lowering was 26%in patients with a reduced GIM extension.

	N	MEDIAN AGE	AGE RANGE	GIM EXTENSION LOWERED	STABLE GIM EXTENSION	GIM EXTENSION RAISED
Females	13	67	56-71	3 (23%)	3 (23%)	7 (54%)
Males	7	64	53-85	4 (57%)	1 (14%)	2 (29%)
OVERALL	20	64	53-85	7 (35%)	4 (20%)	9 (45%)

CONCLUSION: Our results demonstrate that already at 1-year the extension of GIM and, therefore, the risk of developing a gastric cancer GIM-related, worsens in about 45% of the patients. Thus, these data seem to support a more close follow-up in patients with a GIM extension higher than 20% at histologic assessment.
Disclosure of Interest: None declared

P0706 DOES MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING IMPROVE DIAGNOSTIC ACCURACY FOR DEPTH OF INVASION IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA?

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INTRODUCTION: While accurate estimation for the depth of invasion in esophageal squamous cell carcinoma (ESCC) is essential to indicate relevant treatment methods, it is difficult to evaluate conventional endoscopy alone. Microvascular patterns identified using magnifying narrow band imaging (M-NBI) have been reported to be useful for the diagnosis in the depth of invasion for superficial ESCC. Recently, a classification regarding the microvascular patterns of superficial ESCC using M-NBI was advocated from the Japan Esophageal Society, however, it is not clear whether the depth of invasion can be estimated more accurately according to this classification compared with estimation using conventional white light endoscopy (WL) alone.
AIMS & METHODS: The aim of this study was to evaluate whether the diagnostic accuracy of in M-NBI is higher than that in WL alone. In this study, we enrolled patients with superficial ESCC who had undergone pretreatment evaluation using both WL and M-NBI, and who received endoscopic resection or surgery in our institution from June 2012 to December 2013. The patients who had been previously treated with chemotherapy or chemoradiotherapy were excluded. The microvessels of tumor surface observed by M-NBI were classified into 3 groups; type B1 consisted of loop-like vessels with atypia, including dilatation and meandering; type B2 were non-loop vessels; and type B3 were large vessels 3 or more times larger than type B2. Type B1, B2, and B3 vasculatures were correlated with lesions invading to EP/LPM, MM/SM1, and SM2 or deeper, respectively. Investigators who were blinded to the pathological diagnosis estimated retrospectively the depth of invasion in the endoscopic pictures by WL alone, and then using the pictures by M-NBI. We sorted the lesions into 3 groups (EP/LPM, MM/SM1, and SM2/SM3) and the diagnoses for individual modalities were compared to the pathological results. Finally, sensitivity, specificity, and positive predictive value (PPV) were analyzed.
RESULTS: A total of 198 lesions were examined. Sensitivity, specificity, and PPV of WL-alone were 92%, 85%, 90% for EP/LPM; 63%, 89%, 51% for MM/SM1; and 74%, 97%, 90% for SM2/SM3, respectively. Sensitivity, specificity, and PPV of M-NBI were 85%, 71%, 81% for EP/LPM; 50%, 75%, 28% for MM/SM1; and 39%, 100%, 100% for SM2/SM3, respectively. The concordance rate for diagnoses between both modalities was 87% in EP/LPM, 59% in MM/SM1, and 45% in SM2/SM3. In cases of a concordance between WLE and NBI-ME, the PPV was 90% for EP/LPM, 61% for MM/SM1, and 100% for SM2/SM3.
CONCLUSION: While the concordance rates between WL and M-NBI was unfavorable in MM/SM1, and SM2/SM3, PPV was high in the diagnosis was concordant cases between both modalities. However, the difficulty of evaluating the invasion depth for MM/SM1 lesions remains unsolved.
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Disclosure of Interest: None declared

P0707 RJ 4 JUMBO VS. RJ 4 LARGE CAPACITY FORCEPS IN TISSUE SAMPLING IN PATIENTS WITH BARRETŕS ESOPHAGUS: FINAL RESULTS OF A PROSPECTIVE, RANDOMIZED STUDY

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INTRODUCTION: Good quality of biopsy specimen is required for reliable diagnosis of early neoplasia in patients with Barretťs esophagus (BE). Studies comparing large capacity vs. jumbo forceps have shown inconsistent results. The aim of this study was to assess the quality of biopsy specimen obtained by 2 different-sized biopsy forceps (Radial Jaw 4 large capacity (outer diameter 2.4 mm) vs Radial Jaw 4 jumbo (outer diameter 2.8 mm) in patients with BE. We hypothesized that RJ4 ''jumbo'' forceps if used with a standard diagnostic endoscope (channel 2.8 mm) provides a better quality of biopsy specimen as compared to the large capacity forceps.
AIMS & METHODS: A single center, randomized (forceps order), prospective and single blind (pathologist) study. Twenty-one patients with BE (5 women, 16 men) were enrolled. All patients underwent an upper GI endoscopy with trimodal imaging. Targeted or random biopsies with both types of forceps used in random order were obtained from each patient during a single endoscopy with a diagnostic endoscope. Main outcome measurement was specimen adequacy (defined as a well oriented biopsy specimen 2 mm in diameter or greater with mucosa present).
RESULTS: A total of 288 biopsy specimen were analyzed (large capacity: 159, jumbo forceps: 129). A significantly higher proportion of biopsy samples obtained with jumbo forceps was adequate as compared to large capacity forceps (54.3 % vs. 18.9 %, $p < 0.0001$).
Biopsies with jumbo forceps had a larger diameter (median 2.4 mm vs. 2 mm; $p < 0.001$). Muscularis mucosae was detected in 67.4 % of specimen with jumbo forceps vs. 31.4 % with large capacity forceps ($p < 0.0001$). Excellent or good specimen orientation was present in 79.8 % of samples with jumbo forceps and in 59.1 % with large capacity forceps (not significant). Intestinal metaplasia was present in 69.8 % with jumbo forceps vs. 78.6 % of samples with large capacity (not significant). The diagnostic yield of both types of forceps was comparable.
CONCLUSION: Radial Jaw 4 Jumbo biopsy forceps, if used with diagnostic endoscope, provides more adequate biopsy specimen as compared to Radial Jaw 4 large capacity biopsy forceps. The diagnostic yield seems to be comparable.
Disclosure of Interest: None declared

P0708 OPTIMIZED IMPEDANCES OF INJECTION SOLUTIONS LEAD TO IMPROVED CUTTING RESULTS IN ENDOSCOPIC RESECTION

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INTRODUCTION: The endoscopic resection of large (ø > 20 mm) lesions in the gastrointestinal tract is a high challenge for interventional endoscopy and radiofrequency surgery. There is no easy, fast and safe way to remove large lesions en-bloc. An important reason is the interaction between submucosal injection, tissue and high-frequency parameters in respect to electrical impedances. This interaction is only partly understood and poorly investigated. Preliminary studies led to the conclusion that problems in the cutting process like cutting delay, perforation and thermal artifacts are due to unsuitable impedances.
AIMS & METHODS: Our aim was to improve the cuttings results (avoiding of cutting delay and high thermal load of the intestinal wall) by optimizing the impedances of the tissue. Therefore we analyzed various submucosal injection solutions in respect to impedances (surface and tissue) and rf-cutting.
With standardized gold probes (1 mm/15 mm) and a special RF-impedancemeter ($f = 100$ kHz, 10 Ω - 1 MΩ) the specific impedances of various solutions and the impedances on the surface and in the tissue after submucosal injection of 3 ml were measured in a standardized bio-model (porcine stomach). Additionally the elevations during 30 min were observed. The following solutions were injected into the submucosa: 0.9% saline, 4% gelatin, 6% hydroxyethyl starch, 10% glycerol/5% fructose in 0.9% saline, 10% glucose and aqua destillata. Additionally 5% albumin, 20% albumin, human blood and blood plasma and a new experimental substance.
RESULTS: Aqua destillata and 10% glucose showed a highly significant higher ($p \leq 0.0001$) specific impedance compared to the standard 0.9% saline (factor 360). After injection also the impedances on the surface and in the tissue were significantly higher ($p \leq 0.01$, resp. $p \leq 0.0001$). The elevation showed no significant difference between the tested solutions. Cutting experiments in a standardized setting showed the expected improvements: no cutting delay, less thermal load of the intestinal wall, smooth cut without carbonization but with adequate zone of hemostasis.
CONCLUSION: Clinically used injection solutions show a highly significant difference of specific impedances. After injection they lead to different impedances on the surface and in the tissue. Better cutting results (avoidance of delayed cut, high thermal load and thermal artifacts) obviously depend on an optimized impedance of the tissue. Therefore injection solutions with optimal (i.e. higher) impedances should be further investigated and preferred to conventional agents.
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P0709 PERCUTANEOUS TRANSESOPHAGEAL GASTROTUBING WITHOUT RADIATION EXPOSURE WITH ENDOSCOPIC ASSISTANCE

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INTRODUCTION: Percutaneous transesophageal gastrotubing (PTEG) was developed as an alternative route to access the gastrointestinal tract for patients where Percutaneous Endoscopic Gastrostomy was contraindicated with conditions such as prior gastrectomy, gastric anterior wall malignancies, or massive ascites. PTEG was originally developed to be performed under fluoroscopy without endoscopy. However, endoscopy may enhance the safety of the procedure.
AIMS & METHODS: The aim of this study is to evaluate the clinical usefulness of PTEG supported by endoscopy. A rupture-free balloon (RFB) catheter is inserted into the lower esophagus. Percutaneous balloon puncture with a specialized needle is then performed from the left side of patient's neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. We started to perform PTEG under

endoscopy without fluoroscopy in a total of 99 patients (63 men and 36 women, mean age 74.0 years) in whom PEG was not feasible. PTEG was performed for nutrition in 53 patients and for decompression in 46.
RESULTS: Satisfactory results were achieved in all 100 patients. Median follow-up was 60.5 days in patients who received decompression because of the obstruction due to malignancies and 231.0 days in those who received nutrition. Two of the 99 patients in the endoscopic assistance required fluoroscopy because of the tube insertion into the jejunum. There were no major complications, but one patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in six patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. Nine accidental (four self) tube removals occurred more than 2 weeks after the procedure, without any problem in reinsertion. The overall complication rate associated with endoscopically assisted PTEG was 14.1%. No patient required surgical treatment or died after PTEG.
CONCLUSION: PTEG supported by endoscopy is as feasible, safe, and useful as PTEG supported by fluoroscopy, the original procedure. The use of endoscopy enhances the safety of the procedure and allows better confirmation of each step involved.
Disclosure of Interest: None declared

P0710 ASSESSMENT OF THE SIMPLIFIED NARROW BAND IMAGING PATTERN CLASSIFICATION IN BARRETT'S OESOPHAGUS

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INTRODUCTION: Various narrow band imaging (NBI) pattern classifications in Barrett's oesophagus (BO) have been proposed, but are not readily applied to routine clinical practice due to their multiplicity or complexity.
AIMS & METHODS: We evaluate inter- and intra-observer agreement as well as accuracy of a new simplified NBI pattern classification using NBI magnifying endoscopic images.
A simplified binary classification is based upon NBI mucosal and vascular patterns: 1) regular pattern (non-neoplastic BO) 2) irregular (Barrett's neoplasia, BN). Four endoscopists consisting of 2 experts and 2 non-experts assessed 248 NBI magnifying endoscopic images (neoplasia 72, non-neoplasia 176) based on a simplified binary NBI pattern classification. The endoscopists assessed two times a randomly-arranged NBI magnifying endoscopic image sequence. The interval between the 1st and the 2nd assessment was 6 weeks. Primary endpoint was inter-observer agreement among endoscopists. Secondary endpoints were intra-observer agreements in each endoscopist and diagnostic accuracies of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) in predicting BN as well as scores of diagnostic confidence level and image quality.
RESULTS: A median score for image quality was 5 (excellent) in both the 1st and 2nd assessment. Inter-observer agreement (multi-kappa value) among endoscopists for BN prediction was calculated as 0.79 (substantial) and 0.86 (almost perfect) for the 1st and 2nd assessment. Intra-observer agreement (kappa-value) which were 0.95, 0.94 (experts) and 0.83, 0.83 (non-experts), respectively, were all almost perfect. Mean sensitivity and specificity of NBI patterns for predicting BN were 92.7% (experts, 90.3%; non-experts, 95.1%) and 95.9% (experts, 99.4%; non-experts, 92.3%) in the 1st assessment as well as 95.5% (experts, 95.8%; non-experts, 95.1%) and 95.7% (experts, 99.1%; non-experts, 92.3%) in the 2nd assessment, respectively, with high confidence level in both assessments. NPV was 98.9% (experts, 96.2%; non-experts, 97.9%) and 99.3% (experts, 98.3%; non-experts, 97.9%) in the 1st and 2nd assessment, respectively.
CONCLUSION: A simplified binary NBI pattern classification for BO showed substantial to almost perfect inter- and intra-observer agreement and significantly high diagnostic accuracies in both experts and non-experts. A simplified binary NBI pattern classification seems applicable to routine clinical practice.
Disclosure of Interest: None declared

P0711 PREDICTIVE FACTORS FOR LYMPH NODE METASTASIS AFTER NONCURATIVE ENDOSCOPIC RESECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic resection (ER) is widely accepted as an appropriate treatment modality for early gastric cancer. The indication criteria for ER is established, and additional treatment, including gastrectomy with lymph node dissection, is recommended when pathological examination of resected specimens do not meet the criteria. In some non-curative ER cases, pathological examination after additional surgery reveals lymph node metastasis which have not been detected before ER. There is a possibility that the discovery of risk factors of LN-metastasis in non-curative ER case can expand the indications of endoscopic treatment for early gastric cancer.
AIMS & METHODS: The aim of this study is to examine the predictive factors of LN- metastasis which could not be detected before ER in non-curative ER cases. The indication criteria for ER in Japan is as follows; the lesion clinically diagnosed as intramucosal differentiated cancer which is ≦2 cm in size with no ulceration findings. Expanded indications for some differentiated cancers (intramucosal cancers either ≦3 cm in size with ulceration findings or with no ulceration findings regardless of tumor size) and some undifferentiated cancers (intramucosal cancers ≦2 cm in size with no ulceration findings) have been accepted by high volume ER centers like our institution. If the pathological examination of resected specimens show that they do not meet the criteria including expanded indications, we diagnose them as non-curative. From Apr 2000 to Jul 2013, 75 patients underwent ER as the expanded indication lesion, and were diagnosed as non-curative by pathological examination in our hospital. They underwent additional gastrectomy and their pathological findings in ER and surgical specimens were retrospectively analyzed. And the cases with pathological LN- metastasis, which have not been detected before ER, were picked up and their characteristics were analyzed.
RESULTS: LN- metastasis was found in 9 cases (12%). 7 cases were primary gastric cancers, and 2 cases were residual gastric cancers. In the 7 primary cases, 5 cases had no residual cancer in surgical specimen, while LN- metastases existed. Focus on these complete endoscopic resection cases, 1 case was pathologically undifferentiated type and 5 cases were mixed type. The depth of invasion was SM1 in 1 case, and SM2 in 4 cases. Lymphatic-vascular capillary involvement was found in all cases. In these cases, LN- metastases were found only in local D1 lymph node lesion. Lymph node relapse was found in 2 SM2 cases in the complete endoscopic resection cases at an early date, one case was in 5 months and another in 6 months after surgical resection. Both of them had not only lymphatic capillary involvement but also vascular one.
CONCLUSION: Our data indicate that SM1/SM2 gastric cancer with pathologically mixed type, regardless of predominant type, have high risk of LN- metastasis even if complete endoscopic resection of local lesion has been performed. Lymphatic-vascular capillary involvement also may be a predictive factor of LN-metastasis and risk factor of recurrence. In these cases, we should perform gastrectomy with appropriate LN- dissection keeping the risk of recurrence in mind and consider adjuvant chemotherapy according to the risks.
Disclosure of Interest: None declared

P0712 HIGH DEFINITION (HD) ENDOSCOPY WITH I-SCAN FOR THE DETECTION OF MARKERS OF COELIAC DISEASE: A FEASIBILITY STUDY

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INTRODUCTION: Coeliac disease (CD) remains underdiagnosed. Previous studies have shown that up to 13% of patients with CD have undergone a previous gastroscopy where the opportunity to take duodenal biopsies and make a diagnosis had been missed. Clinicians may rely on the presence of endoscopic markers of CD to guide biopsy however these have been shown to lack the required sensitivity. A routine duodenal biopsy approach may solve this problem but this is time consuming and expensive. Methods to improve the macroscopic detection of CD at endoscopy to guide biopsy would seem advantageous. A single trial on I-Scan, a commercially available digital enhancement technique, has shown promising results in identifying markers of villous atrophy (VA)[1]. However this was an uncontrolled, unblinded trial in high prevalence population (35% CD). We aimed to assess the utility of I-Scan in a lower prevalence population in a randomised controlled trial.
AIMS & METHODS: Patients on a single coeliac enriched endoscopy list were randomised into 2 groups. Group 1 standard HD white light endoscopy (WLE) and group 2 WLE plus I-Scan. The presence of endoscopic markers of CD, scalloping, mosaic pattern, nodularity, loss of duodenal folds or increased vascularity was noted throughout the duodenum. All patients received 4 biopsies from the second part of the duodenum and at least 1 biopsy from the bulb. Coeliac serology was taken at the time of endoscopy. Macroscopic markers of CD are compared VA on histology as the gold standard. 3, 10-point likert scales for pain, discomfort and distress were used to assess tolerability.
RESULTS: 253 patients (149 female, mean age 53.3 SD 18.2) have been recruited to date (127 into group 1 and 126 in group 2). In total 27 (prevalence 10.7%) new diagnoses of CD have been made (14 in group 1 and 13 in group 2). I-Scan appears to enhance the appearance of markers for CD and in 2 patients in group 2 CD markers that were not noted to be seen on WLE became apparent. Preliminary results show that endoscopic markers of CD across both groups currently have a sensitivity of 78.6% (58.5 – 91.0), specificity 87.6% (82.4 – 91.5), positive and negative predictive values of 44.0% (30.3 – 58.7) and 97.1 (93.4 – 98.8). Median tolerability scores were good in both groups but better in the I-Scan group than WLE alone (4/30 versus 8/30 p0.005)
CONCLUSION: The addition of I-Scan to standard endoscopy to aid the diagnosis of CD is well tolerated and is feasible. I-Scan appears to enhance the markings of coeliac disease, however a larger study is required to truly evaluate the effectiveness of I-Scan as an adjunct to standard endoscopy to increase CD diagnosis.
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Disclosure of Interest: None declared

P0713 EFFECT OF AGING ON COMPLICATIONS OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY GASTRIC CANCER (EGC)

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INTRODUCTION: As ESD has been widely used as a minimally invasive treatment for EGC, opportunity to perform it for elderly patients is increasing. However, there are few reports about safety and efficacy of ESD for them. We evaluated the effect of aging on complications of ESD for EGC.
AIMS & METHODS: We perform a prospective study of the expanded indication of ESD for EGC (Soetikno, et al. J Clin Oncol. 23(20):4490-8). ESD was performed in 891 patients from April 2006 to March 2013 according to the indication. Patients were divided into elderly group (75 years or older; 344 cases) and non-elderly group (the rest; 547 cases). We compared the incidence of complications such as post-ESD bleeding, perforation, pneumonia, and delirium between the groups.
RESULTS: No emergent surgery was experienced in all cases. One patient in non-elderly group died of pneumonia. The incidence of pneumonia and delirium were significantly higher in elderly group than in non-elderly group (7.0% in elderly group vs 1.7% in non-elderly group; $P<0.01$, 10.2% in elderly group vs 1.0% in non-elderly group; $P<0.01$, respectively). There was no significant difference between two groups in the incidence of post-ESD bleeding and perforation (3.8% in elderly group vs 4.9% in non-elderly group; $p=0.42$, 7.0% in elderly group vs 5.7% in non-elderly group; $p=0.57$, respectively). Among the elderly group, the incidence of delirium was significantly higher in patients who have dementia than in those who haven't (79.2% in dementia patients vs 5% in non-dementia patients; $p<0.01$), and pneumonia was observed relatively more often in patients who have a history of chronic obstructive pulmonary disease (COPD) than in those who haven't (10.9% in COPD patients vs 6.1% in non-COPD patients; $p=0.17$).
CONCLUSION: ESD for EGC were safely performed even in elderly patients without critical complications. However, pneumonia and delirium would be more encountered after ESD in elderly patients, so we have to take care additionally about them.
REFERENCES
Soetikno, et al. *J Clin Oncol* 23: 4490-4498.
Disclosure of Interest: None declared

P0714 ENDOSCOPIC INJECTION OF AUTOLOGOUS BLOOD VERSUS DILUTED EPINEPHRINE FOR CONTROL OF ACTIVELY BLEEDING GASTRODUODENAL ULCERS: A RANDOMIZED CONTROLLED STUDY

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INTRODUCTION: A variety of endoscopic methods are available to achieve hemostasis from an actively bleeding ulcer and reduce the risk of rebleeding e.g. endoscopic injection of diluted epinephrine, applications of endoscopic clips and argon plasma coagulation. Preliminary report showed that autologous blood through tamponade effect, cellular components and its viscosity is effective and easy applicable technique that can control bleeding from the actively bleeding gastroduodenal ulcers.
AIMS & METHODS: The aim of this study was to test if endoscopic injection of autologous blood is superior to endoscopic injection of diluted epinephrine in controlling bleeding from gastroduodenal ulcers. One hundred patients with actively bleeding gastroduodenal ulcers were randomly assigned to autologous blood injection (Group A, $n=50$) or diluted epinephrine (group B, $n=50$) along the edges of the ulcers. Groups were compared for rates of initial hemostasis, rebleeding and complications.
RESULTS:

	Group A (Autologous blood) N = 50 (No & %)	**Group B (Diluted epinephrine) N = 50** (No & %)	**P**
Ulcer size			**0.523**
Small (<2 cm)	**32(64.0)**	**35(70.0)**	
Large (>2 cm)	**18(36.0)**	**15(30.0)**	
Ulcer site			**0.424**
Bulbar	**20(40.0)**	**20(40.0)**	
Antral	**15(30.0)**	**20(40.0)**	
Corporal	**15(30.0)**	**10(20.0)**	
Ulcer type			**1.0**
Forest Ia (spurting)	**30(60.0)**	**30(60.0)**	
Forest Ib (oozing)	**20(40.0)**	**20(40.0)**	
Volume/cc (blood/epinephrine)			**0.022***
Mean±SD	**7.4±1.8**	**8.9±4.1**	
Range	**(5-10)**	**(5-21)**	

All patients initially achieved hemostasis (100%). Rebleeding occurred in 4 cases of group A (8%) and 5 cases of group B (10%) but this difference was not statstically significant. Two cases in group B developed cardiovascular complications (arrhythmia and ischemic heart attack) while none of group A developed complications. Ulcer characteristics showed no difference regarding ulcer size, site and Forrest classification (the table). There was a significant difference in the amount needed for injection, little amounts of blood were needed to achieve hemostasis in group A than the amounts of epinephrine needed in group B ($p=0.022$)
CONCLUSION: Autologous blood is effective, comparable to diluted epinephrine in achieving initial hemostasis from actively bleeding gastroduodenal ulcers, associated with 8% rebleeding rate and had no complications.
Disclosure of Interest: M. Emara: none, E. Darwiesh: none, A. Bihery: none, T. Zaher: none

P0715 ENDOSCOPIC RESECTION AS A DIAGNOSTIC THERAPY FOR BORDERLINE LESION OF GASTRIC CANCER; A MULTICENTRE PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: It is often difficult to discriminate between gastric adenocaricinoma and dysplasia/adenoma using endoscopic forceps biopsy. Endoscopic resection (ER) is, therefore, applied for "borderline malignant" lesions for the purpose of total biopsy in clinical practice. We have reported that about 40% of patients with borderline lesion were diagnosed as adenocaricinoma after ER from a multicenter retrospective analysis (*M. Kato, et al. J Gastroenterol. 2010*). However, true incidence rate of adenocarcinoma is still unknown due to its retrospective study design.
AIMS & METHODS: The aim of this study is to confirm the feasibility of ER for gastric borderline malignant lesions.
This is a multi-centre prospective observational study from 10 hospitals (UMIN Clinical Trials Registry: UMIN000007476). Patients were included if they were diagnosed as Category 3.1 or 4.1 based on Vienna classification using endoscopic forceps biopsy specimen. After inclusion, patients underwent ER in each hospital and data was prospectively collected concerning macroscopic findings (size and morphological type based on Paris classification), findings of magnified endoscopy with narrow band imaging (NBI-ME), outcomes of ER, and pathological findings. Primary endpoint was cancer-bearing rate in patients diagnosed as adenocarcinoma after ER. Secondary endpoints were the association between final diagnosis and findings of macroscopic appearance and NBI-ME, and the short-term outcomes of ER.
RESULTS: A total of 105 patients were included from April 2012 to February 2014. Among them, 48 patients were diagnosed as adenocarcinoma after ER and cancer-bearing rate was 46%. Larger ($\geq$ 20mm) and smaller ($<$ 20mm) lesions were not significantly different in cancer-bearing rates (43% vs 57%, $p=0.2589$). Similarly, depressed and elevated lesions were not significantly different (50% vs 55%, $p=0.7469$). NBI-ME could predict accurately the pathological diagnosis after ER in 52% of the patients. En bloc margin negative resection was achieved in 103 patients (98.1%). Perforation and post-procedural bleeding occurred in 3 patients (2.9%) and 2 patients (1.9%), respectively. All these adverse events were managed conservatively and no patients required emergent operation or blood transfusion.
CONCLUSION: The present study showed that diagnostic ER for gastric borderline malignant lesion is clinically safe and useful because of acceptable complication and high cancer-bearing rate.
Disclosure of Interest: None declared

P0716 THIENOPYRIDINE DERIVATIVE CAN BE A RISK FACTOR FOR POSTOPERATIVE BLEEDING WHEN PERFORMING GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION WITHOUT DISCONTINUATION OF ASPIRIN: STRAP STUDY (SAFE TREATMENT ON ANTIPLATELETS)

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INTRODUCTION: Endoscopic procedures for patients taking aspirin were recently reported[1,2]. However, there was not enough evidence to support these procedures. We evaluated the safety of endoscopic procedures in Asian patients with a high risk of bleeding without perioperative discontinuation of aspirin.
AIMS & METHODS: A multicenter prospective cohort study was conducted at six high-volume endoscopy centres in Japan (UMIN000009176). Patients regularly taking antiplatelet agents and with a high risk of thromboembolism upon discontinuation of administration were enrolled in this study. All patients underwent endoscopic procedures with a high risk of bleeding while continuing aspirin including endoscopic submucosal dissection (ESD), endoscopic mucosal resection (EMR), and endoscopic polypectomy of the upper and lower

gastrointestinal tracts. The primary endpoint was the rate of major bleeding complications after endoscopic procedures.
RESULTS: This study was terminated in accordance with predetermined criteria because seven of 28 consecutive patients experienced major bleeding complications (25.0%; 95% confidence interval, 10.7%–44.9%). All major bleeding complications occurred after ESD (stomach n = 6; colon, n = 1). Univariate analysis revealed that postoperative administration of a thienopyridine derivative was the only significant factor associated with postoperative bleeding ($p = 0.04$). Subanalysis of gastric ESD of 23 lesions in 19 patients also confirmed that administration of a thienopyridine derivative was the only significant factor through multivariate analysis ($p = 0.01$). All complications of postoperative bleeding (postoperative day 11.2 ± 3.5; range, 7–17) occurred after resuming administration of thienopyridine derivatives postoperatively (postoperative day 2.3 ± 2.4; range, 1–7). No patients experienced thromboembolic events during the course of the study.
CONCLUSION: Endoscopic procedures with a high risk of bleeding require careful consideration of the indications for Asian patients taking thienopyridine derivatives. This especially applies to patients undergoing gastric ESD without discontinuation of or with a switch to aspirin.
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P0717 A SECOND-LOOK ENDOSCOPY AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION MAY NOT BE USEFUL FOR PREVENTING POSTOPERATIVE BLEEDING

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INTRODUCTION: Gastric endoscopic submucosal dissection (ESD) has gradually come to be recommended as the optimal treatment for early gastric cancer; however, one of the primary issues is postoperative bleeding. Although second-look endoscopy is conventionally performed to reduce the risk of postoperative bleeding, its benefit has not yet been clearly elucidated. The objective of this study was to elucidate the benefit of second-look endoscopy.
AIMS & METHODS: From among 488 lesions in patients who underwent gastric ESD between May 2004 and April 2013 at our hospital, a total of 29 lesions in patients who had a residual lesion, perforation, or concurrent aspiration pneumonitis, or in patients in whom the treatment modality had been switched to open surgery or there was no evidence of cancer in the resected specimen were excluded, and the remaining 459 lesions were included in the analysis. The patients were divided into those who had bleeding within 24 hours after ESD (immediate bleeding) and those in whom bleeding occurred 24 hours or more after the procedure (delayed bleeding); the underlying disease, age, lesion site, diameter of the resected specimen, and lesion diameter were analyzed to identify the risk factors for postoperative bleeding after ESD.
RESULTS: Post-ESD immediate or delayed bleeding occurred in 23 of the 459 cases (5.0%). Second-look endoscopy was performed in 210 of 447 cases (47.0%) excluding 12 cases with immediate bleeding; in the remaining 237 of the 447 cases (53.0%), it was not performed. Post-ESD delayed bleeding occurred in 6 of the 210 cases (2.9%) and 5 of the 237 cases (2.1%), with no statistically significant difference between the two groups. Overall, the following factors were identified as the risk factors for postoperative bleeding: young age ($P = 0.005$), lesions in the L segment ($P = 0.042$), and large size of the resected specimen ($P = 0.005$). The risk factors identified in the immediate bleeding group were lesions in the L segment ($P = 0.032$), large size of the resected specimen ($P < 0.001$), and large tumor size ($P = 0.011$), and those in the delayed bleeding group were young age ($P = 0.013$) and concomitant renal disease ($P = 0.011$).
CONCLUSION: The results of this study suggest that second-look endoscopy after gastric ESD may not be useful for preventing postoperative bleeding.
Disclosure of Interest: None declared

P0718 EARLY CLINICAL EXPERIENCE OF THE EFFECTIVENESS OF HEMOSPRAY IN ACHIEVING HAEMOSTASIS IN PATIENTS WITH ACUTE NON-VARICEAL BLEEDING

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INTRODUCTION: Despite advances in management, mortality from acute upper gastrointestinal bleeding remains high at 10%1. Current endoscopic modalities have found to be effective in achieving haemostasis in 85-95% of cases, however 5-10% of patients still experience rebleeding despite combination therapy2. Bleeding may occur from sites, which are challenging to access or lesions that are large and actively bleeding causing poor views for effective endoscopic therapy. Hemospray is a novel powder designed to be a simple endoscopic technique in applying to large surface areas even in difficult positions.
AIMS & METHODS: This was a retrospective review of patients at the Queen Elizabeth Hospital Birmingham where Hemospray was used for an acute non-variceal upper gastrointestinal bleed. Eight patients (4 male and 4 female) were identified between May 2012 and February 2013.
RESULTS: The median age was 63 years (range 37 – 84 years). Two patients had a Forrest classification of 1a, 2 were 1b, 1 was 2a and 3 were 2b. Causes of bleeding were duodenal ulcer (4), gastric ulcer (2), oesophageal cancer (1) and Diuelafoy lesion in stomach (1). Hemospray was used as the sole endoscopic modality in 1 patient and in combination with other modalities in 7 patients. Other modalities used were adrenaline (3), clips (1), adrenaline and clips (1), adrenaline and heater probe (1), adrenaline, clips and heater probe (1). Immediate haemostasis was achieved in all 8 patients. 3 patients re-bled within 7 days. All 3 patients had a duodenal ulcer (Forrest classification 1a, 1b and 2b). Two patients required further definitive therapy: radiological coiling of gastroduodenal branches (1) and endoscopic therapy with adrenaline and clips (1).
CONCLUSION: From the small number of patients in this study, we can conclude that Hemospray is an effective method in achieving immediate haemostasis when combined with other endoscopic modalities. However, there is a high rebleeding rate within 7 days in patients with duodenal ulcers, irrespective of their Forrest classification, who mostly required further definitive management. Larger studies are required to assess the efficacy of Hemospray in this particular group of patients to determine whether they are truly at higher risk.
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Disclosure of Interest: None declared

P0719 USEFULNESS OF CHROMOENDOSCOPY WITH INDIGO CARMINE AND ACETIC ACID FOR IDENTIFYING THE DEMARCATION LINE PRIOR TO ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Identification of a precise demarcation line (DL) is indispensable for performing pathological complete en bloc endoscopic submucosal dissection (ESD) for early gastric cancer (EGC). Recently, chromoendoscopy with combination use of indigo carmine and acetic acid was reported as a novel technique for identifying the DL; however, this technique is not effective in all EGC cases.
AIMS & METHODS: The aim of this study was to evaluate the usefulness of chromoendoscopy with indigo carmine and acetic acid for marking dots around lesions during ESD for EGC. We examined 98 consecutive patients with 109 intramucosal EGCs (mean diameter, 17.8 ± 12.4 mm; location, U 21/M 34/L 54; main histologic type, 96 intestinal and 13 diffuse) resected by en bloc ESD after chromoendoscopy with indigo carmine and acetic acid at Hiroshima University Hospital between December 2012 and February 2014. We identified the DL by chromoendoscopy with indigo carmine and acetic acid just before ESD (mean chromoendoscopy observation time, 71.6 s), and then marking dots were placed around the EGC. Four physicians participated in the evaluation of improved EGC visibility. Conventional endoscopic images were presented to each of the physicians in random order for comparison with chromoendoscopy images. Physicians scored each of the chromoendoscopy images for visibility of the DL, and the four physicians' scores for each image were tallied. EGCs were classified into two groups: useful for identifying the DL or useless. The tumor diameter, histologic type (intestinal/diffuse), macroscopic type (elevated, 0-I & IIa & IIb; depressed, 0-IIa+IIc & IIc), tumor lesion (U or M/L), tumor depth (intramucosal/submucosal), tumor color (reddish/normal or pale), atrophic gastritis around tumor (present/absent), intestinal metaplasia around tumor (present/absent), and rate of histologically positive horizontal margin were evaluated in each group.
RESULTS: Forty-two of the 109 cases (38.5%) were useful for chromoendoscopy with indigo carmine and acetic acid, which were compared to the other 67 cases. Univariate analysis showed that histologic type (intestinal type), macroscopic type (elevated type), and atrophic gastritis around the tumor (present) were associated with the usefulness of chromoendoscopy using indigo carmine and acetic acid. Multivariate analysis with logistic regression showed that macroscopic type (elevated type) and atrophic gastritis around the tumor (present) were independently associated with the usefulness of chromoendoscopy using indigo carmine and acetic acid for identifying the DL of EGCs ($P < 0.05$). The histologically positive horizontal margin after ESD was 0% (0/42) in useful cases, and 7.5% (5/67) in useless cases.
CONCLUSION: To make precise markings around EGCs before ESD, chromoendoscopy with indigo carmine and acetic acid is useful for elevated-type EGC or in cases of existing atrophic gastritis around EGCs.
Disclosure of Interest: None declared

P0720 THE DIAGNOSIS OF INVASION DEPTH IN SUPERFICIAL ESOPHAGEAL CANCER: A COMPARISON BETWEEN A MAGNIFYING NARROW-BAND IMAGING (NBI) OBSERVATION AND EUS

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INTRODUCTION: The diagnosis of cancer invasion depth is crucial for selecting the optimal treatment strategy for esophageal cancer. Endoscopic ultrasonography (EUS) is regarded as the standard modality for diagnosing invasion esophageal cancer depth in the West. In Japan, magnifying endoscopy has been used for diagnosis by observing the architecture of the esophageal microvasculature. This modality represents a rapid and simple diagnostic procedure without the need for any additional equipment. However, the accuracy of magnifying endoscopy has not been compared with that of EUS for the diagnosis of cancer invasion depth.
AIMS & METHODS: Patients with esophageal squamous cell carcinoma suspicious for muscularis mucosa or submucosal invasion in non-magnifying white light imaging were included. All patients received magnifying narrow-band imaging (NBI) observation followed by EUS. Magnifying NBI observation was performed by endoscope with magnification (GIF-Q240Z, or H260Z; Olympus, Tokyo, Japan). EUS was performed using a high-resolution probe by jelly-filled method. Before examination, several syringes (5 mL) containing sufficient amounts of jelly (K-Y lubricating jelly, Johnson and Johnson, k. k.) were prepared. After endoscope insertion (GIF-2TQ260M; Olympus) into the target area within the esophagus, a 30-MHz miniature probe was then inserted through the left channel of the endoscope and 30 to 40 mL of echo jelly was instilled through the right channel until the esophageal lumen was filled. Cancer invasion depth was diagnosed as T1a or T1b using both modalities. The diagnostic accuracy of magnifying NBI observation was compared with that of EUS while the histologic diagnosis of resected specimen served as reference standard.
RESULTS: From January 2011 to February 2014, 166 patients with esophageal squamous cell carcinoma were examined using the two modalities. Of the 166 patients, 91 treated with chemoradiotherapy or photodynamic therapy were excluded from analysis because histologic specimens were not obtained. Seventy-five patients treated either by esophagectomy ($n = 15$) or endoscopic resection ($n = 60$) were included in the final analysis. Histologic diagnosis was T1a in 43 lesions, T1b in 31 lesions, and T2 in one lesion. The overall accuracy of diagnosing invasion depth was 66.7% (50/75 lesions) by magnifying NBI and 70.7% (53/75 lesions) by EUS ($P = 0.602$). The accuracy of diagnosing invasion depth in lesions with protrusions was 58.8% (20/34 lesions) and 76.5% (26/34 lesions) by magnifying NBI and EUS, respectively ($P = 0.194$). The accuracy of diagnosing invasion depth in lesions without protrusions was 73.2% (30/41 lesions) and 65.9% (27/41 lesions) by magnifying NBI and EUS, respectively ($P = 0.632$).
CONCLUSION: EUS and magnifying NBI exhibited high diagnostic accuracy in lesions with and without protrusion. Furthermore, there was no significant difference in the overall accuracy of these two modalities. Considering its simplicity of use, magnifying NBI has the potential to be the standard modality for diagnosing invasion depth of esophageal squamous cell carcinoma.
Disclosure of Interest: None declared

P0721 ENDOSCOPIC DIAGNOSIS OF HIATUS HERNIAS - VARIABILITY BETWEEN ENDOSCOPISTS

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INTRODUCTION: There is a wider discrepancy in the diagnosis of hiatus hernias (HH) at upper gastro-intestinal endoscopy (OGD) compared to other techniques, such as manometry and barium swallow, or during surgery.[1] Endoscopic diagnosis may be affected by the method used (eg during intubation or extubation[2]), and variable definition of the gastro-oesophageal junction (eg proximal margin of the gastric folds, squamo-columnar junction or distal margin of the palisade zone).
AIMS & METHODS: Our aim was to assess variability in diagnosis of hiatus hernias by different endoscopists.
A retrospective review of the endoscopy database at Kingston Hospital, was performed. Consecutive OGD were analysed over a 3 month period (2/4/13 - 28/6/13). Complete data was obtained for 451 endoscopies, from 21 different endoscopists. Mean age for patients was 60.1 years (range 20-98), female to make ration of 1:1.04. Unpaired t-test and one-way ANOVA with Tukey's Test were used for normal data, and Chi-squared for proportional differences.
RESULTS: Of the 451 OGD, HH were diagnosed in 168 (36.6%), most HH under 5cm (81.55%). Main indications were for dyspepsia (14.2%), reflux symptoms (17.7%), abdominal pain (22%), anaemia (14%). There was a wide variability in the diagnosis of HH depending on speciality and grade (range 0-100%). Age, indications and gender were similiar between groups of endoscopists. Surgical Consultants were more likely to diagnose HH than Gastroenterology Consultants ($p < 0.002$) or Registrars ($p < 0.04$), and Nurse Endoscopists more likely than Gastroenterology Consultants ($p < 0.0001$) or Registrars ($p < 0.0004$).

Speciality & Grade	Number of endoscopies	Number of HH diagnosed	% HH
Gastroenterology Consultants	142	27	19%
Gastroenterology Registrars	34	6	17.7%
Surgical Consultant	55	23	41.8%
Surgical Registrars	19	11	57.9%
Nurse Endoscopists	189	99	52.4%
GP Endoscopists	12	2	16.7%

CONCLUSION: Endoscopic diagnosis of HH is highly variable and may be affected by level of training and speciality of the endoscopist. This may lead to under or overdiagnosis. A standardised approach to landmark measurement may lead to a more consistent diagnosis of HH.
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Disclosure of Interest: None declared

P0722 THE EFFECT AND USEFULNESS OF CHROMOENDOSCOPY WITH INDIGO CARMINE DYE ADDED TO ACETIC ACID IN DIAGNOSIS OF EARLY GASTRIC CANCER DIFFERS DEPENDING ON ITS MUCIN HISTOCHEMISTRY

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INTRODUCTION: Endoscopic submucosal dissection (ESD) became a very popular technique of therapeutic endoscopy for superficial gastrointestinal neoplasms, and it made possible to perform a reliable en bloc resection with higher success rate and lower recurrence rate compared with conventional endoscopic mucosal resection. For a complete en bloc resection of cancer lesions, it is indispensable to accurately delineate the margin, in other words, the lateral extent of the cancer. Chromoendoscopy with indigo carmine dye added to acetic acid is thought to be useful in the diagnosis of early gastric cancer. Usually this method helps to clarify the lateral extent of gastric cancer. But in some cases, this method can not help satisfactorily to delineate the margin between cancer and non-cancer parts. We assumed that the difference of dyeing pattern arises from quantity and character of mucus secreted from each lesion.
AIMS & METHODS: Subjects were 33 early gastric cancer lesions resected by using ESD technique in our institution, and were divided in two groups. We defined the lesions which were delineated clearly by acetic acid-indigo carmine method as group A ($n = 17$), and lesions which were not delineated clearly enough as group B ($n = 16$). We evaluated the mucin histochemistry of the specimens about stain levels of d-PAS and immunohistochemistry of MUC2, MUC5AC and CD10, and compared between the two groups.
RESULTS: Both group showed lower level of d-PAS stain in its cancer tissue than its non-cancer parts, suggesting that mucin productivity is decreased in the cancer tissue compared with non-cancer parts. Classification grouping using immunohistochemistry of MUC2, MUC5AC and CD10 showed that many cases of group A have intestinal type mucin (68.8%), and group B tends to have gastro-intestinal type mucin (64.7%).
CONCLUSION: Chromoendoscopy with indigo carmine dye added acetic to acid is generally useful and effective in case of early gastric cancer which has intestinal type mucin histochemistry. But on the other hand, cancer lesions having gastro-intestinal type mucin often show unclear margin even if using this technique.
Disclosure of Interest: None declared

P0723 FULL SPECTRUM ENDOSCOPY VS. TRADITIONAL FORWARD-VIEWING COLONOSCOPY WITH AND WITHOUT RIGHT-COLON RETROFLEXION: A RANDOMIZED, BICENTRIC BACK-TO-BACK STUDY

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INTRODUCTION: Colonoscopy can reduce colorectal cancer (CRC) incidence and mortality through early detection and removal of adenomas, but estimates suggest that up to 24% of adenomas are missed; various colonoscopic techniques are evolving to improve its diagnostic yield and avoid interval CRC. Recently a new colonoscopy platform (FUSE^{TM} system, EndoChoice Inc., Atlanta, GA, USA) was introduced with promising initial results. FUSE-colonoscopy (F-C) provides a 330°-field of view instead of the 170° of standard colonoscopy (S-C); this allows polyps hidden behind folds or flexures to be seen easier.

AIMS & METHODS: The aim of this study is to evaluate F-C additive contribution to detection of polyps/adenomas, compared to S-C, with and without the addition of right-colon retroflexion (R-C), in a series of patients undergoing same-day, back-to-back randomized (1:1) tandem colonoscopies in 2 tertiary endoscopy centres. ClinicalTrials.gov Identifier: NCT02117674
RESULTS: Of 150 totally planned, 84 pts have been enrolled until now; 40 (47.6%) of them were randomized to undergo F-C first. There were 7 incomplete cases for both F-C and S-C (including 1 failed case for both F-S and S-C and 1 case where F-C was not performed due to technical failure). Thus, 83 (46 screening/surveillance, 32 symptomatic and 5(6%) with polyps) were included in the per-protocol analyses. R-C was attempted in 57/83 cases; successful in 37. Insertion time did not differ between F-C and S-C (5min, IQR:4-10.25 vs. 5min, IQR: 4-8, respectively, $p = 0.4$), whereas, withdrawal was marginally longer for F-C (8min, IQR:6-10 vs. 7min, IQR:6-9, respectively, $p = 0.05$). Overall, 133 polyps were found (53 right colon); of these 61 were adenomas, 32 in the right colon (histology available for 24/28 pts with polyps).
By per-lesion anlaysis, F-C detected significantly more missed polyps compared to S-C overall (26 vs. 4, $p = 0.033$) and right-sided ones (14 vs. 2, $p = 0.038$) and detected more adenomas (9 vs. 3, $p = 0.162$) overall and right-sided ones (7 vs. 2, $p = 0.184$). R-C offered no additional gain in polyp or adenoma detection in the right colon.
CONCLUSION: Our initial results show that F-C could be an advancement in colonoscopy by detecting more polyps. However, if this improvement actually represents detection of more adenomas requires further investigation.
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P0724 ORALLY ADMINISTRATION OF OTILONIM BROMIDE BEFORE COLONOSCOPY IMPROVES ADENOMA DETECTION RATES

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INTRODUCTION: We aimed in this randomized prospective controlled trial to evaluate the effect of orally administration of Otilonium bromide over the quality of the colonoscopy in the meanings of adenoma detection rate, caecal intubation time, and the tolerability.
AIMS & METHODS: Two-hundred consecutive volunteer outpatients were randomized to Otilonium Bromide group (100 patients) and the control group (100 patients). The patients in the Otilonium Bromide group received 30 mg Otilonium Bromide 3 times a day for five days with the last dose given two hours before colonoscopy. The bowel preparation quality was graded according to the Boston bowel preparation scale. For each colon area, a distension scale was awarded by using a previously validated 5-point scale. The pain experienced during colonoscopy was determined by using a 1-10 visual analog pain scale.
RESULTS: Twenty-one patients in Otilonium bromide group and 22 patients in control group were excluded from the study because of uncompleted colonoscopy. Caecum intubation time was comparable between groups ($p = 0.4$). There was no statistically difference between groups in the terms of mean bowel preparation quality scores ($p = 0.4$), while mean distension score was greater in Otilonium bromide group ($p = 0.007$). Polyp detection rate (26 polyps in 22 patients vs. 14 polyps in 12 patients) (32.9% vs. 17.9%, $p = 0.03$) was significantly higher in OB group. Also, adenoma detection rate (22 adenomas in 21 patients vs. 11 adenomas in 11 patients) (27.8% vs. 14.1%, $p = 0.03$) was significantly higher in OB group. The visual analog pain scale scores were comparable between groups ($p = 0.07$)
CONCLUSION: Otilonium bromide administration before colonoscopy increases colonic distension, polyp detection and adenoma detection rates. Further clinical investigations are required to determine the utility of relieving colonic spasm with oral antispasmodics to improve adenoma detection rates.
Disclosure of Interest: None declared

P0725 NEW GENERATION FLEXIBLE SPECTRAL IMAGING COLOR ENHANCEMENT IS USEFUL TO PREDICT HISTOLOGY OF SMALL COLORECTAL POLYPS

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INTRODUCTION: Prediction of colon polyp histology is decisive as small non advanced adenoma may be discarded after resection and hyperplastic lesions may be left in place. The NICE classification system for NBI endoscopy and magnification has been shown to be effective in prediction of histology. There is only little data for the flexible spectral imaging color enhancement (FICE). Newest generation of endoscopes have over mega pixel CMOS sensors that allow FICE aligned with electronic zoom without loss of image quality. With this new technology, histology prediction may easily be possible during standard colonoscopy without using optical zoom endoscopes.
AIMS & METHODS: To assess the accuracy of endoscopic prediction of histology of small colorectal polyps using white light (WLE) and FICE and CMOS endoscope
Methods:
We randomly assigned patients for colonoscopy using a CMOS colonoscope (EC-600 WM, Fujifilm Europe Düsseldorf). All detected polyps were assigned to Types 1-3 according to the NICE classification system criteria using WLE and FICE (modes 1,8,9) with and without electronic zoom. Classification was assessed during the examination. Before starting the study, the endoscopist underwent endoscopic training using NBI. All detected polyps were removed for histopathology. The concordance of endoscopic classification and histology was calculated.
RESULTS: We investigated 27 polyps in 11 patients. Median polyp size was 4 mm (range 3-20 mm) Polyps location were in the rectum and sigmoid colon ($n = 15$) in the right colon ($n = 10$) and in the left colon ($n = 2$). According to the endoscopic classification 18 polyps were hyperplastic (Type 1) and 9 polyps were adenomas (Type 2). No colorectal cancer or high grade adenoma were identified. Histology proofed that 100 % of polyps were classified correctly. One polyp classified as adenoma revealed serrated adenoma in histology.
CONCLUSION: The NICE classification system criteria can successfully be applied for colorectal polyps being investigated with FICE and electronic zoom using a CMOS colonoscope.
Disclosure of Interest: J. Weigt Lecture fee(s) from: Fujifilm, A. Kandulski: None declared, P. Malfertheiner: None declared

P0726 MEASUREMENT OF COLONIC POLYPS. IS VISUAL ESTIMATION ACCURATE?

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INTRODUCTION: Colon polyp size is a critical biomarker for clinical management of colonic polyps. Larger polyps have a greater malignant potential. During colonoscopy, it is important to correctly measure the size of the polyps because of the direct correlation of size with colon cancer.[1] During polypectomy, size of the colonic polyps encountered are often gauged by visual estimation or the open forceps method.[2] However, some data exists on the questionable reliability of a visual estimate even amongst expert colonoscopists. We aim to compare the estimation of polyp size using the visual estimation of colon polyp with or without the open biopsy forceps technique against actual polyp size measurement by our histopathology department for all polyps >1cm in size.
AIMS & METHODS: A single centre, retrospective analysis using the Unisoft GI auditors software was used to identify patients who have had polypectomies done for polyps >1cm in size from October 2005 till September 2013. The size of the polyps documented in the endoscopy report was then compared to the lab measured actual polyp size.
RESULTS: A total of 39 patients were identified with polyps >1cm in size who has had polypectomy done. Results are as below:

Visual estimated size (mm)	Actual lab measured size (mm)					
	3~9	10~14	15~19	20~24	25~29	>30
3~9						
10~14	XXXXXXX	XXXX	XXXX			
15~19	XXXX	X	X		X	
20~24		XXX	X	X		
25~29	X	X	XXX	X		X
>30	X		X	XX	X	

CONCLUSION: From this study we can conclude that visual estimation with or without the open biopsy forceps technique is completely inaccurate with wide variations between the reported size and the actual size of the polyps when measured in our laboratory. Accurate measurement of colonic polyps is important as inaccuracies can lead to potentially larger polyps not being tattooed and subsequent difficulty in identification during surgery and surveillance. We advocate that the 'gold standard' practice of direct measurement of the polyp once excised and outside the body be adopted and the actual size should be documented according to direct measurement.
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Disclosure of Interest: None declared

P0727 THE VALUE OF ENDOSCOPIC INVESTIGATION IN PATIENTS WITH BOWEL THICKENING ON COMPUTED TOMOGRAPHY IMAGING. A 4 MONTH RETROSPECTIVE STUDY BASED IN A DISTRICT GENERAL HOSPITAL IN THE UK

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INTRODUCTION: Bowel wall thickening is a common and often unexpected finding on abdominal computed tomography (CT) scans, and yet its significance and further investigation is unclear from the literature. This study aims to clarify the incidence of bowel wall thickening, and its investigation and outcomes in a District General setting.
AIMS & METHODS: In this retrospective observational study, all in-patients who underwent abdominal CT imaging were included over a 4 month period regardless of indication. Radiology reports were analysed, and patients with gastrointestinal wall thickening were identified for further analysis.
RESULTS: 1227 patients underwent abdominal CT imaging over the 4 month period, of which 116 (9.5%) were found to have bowel wall thickening. 53 patients subsequently had an endoscopic examination and in 49 cases the area of interest was visualised. 33 patients had positive endoscopic findings at the site of bowel thickening, of which 16 had mucosal inflammation, 8 had malignancy, 6 had diverticulosis and 3 had polyps.
In the remaining 63 patients who did not have endoscopic examination, 42 were investigated by other means including surgery or other imagining modalities, or further investigation was not appropriate. In 21 patients, it was unclear as to why further investigation did not take place.
CONCLUSION: Endoscopic evaluation of gastrointestinal wall thickening found on CT imaging led to a positive diagnosis in 62.3% (33/53) patients of which 15% (8/53) were found to have malignancy. This highlights both the importance of further investigating GI wall thickening and the value of endoscopic visualisation.
Disclosure of Interest: None declared

P0728 THE COMPARATIVE STUDY OF SPLIT-DOSE OF POLYETHYLENE GLYCOL (PEG) BETWEEN LOW VOLUME PEG PLUS ASCORBIC ACID FOCUSING ON THE BOWEL CLEANSING EFFICACY, PATIENTS' AFFINITY TO PREPARATION SOLUTION AND MUCOSAL INJURY: A PROSPECTIVE RANDOMIZED TRIAL

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INTRODUCTION: Adequate bowel cleansing is essential for a high-quality, effective, and safe colonoscopy. The aims of this study were to compare the efficacy and patients' affinity to preparation solution and mucosal injury of split dose of polyethylene glycol (PEG) solution with low volume PEG plus ascorbic acid for outpatients who underwent scheduled colonoscopy.
AIMS & METHODS: This study was prospective randomized investigator-blinded. Overall, 160 patients were enrolled for split-dose of PEG and 159 for the low volume PEG plus ascorbic acid, respectively. The bowel cleansing efficacy of preparation was rated according to the Ottawa bowel preparation scale and patients' affinity to preparation solution was assessed using a questionnaire. All mucosal abnormalities observed during colonoscopy were noted and biopsied. These biopsy specimens were reviewed by pathologists.
RESULTS: Of the 319 patients, 308(96%) ingested more than 75% of the bowel preparation. There was no significant difference between the two groups for the mean total score using the Ottawa bowel preparation scale ($p = 0.376$). Significantly greater residual colonic fluid was observed in the low volume PEG plus ascorbic acid group (0.81 ± 0.54) than in the split-dose PEG group (0.66 ± 0.62) ($p = 0.023$). There was significant difference in the Ottawa bowel preparation score for the middle colon (split-dose PEG vs. low volume PEG plus ascorbic acid: 1.19 ± 0.94 vs. 1.42 ± 0.73; $p = 0.014$). In patients' preference and acceptance, low volume PEG plus ascorbic acid group showed better results ($p = 0.001$). The overall incidence of adverse events was not significantly different between the two groups (69/160 [43.1%], 69/159 [43.4%], $p = 0.972$); however, the split-dose PEG group tended to had less headache and dizziness ($p = 0.056$). Endoscopically, mucosal lesions, possibly associated with two preparation regimen, were observed in total 11 patients (split-dose PEG: 5, low volume PEG plus ascorbic acid: 6, respectively). Mucosal ulceration occurred in 1 patient taking split-dose PEG compared with 2 patients receiving low volume PEG plus ascorbic acid.
CONCLUSION: Low volume PEG solution plus ascorbic acid, compared with split-dose PEG, was associated with more residual fluid, but showed equivalent colon cleansing efficacy and resulted in more patient preference, and acceptance. There was no significant difference in mucosal injury.
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Disclosure of Interest: None declared

P0729 COLON STENTING: CAN WE PREDICT PERFORATION? CONSIDERING FACTORS BEFORE PLACING A COLON STENT

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INTRODUCTION: In the last decade, Colon Stenting has become a well accepted technique for use as "bridge to surgery" or as palliative treatment in cases of malignant colon strictures. None the less, recent meta-analysis had suggested that there is a high rate of complication due to this procedure carrying an increase in morbidity in these patients that in some cases must be treated with emergency surgery due to Peritonitis in relation to colon perforation secondary to the procedure. In that matter we focused our study on identifying factors, before the procedure, that can predict colon perforation.
AIMS & METHODS: Data from 213 ($n = 213$) patients admitted in our hospital between January 2004 to November 2012 were analyzed. All of the items reviewed were before the procedure. Demographic factors were age and sex. Clinical factors include length of symptoms, presence of peritoneal irritation, cardiac frequency, temperature and blood pressure. Laboratory tests were CRP, LDH, WBC, pH and lactate. Radiologic features included the presence of colon dilatation, measurement in centimeters of the cecum and the most dilatated area, function of the ileo-cecal valve and the presence of metastasis in CT scan. Factors analyzed from the procedure include timing (urgent or elective) (<48 hrs or >48 hrs), length of the procedure, level of expertise of the endoscopist, location of the tumor, angulations of the tumor, length of the Stent and the visualization of feces coming through the Stent after released.
RESULTS: We review data from 213 cases, after statistical analysis, rate of colon perforation found was 12% (21 patients); factors with statistic significance related to patients demonstrated that the presence of colonic dilatation in the radiologic study was associated with a higher risk of perforation compared with patients that did not have dilatation (18.1% vs 2.3%, $p = 0.009$), being the risk of perforation increased almost eight times [$R = 7.9$ (IC 95%: 1.1-57.1)]. The mean in centimeters of colon dilatation in patients that had perforation was significantly longer (8.75 cm vs 6.79 cm, $p = 0.012$). In the other hand, factors related to the procedure with statistic significance, revealed that seeing feces coming through the stent after released was associated with a lower risk of perforation (10.3% vs 31,3%, $p = 0.004$), there was an increased risk of three times, for colon perforation, in patients that did not present the pass of feces through the stent after liberation [$R = 3.04$ (IC 95%: 1.5-6.1)].
CONCLUSION: Colon dilatation and the length of dilatation before procedure is an important factor to take in consideration when deciding to place a colon stent, in our study we saw an important increase in colon perforation when the length of the cecum was more than 8 cms. In the other side, seeing feces passing through the stent when it is released, reveals an adequate function of the stent, and demonstrated a less number of perforations. In the future, predictive models taking these factors into consideration might be developed with the objective to select better the patients for this procedure reducing the rate of complications.
Disclosure of Interest: None declared

P0730 THE OFFER OF ADVANCED ENDOSCOPIC IMAGING TECHNIQUES LEADS TO HIGHER ACCEPTANCE RATES FOR COLONOSCOPY – A PROSPECTIVE STUDY

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INTRODUCTION: In Germany patients over the age of 55 years should undergo colonoscopy for colorectal cancer screening. The acceptance rate of patients undergoing screening colonoscopy is still low.
AIMS & METHODS: Aim was to evaluate whether the offer of advanced endoscopic imaging techniques including chromoendoscopy, magnification endoscopy, spectroscopy, confocal laser endomicroscopy, endocytoscopy, capsule endoscopy, CT-colonography or device-assisted enteroscopy may lead to an increased awareness and improved acceptance rates of patients to undergo colonoscopy.
Prospectively, 372 patients were randomly included (168 female, 204 male). At baseline, a standardized questionnaire was developed. Afterwards, knowledge of advanced imaging techniques was inquired and if the patient was motivated by the specific offer of these imaging techniques to undergo colonoscopy. In the second phase, several media campaigns through press, internet, TV coverage, and information events were organized reporting about advanced imaging techniques, followed by repeat evaluation of the patients. This sequence (media campaign and patients' evaluation) was repeated every 3 months over a period of 12 months.
RESULTS: At baseline, 64% of the patients reported that knowledge about new endoscopic methods is completely unknown. After the evaluation period this was reported by only 34% of patients ($P < 0.05$). Despite general information about all advanced imaging techniques was given in the media campaigns, patients were most interested in chromoendoscopy (baseline: 5% - after 12 months: 22%), endomicroscopy (5% vs. 17%), CT colonography (16% vs. 37%) and capsule endoscopy (12% vs. 47%). The overall grade of information increased significantly from 14% at baseline to 35% after 12 months ($P < 0.05$). The percentage of patients who decided to undergo colonoscopy because of the offer of new imaging methods increased significantly from 12% at baseline to 42% after 12 months ($P < 0.05$).
CONCLUSION: Patients were highly interested in advanced endoscopic imaging techniques and patient's knowledge about new imaging methods increased significantly over the study period. The offer of advanced imaging techniques lead to higher acceptance rate for screening or surveillance colonoscopies.
Disclosure of Interest: None declared

P0731 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR HUGE COLORECTAL NEOPLASMS: COMPARISON BETWEEN SESSILE TUMORS AND LATERALLY SPREADING TUMORS

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INTRODUCTION: Although endoscopic submucosal dissection (ESD) is thought as an effective treatment for large laterally spreading tumors (LSTs) of the colorectum, the therapeutic effectiveness of ESD for large sessile colorectal tumors has not been evaluated.
AIMS & METHODS: We aimed to evaluate the outcomes of ESD for the huge colorectal tumors (30 mm or larger in diameter) and compare therapeutic outcomes between sessile tumors and LSTs. We retrospectively reviewed medical records of the patients who underwent ESD for huge sessile tumors and LSTs of the colorectum from July 2007 to November 2013. En-bloc resection rate, complete resection rate, procedure time and procedure-related complications were evaluated in the sessile tumor and LST groups. Multivariate analysis was performed to identify independent factors for incomplete resection.
RESULTS: ESD was attempted for a total of 191 patients with huge colorectal tumors (48 with sessile colorectal tumors and 143 with LSTs) by two endoscopists. The mean (± SD) time required for ESD was 82.5 ± 4.4 minutes (range, 17-392), and mean size and height of the lesions were 43.2 ± 1.1 mm (range, 30-135) and 9.6 ± 0.5 mm (range, 1-33). The rate of en bloc resection and complete resection were 85.9% and 75.9%. With regard to complications, 11.0% (21/191) cases of intra-procedural bleeding and 15.7% (30/191) cases of perforation were observed in total; none of the complications required surgical intervention. In the sessile colorectal tumors, the endoscopic en bloc resection and complete resection rate were 72.9% (35/48) and 62.5% (30/48) respectively. In the LSTs, they were 90.2% (129/143) and 80.4% (115/143) respectively. Although endoscopic findings suggesting submucosal (sm) invasion such as Vi or Vn pit pattern were not different between the two groups, higher sm invasion rate was noted in the sessile tumors than the LSTs (39.6% vs 23.1%, $p = 0.026$). Intra-procedural bleeding was more frequent in sessile tumors than LSTs (22.9% vs 7.0%, $p = 0.002$). There was no significant difference in procedure time and perforation between the two groups. The rate of operation, caused by non-curative resection, was higher in sessile tumors (14.6% vs 5.6%, $p = 0.045$). There was no mortality associated with procedure or operation. On multivariate analysis, sessile morphology (OR 2.125; 95% confidence interval (CI) 1.006-4.488; $p = 0.048$) and presence of fibrosis (OR 2.290; 95% CI 1.216-5.251; $p = 0.013$) were independent risk factors of incomplete resection in ESD of huge colorectal neoplasia.
CONCLUSION: The complete resection rate of ESD for sessile tumors was relatively lower than that of ESD for LSTs. Presence of fibrosis was another independent risk factor of incomplete resection in ESD of huge colorectal neoplasia.
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P0732 THE FEASIBILITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY COLORECTAL NEOPLASM WITH HIGHLY TECHNICAL DIFFICULTY

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INTRODUCTION: Colorectal endoscopic submucosal dissection (ESD), has not been widely spread because of technical difficulty and high incidence of perforation. Before ESD, we need to recognize whether a lesion can be removed with or without technical difficulty. The aim of study is to assess the feasibility of colorectal ESD for lesions accompanied by highly techinical difficulty.
AIMS & METHODS: We established the indication of colorectal ESD as follows: LST-NG, LST-G (mixed nodular type), local recurrent lesion after previous endoscopic piecemeal mucosal resection (EPMR)≧20mm, and Is/Isp≧30mm. 330 colorectal consecutive lesions were enrolled in this study. Flush knife was used in all cases. From the viewpoint of morphological type and tumor size, we defined (1) LST-NG≧40mm, (2) LST-G (mixed nodular type)≧50mm, (3) Is/Isp≧40mm, and (4) local recurrent lesion after EPMR≧20mm, as highly difficult lesion. A lesion except for these four groups was defined as an ordinary lesion (5). We investigated {tumor size(mm), en bloc resection rate(%), operative time(min), perforation/delayed bleeding rate(%), moderate/severe fibrosis rate(%)}, respectively. Each highly difficult group was respectively compared to the group (5) for all factors. A P value $< .05$ was considered statistically significant.
RESULTS: The total average diameter of lesions was 33.8mm. For morphological type, 153 lesions were LST-NG, 110 LST-G, 37 protruded, 15 depressed and 15 recurrent lesions. By histological examination, 226 intramucosal cancers, 49 slightly invasive submucosal cancers, 19 massively submucosal invasive cancers, and 36 tubular adenomas. The average operative time was 85.8 minutes, and the en bloc resection rate was 97.9% (323/330). With regard to complications, postoperative bleeding was observed 0.9% (3/330). Microperforation which occurred in only 1 case was conservatively repaired with endoscopic clipping. The clinical outcome of each group is as follows: (1) LST-NG≧40mm, n = 31 {44.4mm, 93.5%, 149.8min, 0%/0%, 25.8%/6.5%} (2) LST-G(mix)≧50mm, n = 29 {62.9mm, 93.1%, 169.7min, 3.4%/6.9%, 25.8%/6.5%} (3) Is/Isp≧40mm, n = 12 {51.3mm, 100%, 121.3min, 0%/0%, 25.0%/41.7%} (4) local recurrent lesion after EPMR≧20mm, n = 15 {29.9mm, 100%, 118.3min, 0%/0%, 0%/100%} (5) ordinary lesion, n = 243 {28.7mm, 99.2%, 63.3min, 0%/0.4%, 24.7%/2.1%}. The tumor size was significantly larger for the group (1) (2) (3) than the group (5), respectively. Operative time was significantly longer for these four groups than the group (5). En bloc resection rates didn't significantly differ respectively between the two groups. Except for local recurrent lesion, moderate severe fibrosis rates were respectively similar between the two groups. Furthermore, all recurrent lesions had severe fibrosis and the severe fibrosis rate was significantly higher for the group (3) than the group (5). The perforation rates were respectively similar between the two groups. The delayed bleeding rate was significantly higher only for the group (2) than the group (5).
CONCLUSION: It is confirmed that we should regard both LST-NG and Is/Isp≧40mm as lesions with highly technical difficulty. We acquired the high curability and safety even for highly difficult lesions irrespective of longer operative time.
Disclosure of Interest: None declared

P0733 DISTINCT MOLECULAR FEATURES OF DIFFERENT MACROSCOPIC SUBTYPES OF COLORECTAL NEOPLASMS

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INTRODUCTION: Colorectal adenoma develops into cancer with the accumulation of genetic and epigenetic changes. We studied the underlying molecular and clinicopathological features to better understand the heterogeneity of colorectal neoplasms (CRNs).
AIMS & METHODS: We evaluated both genetic (mutations of *KRAS*, *BRAF*, *TP53*, and *PIK3CA*, and microsatellite instability [MSI]) and epigenetic (methylation status of nine genes or sequences, including the CpG island methylator phenotype [CIMP] markers) alterations in 158 CRNs including 56 polypoid neoplasms (PNs), 25 granular type laterally spreading tumors (LST-Gs), 48 non-granular type LSTs (LST-NGs), 19 depressed neoplasms (DNs) and 10 small flat-elevated neoplasms (S-FNs) on the basis of macroscopic appearance.
RESULTS: S-FNs showed few molecular changes except *SFRP1* methylation. Significant differences in the frequency of *KRAS* mutations were observed among subtypes (68% for LST-Gs, 36% for PNs, 16% for DNs and 6% for LST-NGs) ($P < 0.001$). By contrast, the frequency of *TP53* mutation was higher in DNs than PNs or LST-Gs (32% vs. 5% or 0%, respectively) ($P < 0.007$). We also observed significant differences in the frequency of CIMP between LST-Gs and LST-NGs or PNs (32% vs. 6% or 5%, respectively) ($P < 0.005$). Moreover, the methylation level of LINE-1 was significantly lower in DNs or LST-Gs than in PNs (58.3% or 60.5% vs. 63.2%, $P < 0.05$). *PIK3CA* mutations were detected only in LSTs. Finally, multivariate analyses showed that macroscopic morphologies were significantly associated with an increased risk of molecular changes (PN or LST-G for *KRAS* mutation, odds ratio [OR] 9.11; LST-NG or DN for *TP53* mutation, OR 5.30; LST-G for *PIK3CA* mutation, OR 26.53; LST-G or DN for LINE-1 hypomethylation, OR 3.41).
CONCLUSION: We demonstrated that CRNs could be classified into five macroscopic subtypes according to clinicopathological and molecular differences, suggesting that different mechanisms are involved in the pathogenesis of colorectal tumorigenesis.
Disclosure of Interest: None declared

P0734 ENDOCYTOSCOPY CAN PREDICT THE VENOUS AND LYMPHATIC VESSEL PERMEATION OF EARLY COLORECTAL ADENOCARCINOMA

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INTRODUCTION: Endocytoscopy (EC), which enables observation of in vivo cells and nuclei at about 380-fold magnification, provides more detailed information about the lesions.
AIMS & METHODS: The aim of our study is to evaluate the possibility of EC with regard to prediction of venous and lymphatic vessel permeation.
The subjects were 117 colorectal differentiated adenocarcinomas (53 Tis, 41 T1 carcinomas, 12 T2 carcinomas, 11 T3 carcinomas) from 115 patients treated by endoscopic or surgical resection after observation with EC at Showa University Northern Yokohama Hospital from February 2009 to March 2014. In observing EC images, we defined the average scale of four vessels as ''vessel diameter'' and proportion between maximum portion and minimum portion of the vessel as ''vessel caliber variation''. We analyzed the correlationship between these parameters (''vessel diameter'' and ''vessel caliber variation'') and venous or lymphatic vessel permeation.
RESULTS: The mean vessel diameter of venous permeation positive tumors was 41.0μm, and that of negative tumors was 31.4μm. The mean vessel caliber variation of venous permeation positive tumors was 0.45, and that of negative tumors was 0.38 ($P < 0.05$). In lymphatic vessel permeation, the mean vessel diameter of lymphatic vessel permeation positive tumors was 39.1μm, and that of negative tumors was 34.4μm. The mean vessel caliber variation of venous permeation positive tumors was 0.45, and that of negative tumor was 0.40 ($P < 0.05$).

There were differences in vessel diameter and vessel caliber variation between venous permeation positive tumors and that of negative tumors especially in T1carcinomas ($p < 0.05$).
CONCLUSION: EC has the possibility to evaluate the venous and lymphatic vessel permeation by observing the vessel formation, especially in T1 carcinoma.
Disclosure of Interest: None declared

P0736 NATURE OF WHITE OPAQUE SUBSTANCE WITHIN COLORECTAL NEOPLASTIC EPITHELIUM AS VISUALIZED BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING: A NOVEL BIO-MARKER FOR COLORECTAL NEOPLASIA

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INTRODUCTION: Background: We previously reported the presence of a white opaque substance (WOS), opaque to the endoscope light, inside the epithelium when we use magnifying endoscopy (ME) to examine gastric epithelial neoplasia (adenomas and carcinomas) and chronic gastritis (intestinal metaplasia)[1)]. Through further pathohistological study we elucidated that this substance is comprised of minute lipid droplets (LDs) accumulated within the mucosal epithelium of gastric epithelial neoplasia or intestinal metaplasia.[2)] These minute LDs strongly backscatter the projected light, and are visualized as a white substance. When we examined colorectal neoplastic lesions (adenomas and carcinomas) using ME, we observed WOS as in the stomach. However, it is unclear whether WOS in colorectal epithelial tumors is in fact an accumulation of LDs as in the stomach.
AIMS & METHODS: Aims: To elucidate whether WOS observed in colorectal epithelial tumors (adenomas and carcinomas) is composed of LDs.
Methods: We analyzed a continuous series of both 40 WOS-positive and 40 WOS-negative colorectal epithelial tumors. We examined colorectal neoplastic lesions (adenomas and carcinomas), prior to planned treatment, using ME with narrow-band imaging (NBI), determining whether WOS was present in the surface layers of the most anal part of the colorectal epithelial tumor. We took targeted biopsies from this part of the tumor. Biopsy specimens were immediately frozen, slices taken, and the slides were stained for lipids using oil-red O. Slides were examined using light microscopy immediately after staining for the presence of LDs within the neoplastic epithelium. We investigated the correlation between the presence of WOS as visualized by ME with NBI and the presence of LDs in the histological specimens.
RESULTS: The prevalence of LDs in WOS-positive *vs* WOS-negative lesions was 47.5% (19/40) and 5% (2/40), respectively ($P < 0.001$, Fisher's exact test).
CONCLUSION: Conclusion: LDs do not accumulate in the normal colorectal epithelium. However, this study elucidated for the first time that endoscopically visualized WOS may be composed of LDs accumulated in colorectal epithelium. This phenomenon has the potential to be a new biomarker for the pathology and diagnosis of colorectal neoplasia.
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Disclosure of Interest: None declared

P0737 QUANTITATIVE AUTOFLUORESCENCE IMAGING IS USEFUL FOR ASSESSING THE SEVERITY OF ULCERATIVE COLITIS

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INTRODUCTION: Maintaining remission in patients with ulcerative colitis (UC) is the most important achievement for the present treatments. Although precise evaluation of the mucosal inflammation is necessary to keep the remission status as long as possible, the procedures have been inadequate to detect this inflammation. Autofluorescence imaging (AFI) is a novel technology that can capture the fluorescence emitted from living tissues. While AFI has been demonstrated to be useful for diagnosing colorectal neoplasms, it is unclear whether AFI can assess the severity of ulcerative colitis (UC).
AIMS & METHODS: The aim of this prospective study was to evaluate the efficacy of AFI and its quantification for detecting mucosal inflammation in patients with UC. Forty-three patients diagnosed with UC who underwent AFI at Asahikawa Medical University Hospital between 2007 and 2010 were enrolled in this study. One hundred and thirty-five areas of the colon in the enrolled patients were first photographed using conventional endoscopy, followed by AFI. Eleven endoscopists separately evaluated the photographs captured with WLE and AFI, and quantified the intensities of fluorescence. Biopsy specimens were evaluated according to Matts' criteria, and active inflammation was defined when Matts' grade was 2 or higher. 1) When the WLE image corresponded to a Mayo endoscopic subscore 0 or 1, the inflammation was categorized as inactive. AFI images were visually categorized into two groups, green-dominant (G) and magenta-dominant (M) (vAFI). 2) AFI images were quantified using an image-analytical software program. The ratio of the reverse gamma value of green (fluorescence) divided by that of red (reflex) was defined as the fluorescence index (F index). These endoscopic assessments and the F index were compared with the histological findings. A cutoff value for the F index of active inflammation was determined using an ROC analysis. 3) The inter-observer consistency of WLE, vAFI and the quantified AFI for eleven endoscopists was calculated.
RESULTS: 1) The average diagnostic accuracy of WLE and vAFI for the histological activity was 78.5% and 78.6%, respectively. No significant difference was observed between these modalities. 2) The correlation coefficient between the F index and the histological findings was closely associated with the inflammatory grade ($r = -0.558$, $p < 0.0001$). The ROC analysis showed that active inflammation was defined when the F index was less than 0.906. The average diagnostic accuracy of the F index (84.7%) was higher than that of WLE and AFI ($p < 0.01$, $p < 0.05$). 3) The kappa value for inter-observer agreement of WLE, vAFI and the F index by the overall observers, residents and experts were 0.58, 0.56 and 0.95, 0.53, 0.49 and 0.97 and 0.67, 0.64 and 0.93, respectively.
CONCLUSION: The quantified AFI is therefore considered to be a useful and objective modality for assessing the activity of ulcerative colitis, particularly by residents.
Disclosure of Interest: None declared

P0738 EFFICACY OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE TREATMENT OF RESIDUAL OR LOCALLY RECURRENT TUMOR OCCURRING IN THERAPEUTIC SCAR

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been widespread as a treatment of superficial gastric neoplasm even for ulcerative scar cases. This technique has been recently introduced as a treatment option for colorectal tumor; however, the efficacy of ESD for residual or locally recurrent colorectal tumor occurring in therapeutic scar has not been fully evaluated.
AIMS & METHODS: To clarify the clinical outcomes of colorectal ESD for residual or locally recurrent tumor occurring in therapeutic scar.
Between April 2008 and March 2014, 285 consecutive superficial colorectal tumors in 267 patients were treated using ESD. Of these, 17 lesions in 17 patients were treated as residual or locally recurrent tumor with therapeutic scar. These contained 12 that recurred after endoscopic mucosal resection (EMR) and 5 after transanal endoscopic microsurgery (TEM) (scar group). The others were defined as non-scar group and treatment outcomes and complications were evaluated between two groups.
RESULTS: In all patients, the rates of en bloc resection, R0 resection and curative resection were 98.9% (282/285), 90.2% (257/285) and 82.5% (235/285) respectively, and mean tumor size was 33.3 mm, mean treatment time was 67.2 minutes, and perforation rate was 9.5%. All patients with perforation were managed with conservative medical treatment after endoscopic closure with clipping and did not need emergent surgery.
No significant differences were observed between the two groups with respect to the rate of en bloc resection, R0 resection and curative resection; however, univariate analysis showed that perforation rate and treatment time were significantly higher and longer in the scar group compared with the non-scar group.
In addition, we evaluated age, sex, tumor location, tumor depth, tumor size, tumor morphology and the presence of therapeutic scar by multivariate analysis, and found that large tumor size and the presence of therapeutic scar were an independent risk factor for both perforation and long treatment time.
CONCLUSION: This finding implies that colorectal ESD may be used as a treatment choice for residual or locally recurrent tumor occurring in therapeutic scar. However, we need to perform ESD in consideration of the risk for perforation, and it will require cooperation with surgery when treating those cases.
Disclosure of Interest: None declared

P0739 EDUCATION FOR WARD NURSES INFLUENCES ON THE QUALITY OF INPATIENT'S BOWEL PREPARATION FOR COLONOSCOPY

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INTRODUCTION: Although adequate bowel preparation is prerequisite to colonoscopy, preparation for inpatients is often suboptimal.
AIMS & METHODS: This study aimed to evaluate the impact of education for ward nurses on the quality of inpatients' bowel preparation. A prospective, endoscopist-blinded, non-randomized, controlled study was performed. Gastroenterology experts provided the education to nurses who belonged to educated ward and this education was repeated every week for 1 month. 103 inpatients in educated ward and 102 inpatients in control ward of gastroenterology department who were scheduled for colonoscopy were enrolled. The primary outcome was the quality of the bowel preparation using the Ottawa Bowel Preparation Scale (OBPS). The secondary outcomes were polyp detection rate (PDR), patient compliance and subjective feelings.
RESULTS: Baseline data including patient characteristics, indication of procedure, and preparation quality before the study were comparable between 2

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Indication (n)	Ileoscopy abnormal			Ileoscopy normal			P value (all / clinically relevant)
	Number	Biopsy abnormal	Clinically relevant	Number	Biopsy abnormal	Clinically relevant	
Diarrhoea (67)	15	11	9	52	7	3	<0.001 / <0.001
Abdo pain (39)	12	9	8	27	3	2	<0.001 / <0.001
IBD assessment (29)	12	10	9	17	3	3	<0.001 / 0.006
Other* (18)	2	2	1	16	3	1	0.194 / 0.284
Total≠ (129)	34	25	21	95	14	1	<0.001 / <0.001

wards. Mean scores of OBPS were 4.42±2.23 and 6.15±2.38 in educated and control ward, respectively ($p<0.001$). Rate of poor preparation (OBPS <6) in educated ward was significantly lower than that of control (31.1% vs. 58.8%, $p<0.001$). PDR of educated ward was significantly higher than that of control ward (74.8% vs. 52.0%, $p=0.001$). Compliance with preparation and diet instructions in education group was superior to that in control ($p<0.001$). Control group was more likely to be anxious before colonoscopy ($p<0.001$) while education group showed a higher level of satisfaction with better sleep quality ($p<0.001$). In multivariate analysis, no ward nurse education (OR 2.36, $p=0.025$), constipation (OR 6.52, $p<0.001$) and no additional water ingestion (OR 2.05, $p=0.042$) were factors associated with poor bowel preparation.

CONCLUSION: Ward nurse education is effective to improve the quality of inpatient bowel preparation, PDR, and compliance. Additional effort is needed to control constipation and to encourage additional water ingestion for better inpatient bowel preparation.

Disclosure of Interest: None declared

P0740 WHEN SHOULD I TAKE TERMINAL ILEAL BIOPSIES? EXPERIENCE FROM A SINGLE UNIT

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INTRODUCTION: Terminal ileum (TI) intubation at colonoscopy may be useful in the investigation of patients with diarrhoea or possible inflammatory bowel disease.[1,2] The yield of TI biopsies has been shown to be variable and there are no standards for current practice.[2,3] Furthermore, in the UK, concerns remain regarding the potential for prion transmission.

AIMS & METHODS: We aim to establish the yield of TI biopsies in a single unit.

All TI biopsies recorded on the pathology system in a 3-year period were reviewed. Colonoscopy reports for these cases were reviewed, as well as case records to establish if biopsy results were clinically relevant (defined as leading to a change in management). Statistical analysis was performed using SPSS. P values were calculated using the Fisher's exact test to show any difference in biopsy yield between normal and abnormal looking mucosa for each indication. The values were calculated for all abnormal biopsy results, and for clinically relevant biopsy results.

RESULTS: 129 TI biopsies were taken between September 2010 and September 2013, 49 (38%) male and 80 (62%) female. Mean age 44 years (s.d. 17.2). There were 29 (22.5%) cases of known inflammatory bowel disease (IBD). 5 (3.9%) cases were completion colonoscopies after colorectal cancer surgery, where TI biopsies are taken to prove a complete examination.

CONCLUSION: We demonstrate that when investigating patients with diarrhoea, abdominal pain, or IBD, if the terminal ileum is visually normal, biopsies do not add to the clinical picture. There is a higher yield of relevant biopsy abnormalities when the TI appears abnormal. We can recommend within our practice that a visual assessment of a normal terminal biopsy is adequate, thereby reducing unnecessary biopsies. This reduces the workload for pathology laboratories, reduces risk from biopsies, and improves patient care as normal results can be communicated sooner to the patient.

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P0741 PHARMACODYNAMIC AND CLINICAL EVALUATION OF LOW-VOLUME POLYETHYLENE GLYCOL (PEG)-BASED BOWEL CLEANSING SOLUTIONS (NER1006) USING SPLIT DOSING IN HEALTHY AND SCREENING COLONOSCOPY SUBJECTS

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INTRODUCTION: The effectiveness of PEG3350+electrolytes based solutions for bowel cleansing prior to endoscopy is well established but require patients to drink ≥3L of fluid. Reducing this volume without compromising efficacy/safety is the next challenge.

AIMS & METHODS: This open-label, randomised, 2-part (Part A: healthy subjects; Part B: screening colonoscopy subjects), phase II study investigated the pharmacodynamics (stool weight), tolerability, and clinical efficacy of dose- and taste-optimised low-volume PEG-based formulations (NER1006) after split dosing compared with MOVIPREP®. Subjects (40–70y) were randomised to 1 of 4 treatment arms in Parts A and B (1:1:1:1): 3 formulation arms for NER1006; 1 for MOVIPREP. NER1006 consisted of different PEG3350 formulations, mineral salts (including ascorbate), electrolytes and flavouring, reconstituted with water plus additional intake of specified volumes of water (Table). Treatment was administered on Day 1 (evening dose) and Day 2 (morning dose). The primary endpoint in Parts A and B was 24h stool weight (desired target ≥2750g). Cleansing success rate (Harefield Cleansing Scale) was a co-primary endpoint in Part B. Secondary endpoints included time and volume of study drug to reach clear effluent, safety and tolerability (vomiting rate).

RESULTS: 120 subjects were included in each part (n = 30/arm). 24h stool weight was significantly >2750g for NER1006 formulations OPT002 and OPT003 in Part A, and OPT003 and OPT007 in Part B. Reversed order of administration of the split dose (i.e., TF043 morning/TF048 evening) in OPT002 was as efficacious, with a similar safety profile. Most subjects in the NER1006 arms reached clear effluent. Mean volume of study drug required and time to reach clear effluent are shown in the Table. In Part B, cleansing success rate was: 100% for OPT003 and OPT007; 90% for OPT006 and OPT004. For subjects who completed dosing, vomiting rates were <7.0% and <3.5% for all treatments in Parts A and B, respectively, with no significant differences between arms in either part.

CONCLUSION: In healthy and screening-colonoscopy subjects, the new low-volume, split-dose bowel preparation NER1006 achieved high quality bowel cleansing comparable with MOVIPREP. Stool output was consistently higher with NER1006 treatments, and safety/tolerability profiles between treatments were comparable.

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Table Pharmacodynamics of different technical formulations (TF)/administration volumes of NER1006

Arm (formulation)	Evening dose formulation (reconstitution vol+additional vol, mL)	Morning dose formulation (reconstitution vol+additional vol, mL)	Mean stool weight, g (p-value vs target)	Mean time to clear effluent, h	Mean volume of drug required to reach clear effluent, mL
Part A:					
1 (OPT001)	TF048 (750+875)	TF043 (500+875)	2951 (0.2176)	15.8	1139
2 (OPT002)	TF043 (500+875)	TF048 (750+875)	3219 (0.0042)	12.3	900
3 (OPT003)	TF047 (500+1000)	TF043 (500+1000)	3399	17.8	944
4 (OPT004)	MOVIPREP (1000+500)	MOVIPREP (1000+500)	(<0.0001)		
2491 (0.8764)	17.7	1929			
Part B:					
1 (OPT003)	TF047 (500+1000)	TF043 (500+1000)	3050 (0.0268)	14.9	860
2 (OPT007)	TF047 (500+500)	TF043 (500+500)	3215 (0.0004)	16.9	956
3 (OPT006)	TF047 (500+1000)	TF044 (500+1000)	2675 (0.4907)	17.7	935
4 (OPT004)	MOVIPREP (1000+500)	MOVIPREP (1000+500)	2487 (0.9691)	16.3	1790

Disclosure of Interest: M. Halphen Consultancy for: Norgine, B. Tayo Other: Norgine, S. Flanagan Other: Norgine, L. Clayton Other: Norgine, R. Kornberger Financial support for research from: Norgine

P0742 OLYMPUS "NEAR FOCUS" NARROW BAND IMAGING (NBI) VS CONVENTIONAL NBI FOR IN VIVO ENDOSCOPIC HISTOLOGY OF COLONIC POLYPS: A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: A lower diagnostic accuracy of pathologic in vivo diagnosis with NBI has been described in nonacademic settings compared to expert centers. Recently, Olympus has launched the 190 series, which has a pushbutton-controlled optical magnification system (near focus).
AIMS & METHODS: Aims: to assess the reliability of the near focus system compared to conventional NBI in the histologic prediction (adenoma vs hyperplastic) of small (6-9 mm) and diminutive (1-5 mm) colonic polyps. Secondary objective was to assess the fulfillment of PIVI criteria.[1]
Patients and methods: Patients scheduled for colonoscopy were consecutively included. Patients were assigned to 190 series (group 1) or 180 series (group 2) endoscopes using a computer-generated random number sequence. A sample size calculation was performed, and a minimum of 136 lesions per group was programmed. All examinations were performed by the same endoscopist (MBB) with expertise in NBI analysis. NICE classification criteria[2] were used for *in vivo* histological diagnosis.
RESULTS: 98 patients were included (49 women, 50%), median age 63 yr. CRC screening was the most frequent indication (51%). Group 1 was comprised of 51 patients (52%). Finally 333 lesions were included, 82.6% from 1 to 5 mm of diameter, and 231 (69.4%) adenomas. Under NBI examination, the histology of 277 lesions (83.2%) was predicted with high confidence. The 51 patients from group 1 harbored 171 lesions (142 predicted with high confidence) and the 48 patients from group 2 harbored 162 lesions (135 predicted with high confidence). Sensitivity, specificity and diagnostic accuracy for lesions diagnosed with high confidence in both groups are summarized in table 1. There were no differences in diagnostic accuracy between both groups (92.2% vs 89.6%, p = 0.5).

(%) (CI 95%)	Group 1		Group 2	
	High confidence	High confidence Diminutive lesions	High confidence	High confidence Diminutive lesions
Sensitivity	91.8 (85.9-97.7)	90.0 (82.8-97.2)	91.2 (84.8-97.6)	87.7 (78.9-96.5)
Specificity	93.2 (84.6-100)	94.1 (84.7-100)	86.4 (75.1-97.6)	86.4 (75.1-97.6)
Accuracy	92.2 (87.5-97.0)	91.2 (85.6-96.9)	89.6 (84.1-95.1)	87.2 (80.4-93.9)

Six (10.3%) of the 54 diminutive lesions located in rectum and sigmoid colon and diagnosed as hyperplastic with NBI were finally categorized as adenomas. The overall NPV for the diagnosis of adenoma was 89.7%. In 61 (95.3%) out of the 64 patients in whom a colonoscopy control was scheduled, there was an agreement between NBI and the final pathological diagnosis (kappa = 0.9), without differences between groups.
CONCLUSION: The near focus technology does not increase the diagnostic accuracy of conventional NBI at least for an expert examinator. NBI achieves a good accuracy for in vivo pathological diagnosis, fulfilling PIVI criteria; therefore it may represent an alternative to pathological diagnosis in a near future.
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Disclosure of Interest: None declared

P0743 CONFOCAL LASER ENDOMICROSCOPY FINDINGS IN PRIMARY SCLEROSING CHOLANGITIS (PSC) -IBD PATIENTS

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INTRODUCTION: Controversy exists as to whether the colitis seen in patients with primary sclerosing cholangitis (PSC) represents a different entity than that classically observed in patients with Crohn's disease (CD) or ulcerative colitis (UC). Specific differences have been described in the nature of the endoscopic and histological findings. Confocal laser endomicroscopy (CLE) is a new technology which enables real time endoscopy and histological investigation. PSC colitis has not been investigated by CLE.
AIMS & METHODS: To describe the CLE appearance in the colon in patients with PSC, with or without associated IBD. **Patients and Methods** 24 patients (16 male: median age 43y, range 20-71y) with PSC underwent colonoscopy with CLE (Pentax, Tokyo) between 02/12 and 12/13. The Mayo endoscopy sub-score was used to grade endoscopic findings in UC, and the SES-CD score was used to describe the white light findings in CD. CLE findings were classified using the 4 grade classification system of inflammation, describing crypt architecture, infiltration of the cells, microvasculature alteration and leakage of fluorescein. CLE images were collected for each segment of the colon, and targeted biopsies were taken for histologic analysis.
RESULTS: Of the 24 PSC patients, 20 had co-existent IBD (10UC, & 10CD). Absence of rectal inflammation based on CLE findings was seen in 20/24 patients. 10/24 had moderate to severe inflammation present in the right colon with irregular, decreased or necrotic crypts. Two patterns of fluorescein leakage were observed. A) In 10 patients leakage of fluorescein were observed in spaces amongst epithelial cells, or non-uniform abundant leakage in the lumen of the crypts associated with moderate to severe inflammation; B) In 12 patients we observed uniform leakage of the fluorescein into the lumen of crypts in the left side of the colon, associated with normal crypt architecture and micro-vasculature - the absence of active inflammation was confirmed by histology. The remaining 2 patients did not showed leakage of fluorescein. Four patients did not have a diagnosis of IBD but 3 of these patients had subtle inflammation on CLE characterized by cellular infiltration within the lamina propria in the sigmoid colon and rectum (by histology). One had a new diagnosis of UC after examination by CLE and colonoscopy.
CONCLUSION: CLE effectively characterizes the inflammation of PSC –IBD patients, confirming that these patients are likely have a different phenotype with inflammation in the right side of the colon and rectal sparing. The finding of uniform leakage of fluorescein into the lumen of the crypts, in the absence of active inflammation, may represent a defect in the intestinal barrier. Even patients not known to have IBD associated with PSC may demonstrate subtle infiltration of mononuclear cells into the lamina propria as demonstrated at CLE.
Disclosure of Interest: None declared

P0744 ANALYSIS OF THE ENDOCYTOSCOPIC IMAGE OF COLORECTAL LESION FROM THE ASPECT OF MICRO VASCULAR PATTERN

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INTRODUCTION: Endocytoscopy (EC) is an ultra-magnification technique, which can be performed to evaluate structural and cellular atypia with observation of lumens and nuclei in the surface layer of the mucosa. EC has made it possible to diagnose living tumor cells in vivo and to obtain an ultra-magnification pathological image simply by applying the scope to the target mucosa during an endoscopic examination. On the other hand, analysis of the surface microvessels of colorectal lesions using magnifying narrow-band imaging is useful for identifying the appropriate treatment method for colorectal lesions. In addition, the surface microvessels can be analyzed using EC.
AIMS & METHODS: The aim of this study was to investigate whether the observation of surface microvessels using EC was useful in predicting the histopathology of colorectal lesions.
The study included 273 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April 2006 and December 2013. A total of 337 lesions (10 normal mucosae, 23 hyperplastic polyps, 210 adenomas, and 94 submucosally invasive cancers) were retrospectively evaluated. The colonic surface micro-vascular patterns observed using EC were classified into the following 3 groups: EC-V1, the surface microvessels were obscure; EC-V2, the surface microvessels were clearly observed, and their caliber and arrangement were uniform; and EC-V3, the surface microvessels were thick, and their caliber and arrangement were non-homogeneous.
RESULTS: The sensitivity, specificity and accuracy of EC-V1 for diagnosis of hyperplastic polyp were 97.0%, 99.0% and 98.8%, respectively. As regards the sensitivity, specificity and accuracy of EC-V3 for diagnosis of invasive cancer were 84.7%, 97.7% and 94.1%, respectively.
CONCLUSION: Vascular patterns of colorectal cancers observed by endocytoscopy were useful in predicting the histopathology of colorectal lesions.
Disclosure of Interest: None declared

P0745 EXCELLENT PROGNOSIS OF ENDOSCOPICALLY RESECTED RECTAL NEUROENDOCRINE TUMORS DESPITE THE FREQUENT PRESENCE OF LYMPHOVASCULAR INVASION

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INTRODUCTION: Endoscopic resection (ER) is increasingly used to treat small rectal neuroendocrine tumors (NETs). Currently, several guidelines recommend ER as a treatment of rectal NETs less than 10 mm without muscularis invasion. However, limited data are available on the long-term outcomes of rectal NETs treated by ER. In addition, the significance of known risk factors for metastasis of rectal NETs, including lymphovascular invasion, remains elusive.
AIMS & METHODS: The aim of this study was to clarify the prognosis of rectal NET patients treated by ER and to characterize the known risk factors for metastasis of these lesions. Ninety-eight patients underwent ER for rectal NETs at our institution between 1997 and 2011. Among them, 3 patients who underwent colectomy for colorectal cancers after ER of rectal NETs and 8 patients with a follow-up period shorter than 1 year were excluded. Thus, a

total of 87 patients with 91 lesions were included in this study. The patients' records were retrospectively analyzed for clinical outcomes and pathological findings including size, invasion depth, and lymphovascular invasion. Also, we additionally evaluated tumor proliferation by Ki-67 immunohistochemistry and lymphovascular invasion using elastic staining and double staining immunohistochemistry (CD31/synatophysin and D2-40/synaptophysin).
RESULTS: ER procedures included endoscopic submucosal resection with a ligation device (ESMR-L) (n = 82), EMR (n = 5), and ESD (n = 4), with an R0 resection rate of 90.1% (ESMR-L 76/82, EMR 3/5, and ESD 3/4, respectively). No major complications were observed. All cases were followed up without surgery after ER; with the median follow-up period of 68 months (range, 12–167), no metastasis or recurrence was detected and the 5-year overall survival rate was 95.9%. The median tumor size of these cases was 5 mm (range, 2–13) and no lesion showed invasion beyond the submucosal layer. Based on the results of Ki-67 immunohistochemistry, all 91 lesions were classified as NET G1 (WHO 2010 classification). The original diagnoses based on haematoxylin and eosin staining identified no case with lymphatic invasion and only one case with positive venous involvement. However, additional analysis using elastic staining and double staining immunohistochemistry revealed lymphovascular invasions in 33 lesions (36.3%) by elastic staining, 9 lesions (9.9%) by CD31/synaptophysin double staining, and 23 lesions (25.3%) by D2-40/synaptophysin double staining. Collectively, lymphovascular invasion was identified in a total of 42 lesions (46.2%) with at least one of these staining procedures. Size of NETs with lymphovascular invasion (median, 5 mm; range, 3–13) was significantly but only slightly larger than that of NETs without lymphovascular invasion (median, 4 mm; range, 2–10; $p = 0.02$, Mann–Whitney U test).
CONCLUSION: Long-term clinical outcomes of rectal NETs following ER were favorable. While lymphovascular invasion was believed to be a strong risk factor for metastasis, a detailed analysis revealed that it was frequently present even in minute rectal NETs. The present results raise a question on the clinical significance of lymphovasucalar invasion in small rectal NETs.
Disclosure of Interest: None declared

P0746 HIGH PRESSURE JET INJECTION OF VISCOUS SOLUTIONS FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): ABOUT THE 45 FIRST HUMAN CASES IN 4 EXPERT CENTERS

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INTRODUCTION: Long lasting lifting is a key factor during ESD and can be obtained by water-jet injection of saline solution or by injection of viscous macromolecular solutions. In a previous animal study, we assessed the ability of the Nestis Enki II system to combine jet injection and macromolecular viscous solutions. In the present work, we used this combination in humans in the different sites of the digestive tract.
AIMS & METHODS: To assess the effectiveness and safety of Nestis® system using viscous solutions. We report retrospectively all the consecutive cases of ESD procedures made with Nestis Enki II system with injection of viscous solutions. Information was collected about: the lesion (site, histology), the procedure (time, perforations, bleedings, monobloc or piece meal resection), the piece (size, R0, Rx or R1 resection) and the outcomes for the patient (curative treatment, surgery, recurrence, delayed complications).
RESULTS: 45 resections were complete macroscopically. Procedures were performed by 6 operators: 5 experts and one beginner with only one previous experience in human ESD (11). The lesions were: 22 lateral spreading tumors of the rectum 11 gastric lesions, 10 esophageal lesions, 1 of the right colon and 1 of the second duodenum. The average maximal lesion diameter was 4.8 cm (SD 2.4, range 2-11 cm), the average surface was 19.8 cm2 (SD 17.7, range 2.2-72 cm2) and the average time of procedure was 79.9 min (SD +/- 50.3, range 19-225 min). Three adverse events occurred with two diminutive perforations (and two delayed bleedings treated conservatively. R0 resection rate was 91.1%. Obstruction of the catheter occurred in 6 cases in bloody situations.
CONCLUSION: This is the first multicenter report on a new water jet system allowing injection of viscous solutions. This system is safe and effective and allows working in retroflexed position with different viscous solutions.
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P0747 OPTIMISATION OF ENDOSCOPIC FOLLOW-UP WAITING LISTS IN A NEW ZEALAND DISTRICT HEALTH BOARD

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INTRODUCTION: New Zealand (NZ) has the one of the highest bowel cancer death rates in the Western world, so prompt access to lower GI endoscopy for new referrals is of importance in diagnosis, treatment and prevention. However, partly as a result of follow-up colonoscopy demands, waiting lists have increased substantially, and so the NZ Ministry of Health has funded initatives to ensure appropriate clinical investiagtions are being done for the right indication at the right time.
AIMS & METHODS: We sought to evaluate an optimisation exercise of follow-up lower GI endoscopy lists in a single District Health Board covering a population of around 300.000 people in the lower North Island of North New Zealand. Evidence-based criteria were agreed by the endoscopy user multi-disciplinary group for recall criteria for repeat colonoscopy for a number of conditions, including: colorectal cancer resections; colorectal adenoma follow-up; family history of colorectal cancer; and inflammatory bowel disease surveillance. These were then applied to those patients on the waiting list for repeat endoscopic appearances in 2014 by a single consultant gastroenterologist.
RESULTS: Of 511 patients on the waiting list, >97% were for repeat colonoscopies. 164 procedures (32.1%) did not meet the criteria for repeat procedures, and were cancelled. Within 2 months of this exercise, only four primary care practitioners (2.5%) sent queries regarding cancellation, which were dealt with. 183 (35.8%) did meet the criteria, but were not being done at the appropriate time interval, so were deferred (range 6 months - 3 years). 165 (32.3%) did meet the indication for repeat procedure in the appropriate time interval, and were approved and duly listed.
CONCLUSION: Initiatives to apply evidence-based criteria for repeat endoscopic procedures can improve quality, productivity and prevent unnecessary procedures. In this real-life application in NZ, a third of repeat endoscopy workload were removed from waiting lists, and more than an additional third were deferred to a clinically appropriate time, allowing new referrals to be seen sooner. Centrally funded initiatives to apply evidence-based guidelines to help manage waiting lists may be relevant to other populations.
Disclosure of Interest: None declared

P0748 PICOSALAX PROVIDES SUPERIOR BOWEL CLEANSING TO TRADITIONAL POLYETHYLENE GLYCOL IN THE ELDERLY POPULATION

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INTRODUCTION: Lately, life expectancy was prolonged. Therefore, endoscopic procedures are performed in an elderly population too. The level of bowel cleansing during colonoscopy is one of the quality indicators that were determined in order to improve the procedure's efficacy. An elder age is one of the factors for poor preparation.
AIMS & METHODS: Aims: We aimed to evaluate the level of bowel cleansing of the elderly population, by assessing the bowel preparation with Picosalax as compared to polyethylene glycol (PEG).
Methods: Included 6,844 patients aged ≥75y (mean 81.1y±4.6) who underwent colonoscopy at our endoscopy unit during 2003-2013. 3,659 (53.5%) patients were men. 1,258 patients had preparation with Picosalax and 5,444 with PEG. The quality of bowel cleansing was assessed according to the Aronchick scale. Multivariable logistic regression analysis for good preparation were used and included: the patients' age, gender and bowel preparation type.
RESULTS: Total, good preparation was achieved in 1,024 (79.8%) patients who used Picosalax as compared to 3,528 (63.4%) with PEG ($p < 0.001$). Fair preparation was achieved in 183 (14.5%) patients by Picosalax as compared to 1,322 (24.3%) by PEG. Bad and poor preparations were reported in 44 (3.5%) and 7 (0.6%) patients who used Picosalax as compared to 544(10%) and 50 (0.9%), respectively. By using multivariable logistic regression analysis, good preparation, was significantly associated with female gender [OR: 1.38 95% confidence interval (CI) 1.24-1.52, $p < 0.001$] and Picosalax preparation [OR: 2.15 95% CI 1.85-2.5, $p < 0.001$, PEG- ref]. An increased age, was negatively associated with good preparation [OR: 0.9595% CI 0.97-0.99, $p = 0.009$].
CONCLUSION: Female gender is significantly associated with good preparation in patients aged ≥75y. The usage of Picosalax was associated with a 2.15 odds ratio for predicting good bowel preparation. Despite lack of conventional guidelines of bowel preparations regimens for the elderly population, the usage of Picosalax is indicated as an effective preparation for this age group, too.
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Disclosure of Interest: None declared

P0749 MULTIPURPOSE USE OF THE OVER-THE-SCOPE-CLIP SYSTEM: SWISS EXPERIENCE IN A TERTIARY CENTER

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INTRODUCTION: The Over-the-scope-clip (OTSC) system (Ovesco Endoscopy AG, Tübingen, Germany) is a fairly new endoscopic device suitable to close gastrointestinal (GI) perforations, post-surgical fistulae or to resect submucosal tumors. It can also be used as hemostatic tool in GI bleeding and for esophageal stent fixation. To the best of our knowledge, in literature there are only case reports or small case series regarding the efficacy and safety, so far human clinical randomized controlled trials are not available. The available case series and reports are inhomogeneous concerning indication, study design, site of application and definition of success.
We present a prospective case series reflecting our all-day clinical experience with OTSC in a tertiary endoscopy center in Switzerland. This case series illustrates the primary successful closure in over 80% of GI lesions, mainly fistulae or anastomotic leakages and adds data to the increasing experience with this tool.
AIMS & METHODS: Aim: To evaluate the outcome of the over-the-scope-clip system (OTSC) regarding various indications in all-day clinical practice in Switzerland.
Methods: This is a prospective, consecutive case series conducted at a hospital with tertiary care endoscopy from September 2010 until January 2014. Indications were fistulae, anastomotic leakages, perforations, deroofed submucosal lesions for biopsy, refractory bleeding and stent fixation in the gastrointestinal (GI) tract. Primary technical success was defined as an adequate deployment of the OTSC on the target lesion. Clinical success was defined as resolution of the problem, for instance no need for surgery or further endoscopic intervention. In case of recurrence retreatment of a lesion with a second intervention was possible. Complications were classified into those related to sedation, endoscopy or deployment of the clip.
RESULTS: A total of 28 OTSC system applications were carried out in 21 patients (median age 64 years [range 42-85], 33% females). Main indications were fistulae (52%), most of them after percutaneous endoscopic gastrostomy (PEG) tube removal and anastomotic leakage after GI surgery (29%). Further indications were unroofed submucosal lesions after biopsy, upper gastrointestinal bleeding or esophageal stent fixation. 48% of the OTSC were applied in the upper and 52% in the lower GI tract. The range of lesion size was 2-20 mm (mean 8 mm). Primary technical success and clinical success were achieved in 85% and 67%, respectively. In 53% of cases the suction method was used without accessories like Twin grasper or Tissue anchor. No endoscopy-related or OTSC-related complications were described.
CONCLUSION: OTSC is a useful tool for endoscopic closure of various GI lesions like fistulae or leakages. Future randomized prospective multicenter trials are needed.
Disclosure of Interest: None declared

P0750 INVESTIGATING THE INVESTIGATION - INCIDENTAL COLONIC HOTSPOTS ON PET-CT SCANS

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INTRODUCTION: Positron emission tomography (PET) measures metabolic changes at a cellular level enabling detection of early stage disease. Incidental 2-deoxy-[^{18F}F]fluoro-2-D-glucose (FDG) colonic uptake is detected in 1.3-3% of patients with up to a third resulting in false positive results [1]. Follow-up endoscopy is recommended to further distinguish these FDG avid lesions [2]. Cancer detection rates of 7.8-18.9% have been quoted in various studies [1,3]
AIMS & METHODS: Our aim was to evaluate incidental colonic FDG avid lesions on PET-CT by endoscopy.
An analysis of retrospectively collected database of all patients (n = 1564) who had PET-CT for extra-colonic malignancy between January 2011 to September 2013 was performed.
RESULTS: Fifty-nine (3.77%) patients had focal colonic FDG uptake and 44 (2.87%) patients went on to have colonoscopy.
Indications for PET CT for those undergoing endoscopy was lung carcinoma (22), oesophageal carcinoma (5), gastric carcinoma (3), head and neck carcinoma (7), lymphoma (6) and unknown primary (1).
Median age was 68 with a male preponderance (2.4:1).
Location on PET CT was categorized to sigmoid (22), rectal (9), anorectal (4), caecal (3), hepatic flexure (2), transverse (1), splenic flexure (1), ascending (1) and descending (1).
Findings on endoscopy ranged from polyps (21), normal (9), diverticulosis (8), sigmoid cancer (4), caecal cancer (1) and colitis (1).
In total, out of the all patients who had endoscopy, 19 (43.2%) were found to have low-grade tubullovillous adenomas, 5 (11.1%) had cancer, whilst 2 (4.4%) had hyperplastic polyps on histology.
CONCLUSION: These findings are in keeping with other series and suggests to carry on with current practice of following up these "hot-spots" with endoscopic investigations.
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Disclosure of Interest: None declared

P0751 VARIATIONS IN ADENOMA DETECTION RATES IN THE ENGLISH FLEXIBLE SIGMOIDOSCOPY SCREENING PROGRAMME

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INTRODUCTION: The English Bowel Cancer Screening Programme has been expanded to include a one-off flexible sigmoidoscopy offered to all 55 year olds, called BowelScope Screening. Screening commenced in May 2013, with 6 pilot sites performing flexible sigmoidoscopies in the first 8 months of screening.
AIMS & METHODS: We aim to describe ADR in BowelScope Screening. The NHS Bowel Cancer Screening System database was interrogated and ADRs reviewed for each screening centre and screening endoscopist. ADR was reviewed graphically, with a funnel plot, constructed using the log odds method.
RESULTS: 49 endoscopists have performed 4444 sigmoidoscopies at 6 screening centres. Endoscopists had performed 2-330 procedures (median 66, mean 91). 29 endoscopists had performed ≥50 procedures; of these, 17 had performed ≥100 procedures.
Centre 2 has a higher ADR than the other centres. When considering all procedures, this difference reaches statistical significance when compared to centres 3, 5, and 6 ($p < 0.05$), and approaches significance when compared to centre 1 ($p = 0.0687$) and centre 4 ($p = 0.0548$). When considering only the procedures done by endoscopists who have performed ≥50 or ≥100 sigmoidoscopies, there remains a significant difference ($p < 0.05$) between centre 2 compared to centres 5 and 6, but not to the other centres. A funnel plot of individual endoscopist ADRs demonstrates one endoscopist below the 99.8% control limit.
Overall BowelScope ADR is 8.6%. ADR by centre is shown in Table 1.
Table 1 - ADR by centre and endoscopist volume

	Centre 1	Centre 2	Centre 3	Centre 4	Centre 5	Centre 6	**All Centres**	
Endoscopist procedure counts	ADR %	ADR %	ADR %	ADR %	ADR %	ADR %	**ADR %**	**ADR range %**
All	8.8	11.7	8.9	7.6	6.5	7.3	**8.6**	**0.0-60.0**
≥50	8.9	11.3	8.1	8.6	6.4	6.4	**8.6**	**3.1-14.0**
≥100	9.0	11.3	8.9	8.6	3.1	5.2	**8.7**	**3.1-13.0**

CONCLUSION: Adenoma detection rates within BowelScope screening show variation between centres. There is also variation between endoscopists in terms of individual ADRs, although all but 1 endoscopist are above the 99.8% lower control level on funnel plot. These variations require further exploration at both centre and individual level, and feedback and education methods will be used to improve ADRs.
Disclosure of Interest: None declared

P0752 FLEXIBLE SIGMOIDOSCOPY SCREENING IN THE ENGLISH BOWEL CANCER SCREENING PROGRAMME - EARLY RESULTS FROM THE BOWELSCOPE PILOT SITES

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INTRODUCTION: UK population colorectal cancer (CRC) screening has been successfully implemented with Bowel Cancer Screening Programme (BCSP) faecal occult blood testing biannually from age 60-75.
A large UK study of once-only flexible sigmoidoscopy (FSIG) demonstrated a reductions in CRC incidence of 33% & death rates of 43%1. This, with the screening centre infrastructure developed for the FOB programme, allowed provision of a new arm of BCSP, offering FSIG to 55 year olds in England, known as BowelScope screening.
BowelScope screening began May 2013, with 6 pilot sites performing FSIGs in the first 7 months.
AIMS & METHODS: We aim to describe procedural data from the early months of BowelScope screening. Data were obtained from The Bowel Cancer Screening System (BCSS) database for all participants invited and participating in BowelScope FSIGs May-Dec 2013. Procedural data were recorded, including

insertion depth, adenoma detection rates (ADR), cancer detection, discomfort levels, entonox usage & colonoscopy conversion rates.
RESULTS: 13927 people have been invited to or opted into BowelScope screening at 6 screening centres. Overall uptake is 43.5% (range 37.0-51.9%). 4 cancers have been detected. Polyps were detected in 16.4-23.8% of procedures (mean 20.7%). Mean ADR was 8.4%. One centre has a significantly higher ADR than the other 5 sites ($p < 0.05$). (see Table 1).
Table 1 – BowelScope outcomes by anonymised centre

Screening Centre	Invitees	Attended (%)	B/S with adenoma(s)	ADR %	Cancer	Colonoscopy required (%)	Entonox used
1	3125	1128 (51.9)	100	8.9%	1	39 (3.5)	121
2	1866	524 (37.0)	64	12.1%	0	23 (4.4)	94
3	3779	1070 (40.9)	90	8.4%	0	50 (4.7)	60
4	986	311 (46.6)	25	8.0%	0	12 (3.9)	15
5	1970	625 (47.4)	38	6.1%	2	21 (3.4)	28
6	2181	479 (37.2)	30	6.2%	1	18 (3.8)	25
TOTAL	**13927**	**4135**	**347**	**8.4%**	**4**	**163 (3.9)**	**343**

Most (52.7%) procedures were completed in 6-10 minutes. 78.6% of procedures were reported as causing no or minimal pain only, with only 34 procedures (0.8%) reporting severe pain.
CONCLUSION: Uptake has varied between centres, but is lower than for the FOB arm of the BCSP. The average ADR is 8.4% (range 6.1-12.1%), lower than in the UK flexible sigmoidoscopy screening trial (12.1%, range 8.6-15.9%[1]) although the age range studied in the trial differs from this cohort.
Further work will be required to investigate the variation in uptake rates and to improve these rates. ADR variations may also need to be addressed in future work.
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Disclosure of Interest: None declared

P0753 PATIENT-REPORTED EXPERIENCE OF COMFORT AND DIGNITY IN FLEXIBLE SIGMOIDOSCOPY: DATA FROM THE NHS BOWEL SCOPE SCREENING PILOT

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INTRODUCTION: The NHS Bowel Cancer Screening Programme started flexible sigmoidoscopy (FS) screening (also known as Bowel Scope Screening, BSS) at six centres across England (Gateshead, Guildford, London, Medway, Norwich, Wolverhampton) in March 2013. The aim of this analysis was to investigate the extent to which high levels of patient satisfaction recorded in previous UK trials can be replicated in the early stages of a routine screening programme.
AIMS & METHODS: We used data from an ongoing study monitoring patient-reported experience in the pilot phase of the BSS Programme. We report data from the 'post-AM questionnaire' which is given to patients at the end of their FS appointment and supposed to be completed on the following day.
RESULTS: As of January 2014, we had received 2,324 questionnaires. Satisfaction with the test was high with 98.8% of patients being either satisfied (21.1%) or very satisfied (77.7%). Nonetheless, 43% of patients reported moderate (34%) or severe pain (9%) which was high compared with the St Marks' demonstration programme[1] and the UK Flexible Sigmoidoscopy Trial[2]. Women were three times as likely to report severe pain during the test than men (14.3% vs 4.6%), and twice as likely to find the test as more painful than they had expected (39.9% vs 20.1% respectively). Only about 1 in 10 patients reported being moderately (9.8%) or severely (1.4%) embarrassed during the test, with women being slightly more likely than men to fall into these categories (13.4 vs. 8.9%). Women also had a much stronger preference for the test to be carried out by a female practitioner than men (41.2% vs 7.1% respectively).
CONCLUSION: The vast majority of patients were satisfied with their experience of FS screening. However, levels of pain appear high when compared with previous trials. Emphasis should be placed on ensuring that patients have as comfortable a procedure as possible. Additional consideration should be given to women being able to choose the sex of the practitioner performing the test.
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Disclosure of Interest: None declared

P0754 PATIENTS' EXPERIENCE OF COLONOSCOPY IN THE ENGLISH BOWEL CANCER SCREENING PROGRAMME

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INTRODUCTION: In the English Bowel Cancer Screening Programme, colonoscopy is the standard investigation to exclude cancer in participants who receive a positive faecal occult blood test result. A questionnaire is sent to all patients 30 days post-test. These data were used to assess patients' experience of colonoscopy.
AIMS & METHODS: Anonymised data were extracted from the Bowel Cancer Screening System. These included all patients who had colonoscopy between 01/01/11 and 31/12/12. Questionnaire items on the pre-test experience (whether patients understood the risks/benefits), the hospital experience (the test itself, issues of dignity/privacy) and post-test complications (bleeding/pain) were analysed. Pearson chi-square tests were used to compare experiences by gender, high vs. low levels of socioeconomic deprivation (using Index of Multiple Deprivation scores), and whether patients reported receiving sedation or not.
RESULTS: After excluding patients outside the target date range and those who did not have colonoscopy, 76,717 patients were eligible for analysis, of whom 60,581 (79.0%) responded to the questionnaire. Nearly all patients felt they understood the risks (95.7%) and benefits (98.2%) of the test, and 97.8% felt the preparation instructions were clear. Comparison by gender and deprivation did not yield clinically meaningful (≥3%) differences. In terms of the hospital experience, virtually all patients felt they were treated with respect (98.5%) and had privacy (98.0%), but 20.8% experienced more discomfort than expected (although only 5.2% asked for the test to be stopped/paused). Procedural discomfort was moderated by gender, with more women than men reporting higher-than-expected discomfort (25.4% vs. 17.9%; $p < .0005$), and requesting that the test be stopped/paused (7.1% vs. 3.9%; $p < .0005$). Use of sedation showed only a weak association with patient experience: 22.2% of sedated vs. 20.2% of non-sedated patients reported unexpected discomfort; 6.4% vs. 4.8% asked for the test to be stopped/paused; both p-values $< .0005$). Post-test, 14.3% of patients reported pain and 6.9% reported rectal bleeding. Pain was more common in women (18.0% vs. 11.9%; $p < .0005$) but there were no other clinically meaningful differences post-test related to gender or deprivation level.
CONCLUSION: Most patients referred for colonoscopy as part of the Bowel Cancer Screening Programme have a positive colonoscopy experience. The most negative aspect of the experience was the test being unexpectedly uncomfortable. Patients are extensively counselled pre-procedure but more emphasis on managing expectations, along with continued measures to reduce discomfort and pain are required, particularly for women.
Disclosure of Interest: None declared

P0755 ENDOSCOPIC RESECTION OF GIANT COLONIC POLYPS – SIZE MATTERS!

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INTRODUCTION: Colonic polyps sized 50mm and above are traditionally treated by surgical resection. Endoscopic resection has now become increasingly common as the expertise of western endoscopists improves. There is very little published literature on endoscopic resection of these giant polyps.
AIMS & METHODS: The aim of the study was to evaluate the feasibility, safety and efficacy of endoscopic resection of giant polyps ≥50mm in size.
This was a prospective cohort study. All patients who underwent endoscopic resection of colonic polyps ≥50mm from 2007-2013 were prospectively entered into a database. We excluded all polyps with fibrosis related to previous intervention. All patients were tertiary referrals from experienced gastroenterologists. All procedures were performed by a single experienced endoscopist.
RESULTS: N = 124 polyps in 122 patients. Mean polyp size = 71mm. Range 50-170mm. 27(22%) in right colon and 97 (78%) in left colon. M:F ratio 1.1:1. All polyps were resected in a piecemeal fashion. The mean procedure time was 120 minutes (range 90 to 240).
The complication rate was 11/124(8.9%). All these patients required inpatient stay. There were 9 bleeds (3 immediate and 6 delayed), 1 post polypectomy syndrome and 1 case of split muscle fibres (clipped endoscopically). 1 case of immediate bleeding required surgery to control the bleeding. All the others were managed conservatively. 4 of the 9 bleeds required blood transfusion. The complication rate was independent of polyp size, resection technique or site of the lesion.
Follow up data was available for 90 polyps. The recurrence rate was 21/90(23.3%). Of the 21 recurrences, 16/21(76%) patients achieved complete clearance with a further 1 to 2 endoscopic procedures. The recurrence rate was significantly dependent on polyp size and was not dependent on the resection technique or the site of the lesion. Recurrence gradually increased with an increase in polyp size up to 70mm. Recurrence was seen in 3/34(8.8%) polyps ≤55mm, in 7/54(12.9%) polyps ≤60mm and in 9/63(14.2%) polyps ≤70mm. However, in polyps >70mm, the recurrence rate greatly increased to 12/27(44%) **(p = 0.002)**.

	Size			
Recurrence 21/90 (23.3%)	**≤55mm** 3/34 (8.8%)	**≤60mm** 7/54 (12.9%)	**≤70mm** 9/63 (14.2%) **p = 0.002**	**>70mm** 12/27 (44.4%)

CONCLUSION: 1) It is safe and feasible to endoscopically resect polyps 50-170mm in size.
2) Recurrence is significantly dependent on polyp size.
3) Giant polyps resected endoscopically have a significant recurrence rate. The majority of these can be cleared by further endoscopic procedures. However, we believe that the recurrence rate in polyps above 70mm is very high and surgery should be considered in these cases.
4) Complication rates are independent of size.
Disclosure of Interest: None declared

P0756 ADVISABILITY OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN ELDERLY: TREATMENT AND LONG-TERM OUTCOMES

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is becoming widespread as a treatment of superficial colorectal neoplasm; however, the efficacy and safety of colorectal ESD in elderly patients has not been fully evaluated.
AIMS & METHODS: In the present study, we assessed the treatment and long-term outcomes of colorectal ESD in elderly patients.
Between April 2008 and March 2014, 285 consecutive superficial colorectal tumors in 267 patients were treated using ESD. Patients were divided into two groups; elderly (75 years of age or older) and non-elderly (less than 75 years of age), then were retrospectively compared to patient and tumor characteristics and treatment outcome.
Long-term outcomes in elderly patients were also evaluated.
RESULTS: The elderly group comprised 93 lesions in 83 patients and non-elderly group comprised 192 lesions in 184 patients.
No significant differences were observed between the two groups with respect to patient and tumor characteristics as the following factors: sex, tumor location, tumor depth, tumor size, tumor morphology.
In all patients, the rates of en bloc resection, R0 resection and curative resection were 98.9% (282/285), 90.2% (257/285) and 82.5% (235/285) respectively. Mean procedure time was 67.2 minutes (range 10-273 minutes), the rate of delayed bleeding was 3.9% (11/285) and the rate of perforation was 9.5% (27/285). There were no significant differences between the two groups in the rates of en bloc resection, R0 resection, curative resection, delayed bleeding, perforation, and procedure time.
In 83 elderly patients, during a median follow-up period of 20.2 months (range 1.4-63 months), 6 patients were excluded from the long-term prognosis analysis because of missing follow-up. Four of 16 patients who judged as non-curative resection underwent additional surgery, and the others requested only observation. Two of 77 patients (2.6%) died of infection of unknown cause (n = 1) and heart failure (n = 1). The 3- and 5-year overall survival rates were 96.4% and 87.7%, respectively. However, we did not observe local or distant recurrences in any of the patients were followed up. Therefore, the 3- and 5-year disease-specific survival rates were 100%.
CONCLUSION: Because there was no significant difference in treatment outcome between in elderly and non-elderly group, colorectal ESD could be used as a treatment choice for superficial colorectal tumors in elderly patients. However, many of the elderly non-curative cases were observed without additional surgical treatment, implying that such patients are necessary for careful follow-up by computed tomography (CT) or measuring tumor markers.
Disclosure of Interest: None declared

P0757 A COMPARATIVE STUDY OF TWO DIFFERENT SNARES FOR THE COMPLETENESS OF POLYP EXCISION

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INTRODUCTION: Polypectomy with cold snare is a frequently used technique for the removal of small colorectal polyps. The influence of snare type on completeness of excision is unknown. We have therefore compared the effectiveness of two different snares.
AIMS & METHODS: Patients attending for colonoscopy at Sheffield Teaching Hospitals, England were prospectively included in the study. We assessed the endoscopic and histological completeness of excision following cold snare of 3-7mm polyps using the Exacto mini-snare (diameter 0.30mm) and Olympus mini-snare (diameter 0.47mm). Prior to the study, consensus regarding the endoscopic completeness of excision was standardised to complete, incomplete or uncertain using the Delphi method. Completeness of excision was aided by chromoendoscopy (indigo carmine 0.1%). The primary outcome was endoscopic completeness of excision. Secondary outcome measures included: completeness of histologic excision, polyp 'fly away', retrieval rate, early bleeding (48 hours), delayed bleeding (2 weeks) and perforation.
RESULTS: A total of 157 polyps were removed. Median (range) polyp size was 4.0mm (3-7mm). There was no significant difference in the patients' demographic details or polyp characteristics between the two groups. Endoscopic completeness of excision was significantly higher with the Exacto snare compared to the Olympus snare (90.2% vs. 73.3%, $p < 0.05$). There was also a trend towards a higher complete histological excision rate with the Exacto snare (71.9% vs. 64.4%), but this did not reach statistical significance ($p = 0.4$). Polyp 'fly away' occurred less often with the Exacto snare (14.6% vs. 35.3%, $p < 0.05$), but there was no significant difference in the polyp retrieval rate (84.3% vs. 83.8%, $p = 0.9$). There were no significant complications with either snare. Where the completeness of excision was assessable (complete or incomplete), there was a fair level of agreement (kappa = 0.36) between endoscopic and histological assessment.
CONCLUSION: This is the first study we are aware of that compares completeness of excision with different snares. Our findings suggest that snare type may be an important factor determining completeness of excision when removing small polyps by the cold snare techniques.
Disclosure of Interest: None declared

P0758 THE ROLE OF CONFOCAL LASER ENDOMICROSCOPY IN THE MANAGEMENT OF PATIENTS WITH COLORECTAL LESIONS: A CONSENSUS REPORT BASED ON CLINICAL EVIDENCE

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INTRODUCTION: Recent studies have highlighted the role of Confocal Laser Endomicroscopy (CLE) for the characterization of colorectal lesions *in vivo*, specifically for the real time characterization of polyps and endoscopic mucosal resection (EMR) sites.
AIMS & METHODS: We sought to develop consensus recommendations for the role of CLE in the management of patients with colorectal lesions. To this end, a single CLE expert developed a series of preliminary statements on the use of CLE for the characterization of colorectal lesions based on the available clinical evidence. Twenty statements were submitted for external review by a group of 16 gastrointestinal CLE experts using a modified Delphi approach. After two rounds of votes to assess the quality of evidence and strength of recommendations based on relevant studies, statements were adopted if the threshold of agreement exceeded 75%.
RESULTS: 15 of 20 statements achieved consensus and were adopted: CLE has been shown to be highly accurate for real-time histopathological classification of colonic neoplasia *in situ*. CLE criteria can be used to accurately and reliably identify normal, hyperplastic, adenomatous (dysplastic), and cancerous mucosa; criteria for serrated neoplasia require further validation. CLE criteria characterize colonic tissue accurately both in real time during endoscopy as well as off-line. CLE can be used to define the extent of flat lesions. The combination of CLE and virtual chromoendoscopy (VCE) is highly accurate for classifying colonic polyps < 5 mm both in real time and offline and should undergo further study toward enabling a resect-and-discard approach. A diagnosis of intramucosal carcinoma and/or high-grade dysplasia by CLE alone is sufficient to trigger an appropriate therapeutic resection. CLE can be used to classify lesions and define margins for EMR/ESD. CLE has a role in resurveillance 3-12 months following EMR/ESD of advanced colonic neoplasia. Absence of residual neoplasia by CLE and VCE at 3-12 months obviates the need for re-EMR/ablation. The extent of therapy for residual neoplasia post-EMR can be guided in real time by the combination of CLE and VCE.
CONCLUSION: According to a panel of 16 gastrointestinal endoscopy experts in Confocal Laser Endomicroscopy, CLE is an important adjunct to current endoscopic practice for the management of colorectal lesions. Standardized guidelines are in development to serve as an educational resource for physicians to provide increasingly personalized, state-of-the-art care for their patients.
Disclosure of Interest: None declared

P0759 IMMEDIATE AND DELAYED BLEEDING AFTER ERCP: RESULTS FROM SINGLE CENTRE EXPERIENCE AT A DISTRICT GENERAL HOSPITAL IN JAPAN

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INTRODUCTION: Bleeding following endoscopic retrograde cholangiopancreatography (ERCP) including endoscopic sphincterotomy (ES) is one of the most frequent complications, and has been reported in 1-10% of patients. Haemorrhage that cannot be controlled by conservative management needs to be controlled endoscopically, radiologically, or surgically. However, there are few reports about the incidence and the outcomes at a district hospital.

AIMS & METHODS: The aim of this study was to assess the incidence of ERCP-related haemorrhage and the clinical outcomes in the district general hospital setting. A review of all patients undergoing ERCP at our institution from April 1996 and March 2014 was performed to assess the ERCP-related haemorrhage. ERCP-related haemorrhage was classified according to the timing of bleeding. Immediate bleeding was defined as any haemorrhage during ERCP and warranting endoscopic haemostasis within the procedure following epinephrine spray. A diagnosis and severity of delayed bleeding was made according to Cotton's classification (GIE 1991).
RESULTS: Out of 6002 ERCPs, we performed ES in 975 patients, needle knife sphincterotomy (NKS) in 195 patients, NKS followed by ES in 22 patients, endoscopic papillectomy in 12 patients and endoscopic large balloon dilatation in 47 patients. No patients were taking anticoagulants at the time of ERCP. During ERCP, 48 patients (0.80%) experienced immediate bleeding. All patients underwent endoscopic haemostatic method including balloon tanponade, dilute epinephrine (1:10000), heater probe, clipping, covered metallic stent and combined hemostatic procedures. Initial haemostasis was achieved in all patients. However, delayed bleeding occurred in 3 patients (6%). By definition, delayed bleeding occurred in 26 patients (0.43%). There were 14, 5 and 7 cases of mild, moderate and severe bleeding, respectively. The time period between ERCP and haemorrhage ranged from 1 d to 14 d (median 4 d). The time to onset of delayed bleeding was not significantly different between patients with or without immediate bleeding. Seventeen out of 26 (65%) were managed endoscopically with various haemostatic methods including dilute epinephrine, heater probe, argon plasma coagulation, clipping, fibrin glue, covered metallic stent and combined procedures. Initial haemostasis was successfully attained in all patients. The re-bleeding rate was 15% (4 of 26). The treatment for the 4 patients with re-bleeding was as follows: 1 underwent 1 session, 1 underwent 2 sessions and 2 underwent 3 sessions of endoscopic combined procedures (2 patients required fibrin glue) and the bleeding was finally controlled. No patients required angiographic embolisation and surgery. No complications of the hemostatic procedure occurred in any patients. There was no bleeding-related death.
CONCLUSION: Early recognition and appropriate management of ERCP-related haemorrhage is crucial for optimal results.
Disclosure of Interest: None declared

P0760 USEFULNESS OF CAP-ASSISTED ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH DIFFICULT CANNULATION DUE TO PERIAMPULLARY DIVERTICULUM

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INTRODUCTION: Successful biliary cannulation is an essential for therapeutic retrograde cholangiopancreatography (ERCP). In special cases of difficult cannulation due to anatomy, diverticulum, lack of space or bulky papilla other methods are needed. Various methods depending on the practices of the endoscopist have been developed to overcome difficult cannulation.
AIMS & METHODS: We report a retrospective case series of patients with difficult cannulation due to periampullary diverticulum and assess the utility and safety of cap-assisted ERCP for biliary cannulation.
From November 2013 to March 2014, inclusion criteria were: (a) documented periampullary diverticulum; and (b) use of cap-assisted ERCP as a rescue method on the first endoscopic encounter after failed attempts to perform ERCP with a standard side-viewing endoscope. Among 73 patients with periampullary diverticulum, 5 consecutive patients (6.8%) underwent therapeutic ERCP using a cap-fitted forward-viewing endoscope as a rescue method due to difficult biliary cannulation.
RESULTS: There were three men and two women, with median age of 69 years (range 53–90 years). The indications for ERCP were bile duct stones (n = 4) and common bile duct stricture (n = 1). All of the ampulla is located at 6 o'clock. The causes of difficult biliary cannulation were tangential approach in two patients and hidden papilla in three patients. A selective biliary cannulation was achieved with needle knife fistulotomy in four patients. The mean number of ERCP sessions was 1.8 per patient and the mean procedure time was thirty eight minutes. Therapeutic ERCP was successfully performed in all patients. In four patients, the therapeutic ERCP was completed with a cap-fitted forward-viewing endoscope. But in the only one patient who had a pyloric stenosis with bulbar deformity due to duodenal ulcer scar, CBD stones were successfully removed by percutaneous procedure combined with rendezvous method although we performed endoscopic balloon dilation of the stenosis. The one patient undergoing biopsy was pathologically confirmed to carcinoma of ampulla of Vater. This patient was managed previously with biliary stent insertion due to biliary stricture.
Two patients experienced complications; post-ERCP pancreatitis and hyperamylasemia. But their complications were not clinically significant and self limitied.
CONCLUSION: As a rescue method, cap-assisted ERCP is effective and safe technique in patients with difficult cannulation due to periampullary diverticulum.
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Disclosure of Interest: None declared

P0761 SEQUENTIAL PERFORMANCE OF DOUBLE GUIDEWIRE TECHNIQUE AND TRANSPANCREATIC PRECUT SPHINCTEROTOMY IN DIFFICULT BILIARY CANNULATION

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INTRODUCTION: Double guidewire technique (DTG) and transpancreatic precut sphincterotomy (TPS) are alternative techniques in failed standard biliary cannulation during endoscopic retrograde cholangiopancreatography (ERCP) when a guidewire proceeds into the pancreatic duct. However, the sequential performance of TPS after DTG has not been evaluated.
AIMS & METHODS: We aimed to investigate the usefulness and complications of seqeuntial DTG-TPS in comparison with needle knife precut (NK). We consecutively enrolled 612 patients with naïve papilla undergoing ERCP for biliary cannulation between March 2010 and April 2014. In cases of unsuccessful standard technique, DTG or NK was performed according to the guidewire passage through the pancreatic duct. TPS was sequentially performed when DTG had failed. Patients' demographics, laboratory, and procedure-related data were analyzed retrospectively.
RESULTS: During 612 ERCPs, DTG and NK was attempted in 67 and 58 patients, respectively. Sequential DTG-TPS were performed in 38 patients. Successful biliary cannulation was performed in 42%, 74%, and 66% of the DTG, TPS, and NK group, respectively ($P = 0.002$). The cannulation rate was higher in the sequential DTG-TPS group (85%) than in the NK group ($P = 0.014$). Post-ERCP pancreatitis (PEP) occurred in 37% of the sequential DTG-TPS group and in 10% of the NK group ($P = 0.002$). In the sequential DTG-TPS group, PEP developed in 24% patients with pancreatic duct (PD) stent, but in 62% patients without PD stent ($P = 0.023$). Among them, one patient without PD stent expired due to severe pancreatitis.
CONCLUSION: The sequential DTG-TPS is a useful alternative technique for biliary cannulation compared with NK in patients who have failed standard technique. Their rate of PEP was higher than that in the NK group, but PD stent had a protective role over PEP.
Disclosure of Interest: None declared

P0762 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR SUSPECTED CHOLEDOCHOLITHIASIS – FROM GUIDELINES TO CLINICAL PRACTICE

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INTRODUCTION: Patients suspected of having choledocholithiasis are diagnosed with a combination of laboratory tests and/or imaging studies. The American Society for Gastrointestinal Endoscopy (ASGE) proposes a stratification of patients according to the risk for choledocholithiasis, influencing subsequent management.
AIMS & METHODS: The aim of this study was to assess the practical applicability and to validate the current ASGE guidelines in our population. This was a retrospective single center study, covering a 4-year period, from January 2010 to December 2013. All patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) for suspected choledocholithiasis were included. Based on the presence or absence of predictors of choledocholithiasis (clinical ascending cholangitis, common bile duct (CBD) stones on ultrasonography (US), total bilirubin >4mg/dL, dilated CBD on US, total bilirubin 1,8-4mg/dL, abnormal liver function test, age >55 years and gallstone pancreatitis), patients were stratified in low, intermediate or high risk for choledocholithiasis. For each predictor and risk group we used the Chi-square to evaluate the statistical associations with the presence of choledocolithiasis at ERCP. Statistical analysis was performed using SPSS version 21.0. A p value of less than 0.05 was considered statistically significant.
RESULTS: A total of 268 ERCPs were performed for suspected choledocholithiasis. Except for gallstone pancreatitis ($p = 0.063$), all other predictors of choledocholitiasis (clinical ascending cholangitis, $p = 0.001$; CBD stones on US, $p < 0.001$; total bilirubin >4mg/dL, $p = 0.035$; total bilirubin 1,8-4mg/dL, $p = 0.001$; dilated CBD on US, $p < 0.001$; abnormal liver function test, $p = 0.012$; age >55 years, $p = 0.002$) showed a statistically significant association with the presence of choledocholithiasis at ERCP. Approximately four fifths of patients in the high risk group (79.8%, 154/193) had confirmed choledocholithiasis on ERCP, versus 34.2% (25/73) and 0 (0/2) in the intermediate and low risk groups, respectively. The definition of "high risk group" had a sensitivity of 86%, positive predictive value 79,8% and specificity 56.2% for the presence of choledocholithiasis at ERCP.
CONCLUSION: The use of clinical, analytical and imaging predictors, as well as risk stratification according to ASGE guidelines, may improve risk estimation of choledocholithiasis and should be considered to optimize patients' selection for ERCP. However, even in the "high risk group" the specificity was low (56.2%), meaning that a significant proportion of patients (20%) will still perform ERCP unnecessarily. Thus, at this point, it seems advisable that also "high risk" patients undergo further testing before being submitted to ERCP, similarly to those patients with "intermediate risk", while for patients with "low-risk" of choledocholithiasis a watchful waiting strategy seems adequate.
Disclosure of Interest: None declared

P0763 THE EFFECT OF RECTAL KETOPROFEN IN THE PREVENTION OF POST ERCP ACUTE PANCREATITIS

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INTRODUCTION: Acute pancreatitis is the most common and the most fearful complication of endoscopic retrograde cholangiopancreatography (ERCP). A recently published meta-analysis reported that a single dose of indomethacin or diclofenac (100 mg) administred rectally before or immediately after ERCP decreases the incidence of post ERCP pancreatitis (PEP).
AIMS & METHODS: A retrospective single-center non randomized study was conducted with 304 patients who underwent a primary ERCP. Patients were divided into 2 groups. The patients in the first group had a single dose of ketoprofen 100mg administred rectally immediately after ERCP. The 2nd group was a control group.
The aim of this study was to determine whether prophylactic rectal ketoprofen will reduce the incidence of PEP and to determine the risk factors of this complication.
RESULTS: Three hundred and four patients (M/F = 197/107, Mean age = 62.4 y.o) were included. 107 patients (35.2%) were in the first group. The groups were similar with regard to patient demographics and to patient and procedure risk factors for PEP. The overall incidence of PEP was 6.9%: 4.6% (5/107) in the group 1 versus 8.1% (16/197) in the placebo group (p = 0.34, IC = 95%). The pancreatitis was graded as severe in 33% of the patients. There was no significant difference between the groups in the frequency or severity of PEP. Two risk factors were associated with a higher incidence of PEP:a difficult cannulation of the common bile duct (52.4 vs 16%, p = 0.0004. IC = 95%) and contrast injection into the pancreatic duct (47.62 vs 24.38 %, p = 0.008, IC = 95%).
CONCLUSION: Prophylactic rectally administered ketoprofen (100mg) did not affect the frequency or severity of PEP. Prospective randomized studies with a higher number of patients are needed.
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Disclosure of Interest: None declared

P0764 ANALYSIS OF THE ROLE OF PANCREATIC DUCTAL FUSION ANOMALIES AS A RISK FACTOR FOR DEVELOPMENT OF POST-ERCP PANCREATITIS

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INTRODUCTION: Pancreatic ductal fusion occurs in the early weeks of gestation. It has been suggested the possible association between pancreatic ductal morphology and the incidence of post-ERCP pancreatitis.
AIMS & METHODS: Our aim was to evaluate the possible association between abnormal fusion of the pancreatic duct and the development of post- ERCP pancreatitis. We reviewed the pancreatic ERCPs (PERCP) performed in our center from June 2009 to June 2013. The wirsungrafies were blindly reviewed by one ERCPist who classified the pancreatic ductal fusion unaware of the identity and evolution of patients after PERCP. The ductal fusion was classified into four groups: Normal (Group I), when the dorsal duct joined the upper branch of the ventral duct and Santorini duct; Ansa Pancreatica (Group II), when the dorsal duct was fused to the upper branch of the ventral duct but the Santorini duct was fused to the lower branch of the ventral duct; Pancreatic Loop (Group III), when the dorsal duct was fused to the lower branch of the ventral duct; and Pancreas Divisum (Group IV), when there was no fusion between dorsal and ventral duct. Incomplete wirsungrafies which could not be classified in either group were considered indeterminate and not analyzed. Groups II, III and IV were considered together as Fusion Anomalies Group (FA). We compared the incidence of post-ERCP pancreatitis in each of the groups with respect to the rest and the AF group with Group I.
RESULTS: We performed 134 PERCPs in 68 patients during the inclusion period. We were able to determine with certainty the type of ductal fusion in 56 patients (40 men). Twenty-seven patients suffered a previous acute pancreatitis bout and 28 had chronic pancreatitis. Women had significantly more FA (69 % vs 37 %, p = 0.04). Thirty patients were included in Group I; 10 in Group II; 3 in Group III and 13 in Group IV. Thus, 26 patients were included in FA Group. Complications occurred in 8 patients (14 %), pancreatitis in 5 of them (8.9%). Only Group III was significantly associated with a higher rate of post-ERCP pancreatitis (67%vs11.3%,p = 0.019). The incidence of post-ERCP pancreatitis in Group II and IV was 10 % and 15.4 % respectively. FA Group showed a significantly higher incidence of post-ERCP pancreatitis compared with Group I (19.2%vs0%,p = 0.017) and this comparison remained significant after adjusting for sex (p = 0.017). Variables such previous acute or chronic pancreatitis, sex and placement of pancreatic stent did not influenced post-ERCP pancreatitis incidence (p > 0.05).
CONCLUSION: Pancreatic ductal fusion anomalies are a risk factor for development of post-ERCP pancreatitis. This association should be confirmed by means of prospective comparative studies.
Disclosure of Interest: None declared

P0765 RETROPERITONEAL DUODENAL PERFORATION (TYPE II) AFTER ERCP IS A RARE BUT SEVERE COMPLICATION. A SINGLE - CENTER REVIEW OF TEN - YEAR EXPERIENCE

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INTRODUCTION: Duodenal perforation in the periampullary region due to sphincterotomy (Type II) is a rare post - ERCP complication with significant mortality. The aim of this study was to determine the incidence of retroperitoneal duodenal perforations after periampullary interventions, management options, and clinical outcome.
AIMS & METHODS: All cases of retroperitoneal duodenal perforation (Type II) after ERCP during a ten year period (1/2004 - 12/2013) in our Department were retrospectively reviewed. All patients were initially treated with broad-spectrum antibiotics, nasogastric aspiration and parental nutrition and/or CT-guided drainage when needed.
RESULTS: A total of 19 patients with retroperitoneal duodenal perforation (Type II) after 3428 ERCPs (0.55%) were managed. Indications for performing a periampullary procedure were known or suspected choledocholithiasis in 15 (79%) and biliary stricture in 4 patients. Diagnosis was made during the first 12h, (during the procedure in 3 cases). Radiological drainage was performed in 7 patients (36%) and were successful in all patients except one who eventually required surgery. Surgical intervention was required in 4 patients (21%). Total parental nutrition was given to 4 patients (21%). Three patients died (two post - postoperatively) giving an overall mortality of 15.8%.
CONCLUSION: Retroperitoneal duodenal perforation (Type II) is a rare complication after ERCP with high morbidity and mortality but aggressive conservative management seems effective for the majority of cases.
Disclosure of Interest: None declared

P0766 USEFULNESS OF ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION IN THE TREATMENT OF LARGE OR MULTIPLE COMMON BILE DUCT STONES: COMPARISON WITH ENDOSCOPIC SPHINCTEROTOMY ALONE

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INTRODUCTION: Endoscopic sphincterotomy (EST) is currently recognized as the main treatment for choledocholithiasis. However, the treatment of large common bile duct stones (≥15 mm in diameter) or multiple common bile duct stones (3 or more stones) by EST alone is difficult, and a new therapeutic procedure to supplant EST is needed. Sporadic reports have shown the usefulness of endoscopic papillary large balloon dilation (EPLBD) in the treatment of common bile duct stones, and this technique is anticipated to replace use of EST alone. This study aimed to comparatively assess the therapeutic outcomes and short-term complications of EST versus EPLBD in cases of biliary tract stones ≥15 mm in diameter or multiple (3 or more) stones presumed to be rather refractory to EST alone.
AIMS & METHODS: Data from 70 cases of choledocholithiasis (≥15 mm in diameter or ≥3 stones) that were treated (EPLBD, n = 34; EST, n = 36) in our department between April 2010 and March 2013 were comparatively reviewed and analysed with respect to stone removal success rate, success rate of complete stone removal in 1st session, procedure time, concomitant mechanical lithotripsy (ML) application status, and short-term complications. Stone size and number were checked by endoscopic cholangiography, and the patients treated using EPLBD underwent EST before balloon dilation. EPLBD was performed using 12–18-mm-diameter balloons, and stone collection was performed using a Dormia basket or retrieval balloon. ML was added to the procedure in case of difficulty in expelling the stones.
RESULTS: The stone removal success rate was comparable between groups (EPLBD 100% vs. EST 89%, $p = 0.115$). The EPLBD group exhibited a significantly higher success rate of a complete stone removal in 1st session (EPLBD 88% vs. EST 56%, $p = 0.03$). Further, the procedure time was significantly shorter for the EPLBD group (EPLBD 42 min vs. EST 67 min, $p = 0.011$), and the concomitant ML application rate was significantly lower for the EPLBD group (EPLBD 50% vs. EST 94%, $p < 0.001$). Short-term complication included pancreatitis in 2 patients and haemorrhage in 1 patient of the EPLBD group and pancreatitis in 8 patients and haemorrhage in 2 patients of the EST group (EPLBD 9% vs. EST 25%, $p = 0.112$), but there was no statistically significant intergroup difference.

CONCLUSION: We successfully treated large moulded (≥15-mm diameter) stone or multiple stone choledocholithiasis by EPLBD with fewer sessions and a shorter procedure time compared to EST alone. Our findings suggest the usefulness of EPLBD for difficult cases. However, it is necessary to accumulate further experience of cases and examine long-term complications.
Disclosure of Interest: None declared

P0767 PER ENDOSCOPIC MANAGEMENT OF ALVEOLAR ECHINOCCOSIS BILIARY COMPLICATIONS: A EUROPEAN SURVEY

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INTRODUCTION: Cholestasis and cholangitis are among the most common and life-threatening complications of Alveolar Echinococcosis (AE) of the liver, because of the liver invasion by the metacestode associated with extensive fibro-inflammatory host reaction. Biliary complications of AE are usually treated by surgery or radiological percutaneous biliary drainage. During the last decade the indication of per-endoscopic biliary drainage following endoscopic retrograde cholangio-pancreatography (ERCP) has markedly increased in various benign or malignant biliary tree obstructions, because of its less invasive nature and better outcome. AE is an emerging indication in this field; only little is known about its efficacy and safety.
AIMS & METHODS: Our aim was to collect and analyse the European experience in per-endoscopic management of AE biliary complications. All European physicians practicing ERCP and/or in charge of AE patients were recruited directly or through various professional/scientific associations to participate in the retrospective survey. Data were collected from May, 2013 to January, 2014. Physicians were asked to report any AE case with ERCP. Data on patients' and disease characteristics, endoscopic techniques and follow-up filled-out through an online questionnaire were analysed. Ethical Committee of Franche-Comté Hospitals approved this study.
RESULTS: Between 1986 and 2014, 12 centres performed ERCP for AE in Europe. Detailed data available for 23 patients (18 men and 5 women) in 8 centres were analysed. Sixty-one ERCP were performed (median: 2 {1-9} ERCP per patient). Patients were 55-years-old at the time of AE diagnosis and 60-years-old at the time of the first ERCP. Indications for ERCP were: biliary pain, 14 (23%), cholangitis, 24 (39%), jaundice or chronic cholestasis, 22 (36%). Seventy-four plastic stents and 7 fully (5) or partially (2) covered self expandable metallic stents (SEMS) were placed in the biliary tree. The average time between two stenting procedures was 19.5 weeks (1-98). Two patients needed surgical intervention or radiological drainage because of endoscopic treatment failure. There were 11 adverse events (18%): 1 perforation, 1 hepatic collection, 4 acute pancreatitis, and 5 cholangitis. Resolution of cholestasis was obtained in 42/44 therapeutic ERCP (95.4 %). Biliary duct calibration was obtained by stent placement in 8 patients after an average of 2 procedures; definitive stent removal was possible after a median time of 45 weeks of treatment. Among them, recurrence of stenosis led to a new stent placement 4 years later in 1 patient and gallstones extraction in 2 patients.
CONCLUSION: Endoscopic retrograde drainage is efficient in AE with biliary obstruction. ERCP and stenting, which are less invasive than surgery and avoid long-term external drainage, may be proposed as a valid alternative to radiological and surgical drainage. Several procedures with stenting are usually needed to ensure long-term efficacy and using of antibiotics are necessary during and after the ERCP.
Disclosure of Interest: None declared

P0768 A STUDY TO INVESTIGATE RISK FACTORS FOR ASPIRATION PNEUMONIA AFTER ERCP

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INTRODUCTION: Aspiration pneumonia is the one of complications of various Endoscopic procedures. But there have been few reports of that complication after Endoscopic retrograde cholangiopancreatography (ERCP).
AIMS & METHODS: The aim of this study is to identify the rate and risk factors for aspiration pneumonia after ERCP.
978 consecutive patients who underwent ERCP between January 2011 and December 2013 were included. The cumulative rate and potential risk factors for aspiration pneumonia, such as patient attributes (Age, sex, underlying conditions, and medication) and ERCP procedures were retrospectively investigated.
RESULTS: Of the 978 patients 673 patients were male (68.8%). The median age was 71.4 years (29-99y.o). 55 patients (5.62%) were diagnosed with aspiration pneumonia after ERCP. Age over 75years (OR:5.11 P < 0.0001), a procedure time of >30min (OR2.31 P < 0.0059), the infusion of naloxone (OR :3.68 p = 0.0151), history of heart disease (OR: 2.24 p = 0.0083), eGFR < 30 (OR :5.45 P < 0.001), hemodialysis (OR :5.95 P < 0.0001), cancer-bearing (OR :1.96 p = 0.03), diabetes (OR :2.08 p = 0.0213), history of cerebral infarction (OR:3.68 P < 0.0001) and serum Alb < 3.5mg/dl (OR:5.76 P < 0.0001)were identified as the risk factors for the pneumonia by the univariate analysis. Multivariate analysis showed age over 75years (OR:3.26 p = 0.0018), a procedure time of >30min (OR:2.55 p = 0.0062), history of cerebral infarction (OR:3.06 p = 0.0063), serum Alb < 3.5mg/dl (OR:3.11 p = 0.00016)and hemodialysis (OR:2.59 p = 0.048)were revealed to be the significant risk factors for aspiration pneumonia after ERCP.
CONCLUSION: Age over 75years, a procedure time of >30min, history of cerebral infarction, serum Alb < 3.5mg/dl and hemodialysis are the independent risk factor for the aspiration pneumonia after ERCP. Careful attention should be taken when managing patients with these attributes.
Disclosure of Interest: None declared

P0769 EVALUATION FOR ERCP USING A BALLOON ASSISTED ENDOSCOPY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY: COMPARISON OF A SHORT TYPE DOUBLE BALLOON ENDOSCOPE AND A NEWLY DEVELOPED SHORT TYPE SINGLE BALLOON ENDOSCOPE

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INTRODUCTION: The advent of the short type double balloon endoscope (s-DBE) and the short type single balloon endoscope (s-SBE) radically made the endoscopic approaches feasible for pancreatobiliary diseases in patients with altered gastrointestinal anatomy, which had been considered unpractical. Recently many papers are published to report the efficacy of using these techniques, however, there are so far few studies regarding the comparison of s-DBE and s-SBE.
AIMS & METHODS: This present study aimed to evaluate the usefulness of a newly developed s-SBE for therapeutic ERCP in patients with gastrointestinal anatomy, and also to make a comparative assessment of the respective features and the distinctions of s-DBE and s-SBE. From March 2013 to November 2013, ERCP using a s-SBE (s-SB-ERCP) was performed in 26 postoperative patients who had a reconstructed intestine in our hospital. We retrospectively evaluated the success rate of reaching the blind end, the mean time required to reach the blind end, the diagnostic success rate, the therapeutic success rate, the mean procedure time, and complications. Among 26 patients, the s-SB- ERCP was applied to those 18 patients who previously had undergone s-DB-ERCP and required the recurrent procedure. It allowed us the unique comparison of the s-DBE and the s-SBE in the same patients analyzing the data of the mean time required to reach the blind end and the mean procedure time.
RESULTS: The success rate of reaching the blind end was 92.3% (24/26 patients). As for 2 patients in whom s-SBE failed to reach the blind end, the procedure was successfully accomplished after switching the scope to s-DBE. The mean time required to reach the blind end was 28.6 min. (range, 5–58 min). The diagnostic success rate was 91.7% (22/24 patients). Regarding 2 patients in whom cholangiography failed using s-SBE, they were the cases with Roux-en-Y gastrectomy and with naïve papilla. Switching the scope to s-DBE, the procedure was successfully accomplished subsequently in both cases. Therapeutic success rate was 100% (24/24 patients). Complication occurred in 1 patient (3.8%; 1/26 patients). Regarding the 18 patients who had previously undergone s-DB-ERCP, s-SB-ERCP was successfully completed in 17 patients. The mean required time of s-SBE to reach the blind end was 24.7 min. (range, 7-50 min.), whereas that of s-DBE was 13.5 min. (range, 3-31 min.). The mean procedure time of s-SB-ERCP was 52.3 min. (range, 16-107min.), whereas that of s-DB-ERCP was 70.4min. (range, 21-168min.).
CONCLUSION: ERCP using a newly developed s-SBE for patients with gastrointestinal anatomy is safe and effective. In comparison with s-DBE, for the present, we conclude that a newly developed s-SBE is advantageous in the point of efficiency of performing ERCP-related interventions.
Disclosure of Interest: None declared

P0770 IMPACT OF PREOPERATIVE ENDOSCOPIC BILIARY DRAINAGE ON POSTOPERATIVE COMPLICATIONS AFTER PANCREATICODUODENOSTOMY FOR PERIAMPULLARY CANCER

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INTRODUCTION: The clinical impact of preoperative endoscopic biliary drainage (P-EBD) on the outcome after pancreaticoduodenostomy (PD) for periampullary cancer with obstructive jaundice is not well known.
AIMS & METHODS: The present study was aimed to investigate whether P-EBD was associated with increased morbidity after PD in patients with periampullary cancer. Patients with periampullary cancer, including pancreatic carcinoma, cholangiocarcinoma, and ampullary cancer, who underwent PD from October 2003 to September 2013 were analyzed retrospectively. At our institution, P-EBD was routinely performed with a 7 Fr or 8.5 Fr plastic stent. In addition, endoscopic nasobiliary drainage (ENBD) or switching to a larger caliber stent was done if biliary drainage was insufficient after P-EBD.
RESULTS: One hundred and sixty-seven patients who underwent PD (85 with pancreatic carcinoma, 47 with cholangiocarcinoma, and 35 with ampullary carcinoma) were analyzed. 98 patients received P-EBD before PD and their mean bilirubin level before P-EBD was 7.78 mg/dl. The other 69 patients underwent

PD without preoperative biliary drainage and their mean bilirubin level before PD was 1.59 mg/dl. Complications of P-EBD occurred in 34 patients (mild post-ERCP pancreatitis in 10, minor bile duct perforation by the guidewire in 1, stent occlusion in 7, and insufficient biliary drainage in 16). There was no significant difference in the time from the diagnosis of periampullary cancer until PD between the patients with and without complications of P-EBD. Multivariate regression analysis was performed to clarify the influence of P-EBD on post-operative complications, including pancreatic fistula. This analysis showed that cholangiocarcinoma and ampullary carcinoma, but not pancreatic carcinoma, were independent risk factors for postoperative complications ($p = 0.002$, $OR = 4.9$), while P-EBD had no influence on postoperative complications. Insufficient biliary drainage was also associated with postoperative complications, but not significantly ($p = 0.06$, $OR = 4.1$).
CONCLUSION: P-EBD was not associated with a higher incidence of post-operative complications. However, insufficient biliary drainage after P-EBD was associated with postoperative complications, so the development of more effective P-EBD might be useful to prevent such complications. The present findings showed that P-EBD is a safe and effective procedure for distal malignant biliary stricture due to periampullary cancer.
Disclosure of Interest: None declared

P0771 TECHNICAL SUCCESS WITH WIRE-GUIDED CANNULATION FOR CHOLANGIOGRAPHY USING EARLY PANCREATIC GUIDE WIRE PLACEMENT WITHOUT PRECUT SPHINCTEROTOMY

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INTRODUCTION: Wire-guided cannulation (WGC) and pancreatic guidewire (P-GW) placement may increase the success rate of deep cannulation of the common bile duct (CBD) and reduce the risk of complications compared with contrast-assisted cannulation (CC); however, the data is still unclear. Previous studies have suggested that repeated and unintentional injections or P-GW insertions may cause post-ERCP pancreatitis due to mechanical trauma or an increase in the hydrostatic pressure of the main pancreatic duct. Therefore, we compared the effect of early P-GW placement on the success of deep cannulations and the risk of post-ERCP pancreatitis with the outcomes of WGC or CC procedures.
AIMS & METHODS: We retrospectively assessed 143 patients who required ERCP because of known or suspected biliary duct disease; we excluded patients who had previously undergone endoscopic manipulations. Early P-GW placement was defined as placing a guidewire after one or two attempts into the main pancreatic duct without accomplishing cannulation of CBD. We performed ERCP with CC as the initial option for CBD cannulation in the early period and utilized WGC during the late period. The success rate of bile duct cannulation, the frequency and risk of post-ERCP pancreatitis and the frequency of requiring a pre-cut sphincterotomy were evaluated.
RESULTS: Conventional cannulation was attempted in 47 patients and WGC in 80 patients. The success rate of CBD cannulation was 96.0% in all cases, with 91.4% in the CC group and 97.5% in the WGC group. The frequency of early P-GW placement was 20.4% in all cases, with 10.9% in the CC group and 27.5% in the WGC group. Pre-cut sphincterotomy was performed in only one patient in the CC group. The frequency of post-ERCP pancreatitis was 7.6% in all cases and was 9.2% in the CC group and 7.9% in the WGC group. There were no significant differences among the groups with regard to each cannulation, the surgeon, actual pancreatic guide wire placement and IDUS.
CONCLUSION: Early P-GW placement can lead to a high success rate for CBD cannulation without the use of pre-cut sphincterotomy, and it does not increase the incidence of post-ERCP pancreatitis. In addition, WGC may be more suitable for early P-GW placement when compared with CC. WGC with early P-GW placement may be an ideal option for CBD cannulation in difficult cases and may involve a low rate of pre-cut sphincterotomy.
Disclosure of Interest: None declared

P0772 DOWNSTREAM REVENUE GENERATED BY PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY (PCLE) IN UNDETERMINED PANCREATICO-BILIARY LESIONS

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INTRODUCTION: Probe-based Confocal Laser Endomicroscopy (pCLE) increases diagnostic accuracy via targeted biopsies and greatly impacts management decisions, with accuracy rates above 80%. The improved diagnostic capability of pCLE may result in high post-procedure health resource utilization with increases in subsequent surgical and interventional procedures. Our aim was to examine downstream revenue and profit generated from surgical and interventional radiology procedures after pCLE.
AIMS & METHODS: A retrospective chart review was performed in a tertiary care institution. We identified patients who underwent diagnostic pCLE between August 2011 and December 2012 for indeterminate pancreaticobiliary lesions. Revenue data was generated using AllScripts EPSi and billing information to generate financial estimates.
RESULTS: 67 patients underwent diagnostic pCLE for indeterminate pancreaticobiliary lesions during the study period. Of these, 12 (18%) patients had subsequent procedures related to their diagnosis. Diagnoses included adenocarcinoma ($n = 8$), intraductal papillary mucinous neoplasm ($n = 1$) and benign disease ($n = 3$). Major post pCLE procedures included pancreaticoduodenectomy ($n = 4$), exploratory laparotomy ($n = 2$) and orthotopic liver transplant ($n = 1$). Average revenue generated from procedures was 100,512 dollars while the average net profit was 25,592 dollars per person.
CONCLUSION: For indeterminate pancreaticobiliary lesions, PCLE has major economic implications. Profit generated from surgical and interventional radiology procedures after pCLE is significant and negates the cost of the procedure itself. A large scale study examining the downstream financial impact of pCLE in otherpathologic settings may be useful for further analysis.
Disclosure of Interest: None declared

P0773 EUS-GUIDED DRAINAGE OF PERI-PANCREATIC COLLECTIONS USING A FULLY COVERED SELF EXPANDING METAL STENT WITH DOUBLE WALLED LUMEN APPOSING FLANGES IN AN ELECTROCAUTERY ENHANCED DELIVERY SYSTEM

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INTRODUCTION: To analyze the safety and clinical effectiveness of EUS guided drainage of peri-pancreatic collections (PPCs) using a fully covered self-expanding stent incorporated in an electrocautery enhanced delivery system, the Hot-AXIOS system (Xlumena Inc. Mountain View, Ca, USA).
AIMS & METHODS: Retrospective analysis of consecutive patients with PPCs who underwent EUS guided drainage using the Hot-AXIOS system in 12 European Endoscopy Centers.
RESULTS: From March 2013 to April 2014, 72 patients (median age 60 yrs; 55 male) with PPCs underwent drainage using the Hot AXIOS system. Median diameter of PPCs was 100 mm (range 38-246). 18 were pseudocysts, 35 WOPN, 15 abscesses, and 4 were acute PPCs. 41/72 PPCs were infected. In 57/72 cases (79%) the Hot-AXIOS system was used to enter the PPCs, while in the remaining 15 cases (21%) a 19G needle was utilized. The main approach was transgastric (68/72), and all were technically successful with all but one procedure described as easy to be performed. Early complications were mild fever in 2 cases and self-limiting bleeding in 2 other cases. Late complications were: Infection (1); self-limiting pneumoperitoneum (1); perforation (1); massive bleeding (1). Both last two complications were related to the naso-cystic drainage placement. 3 out of these 4 patients required surgery. Direct necrosectomy was performed in 29 cases. Overall, resolution of PPCs was achieved in 69/72 cases (95.8%). Stent removal was done after a median of 61 days. Recurrence was seen in only two of 69 cases (2.9%), one of which was treated with repeat EUS-guided drainage while the other did not require treatment. At the end of follow up 69 patients are alive and asymptomatic. Complications of the PPCs was the cause of the death in two out of the three patients who died.
CONCLUSION: EUS guided drainage with the Hot AXIOS system is a safe, easy to use, and highly effective minimally invasive treatment modality for peri-pancreatic collections.
Disclosure of Interest: None declared

P0774 CRYPTOGLANDULAR ANAL FISTULA OR CROHN'S ANAL FISTULA: THE ROLE OF ULTRASONOGRAPHY IN DIFFERENTIAL DIAGNOSIS

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INTRODUCTION: Endoanal ultrasonography shows good accuracy in definition of the anatomy of perianal fistulae, including those associated with Crohn's disease (CD). Several studies have been proposed ultrasonographic features to discriminate anal fistulae associated with CD in relation to cryptoglandular fistulae.
AIMS & METHODS: Our aim was to evaluate several ultrasonographic features that may distinguish these two types of fistulae.
Retrospective study including fifty-eight patients who underwent endoanal ultrasonography 2D between 2008 and 2013. The perianal fistulae variables studied were the complexity, transversal diameter, presence of secondary tracks and fistulous debris. For patients with CD was also calculated the adapted perianal disease activity index (PDAI excluding the influence in sexual activity).
Statistical analysis was performed using the SPSS program vs20.0 and a p value of less than 0.05 was considered statistically significant.
RESULTS: Fifty-eight patients were included, 48% with CD with a mean PDAI of 7.6 ± 3.2. In CD patients a higher PDAI was statistically associated to more

complex fistulae (8.5 vs 5.5, p = 0.028). 38% of all patients had been previously submitted to a surgery intervention for fistula resolution. The ultrasonographic features that correlated with the presence of fistulae associated with CD were the complexity (OR:5; IC95% 1.6-15.3; p = 0.004), the presence of secondary tracks (OR:3.2; IC95% 1.1-9.5; p = 0.036) and the presence of fistulous debris (OR:5.9; IC95% 1.6-15.3; p = 0.002). There was no statistical difference between cryptoglandular fistulae and fistulae associated with CD with respect to dimensions (4.1mm vs 4.9mm, p = 0.24).
CONCLUSION: In our study, the complexity of the perianal fistulae and also the presence of secondary tracks and debris revealed to be strong predictors of Crohńs related perianal fistulae.
Disclosure of Interest: None declared

P0776 NOVEL COMPUTER-AIDED QUANTITATIVE ANALYSIS OF THE DISTRIBUTION OF CONTRAST IN CONTRAST-ENHANCED EUS FOR DIFFERENTIAL DIAGNOSIS OF PANCREATIC TUMORS

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INTRODUCTION: Differentiating between pancreatic carcinoma (PC) and chronic pancreatitis (CP) with pseudotumor is still challenging, even with contrast-enhanced EUS (CE-EUS) or EUS-FNA. We developed the novel computer-aided diagnostic software (Madara, Inspeedia Inc., Kariya, Japan) to quantify the pattern of contrast distribution in CE-EUS.
AIMS & METHODS: The aim of this study was to evaluate the utility of CE-EUS with Madara for differential diagnosis of PC and CP with pseudotumor. Consecutive patients who had PC or CP with pseudotumor and underwent CE-EUS from January 2011 to December 2013 were retrospectively analyzed. A curvilinear echoendoscope (GF-UCT260), Aloka Prosound α10 processor and intravenous administration of 0.015ml/kg of Sonazoid were used for CE-EUS. Using our software, a region of interest (ROI) which divided into 100 cells was placed to cover an area within pancreatic mass. Differences of grade of gray scale levels between the adjoining cells within the ROI were detected, and the number of adjoining cells which showed a difference of the gray scale level was automatically calculated in each frame rate of CE-EUS (heterogeneity index). A heterogeneity index curve was also automatically generated to depict the changes of the heterogeneity index over time, and the mean heterogeneity index from start to one minute after injection of Sonazoid was calculated. Moreover, using a conventional software to quantify the degree of enhancement, in which ''time intensity curve (TIC: Hitachi/Aloka Co., Ltd., Tokyo, Japan)'' was generated to depict the changes in the signal intensity, maximum intensity gain (MIG: peak intensity – base intensity) was also calculated. The final diagnosis of PC was based on the results of surgery or EUS-FNA, while CP was diagnosed from EUS-FNA, the clinical course and other imaging tests.
RESULTS: Fifty-nine patients (39 with PC and 20 with CP) were analyzed. The heterogeneity index curve showed ''bell and flat curve type'' in 9 patients with CP, ''irregular curve type'' in 11 patients with CP and 37 with PC, and ''flat curve type'' in 2 with PC. Thus, ''bell and flat curve type'' was specific to CP, while ''flat curve type'' were specific to PC. The mean heterogeneity index in PC patients was significantly higher than CP patients (15.6 vs. 6.1, p < 0.0001). Flat curve type of heterogeneity index curve and the mean value of heterogeneity index showed sensitivity of 92.3% and specificity of 90% for differentiating between PC and CP with pseudotumor. On the other hand, MIG in CP patients was significantly higher than PC patients (21.1 vs. 15.7, p = 0.01), and showed sensitivity of 71.8% and specificity of 65%. Combined assessment of heterogeneity index curve and MIG with time intensity curve, using the cut-off value of heterogeneity index of 10.3 and MIG of 14.3, yielded sensitivity of 94.3% and specificity of 95% to differentiate between PC and CP with pseudotumor.
CONCLUSION: CE-EUS with ''Madara'' diagnostic software to quantify the pattern of contrast distribution might be useful for making a differential diagnosis between PC and CP with pseudotumor.
Disclosure of Interest: None declared

P0777 TRANSMURAL STENT PLACEMENT AS THE DOMINANT STRATEGY FOR ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE

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INTRODUCTION: There are several ways to perform endoscopic ultrasound-guided biliary drainage (EUSBD): transductal (rendezvous [RV] and direct antegrade [DAG] options) or transmural (intrahepatic [hepaticogastrostomy, HGS] and extrahepatic [choledochoduodenostomy, CDS] options). Best approach remains contentious, while patient selection and case-volume confound evidence from limited available comparative data.
AIMS & METHODS: To identify current dominant strategy for EUSBD at high-volume Unit. Data from 44 patients (male 25, mean age [SD] 75 [13], malignant/benign 77% / 33%) undergoing EUSBD from Jan-Dec 2012 at single Unit were prospectively captured. Standardized techniques (single-puncture following comprehensive target choice, minimal needle-guidewire interplay, graded-dilation with salvage-only 6.5F cystotome use) and algorithms for access (intrahepatic for hilar strictures and/or altered GI anatomy; extrahepatic for the opposite when stable scope) and drainage (transductal if early guidewire passage or if failed cannulation of native papilla in benign obstruction, transmural if otherwise) were used. Caliber of access duct was 9.1 mm (IQR 6.3-15.6) for extrahepatic (27%) and 5.5 mm (IQR 4.0-7.9) for intrahepatic access (73%). Number of ERCP/PTBD over study period was 1048/5 (EUSBD = 4.2% of ERCP; PTBD = 11% of EUSBD). Clinical success was defined as bilirubin < 80% baseline values, symptom disappearance and hospital discharge. Adverse events as per consensus. Follow-up through chart review and phone contact.
RESULTS: Technical success was achieved in 43 patients (97.7%) and clinical success in 70%. There were adverse events in 6 patients (13.6%): 5 mild (3 mild bleedings, 1 acute pancreatitis, 1 hypoxemia) and 1 fatal case of cholecystitis. Transductal EUSBD was performed in 11 patients (7 DAG and 4 RV techniques), and transmural EUSBD in 36 (26 HGS/hepaticojejunostomy and 10 CDS/choledocogastrostomy, including dual DAG-HGS in 4). Fully covered metal stents were used in 90.6% for transmural EUS-guided biliary drainage (22 Hanaro stent, 7 Wallflex stents). A variety of stent-anchorage techniques were employed in 65% of these patients (hemoclips, flaps, double pig-tails, balloon expansion or more than one anchorage technique). Accurate follow-up was obtained in 35 patients. After a mean of 146 days (SD 141), 5 dysfunctions occurred (2 patients with plastic stents [1 migration, 1 occlusion], 3 with metal stents [2 angulation, 1 late migration]).
CONCLUSION: After a decade-long usage, the dominant strategy for EUSBD was transmural fully covered metal stents with ancillary anchorage. No short-term migration, minimal late dysfunction and comparable adverse event rate to purported less invasive RV were found. Intriguing higher rate of intrahepatic Vs extrahepatic possibly explained by patient selection/PTBD use patterns warrants clarification.
Disclosure of Interest: None declared

P0779 FACTORS ASSOCIATED WITH THE ACCURACY OF EUS-GUIDED FINE NEEDLE ASPIRATION FOR THE DIAGNOSIS OF SOLID PANCREATIC MASSES

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INTRODUCTION: Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) and biopsy (FNB) are accurate techniques for sampling pancreatic solid lesions. Diagnostic yield of FNA/FNB may be influenced by different factors, but information on this regard is lacking.
AIMS & METHODS: Aim of our study was to evaluate potential factors associated with the diagnostic accuracy of EUS-FNA/FNB for the differential diagnosis of solid pancreatic masses.
447 consecutive patients (mean age 66.4 years, range 17-92, 262 male), who underwent EUS-FNA/FNB for the evaluation of solid pancreatic lesions over the last 4 years were identified from a prospectively collected endoscopy database, and included in the study. EUS was performed using a convex array echoendoscope (Pentax EG-3870UTK and EG-3270UK). FNA/FNB was performed with standard cytology and Procore™ histology needles (Cook Medical Inc, Limerick Ireland). The impact of the type of scope, location and size of the lesion, on-site cytopathological evaluation, number of needle passes and type of needle on the diagnostic accuracy of FNA/FNB was evaluated. Overall diagnostic accuracy was calculated by using surgical histopathology in operated cases and global clinical and radiological assessment and follow-up in non-operated cases as gold standard. Data were analyzed by multivariate stepwise logistic regression.
RESULTS: Mean size of solid pancreatic masses was 36.1±16.4 mm. 283 tumors were located in the head of the pancreas, 124 in the body, and 40 in the tail. Final diagnosis was pancreatic adenocarcinoma in 294 cases, inflammatory lesions in 74 cases, neuroendocrine tumor in 23 cases, pancreatic metastasis in 17 cases, cystic lesions with solid components in 36 cases and pancreatic lymphoma in 3 cases. Overall diagnostic accuracy was 87.5% (95%CI 84.1-90.2). Size of the lesion (OR 1.03; 95%CI 1.00-1.06; p = 0.014), onsite evaluation of the FNA/FNB sample (OR 4.36; 95%CI 1.3-14.9; p = 0.019), and the use of Procore™ needles (OR 3.02; 95%CI 1.4-6.5; p = 0.005) were independently associated with a correct diagnosis after FNA/FNB.
CONCLUSION: EUS-guided FNA/FNB is an accurate technique. Factors associated with a higher diagnostic yield are large lesions, onsite cytopathological evaluation and the use of the Procore™ needles.
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P0780 DOES EUS-BASED CHRONIC PANCREATITIS PROGRESS TO OBVIOUS CHRONIC PANCREATITIS? - THE FOLLOW-UP STUDY USING EUS

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INTRODUCTION: Endoscopic ultrasonography (EUS) has been commonly used for diagnosis of chronic pancreatitis (CP) and assessment of its severity. In 2009, ''Rosemont criteria'' was proposed as EUS-based criteria for CP. EUS

can detect minimal changes in the pancreatic duct and parenchyma, and may reveal early pancreatic abnormalities. However, it is not clear whether the pathological condition revealed by EUS will progress to obvious CP or not.
AIMS & METHODS: The aim of this study is to clarify a clinical significance of EUS-based CP.
We retrospectively reviewed all the medical records and EUS images of the patients who had underwent EUS for pancreas from April 2010 to March 2012 in our center. The study patients were picked-up fulfilling criteria as follows; 1) the patients who had pancreatic abnormalities (Hyperechoic foci with/without shadowing, Lobularity with/without honeycombing, Cysts, Strands, MPD calculi, Irregular MPD contour, Dilated side branches, MPD dilation, Hyperechoic MPD margin) on the initial EUS, 2) the patients who were followed by EUS more than twice until April 2014. These patients were classified into 4 categories by Rosemont criteria; Consistent with CP (C-CP), Suggestive of CP (S-CP), Indeterminate for CP (I-CP), and Normal (N). We assessed the progression of pancreatic condition in each patient.
RESULTS: 10 of 22 patients who had pancreatic abnormalities on initial EUS had undergone EUS more than twice (M/F:8/2, mean age: 73.5 (58-82)). Initial diagnosis was C-CP in 1, S-CP in 2, I-CP in 3 and N in 4, respectively. In 10 patients, 5 were aggressively intervened (abstinence, taking orally protease inhibitor), and the other 5 were not taken medical intervention. In intervention group, the number of EUS criteria increased in 2 patients. However, there was no patient who changed the category of Rosemont classification between initial and follow-up EUS. On the other hand, in no intervention group, the number of EUS criteria increased in 4 patients. Moreover, 3 patients got worse the category of Rosemont classification from N to I-CP.
CONCLUSION: It was considered that early medical intervention might be necessary in patient with pancreatic abnormalities on EUS, even if Rosemont classification indicated ''Normal''.
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Disclosure of Interest: None declared

P0781 DIFFERENT SITES OF ASPIRATION IN EUS-FNA OF PANCREATIC ADENOCARCINOMA: A PROSPECTIVE, MULTICENTER, SINGLE-BLINDED STUDY

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INTRODUCTION: EUS-FNA is widely used to diagnose pancreatic malignancies. Few studies have compared different sites of aspiration when performing EUS-FNA of pancreatic lesions.
AIMS & METHODS: to evaluate the diagnostic accuracy between center and margin of pancreatic adenocarcinoma. 69 consecutive patients with a solid pancreatic lesion, with long axis ≥2cm, were included in this study between January 2012 and December 2013 in 3 hospitals. All FNA procedures were performed using a 22G needle with 5ml suction, 7-8 uniform to-and-fro movements with 2cm depth of insertion were made within the lesion. The first puncture was performed within the central part of the lesion and the second was along the edge of lesion closed to unaffected tissue. A liquid-based cytologic (LBC) preparation was used to rinse the aspiration needle and fix the cytologic specimen after every puncture and specimens were evaluated by expert cytotechnologists. An expert cytopathologist, blinded for the sites of aspiration, reviewed the slides for diagnosis and assessed sampling quality. The final diagnosis was based on pathological examination of tissues obtained either surgically or by EUS-FNA, pathological negative cases need at least 6 months' follow-up to rule out benign diseases. Data were analyzed with Student's t-test and chi squared test, assuming a significant p-value of 0.05.
RESULTS: 64 patients were confirmed with pancreatic adenocarcinoma. The sensitivity of central site is 71.9%(46/64) and 48.4%(31/64) in marginal site ($p = 0.039$).
CONCLUSION: Our study shows EUS-FNA in center of tumor is more sensitive for the diagnosis of pancreatic adenocarcinoma.
Disclosure of Interest: None declared

P0782 PREDICTIVE VALUE OF PRE-OPERATIVE STAGING AND GRADING IN PANCREATIC NEUROENDOCRINE NEOPLASMS

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INTRODUCTION: Pancreatic NeuroEndocrine Tumors (P-NETs) are a heterogeneous group of neoplasms with highly variable clinical behavior. In the attempt to assess a better prognostic description, The European Neuroendocrine Tumors Society (ENETS) proposed a new grading and TNM-based staging system.
AIMS & METHODS: To compare pre-operative and post-operative Staging and Grading in P-NETs and their prognostic significance; secondary to determine if a new cut-off value of Ki-67 proliferative index for P-NETs Grading can improve the accuracy of prognostic stratification.
Our retrospective long-term survival case study is composed of 285 patients with P-NETs observed at San Raffaele Scientific Institute from 1988 to 2012. 274 neoplasms were classified according to ENETS classification models; out of these, 90 and 42, respectively, were classified according to a new pre-surgical classification, composed of pre-operative Staging (CT, MRI, EUS) and Grading (EUS-guided fine needle aspiration and cytological Ki-67 evaluation). Comparison between pre- and post-operative models (Pre-Stage vs. Stage e Pre-Grade vs. Grade) was possible for 88 and 33 neoplasms, respectively. Ki-67 proliferative index was evaluated through immunocytochemical (Pre-Grade) and immunohistochemical (Grade) analyses. Agreement between pre-operative and post-operative models was performed through k-statistics (Cohen). A p-value < 0.05 was considered significant.
RESULTS: Among all pre-operative and post-operative models, Pre-Grade shows the highest Harrell's C (0.97), resulting the best tool for a proper prognostic stratification. When comparing pre-operative and post-operative models, percent agreement between Pre-Stage and Stage was good (83%, $k = 0.74$), otherwise agreement between Pre-Grade and Grade was moderate (70%, $k = 0.42$), when used a 2% cut-off for Grade 1 tumor definition; contrarily, when used a 5% cut-off, Pre-Grade and Grade showed a good agreement (88%, $k = 0.66$). The definition of a new 5% cut-off for cytological and histological Ki-67 index improved the accuracy of patients' prognostic stratification, being not significant the difference between patients' 10-year survival for Ki-67 levels within 5% (93.75% vs. 90%).
CONCLUSION: The new proposed pre-surgical classification, based on Pre-Stage and Pre-Grade, is comparable to post-surgical models. This system shows a good agreement with post-surgical one, being efficient in pre-surgical disease's biology evaluation.
Disclosure of Interest: None declared

P0783 DUPLICATION CYSTS: THE ROLE OF ENDOSCOPIC ULTRASONOGRAPHY

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INTRODUCTION: The duplication cysts are uncommon congenital anomalies and rarely diagnosed in adults. They can be found in any part of the digestive tract. The cysts are typically discovered incidentally on endoscopy or radiologic imaging since they are usually asymptomatic. However complications such as infection, bleeding, perforation, ulceration, obstruction and malignant transformation can occur. Their management can be challenging and increased availability of new diagnostic modalities such as endoscopic ultrasonography (EUS) may change their approach.
AIMS & METHODS: To describe the experience of a center in the diagnosis of duplication cysts by EUS.
We performed a retrospective analysis to the upper EUS performed between 2000 and 2013, with the diagnosis of duplication cyst. The patient characteristics and the endoscopic/imaging findings were analyzed. The contribution to the diagnosis of fine needle aspiration (FNA) was also evaluated.
RESULTS: Between 2000 and 2013, 23 patients (16 men (69.6 %)) with a mean age of 51.9 ± 15.9 years underwent EUS, whose final diagnosis was duplication cyst. Prior to EUS: 19 underwent gastrointestinal endoscopy (EGD), 13 of them by symptoms such as dyspepsia ($n = 9$) and dysphagia ($n = 4$). Of the 19 EGD performed, 3 had no endoscopic abnormalities and 16 had suspection of subepithelial lesions (10 esophageal); Four patients had previous imaging study by computed tomography (CT), 2 with suspected esophageal duplication cysts. EUS detected 16 anechoic lesions with endosonographic criteria of duplication cyst in the esophagus (average size 24.2 x14, 2 mm; 7 with echogenic material inside) and 7 in the stomach (average size 23.6 x14, 1 mm, 2 with fluid levels and septae). There were 8 cases where EUS FNA was performed (5 esophagus); in 75% of cases one pass FNA was done using a 22 Gauge needle. There was cytological confirmation in 3 cases, and in 3 other cases other entities besides cysts were excluded. A CT scan was performed in four patients after EUS, with diagnostic agreement in one case. Annual EUS follow up was performed in 9 patients, with no changes in the lesions characteristics.
CONCLUSION: EUS plays a central role in the diagnosis and monitoring of an entity which, although rare, has potential serious risks and complications associated.
Disclosure of Interest: None declared

P0784 DECISION TREE ANALYSIS OF THE DIAGNOSTIC VALUE OF EUS IN DETERMINING ESD INDICATION IN EGC

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INTRODUCTION: In recent years, due to the spread of endoscopic submucosal dissection (ESD) for early gastric cancer (EGC), preoperative determination of ESD indication has become increasingly important.
AIMS & METHODS: In determining the ESD indication for EGC, we diagnose the depth of invasion by endoscopic ultrasonography (EUS) in all cases as much as possible in our hospital. We investigated its efficacy by decision tree analysis. We performed EUS in 179 cases from January 2011 to March 2014. We performed EUS using 20MHz small-diameter probe. The average age was 69 years

old. Male-to-female ratio was 142:37. We classified the invasion depth into M, M-SM and SM. We evaluated the accuracy of the invasion depth by area, morphological type, histological grading and UL according to the pathology specimen after resection.
RESULTS: The accuracy of all 179 cases was 89 %. It was 91 % in the 150 cases that ESD was performed, and 75% in the 29 cases that surgery was performed. Total cases and accuracy according to area was 83% in 42 U area cases, 93% in 80 M area cases, and 88% in 57 L area cases. According to the macroscopic type, accuracy was 91% in 89 0-IIc type cases, 88% in 60 0-IIa type cases, 92% in 13 0-IIb type cases, 60% in 10 0-IIa+IIc type cases, and 100% in 7 0-I type cases. Accuracy was 68% in 32 UL (+) cases. According to histological type, accuracy was 92% in 155 differentiated type cases, 75% in 24 undifferentiated type cases. 164 cases were diagnosed as M or M-SM, which are indications for ESD, and correct diagnostic rate was 91%. 15 cases were diagnosed as SM, in which surgical treatment is indicated, and accuracy was 67%. In decision tree analysis, accuracy was 69% in UL(+) cases, and as low as 84% in undifferentiated UL (-) cases, and 97% in other cases.
CONCLUSION: In ESD cases, decision tree analysis enabled differentiation between high and low accuracy groups in diagnosis of the depth of invasion.
Disclosure of Interest: None declared

P0785 EUS-FNA OF NON MASS-FORMING CHOLANGIOCARCINOMA WITH A 25 G PROCORE NEEDLE. A CASE SERIES

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INTRODUCTION: Preoperative pathological diagnosis in patients with biliary strictures suspected for malignancy is often difficult. The diagnostic yield of endoscopic retrograde cholangio-pancreatography (ERCP) guided brushing is low and endoscopic ultrasound fine needle aspiration (EUS-FNA) may be difficult to perform in non-mass forming lesions. We report a case series of patients affected with suspected cholangiocarcinoma in which a cytological diagnosis was attempted by EUS-FNA.
AIMS & METHODS: All the cases of EUS-FNA performed in patients with biliary strictures suspected for malignancy from June 2012 to October 2013 were reviewed. Patients were excluded if the EUS examination showed a mass lesion. Only patients in whom an EUS-FNA was attempted were included in the analysis.
RESULTS: During the study period 12 patients (8 males, mean age of 75, range 60 to 85) diagnosed with a non mass forming biliary stricture underwent EUS-FNA. The stenosis was distal from the cystic duct insertion in 8 cases. Aspirates were carried out using a 25 G core needle with the capillary suction technique. The material was put on smears and processed in the standard fashion. The results were definite for malignancy in 9 patients and suspected in 2 patients. In one patient the cytological results were inconclusive. All the patients were resected. The surgical pathology results showed a cholangiocarcinoma in all these patients. The sensitivity of EUS-FNA was 75% considering only the positive cytology and 91% considering also the suspected ones. No complications were reported.
CONCLUSION: Our results suggest that EUS-FNA is a safe and useful procedure for investigating biliary strictures suspected of malignancy even without a mass. Although false-negative diagnosis can still occur, core biopsy needle seems to improve the diagnostic yield of cytology.
Disclosure of Interest: None declared

P0786 LIMITATIONS OF CAPSULE ENDOSCOPY - A SINGLE CENTER STUDY ON 1193 CONSECUTIVE EXAMINATIONS

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INTRODUCTION: Over the past years, capsule endoscopy (CE) has been established as an imaging technique in the diagnosis of small bowel diseases. The aim of this study was to examine the limitations of this method by analysing a large number of consecutive CEs.
AIMS & METHODS: This was a retrospective study, including 1193 consecutive examinations performed at our centre in 1091 patients (male/female = 517/574, mean age ± SD: 61.83 ± 17.46a, range: 9-93a) between 2002 and 2012. In 1061 examinations the system of Given® (Yoqneam, Israel) was used. In 132 examinations the capsule endoscope MiroCam® (IntroMedic, Seoul, South Korea) was used.
RESULTS: *Complications* requiring an endoscopic or surgical intervention occurred in 0.34% (4/1193) of examinations: In two patients the capsule was retained in a duodenal diverticulum or a hiatal hernia, respectively. In both cases the capsule could be removed endoscopically. In one patient with Crohn's disease (CD) the capsule was retained in a stenosis of the terminal ileum and was removed during colonoscopy after dilation of the stricture. One patient underwent surgery after the capsule was retained in a stenosis caused by CD.
Technical defects of the capsule or the data recorder occurred in 16 (1.34%) CEs: Hence the passage through the small intestine was not completely recorded (n = 12) or the pictures could not be used for further evaluation (n = 4).
Transit abnormalities: In 1017 examinations (85.25%) the cecum was reached within the recording period.
Visibility conditions were classified as very good 54.41%, as partly limited in 32.05% and as severely limited during the most part of recording in 13.54% of examinations.
CONCLUSION: Complications of CE requiring endoscopic or surgical intervention are very rare (0.34%). However, technical defects as well as transit abnormalities and limited visibility may decrease the diagnostic yield of CE in some cases.
Disclosure of Interest: None declared

P0787 OESOPHAGEAL CAPSULE ENDOSCOPY VERSUS STANDARD OESOGASTRODUODENOSCOPY FOR THE SCREENING OF OESOPHAGEAL VARICES. RESULTS OF A PROSPECTIVE TRIAL IN PATIENTS WITH LIVER CIRRHOSIS

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INTRODUCTION: Oesophageal capsule endoscopy (OCE) is a non-invasive technology that allows the investigation of the oesophagus. Our aim was to evaluate prospectively the diagnostic yield of OCE in patients with cirrhosis and suspected portal hypertension (PHT).
AIMS & METHODS: 330 patients with cirrhosis and without known oesophageal variz (OV) were enrolled. Patients first underwent OCE, then OGD; endoscopists who performed OGD were blind to OCE result. In case of discrepancy for the presence of VO, a second exploration by OGD was immediately performed. Patient's satisfaction was assessed by an VAS (visual analogic scale, maximal score = 100).
RESULTS: Thirty patients were not included in the analysis because neither OCE nor OGD were performed. Patients (216 male, mean age 56 years) had mainly alcoholic (45%) or viral (22%) cirrhosis. The diagnostic yields of OCE to detect, and to adequately classify, OV were as follows: sensitivity 76% [95% CI, 69% - 83%] and 64% [95% CI, 50% - 78%], specificity 91% [95% CI, 86% - 95%] and 93% [95% CI, 87% - 100%], positive predictive value 88% [95% CI, 82% - 93%] and 88% [95% CI, 77% - 99%] and negative predictive value 81% [95% CI, 75% - 87%] and 78% [95% CI, 68% - 87%] respectively. OCE patient satisfaction scored significantly higher than OGD (87±22 vs. 58±35; $p < 0.0001$).
CONCLUSION: OCE was well tolerated and safe in patients with liver cirrhosis and suspicion of PHT. The sensitivity of OCE is not currently sufficient to replace OGD as a first exploration in these patients. However, due to its excellent specificity and PPV, OCE may have a role in cases of refusal or contra-indication to OGD. OCE might also improve compliance to endoscopic follow-up and help in making important therapeutic decisions in the prophylaxis of bleeding.
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P0788 ARE NON-INVASIVE MARKERS OF GASTRO-INTESTINAL DISEASE PREDICTORS OF ENTEROPATHY AT SMALL BOWEL CAPSULE ENDOSCOPY?

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) represents the gold standard diagnostic technique in case of obscure gastrointestinal bleeding. Moreover, its use is gaining acceptance also as diagnostic procedure when an organic disease of the small bowel (i.e. duodenum/jejunum/ileum) is suspected. On the other hand, SBCE is an expensive, invasive tool and data about its cost/effectiveness are lacking. Thus, non-invasive markers of small bowel disease are desirable in order to increase the rate of positive SBCE examinations.
AIMS & METHODS: We aimed to evaluate the role fecal markers of inflammation (i.e. fecal calprotectin and lactoferrin) and intestinal permeability test (i.e. lactulose-mannitol ratio, L/M) in predicting the presence of enteropathy at SBCE. We included consecutive patients who underwent SBCE because of symptoms suggestive of small bowel disease (i.e. chronic diarrhea, chronic anemia, signs of malabsorption) and with negative upper and lower endoscopy. Patients dosed levels either of fecal calprotectin (normal values, n.v., 0-50 ug/g) or lactoferrin (n.v. 0-7 ug/ml) and performed L/M test (n.v. < 0.030) at the time of SBCE. Erosions, aftous lesions, ulcers and vascular abnormalities at SBCE were considered positive for small bowel disease presence.
RESULTS: In this retrospective analysis of prospective collected data, 101 consecutive patients (66F/35M; mean age 40 years) with dosed levels either of fecal calprotectin or lactoferrin were included. In 51 (50%) patients, SBCE detected the presence of small bowel disease. Sixty-three (62%) patients had increased levels of fecal markers, whereas in 38 (38%) patients these markers were normal. The diagnostic accuracy of fecal markers for the detection of small bowel disease was 62.4%, with 75% sensitivity and 46% specificity, a positive

likelihood ratio (PLR) of 1.49 and a negative likelihood ratio (NLR) of 0.51. Sixty-seven out of 101 patients performed also L/M test. This was abnormal in 46 (69%) patients and normal in 21 (31%). In 36/67 (54%) patients, SBCE was positive for small bowel disease. The diagnostic accuracy of L/M test for the detection of small intestine disease was 76%, with 75% sensitivity and 56% specificity, a PLR of 1.7 and a NLR of 0.45. The alteration of at least one between fecal markers and L/M test has a diagnostic accuracy of 56.7%, whereas having both fecal markers and L/M test abnormal had a diagnostic accuracy of 64.6%.

	N° patients	Sensitivity % (95%CI)	Specificity % (95%CI)	PLR (95%CI)	NLR (95%CI)
Fecal markers	101	75 (60-86)	50 (34-64)	1.36 (1.08-2.05)	0.57 (0.30-0.88)
L/M test	67	75 (58-88)	56 (40-71)	1.70 (1.15-2.50)	0.45 (0.24-0.84)
At least 1 abnormal	67	83 (67-94)	26 (12-45)	1.12 (0.87-1.45)	0.65 (0.25-1.66)
Both abnormal	48	79 (60-92)	42 (20-66)	1.37 (0.89-2.10)	0.49 (0.20-1.19)

CONCLUSION: Although fecal calprotectin and lactoferrin are established markers of colonic inflammation, their diagnostic yield in detecting small intestinal disease through SBCE seems suboptimal. Their combination with L/M test minimally improves this diagnostic accuracy, whereas that of L/M test alone appears the most satisfactory. It remains to establish whether performing either fecal markers or L/M test (or both) might be cost-effective in the selection of patients to address for SBCE when a small bowel disease is suspected.
Disclosure of Interest: None declared

P0789 A THERAPEUTIC WIRELESS ROBOTIC ENDOSCOPE CONTROLLED VIA THE INTERNET REMOTELY

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INTRODUCTION: A few researchers have tried to make the paradigm shift "from diagnosis to treatment with the capsule endoscopy (CE) application". Though technical innovation is rapidly spreading throughout the CE field, there are still several crucial problems with both the hardware and software which were highlighted by the system we presented at the last UEGW in Berlin. This report presents a wirelessly controlled robotic endoscope equipped with some newly developed tools; a syringe for injecting or spraying drugs or contrast medium, a scalpel for cutting and a rubber band for suturing.
AIMS & METHODS: Our goal is to realize a patient-friendly, swallowable, therapeutic and wirelessly controlled robotic endoscope. We tested three newly developed therapeutic tools in a phantom, which had part of its inner wall covered with a patch of porcine stomach. 1) A 0.3ml syringe for injecting or spraying was driven by a spring and switched on electrically. The amount used was dependent on the drug, dye or contrast medium. 2) The rubber band (similar to a variceal ligater) was held between two cylinders and released by a spring. When the spring was released the outer cylinder pushed the band over the mucosa. 3) The scalpel blade was vibrated by a motor similar to a harmonic scalpel. All the tools were triggered by signals originating from a controller in the hospital via a smartphone next to the phantom. In addition, similar to the previous version the tools were controlled via the Internet.
RESULTS: It was possible to control all the new tools in the phantom both locally (Bluetooth) and via the Internet. However, the cuts made by the scalpel in the mucosa were a little bit jagged. In retrospect, it would have been better to move the robotic endoscope slowly backwards during cutting to improve the operator's view of the lesion, so that they could have made a cleaner cut. The tools occupied a large volume and therefore it was difficult to fit all the tools in a single robotic endoscope. To enable the robotic endoscope to be swallowed, it will be necessary to equip it with only one or two tools. The best approach might be to build several specialized robotic endoscopes and the number of endoscopes that a patient would swallow would be determined by their circumstances.
CONCLUSION: This study has built on the previous study by increasing the number of therapeutic tools from two to five and hopefully, it has brought treatment by a robotic endoscope, a little bit closer. However, the current prototype has a number of limitations (e.g. too large to be swallowed and the tools could only be used once) and these will need to be addressed if treatment by robotic endoscope is to become a reality.
Disclosure of Interest: H. Ohta: None, S. Katsuki: None

P0790 KINETICS OF COLON CAPSULE ENDOSCOPY: A NEW MODEL OF PREPARATION

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INTRODUCTION: Up until now, the use of colon capsule endoscopy (CCE) has been limited by the inabilities to achieve a complete examination. A pilot study was conducted to determine the efficacy of a new preparation based on associating Prucalopride (Resolor) and polyethylene glycol plus ascorbic acid (Moviprep). Prucalopride is a highly selective serotonin 5HT4 receptor agonist which stimulate the release of acetylcholine necessary for smooth bowel muscle contraction and therefore peristalsis. After observing its benefits on the treatment for constipation, we believe that Prucalopride could be useful in the preparation of colon capsule endoscopy, speeding up intestinal transit and therefore making the examination shorter, increasing the excretion rate. This article presents the results obtained in terms of transit times, total examination time and expulsion rates.
AIMS & METHODS: Pilot study with 50 patients (cases) with the new preparation compared with 50 control patients with the standard preparation (PEG/ Fosfosoda/). Each video is read by two researchers.
Preparation protocol: - Two days of residue-free diet - Day before the test, liquid diet - Resolor 2 mg, 1 on each day of the diet and 2 on the examination day - Moviprep, 1 liter in the evening prior to the examination and 1 liter in the morning of the examination – Then 2 boosters of half a liter each in alarms 1 and 2.
RESULTS: A cohort with 41 men and 59 women, mean age of 54.6 years old (10-90). Expulsion rate over time of 87% in the cases with respect to 55.5% in the controls ($p = 0.188$). The mean gastric transit time (75 vs. 49.5 minutes; $p = 0.12$), intestinal transit time (81.4 vs. 44 minutes; $p = 0.001$) and colon transit time (252 vs. 232 minutes; $p = 0.79$) were shorten.
CONCLUSION: The higher excretion rate as well as the shortened gastric and intestinal transits, without modifying the colon transit, with the new preparation (Prucalopride+Polyethylene glycol plus ascorbic acid), allow conducting a higher quality study of the colon over time and with less adverse effects and better tolerance as a result of excluding sodium phosphate.
This procedure may be considered as an alternative, particularly for patients in whom sodium phosphate-based preparations are contraindicated.
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Disclosure of Interest: None declared

P0791 COMPARATIVE STUDY OF SMALL BOWEL TRANSIT TIME IN TWO SMALL-BOWEL CAPSULE ENDOSCOPY SYSTEMS

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INTRODUCTION: Some studies[1] suggest that the MiroCam ® endoscopy capsule (CE) has a small bowel transit time (SBTT) greater than Given® CE, which may result in greater detection of positive lesions.
AIMS & METHODS: Aims: To compare the SBTT, the detection of positive lesions and percentage of complete studies between Mirocam ® and Given ®.
Methods: retrospective study of 429 patients who underwent CE between 2005-2013. Lesions were considered positive according to the indication of CE: obscure gastrointestinal bleeding (OGIB) - multiple erosions/ ulcers, typical angiodysplasias, tumor and blood; suspected Crohn's disease (CD)/ evaluation of the extension of CD - multiple erosions/ ulcers and blood; abdominal pain - tumor, multiple erosions / ulcers and blood. Statistical tests: t-student; X^2
RESULTS: The mean age was 54.2 years. MiroCam® CE was performed in 48.7% of patients and Given® CE in 51.3% patients. Indications for performing CE: OGIB – 62.5%, suspected CD/ evaluation of the extension of CD - 21.2%, polyposis – 5%, abdominal pain – 4.4% and others – 6.8%.
The mean gastric transit time (GTT) in MiroCam ® and Given ® CE was identical – (38min vs 41min, $p = 0.52$). The mean SBTT of MiroCam ® CE was superior to Given® CE - 5h17min vs 4h45min, $p = 0.004$. We did not find any differences between the two CE with respect to mean age (MiroCam® - 54.9 years; Given® - 53.6 years, $p = 0.46$), sex (Mirocam ®- female sex 57%; Given® - female sex - 61.3%, $p = 0.35$), percentage of diabetic patients (10.1% MiroCam® - 10.1%; Given® - 14.5%, $p = 0.2$), percentage of complete exams (MiroCam® - 90%; Given® - 89%, $p = 0.63$) and positive lesions (MiroCam ® - 38.2%, - Given® - 39.5%, $p = 0.78$). There were also no differences regarding the indications for CE ($p = 0.051$).
CONCLUSION: Our study suggests that the SBTT of MiroCam ® CE was superior to Given ® CE, but it does not influence the positive findings or complete examination rate. However, a longer SBTT is associated with a longer reading time, an important aspect in daily clinical practice.
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Disclosure of Interest: None declared

P0792 THE USE OF SMALL BOWEL CAPSULE ENDOSCOPY IN OCTOGENARIANS; THE EDINBURGH EXPERIENCE

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INTRODUCTION: Over the last 13 years, the clinical use of capsule endoscopy (CE) has revolutionised the investigation pathways for the small-bowel. Although (as procedure) non-invasive, there are reports of capsule aspiration in certain patient-groups.[1] Moreover, CE video sequence review is a time-consuming process and – on occasions – with limited diagnostic yield (DY). There is scarcity of data on the use of CE in octogenarians.[2-4]
AIMS & METHODS: Aim: We aim to report our centre's experience in using CE in octogenarians. **Setting:** University hospital & tertiary referral centre for CE for the South East of Scotland. Retrospective study; the small-bowel CE database of our unit was interrogated for patients > 80 years of age who underwent CE. Categorical data are reported as mean ±SD (range). The *Fischer's* exact, the *chi-square* and the *t* (unpaired) tests were used to compare datasets. A two-tailed *P* value of <0.05 was considered statistically significant.
RESULTS: 1,477 patients underwent small-bowel CE between 2005 and 2013. 93 CE were performed in 84 (35M/59F) octogenarians; mean age 84 ±2.9 years. PillCam®SB1/SB2 & MiroCam® were used in 61 & 32 CE examinations, respectively. Ten (11.9%) patients had more than 1 CE. One patient was unable to swallow the capsule, and in another the capsule was retained in the stomach. The CE report was unavailable in one case. Indications for small-bowel CE were iron deficiency anaemia (IDA): 44, obscure gastrointestinal bleeding (OGIB): 29, OBIG+IDA: 6, diarrhoea: 4,?small-bowel varices:1. Forty-five (53.6%) patients subsequently died. The mean time from small-bowel CE to death was 23 ±20.9 months, (range: 0.13-83 months). The DY (all findings) of CE in our octogenarian cohort was 56.8%. Vascular lesions (any P class)/active bleeding were found in 33, inflammatory pathology in 9, and other findings in 4 CE. No neoplastic pathology was identified. The DY was independent to the indications for the procedure ($P=0.166$), the small-bowel CE system used ($P=0.068$), the patient final outcome i.e. deceased/alive ($P=0.051$) and/or the time from CE to death ($P=0.053$).
CONCLUSION: CE in patients >80 years of age has high DY, but sinister pathology in this cohort is rare. Furthermore, small-bowel CE has limited impact on the final patient outcome in this patient-group.
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P0793 USEFULNESS OF FLEXIBLE SPECTRAL IMAGING COLOR ENHANCEMENT (FICE) IN DIFFICULT TO INTERPRET MUCOSAL ULCERATIVE LESIONS OF THE SMALL BOWEL

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INTRODUCTION: Identification of subtle small bowel mucosal lesions can sometimes be challenging, as small differences in mucosal hue or pattern are difficult to detect. To overcome this problem, chromoendoscopy virtual techniques based on narrowing the bandwidth of the conventional white light endoscopy (WLE) image were imagined, possibly allowing for contrast-enhanced assessment of the nature of small-bowel mucosal lesions. However, data on the already implemented FICE (Flexible spectral Imaging Color Enhancement) software application in videocapsule endoscopy (VCE) are limited.[1-3]
AIMS & METHODS: This is a multicenter study involving a selection of mixed de-identified images of 250 difficult to interpret small bowel ulcerative lesions (selected as the least representative visualization of an unequivocally confirmed erosion from a succession of images, comprising small or shallow mucosal defects, erosions lacking a clear rim of erythema or located marginally in the field of view, or lesions with a poor image quality due to luminal content), and 50 artifacts mimicking ulcerative lesions, all selected from the 64 VCE recordings in a prospective study (*ClinicalTrials.gov ID NCT00768950*). The evaluation was performed by three blinded experienced VCE readers in two steps, initially as white light images, then with the addition of all available FICE settings (1,2,3 and Blue), labeling them as real or faked lesions and rating each FICE setting as useful or not. The comparison of accuracies in correctly categorizing the images was performed between the two readings (McNemar's test).
RESULTS: Between the first (WLE only) and the second (FICE aided) reading, in terms of accuracy, there was a 19.5% [95% CI:15.7% to 23%] improvement (from 52% to 71.5%) in the global evaluation of all images ($p<0.001$), coming from a 26% [95% CI: 22% to 30%] improvement (from 47% to 73%) in the evaluation of true ulcerative images ($p<0.001$), and a 12% [95% CI: 3.5% to 22%] decrease (from 75% to 63%) in the evaluation of faked ulcerative images ($p<0.01$), results reproduced for all three readers. FICE 1 and 2 settings were rated as most useful.
CONCLUSION: This study demonstrates that FICE virtual chromoendoscopy (mostly settings 1 and 2) applied for VCE is useful to enhance surface patterns and color differences and to better categorize difficult to interpret small bowel mucosal ulcerative lesions. However, care must be taken, and individual images should only be evaluated as part of a succession in a recording, as the technology could also misguide the interpretation of artifacts as ulcerative lesions.
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Disclosure of Interest: None declared

P0794 THE CORRELATION OF WIRELESS VIDEO CAPSULE ENDOSCOPY AND OTHER RADIOLOGICAL IMAGING IN THE INVESTIGATION OF SUSPECTED AND ESTABLISHED SMALL BOWEL CROHN'S DISEASE

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INTRODUCTION: Background: In recent times there have been significant advances in both the radiological, CT and MRI Enterocolysis (CTE / MRE) and the endoscopic, video capsule endoscopy (CE) investigation of small bowel disease. The optimal complimentary and appropriate use of various new evolving and standard diagnostic modalities remains to be established. In particular, their role in identifying small bowel Crohn's disease remains unclear. Early identification of ileal Crohn's disease is desirable to guide treatment and impact on long-term outcome.
AIMS & METHODS: Aim: To compare the diagnostic performance of CE and radiological imaging in detecting small bowel Crohn's disease in the local population and to correlate the findings of CE with other various imaging modalities. Method: A retrospective analysis was undertaken of a database of patients who underwent capsule endoscopy from 2009 to 2013 at Tallaght Hospital. Those patients who underwent CE for known histologically-confirmed or suspected Crohn's disease were identified. This cohort was cross-referenced with the Hospital Radiology Report system "Keogh" for the same period. Patient demographics, radiological procedures, CE and radiology findings were recorded. The diagnostic yield and correlation coefficient was calculated for radiological tests compared to CE.
RESULTS: Results: In all, 263 patients, 155 female (59%), mean age 41 years, had a CE for known (n = 29, 11%) or suspected (n = 234, 89%) Crohn's disease. In all 110 (42%) had active disease on CE. In only 96 (37%) patients additional radiological tests were available for comparison, 73 (76%) and 23 (24%) in positive and negative CE cases. Of 28 CTEs, 28 SBFTs and 17 Abdominal CTs performed in positive CE subjects only 37 (51%) also reported evidence of active Crohn's disease, overall correlation coefficient k = 0.49, 95% CI 0.37-0.61. SBFT was the least sensitive test, 32% (9/28), while CTE and Abdominal CTs had similar diagnostic yields of 64% (11/17) and 61% (17/28). Correlation was better among patients without active Crohn's disease, with 20 of 23 radiological tests, 7 CTEs, 7 SBFTs and 9 Abdominal CTs also being reported as normal, correlation coefficient k = 0.87, 95% CI 0.72-1.0. The incremental diagnostic yield for CE in patients with suspected or known Crohn's disease in our cohort compared to radiological investigations was 34%, CE 76% and all Radiology 42%. Table 1: Diagnostic yield according to test.

Number (%)	CE	CTE	CT-Abd	SBFT
Positive	73 (76%)	18 (51%)	11 (42%)	11 (31%)
Negative	23 (24%)	17 (49%)	15 (58%)	24 (69%)
Total	96	35 (36%)	26 (27%)	35 (36%)

CONCLUSION: Despite its poor diagnostic yield and the advent of new diagnostic modalities SBFT remains a frequently employed test in CD. Notwithstanding the inherent bias in our study, the findings suggest the correlation between CE and standard and targeted small bowel radiology is at best moderate, with CE having a higher diagnostic yield. CE should be considered in all subjects with suspected Crohn's disease.
Disclosure of Interest: None declared

P0795 PROSPECTIVE FOLLOW-UP OF MESENTERIC PANNICULITIS IN A FRENCH UNIVERSITY HOSPITAL; SHOULD WE GO ON WITH CLOSED FOLLOW UP OF PATIENTS?

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INTRODUCTION: Mesenteric panniculitis (MP) is a rare, non-specific inflammatory process affecting the adipose tissue of the mesentery. Symptoms may be absent or there may be fever, abdominal pain, vomiting or diarrhea. MP is characterised on computed tomography (CT) scan by an increased mesenteric fat density called "misty mesentery" and the presence of lymph nodes within the fatty mass; and sometimes the presence of a hypodense halo surrounding blood vessels and nodes called "fat ring sign", and/or a hyperdense pseudocapsule surrounding the mesenteric fat. Prior studies suggested an association of MP with malignancy and also with acute abdominal disorders, infectious or inflammatory diseases. However data are heterogeneous and mainly retrospective and patients' care and follow-up remain unclear.
AIMS & METHODS: We aimed to evaluate the prevalence of cancer in patients with MP on abdominopelvic CT scans, and to study clinical and radiological course of patients. A prospective and descriptive study was performed in a French University hospital. All CT scans performed in the Radiology department between January 2012 and February 2013 with a diagnosis of MP were recorded. The diagnosis of MP was defined as the presence of "misty mesentery", infracentimetric nodes, and the absence of invasion of the adjacent small-bowel loops and vascular structures. Clinical and radiological characteristics of patients with MP were recorded, and patients with isolated MP were followed-up in the Gastroenterology department. An initial search for associated disease, especially for cancer, was performed and prospective 1-year follow-up was proposed.
RESULTS: MP was diagnosed based on CT findings in 100 consecutive patients among 9027 abdominopelvic CT scans (1.1%) over the study period; 54 patients (54%) had cancer, of which 12 (22 %) were melanomas and 11 (20 %) were lymphomas. MP was present at the time of diagnosis (35/54), or appeared within the subsequent months (7/54). Twenty-two patients had MP associated with acute abdominal disorders, and 24 patients had isolated MP. Among those patients and during the prospective follow-up only one cancer was diagnosed, and it was a basal cell carcinoma. Regarding radiological aspects of MP: a pseudocapsule was found in 58 % of cases, a fat ring sign in 63 % of cases and a left-sided location in 88 % of cases. There were no significant difference between the radiological characteristics of MP according to the associated diseases, especially cancer.
CONCLUSION: This study is one of the largest to describe MP diagnosed at CT scan and the first to propose prospective evaluation of patients. MP is frequently associated with cancer, mainly melanoma and lymphoma, already documented at the time of MP diagnosis. However data from follow-up suggest that when PM is isolated, or associated with other disease there does not appear to be underlying or incidental cancer.
Disclosure of Interest: None declared

P0796 CT RADIOLOGICAL MODELLING OF THE UPPER GI TRACT ANATOMY; ESSENTIAL CLUES TO PERFORMING MAGNETIC ASSISTED CAPSULE ENDOSCOPY (MACE)

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INTRODUCTION: Capsule endoscopy, employed to investigate the small bowel, is now being further developed to visualise the upper GI tract. In a pig model, using a hand held magnet, we have demonstrated that magnetic assisted capsule endoscopy (MACE) in the stomach is feasible. However, it is unclear what the best methodology is to achieve complete gastric luminal views in humans. Our aim was to utilise CT modelling of the abdomen to determine the optimal placements of a capsule endoscope in the stomach to allow complete mucosal visualisation and to determine the optimal placement of the hand held magnet to aid pyloric traversing.
AIMS & METHODS: Using multiplanar reformatting, 100 good quality contrast abdominal CT scans were analysed to assess luminal visualisation by a magnetic capsule endoscope from 5 fixed stations throughout the stomach. From each station, we assessed the ability of a capsule endoscope to visualise 6 anatomical landmarks (cardia, fundus, body, incisura, antrum and pylorus). Success of visualisation of an anatomical area was only accepted when >90% mucosal visualisation was achieved from a particular station. The pyloric canal angles were calculated to create a vector. We mapped the position of this vector on the patient's skin (pyloric canal vector surface point) to determine the optimal placement of the magnet that would allow traversing of the capsule endoscope through the pylorus.
RESULTS: There were 65 female and 35 male patients. Mean age of patients was 53 years (s.d+/-18 years). Best mucosal visualisation of the stomach landmarks was achieved from 3 stations; fundal dependant, antral dependent and opposite the antral dependent points. Maximal visualisation of the whole of the stomach, required combining 2 stations as shown in Table 1

Station	Cardia (%)	Fundus (%)	Body (%)	Incisura (%)	Antrum (%)	Pylorus (%)
Station 1 + Station 3	87	99	99	100	100	45
Station 1 + Station 4	92	99	99	100	100	86

The optimal positioning of the magnet to aid pyloric traversing was posteriorly between vertebrae T5 to L2, in an area 10cm to the left and 18cm to the right (83% cases). Age > 55yrs ($p = 0.03$) and the ability to view the pylorus from station 3 ($p = 0.04$) was associated with an extreme pyloric canal vector.
CONCLUSION: CT modelling has provided important data regarding the optimal stations in the stomach to position a magnetic capsule endoscope to allow maximal luminal mucosal visualisation and traversing the pylorus. Although there is some extreme variation in the upper GI anatomy, the majority of cases will allow the use of a single standard method in performing MACE which may be very useful for screening purposes.
Disclosure of Interest: None declared

P0797 INVESTIGATION OF URGENT REFERRALS WITH UNEXPLAINED IRON DEFICIENCY ANAEMIA: IS A CT SCAN RELEVANT?

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INTRODUCTION: Anaemia is a common medical problem and can be due to deficiency of one or more nutrients, blood loss or a variety of medical problems. Generally, anaemia of almost any degree requires medical assessment so that the correct cause can be ascertained and appropriate treatment given. The patient's symptoms and initial FBC findings will influence both the urgency and direction of initial clinical investigation. Upper and lower GI investigations should be considered in all males and post-menopausal females with iron deficiency anaemia unless there is an obvious alternative cause. NICE guidelines for referral for suspected colorectal/ Upper GI cancer includes referral of patients with unexplained iron deficiency anaemia who are men of any age with a haemoglobin of 11 g/100 ml or below and who are non-menstruating women with a haemoglobin of 10 g/100 ml or below. Unexplained iron deficiency anaemia does not usually prompt a referral to chest physicians, gynaecologists nor the urologists.
AIMS & METHODS: All our urgent referral patients with iron deficiency anaemia are investigated with upper and lower GI endoscopy where possible and a CT scan of the chest abdomen and pelvis. We aimed to evaluate our management of these patients with respect to investigations performed, especially the cost effectiveness of a adding on a CT scan to the upper and lower GI scopes that are always part of this investigation.
All Urgent referrals to the Colorectal unit over a 3 month period were retrospectively analysed. CT scan, Colonoscopy and Flexible sigmoidoscopy data was collected as well as any histology obtained from biopsies taken.
Of 73 urgent referrals, 54 were referred with Iron deficiency anaemia. Of these, 46 (85%) underwent a Lower GI scope (37 Colonoscopy and 9 Flexible sigmoidoscopy); 8 did not undergo any scope - 1 failure, 1 refusal (both underwent CT pneumocolon) and 6 patients who were considered too frail, poor mobility etc. 43% patients undergoing colonoscopy were reported normal; of the 57% with findings, 28% were found to have bowel cancer. 98% patients referred urgently with unexplained iron deficiency anaemia underwent a CT scan; of these, 15 (28%) were normal. Of the remaining 38 patients, 47% had significant findings with respect to malignancy (half of which were bowel related) and the remaining 53% had other relevant non-cancer pathology (40% of which was bowel related). Hence, CT scans picked up non bowel related pathology that would not have been found on colonoscopy alone in 39% patients referred urgently with iron deficiency anaemia, 17% of which was significant with respect to malignancy.
CONCLUSION: Patients with iron deficiency anaemia are generally referred to gastroenterology / colorectal surgery for further investigations, with appropriate urgency. These patients are usually investigated with a gastroscopy and colonoscopy. We found our routine use of an addition of a CT scan chest, abdomen and pelvis yielded useful results, both related to malignant and non malignant non-bowel related pathology. This helped us guide further management appropriately, with an urgency dependent on the causative pathology. We would therefore recommend the routine use of a CT scan in the investigation of a patient referred urgently with iron deficiency anaemia, unless contraindicated for any reason.
Disclosure of Interest: None declared

P0798 PATIENT-RELATED FACTORS AFFECTING PATIENT ACCEPTANCE FOR REDUCED-LAXATIVE CT COLONOGRAPHY: WHO DOES PREFER TO CT COLONOGRAPHY?

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INTRODUCTION: Although CT colonography (CTC) is minimal invasive procedure, the actual patient acceptance for CTC varies between patients.
AIMS & METHODS: The aim of this prospective study was to assess patient tolerance and to identify the patient-related factors affecting the patient

acceptance of reduced-laxative CTC in screening purpose. A total of 1242 outpatients at average risk for colorectal cancer were consecutively enrolled in this study. All patients underwent reduced-laxative fecal-tagging CTC with 64-detector row CT using carbon dioxide insufflation. Patient's age, gender, height, weight, and the bowel habits were recorded before the procedure. After the procedure, acceptance and preference were evaluated using self-assessed questionnaires regarding tolerance assessment for overall procedure and preference for future testing.
RESULTS: Percentages of patients in good tolerance category for CTC were 83.9% (897/1069). Sixty percent (641/1062) of patients were willing to accept CTC as a future method of examination. Discomfort factors during CTC were abdominal distention (64.8%) and abdominal pain (4.9%). Among the patient factors, only the older age affected the degree of discomfort during CTC (over 60 vs. under 60, odds ratio = 1.59, p = 0.006). Patient factors of gender, BMI, constipation/laxative use, history of abdominal surgery, and previous colonoscopy or barium enema experiences were not related to patient tolerance during CTC.
CONCLUSION: An uncomfortable CTC procedure may be expected in elder patients. Overall, reduced-laxative CTC has excellent patient tolerance.
Disclosure of Interest: None declared

P0799 INCIDENTAL SLIDING HIATAL HERNIA: FINDINGS AND RELATIONSHIP WITH CT WITH WATER ENEMA AND CT COLONOGRAPHY

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INTRODUCTION: Barium-contrast radiography originally constituted the first development in diagnosing hiatal hernia (HH) and reflux disease however, conventional radiology is no more a gold standard investigation for their assessment. We observed in clinical practice a worrisome rate of HH type I reported as extracolonic finding during CT with water enema (CT-WE) and CT colonography (CTC), likely induced by increased intra-abdominal pressure due to colon distension. HH has been positively related with the incidence and severity of reflux disease and with the risk of its complications. Although HH is not a life-threatening condition it is our opinion that erroneous reporting of HH may trigger consecutive diagnostic unnecessary processes that induce unmotivated anxiety and expensive and time-consuming for the patient and the socio-sanitary system.
AIMS & METHODS: To determine whether colonic distension at CT-WE and CTC can induce a small incidental physiologic sliding hiatal hernia and whether exist differences between water and gas distension achieved with the two different techniques. We retrospectively evaluated 400 consecutive patients, 200 undergoing CT with water enema and 200 undergoing CT colonography, including 59 subjects who also underwent a routine abdominal CT evaluation at a different time, used as internal control, while a separate group of 200 consecutive patients who underwent abdominal CT evaluation was used as external control. Two abdominal radiologists assessed the CT exams for the presence of a sliding HH, grading the size as small, moderate, or large; the internal control groups were directly compared with the corresponding CT-WE or CTC study looking for a change in hernia size. We used the Fisher exact test applying a size-specific correction factor, in order to account for the effect of colonic distention: these "corrected" values were then individually compared with the external control group.
RESULTS: Sliding HH was present in 51% (102/200) of the CT-WE patients and in 48.5% (97/200) of the CTC patients. Internal control CT of the 31 patients with a hernia at CT-WE showed resolution of the hernia in 58.1% (18/31) of patients, including 76.5% (13/17) and 45.5% (5/11) of small and moderate HH. Comparison CT of the 28 patients with HH at CTC showed absence of the it in 57.1% (16/28) patients, including 68.8% (11/16) and 50% (5/10) of small and moderate HH. Its prevalence in the external control group was 22% (44/200), lower than the CT-WE and CTC cohorts' prevalence of 51% ($p < 0.0001$) and 48.5% ($p < 0.0001$). After applying the correction factors for the CT-WE and the CTC groups, the estimated residual prevalences (16% and 18.5%, respectively) were much closer to that of the external control patients ($p = 0.160$ for CT-WE and $p = 0.455$ for CTC).
CONCLUSION: Incidental findings at CT-WE and CTC should be considered according to the clinical background. Small sliding HH should not be reported in patients with unrelated symptoms undergoing CT-WE or CTC: when encountering these findings, accurate anamnesis and review of medical history looking for GERD-related symptoms are essential, in order to address these patients to a correct diagnostic iter, taking advantage from appropriate techniques such as GI endoscopy or esophageal manometry.
Disclosure of Interest: None declared

P0800 THE POTENTIAL OF MR COLONOGRAPHY AS A SCREENING TOOL FOR COLORECTAL CANCER: A COST-EFFECTIVENESS ANALYSIS

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INTRODUCTION: For colorectal cancer (CRC), a range of screening modalities is available. Based on diagnostic accuracy, colonoscopy is the preferred test but there is a low risk on serious complications and, due to the burdensome procedure, the population uptake is low. MR colonography may have potential as a CRC screening tool since it has comparable test characteristics as colonoscopy but is less invasive. Furthermore, innovators in the field of MR technology are striving to develop a targeted contrast agent that specifically detects adenomas at high risk of progressing to CRC. This might even further increase the potential of MR colonography for CRC screening.
AIMS & METHODS: To explore the potential of conventional and targeted MR colonography in terms of (cost-)effectiveness using the Adenoma and Serrated pathway to Colorectal CAncer (ASCCA) model.
Thirteen screening strategies were evaluated, differing in primary screening instrument and number of screening rounds. The strategies under consideration were conventional MR colonography, targeted MR colonography, colonoscopy and CT colonography with two, three and four screening rounds at a ten year screening interval. In addition, eleven rounds of biennial faecal immunochemical test (FIT) screening were evaluated because this is the current Dutch screening programme. For each strategy, both realistic and perfect participation rates were taken into account. Incremental costs and effects were estimated from a societal perspective with an ICER less than the Dutch GDP per capita in 2012, i.e. €35,823/LYG, considered as cost-effective.
RESULTS: All screening strategies were cost-effective compared to no screening. For conventional MR colonography, the ICER ranged between €1,271/LYG to €3,003/LYG for two to four screening rounds at a participation rate of 34%. For participation rates of 62% and 100%, this range was respectively €1,576/LYG to €3,777/LYG and €1,971/LYG to €4,577/LYG. However, conventional MR colonography screening was more expensive than other screening strategies at comparable LYG, for all participation rates. For example, colonoscopy at two to four screening rounds at realistic participation (22%) led to cost-savings of €71 to €87 at 0.025 to 0.035 LYG per person. The effectiveness of targeted MR colonography was only slightly higher than of conventional MR colonography but it was considerably more costly, even under the most favourable assumptions regarding test characteristics and costs per test.
CONCLUSION: This is the first study to evaluate the cost-effectiveness of MR colonography screening for CRC. Although conventional and targeted MR colonography are cost-effective compared to no screening, at the moment they cannot compete with more established screening tests because of the high costs per test.
Disclosure of Interest: None declared

P0801 PRELIMINARY STUDY OF PHOTODYNAMIC DIAGNOSIS USING 5-AMINOLEVULINIC ACID IN GASTRIC AND COLORECTAL TUMORS

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INTRODUCTION: Photodynamic diagnosis (PDD) using 5-aminolevulinic acid (5-ALA), has been performed to detect the accumulation of fluorescent protoporphyrin IX (PpIX) in tumors. 5-ALA is a precursor of the fluorescence-emitting PpIX, and PpIX accumulates specifically in tumor cells and emits fluorescence when the excitation light irradiated on them. This property of 5-ALA may improve the endoscopic diagnosis of gastric and colorectal tumors.
AIMS & METHODS: In this preliminary study, we investigated the utility of 5-ALA using PDD in the detection of gastric and colorectal tumors. This prospective single-center study investigated inter-subject variability in patients with early stage gastric or colorectal tumor indicated for endoscopic resection. Patient selection criteria were age 20–80 years, either sex, and provision of informed consent. After oral administration of 5-ALA, endoscopic resection of gastric or colorectal tumors was performed, then the resected specimens were subjected to fluorescence endoscopy to examine for red fluorescence. Endoscopic, macroscopic, and histopathologic findings of the tumors were assessed.
RESULTS: Ten patients (7 men and 3 women) with a total of 13 lesions (10 gastric and 3 colorectal tumors) were enrolled in this study. Fluorescence was detected in 7 (53.8%) of the 13 lesions. No significant differences were observed in sex, age, color of the tumor, tumor diameter, macroscopic type, histological type, invasion depth, lymph node metastasis, or procedure time between the cases with and without fluorescence. The detection rate of fluorescence tended to be high for elevated lesions. Liver dysfunction developed in 4 (40.0%) of the 10 patients.
CONCLUSION: The results of this preliminary study suggest the utility of PDD using 5-ALA for screening gastric and colorectal cancers.
Disclosure of Interest: None declared

P0802 INCREASED VISCERAL TO SUBCUTANEOUS FAT RATIO IS ASSOCIATED WITH LOWER RISK OF IBD RELATED SURGERY IN PATIENTS WITH CROHN'S DISEASE ON INFLIXIMAB

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INTRODUCTION: Fat wrapping and mesenteric hypertrophy are characteristics of Crohn's disease (CD). In patients with CD, mesenteric adipose tissue releases higher levels of adiponectin, which could up-regulate production of tumor necrosis factor-α and increase the risk for aggressive disease. We have

previously shown that a higher visceral to subcutaneous fat ratio was associated with complicated (stricturing or fistuling) CD (reference).
AIMS & METHODS: The aim of this study was to investigate the effect of visceral fat accumulation on clinical outcomes in patients with CD on Infliximab. We identified patients with a confirmed diagnosis of CD on Infiximab who had computed tomography or magnetic resonance imaging scans of their abdomens within 12 weeks of starting infliximab, from the biologics database of Leeds Teaching Hospital NHS Trust. Areas of subcutaneous and visceral fat were measured in 1 cross-sectional scan, taken at the level of the umbilicus using a previously validated method. All measurements were made using Adode™ CS3 with magic wand function. The outcomes of interest were 1) IBD related flare (defined as increase in dose or steroid use or need for IBD related hospitalization or surgery), 2. Any IBD related surgery and 3) IBD related resectional surgery.
RESULTS: 150 patients with CD on Infliximab met our predefined inclusion criteria. The mean age of the patients was 37.2 ± 13.9 years. On multivariate analysis a higher visceral to subcutaneous fat ratio was associated with a lower risk of all IBD related surgery (HR 0.125 and 95% CI 0.02 0 0.81) and a lower risk of an IBD related flare that almost reached significance (HR 0.39, 95% CI 0.13-1.14). Females were less likely to need IBD related surgery ($p = 0.03$) and ileal and ileo-colonic disease was associated with a higher risk of surgery compared to colonic disease ($p = 0.03$). Only structuring and fistulating disease phenotype was significantly associated with a higher risk of resectional surgery ($p = 0.0.2$).
CONCLUSION: Higher visceral to subcutaneous fat on cross sectional imaging at baseline is associated with better clinical outcomes in patients with CD on Infliximab. This could imply that mesenteric fat hypertrophy has a protective role in CD.
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Disclosure of Interest: None declared

P0803 "DOUBLE-DUCT" SIGN - WHAT IS THE CLINICAL SIGNIFICANCE?

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INTRODUCTION: "Double-duct" sign on endoscopic retrograde cholangiopancreatography (ERCP) is considered suggestive of pancreatic or biliary malignancy [1]. This sign is frequently encountered in radiological imaging. We wish to investigate the prognostic value of the "double-duct" sign in patients who undergo magnetic resonance cholangio-pancreatogram (MRCP), attempting to define the associated features, which would predict underlying malignant disease [1,2].
AIMS & METHODS: An analysis of retrospectively collected database of all patients (n = 2,741) who had MRCP over a four-year period; January 2010 to December 2013 was performed. All the radiological reports showing both a dilated common bile duct (CBD) and pancreatic duct (PD) or the "double-duct" sign were included. These were all interpreted and reported by specialist gastrointestinal radiologist. The demographics, liver biochemistry, final diagnosis and outcome for all patients with the "double duct" sign were accessed using the radiology PACS® system, biochemical results WebICE®, hospital letters and case notes. Follow up information was available for a mean of 36 months (range 12-48 months).
RESULTS: 81 patients (annual incidence 2.2% - 3.3% incidence) had "double-duct" sign with a mean age of 71 years. The ratio of male to female patients was (F: M) 1.2:1. The commonest cause of double duct sign was choledo-cholithiasis (27.2%) followed by malignancy (20%). Patients with jaundice in the context of "double-duct" sign had a higher incidence of malignancy (48%). More than half of the patients, (48/81; 59%) with "double-duct" sign were anicteric. None of the anicteric patients were found to have malignancy ($p = 0.002$). Of the anicteric patients, 25% (12/48) had completely normal liver test and the remaining 75% (36/48) had some abnormality of the liver enzymes (raised GGT and/or Alkaline phosphatase). Four patients in the anicteric group had benign tumours (1 case of benign IPMN [Intra-ductal papillary mucinous neoplasm] and 3 cases of benign ampullary tumour, histology confirming low grade and high grade dysplasia without evidence of invasive malignancy on resection specimens). The benign nature was confirmed on clinical, pathological and radiological follow-up. All four patients remained anicteric over the period of follow-up (mean 24 months; and one unrelated death at 18 months). Our results show that "double duct" sign in the absence of jaundice makes a malignant aetiology unlikely.
CONCLUSION: In patients with cross-sectional imaging evidence of "double-duct" sign, the absence of jaundice makes a malignant aetiology unlikely. Conversely, in jaundiced patient a malignant cause is much more likely.
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Disclosure of Interest: None declared

P0804 QUANTITATIVE ASSESSMENT OF GLOBAL SMALL BOWEL MOTILITY IN CHRONIC INTESTINAL PSEUDO-OBSTRUCTION AND CONTROLS: A PRELIMINARY STUDY

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INTRODUCTION: In this preliminary report, we present the initial results of a prospective investigation comparing MRI quantified global small bowel motility in healthy controls and patients with proven clinical and radiological Chronic Intestinal pseudo-obstruction (CIPO). Diagnosis is initially difficult and often delayed, many patients undergoing unnecessary surgical intervention prior to final diagnosis. MRI offers a potential non-invasive modality of diagnosis and monitoring, employing post-processing quantitation of global metrics describing small bowel motility[1].
AIMS & METHODS: Subject selection: 11 healthy non-smoking volunteers (7 Male, mean age 33[22 to 48]) and 5 CIPO patients (3 Male, mean age 53[32 to 82]) were recruited. CIPO patients stopped any medications that influenced small bowel motility for one week prior to scan including opioids, anti-emetics & anti-diarrhoeals.
Study overview: Participants underwent a single MRI motility scan before and immediately after an injection of 0.5mg IV neostigmine, a cholinomimetic with potent prokinetic action.
MR Protocol: The motility scan protocol used a 3D Balanced Turbo Field Echo (BTFE) motility sequence capturing one coronal volume through the abdomen and pelvis per second over a 20 second breath hold (2.5x2.5x10 in mm resolution, FA 20, TE = 1.7ms, TR = 3.5ms, 15cm thickness in 15 reconstructed slices)
Motility Analysis: Dynamic time-series data was registered using a modified 2D optic-flow technique for each slice through the abdominal volume[2]. The deformation fields generated by the registration process were used to provide a motility metric (arbitrary unit, AU) expressed as the standard deviation of pixel's Jacobian (a measure of local area change) and averaged across a user defined ROI.
ROI Placement: A radiologist, with 5 years experience reading MRE, placed regions of interest (ROIs) around the small bowel in each coronal slice over the 15-slice volume. The radiologist was blinded both to subject group and whether the scan was pre-
RESULTS: 1) Mean baseline small bowel motility scores in CIPO patients was 0.19AU (range 0.1 to 0.25) and in controls 0.35AU (range 0.275 to 0.37) with a statistically significant difference of 0.17AU, ***p = 0.0026*** (CI 0.09 to 0.23).
2) The mean percent increase in small bowel motility scores in CIPO patients following noestigmine was 29% (95% CI from 19 to 50%) and in controls 10% (range 0 to 34) with a statistically significant difference in groups response to neostigmine of 19%, ***p = 0.029*** (95% CI from 4 to 40%).
CONCLUSION: This study demonstrated significant differences in both resting and cholinomimetic-induced global motility between CIPO patients and healthy controls. Despite marked bowel distension in the CIPO patients, motility appeared present but reduced compared to controls, and responded to provocation with neostigmine suggesting the bowel still exhibits the expected pro-kinetic effects following pharmacological stimulation. With just five patients this is a preliminary study, nevertheless initial results appear promising and support our ongoing investigation program.
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P0805 MALIGNANT GASTRODUODENAL OBSTRUCTION – TREATMENT WITH SELF-EXPANDABLE METALLIC STENTS IN A SINGLE REFERRAL CENTRE

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INTRODUCTION: Endoscopic treatment is a valid choice in treating malignant gastroduodenal obstruction, when patients are not candidates to surgery. Self-expandable metallic stents (SEMS) have been increasingly used in this context.
AIMS & METHODS: To retrospectively analyze the use of SEMS in malignant gastroduodenal obstructions, in one referral centre, over a period of 8 consecutive years.
RESULTS: SEMS were successfully inserted in 43 patients in this period (male sex 21 (48.8%); mean age 70.67+/-13.46 years), all of them complaining with stasis symptoms. Primary tumor was gastric adenocarcinoma in 26 patients (60.5%), pancreatic adenocarcinoma in 12 patients (27.9%), and cholangiocarcinoma, gallbladder and colon cancer in 5 patients (11.6%). The median time between tumor diagnosis and stent placement was 27.5 days (range 0-980). Complications to the procedure occurred in 3 patients (7%): hypovolemic shock, perforation and aspiration pneumonia. Clear clinical improvement (tolerance to oral intake) was seen in 26 patients (60.5%). In 10 patients (23.3%), reintervention due to stent occlusion was necessary, including stent-in-stent placement in 6 patients, balloon dilation in 2 and argon plasma coagulation in 2. Median survival after sent insertion was 42 days (range 1-420), with 15 patients (34.9%) dying within less than 30 days after the procedure, with no statistical significant differences between different ages and different types of primary tumor.
CONCLUSION: When feasible, SEMS placement is a safe and efficient therapy for malignant gastroduodenal obstruction. The relatively high percentage of patients that were dead one month after stent placement, in our series, may reflect an over-selection of patients that had too advanced a disease to benefit from this technique.
Disclosure of Interest: None declared

P0806 SELF EXPANDIBLE METAL STENTS IN VARICEAL BLEEDING AS THE BLAKEMORE-SENGSTAKEN TUBE OF NOWADAYS? – A SINGLE INSTITUTION EXPERIENCE

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INTRODUCTION: Despite a dramatic reduction of lethality rates due to upper gastrointestinal bleeding, esophageal variceal bleeding remains a challenge and still accounts for a mortality rate of up to 50 % within the first 6 weeks. Rapid and efficient varical ligations in combination with vasoactive terlipressin are key requirements for the initial patients stabilization. However, a relevant proportion of esophageal varical bleeding remains refractory, thus, making a call for additional tools to achieve hemostasis. Self expandible metal stents (SEMS) incorporate such a tool.
AIMS & METHODS: We report 12 cases of stent application in patients with variceal bleeding between 2011 and 2014. A retrospective analysis reporting a series of clinically relevant parameters in combination with bleeding control rates and adverse events was performed.
RESULTS: The initial bleeding control rate was 100 %. Despite this success, we observed a 30% mortality within the first 42 days due to non-hemorrhage associated reasons in the cirrhotic patients. Interestingly, we found in 7 out of 12 patients stent dislocation even after a proven correct position 24 h after hemostasis. The stent removal procedure appeared to be safe with slight reactivation of bleeding in only one of our patients. Of note, our study cohort required an extensive amount of hospital care.
CONCLUSION: Self expandible metal stents seem to be safe and efficient in patients with therapy refractory variceal bleeding. Despite high rates of stent migration no serious adverse events were observed in short term observation. This contrasts strongly with the formerly used Blakemore-Sengstaken tubes. Thus, SEMS should be considered as the new Gold standard in case of refractory esophageal bleeding.
Disclosure of Interest: None declared

P0807 SAFETY AND EFFICACY OF COLONIC STENTING: 7 YEAR EXPERIENCE FROM A DISTRICT GENERAL HOSPITAL IN THE UK

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INTRODUCTION: A significant proportion of patients with colon cancer present with partial or complete bowel obstruction. Emergency decompression surgery may be associated with up to 25% mortality[1]. Self expandable metal stents (SEMS) provide an alternative low-risk option for managing these patients[2] and have been routinely used as the first line of treatment of these patients in our hospital. The aim of this study was to assess the safety and efficacy of SEMS in malignant colonic obstruction (MCO) in a district general hospital (DGH) setting.
AIMS & METHODS: A retrospective study of patients presenting with MCO and treated with uncovered SEMS between 2007 and 2013 was carried out. All stents were deployed by experienced gastroenterologists. Data including patient demographics, indication and treatment intent, site of lesion, stent type, procedure outcome, adverse events, and outcome at six months were obtained using the endoscopy reporting software and hospital patient record.
RESULTS: 78 patients were included. 53 (68%) had elective and 25 (32%) had emergency stenting. Median age was 77 years (range 47-96 years). 53 (68%) patients were male. 4 (16%) out of 25 patients who underwent emergency stenting subsequently had curative surgery. 6 (11.3%) patients in the elective stenting group (n = 53) had curative surgery. Overall, SEMS was used as a bridge to surgery in 10 (12.8%) patients while 68 (87.2%) underwent palliative stenting. The sites of malignancy were as follows: sigmoid colon 40 (51.3%), descending colon 15 (19.2%), rectum 14 (17.9%), transverse colon 7 (9.0%) and anastomotic recurrence post left hemicolectomy 2 (2.6%). Procedure related serious complications included one case of stent related perforation (proceeded to palliative rescue Hartmann's procedure) and one of contrast extravasation (successfully managed conservatively). 3 patients presented with early stent failure from blocked stent – patency was restored in one with endoscopy, one underwent Hartmann's procedure and the third patient chose to be palliated. The stents did not adequately restore luminal patency in 2 patients despite optimal positioning. Stent migration was discovered in 2 patients who represented with partial obstruction. 2 patients with rectal stents complained of discomfort and were managed conservatively. The technical success rate was 98.7% (n = 77) and the clinical success rate (functional stent without complication) was 88.5%. The 30-day all-cause mortality was 10.3% (n = 8) with none being attributable to the procedure.
CONCLUSION: Our study shows that a safe and effective colonic stenting service can be delivered in a DGH setting. There was no procedure related mortality compared to emergency decompression surgery which has a higher mortality rate[1]. This relates to service delivery by experienced operators. We suggest that all DGH with acute surgical admissions should provide this service to reduce the morbidity and mortality related to emergency decompression surgery.
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Disclosure of Interest: None declared

P0808 ENDOSCOPIC STENT PLACEMENT OR SURGICAL GASTROJEJUNOSTOMY FOR THE PALLIATION OF MALIGNANT GASTRIC OUTLET OBSTRUCTION CAUSED BY UNRESECTABLE OR METASTATIC GASTRIC CANCER

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INTRODUCTION: Malignant gastric outlet obstruction (GOO) is traditionally treated with gastrojejunostomy (GJJ). Recently, endoscopic placement of a self-expanding metal stent (SEMS) to the GOO was covered by insurance and spread widely in Japan because it was a minimally invasive and effective method. The aim of this study was to verify the usefulness of SEMS compared with GJJ.
AIMS & METHODS: We conducted a retrospective study comparing the patients treated with endoscopic SEMS placement from April in 2010 to December 2013 with those treated with GJJ from April in 2000 to December 2013 in the management of malignant GOO caused by gastric cancer. Endoscopic SEMS placement was performed by using WallFlex duodenal stent (Boston Scientific, Tokyo, Japan). Following variables were evaluated between the SEMS group and the GJJ group; age, gender, clinical stage of gastric cancer, procedure time, Gastric Outlet Obstruction Scoring System (GOOSS) score, fasting period after placement, period of hospitalization after placement, survival period after placement, and complications.
RESULTS: The study subjects consisted of 16 patients in the SEMS group and 28 patients in the GJJ group. Between the 2 groups, there were no significant differences in median age (70 years vs. 72 years), percentage of women (31% vs. 18%), percentage of clinical stage at IV (81% vs. 89%), median GOOSS score (1 vs. 1). The technical success rates were 100% both in the SEMS group and the GJJ group. Median procedure time for SEMS stent placement was shorter than that for GJJ (25 minutes vs. 128 minutes; $P < 0.0001$). The clinical success rates were 88% in the SEMS group and 71% in the GJJ group ($p = 0.28$). The median GOOSS score after SEMS placement was similar to that after GJJ (3 vs. 3). However, the time to oral intake was significantly less in the SEMS group than in the GJJ group (2 days vs. 7 days; $p < 0.0001$). Early adverse event (occurring < 1 week) rates did not differ significantly between the 2 groups: (6% in the SEMS vs. 7% in the GJJ group). The median postprocedure length of hospital stay was shorter in the SEMS group than in the GJJ group, but not significant (17 days vs. 26 days; $p = 0.13$). Median postprocedure survival periods was similar in 2 treatment groups (68 days vs. 109 days; $p = 0.85$). Late adverse event (occurring ≥ 1 week) occurred in 2 patient in the SEMS group and 3 patients in GJJ group.
CONCLUSION: Endoscopic stent placement is preferable to GJJ in terms of shorter treatment time and more rapid improvement of food intake. Endoscopic stent placement seems to contribute to improve quality of life for the palliation of malignant GOO cause by gastric cancer.
Disclosure of Interest: None declared

P0809 ESOPHAGEAL COVERED STENTS FIXATION USING ENDOSCOPIC OVER-THE SCOPE CLIPS VERSUS ENDOSCOPIC SUTURING SYSTEM (WITH VIDEO)

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INTRODUCTION: Endoscopic prosthesis migration from the originally stented area occurs in up to 40% of cases and may lead to serious life-threatening complications. Endoscopic suture fixation of the stent using the OverStitch™ Suturing System (Apollo Endosurgery, Inc.) significantly reduces migration. However, suturing with the OverStitch™ has a steep learning curve and is time-consuming. A novel memory shape over-the-scope endoscopic clip, the Padlock™ clip, has been developed recently by Aponos Medical. The device is a preloaded "point & shoot" single-use instrument.
AIMS & METHODS: The aim of this study was to demonstrate that the anchoring of a covered Self-Expandable Metallic Stent using the Padlock™ clip is as effective as endoscopic suturing by means of the OverStitch™ and that Padlock™ fixation can be faster and user-friendly. Eleven pigs were involved in this experimental study. A fully covered esophageal stent (Wall-Flex, Boston Scientific) of 12.3cm in length, 18mm in diameter, was placed under endoscopic guidance at the esophagogastric junction. Five pigs underwent stent fixation with 1 figure-of-eight suture using the OverStitch™. In 4 pigs, the stent was fixed by firing the Aponos Clip over a loop of Vicryl 0, which was attached to the upper edge of the stent. In two pigs, the stent was placed but not fixed and was used as a control. A laparotomy was performed and a specifically designed pulling device made of 4 fishing hooks attached to a plastic ring was anchored to the distal part of the stent at 4 cardinal points after performing a gastrotomy. A suture attached to the plastic ring was passed over the holding hook of a Digital Dynamometer (Chatillon II, Ametek, Inc.). Constant traction was applied on the sutures until full stent mobilization was achieved. The force required to remove the stent was recorded.
RESULTS: Mean force to mobilize the stent was higher in the OverStitch™ group when compared to the Padlock™ group (23.99N; SD 14.91 vs. 19.97N;

SD 7.62), but the difference was not statistically significant. In the 2 control pigs, the force required was 7 and 11 Newtons respectively. Mean suturing time was statistically significantly higher when compared to the time required to apply the Padlock™ clip (455.4sec; SD 144.83 vs. 155sec; SD 12.9; p = 0.002).
CONCLUSION: Full-thickness Padlock™ clip application is faster and may achieve a comparable stent fixation when compared to endoscopic suturing with the OverStitch™.
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P0810 ENDOSCOPIC DILATATION OF BENIGN PYLORIC STENOSIS: IS IT A GOOD ALTERNATIVE TO SURGERY?

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INTRODUCTION: Pyloric stenosis is a common complication of ulcerative disease which requires surgery. The endoscopic dilatation is now a good alternative.
AIMS & METHODS: Aim: evaluate the efficiency of the endoscopic dilatation in the managment of benign pyloric stenosis due to ulcer diseases.
It is a prospective study from January 2009 to January 2014 including 21 patients. The dilatation was performed using a hydrostatic balloon.
RESULTS: There were 13 men and 8 women. Mean age was 48 years (35-70 years). 58 dilations were performed. In 11 cases (52 %), patients had ulcer disease and in 6 cases (29 %) non steroidal anti -inflammatory medication. The duration of symptoms was 13 months (3 months - 3 years). Vomiting and epigastric pain were the predominant clinical signs (90%). All patients underwent an upper endoscopy and had pyloric stenosis and / or pyloro - bulbar stenosis. 12 cases (57%) had impassable strictures. The average number of dilatations was three per patient (1-5). 17 patients (81%) had favorable response. The average follow-up time was 30 months (3-60 months).
CONCLUSION: Through this prospective study, we identified factors of success and failure of endoscopic dilation in benign pyloro-bulbar stenosis: the passable nature of the stenosis, the extent of the stenosis, the distance between the pylorus and the dental arches reflecting gastric distension and food stasis.
Disclosure of Interest: None declared

P0811 PREVIOUS BILIARY STENTING IS NOT REQUIRED BEFORE ENDOSCOPIC PLACEMENT OF DUODENAL COVERED SELF EXPANDABLE METAL STENTS

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INTRODUCTION: Gastroduodenal uncovered Self Expandable Metal Stent (SEMS) placement is the first line treatment in advanced malignant gastroduodenal obstruction. The main disadvantage of uncovered stents is recurrent obstruction, mainly due to tumor ingrowth. Covered SEMS (cSEMS) reduce the re-obstruction rate. As cSEMS are removable they could represent an alternative to surgery or endoscopic dilation in benign stricture. However, cSEMS placement covering the major papilla has been suspected to be responsible of mechanical occlusion the ampullary of Vater, which could lead to cholangitis or pancreatitis. Despite the lack of data, some authors recommend concomitant biliary stenting to guarantee the adequate bile outflow before duodenal cSEMS placement. Nevertheless, the need for biliary stenting in patient without concomitant biliary stricture before cSEMS placement remains unknown.
AIMS & METHODS: The aim of our study is to compare the occurrence of jaundice or pancreatitis after duodenal cSEMS placement in patients with biliary stenting *vs* patients with no biliary stenting.
All consecutive patients who underwent endoscopic duodenal cSEMS placement in the second duodenum area between June 2005 and March 2014, because of obstructive symptoms were assessed. Biliary stenting was performed when patients presented with associated biliary stricture. Patients with previous or concomitant biliary stenting (cSEMS+BS group) were compared to patients with no biliary stent (cSEMS group). The primary end point was the occurrence of jaundice during an observation period of 90 days. Secondary end points were bilirubinemia at baseline compared to day 10, technical success, clinical effectivenes and complications rates, during a follow-up period of 90 days.
RESULTS: 106 patients were included: 53 patients in the cSEMS group (58% male, mean 66.4+/-13.3 y/o) and 53 patients in cSEMS+BS group (60% male, mean 70.4+/-11.6y/o). The obstruction was due to cancer in 45% in cSEMS group and 87% in cSEMS+BS group. **No case of jaundice was reported in the cSEMS group or in the cSEMS+BS group.** We report one case (2%) of edematous pancreatitis after stent removal 90 days after stent placement in the cSEMS group (p = 1). In cSEMS group the mean bilirubin level (µmol/L ± SD) was 9.3± 5.8 at baseline and 8.4± 4.5 at day 10, while in the cSEMS-BS group it was 90.3±106.9 at baseline and 34.7 ±39 at day 10. No significant difference was observed between the two groups in term of technical success, clinical effectiveness, migration and other complications. In all patients, endoscopic duodenal stenting was successful. The global clinical effectiveness was 90%. The overall migration rate was 25% and the symptomatic migration rate, defined as obstructive symptoms recurrence, was 16%. Other reported complications were gastrointestinal bleeding (2% in cSEMS group vs 4 % in cSEMS-BS group), Duodenal perforation (0% in cSEMS group vs 4% in cSEMS-BS group), death from all causes (13% in cSEms group vs 28% in cSEMS-BS group, p = 0.06). We report 3% of stent obstruction due tumor ingrowth.
CONCLUSION: Concomitant biliary stenting is not recommended before covered duodenal SEMS placement in patients with no concomitant biliary obstruction.
Disclosure of Interest: None declared

P0812 ENDOSCOPIC THERAPY OF ESOPHAGEAL LEAKS WITH STENTS: EXPERIENCE IN A REFERRAL CENTER

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INTRODUCTION: Esophageal leaks have an important morbi-mortality. The best approach is still unclear; some studies show a potential benefit of stents. Randomized controlled trials are difficult in this area.
AIMS & METHODS: The aim of this study was to evaluate the efficacy of esophageal stents for the treatment of esophageal leaks.
Retrospective analysis of stent use for esophageal leaks. In a period of 60 months demographic data, leak etiology, endoscopic procedures, time until closure and fistula's relapse were analyzed.
RESULTS: 45 consecutive patients were included (29 males; mean age 63 years). 42% had post-operative leaks (10 after gastric sleeve, 6 after Y-Roux and 3 after subtotal esophagectomy), 42% had malignant esophagopulmonary fistulas (16 esophageal and 3 bronchogenic), 7% had boerhaave syndrome and 9% had iatrogenic perforation (2 foreign body and 2 after esophageal dilation). The median time for post-operative fistula detection was 16 days (4-145).
In 36 of the 45 patients the initial approach was using a stent. Of these, in 16 patients this was the only endoscopic therapy done. Metallic stents were inserted in 40 (13 partially covered, 27 fully covered) and plastic in 5. The rest of patients had another therapeutic endoscopic procedure - another stent (n = 10), through-the-scope (TTS) clip (n = 3), nasoenteric tube (n = 10), over-the-scope clip (n = 2) and argon-plasma coagulation (n = 6).
The median time for leak closure was 48.5 days (13-308). In 6 cases the fistula's closure wasn't documented.
In 4 patients there was relapse of the leak in a median of 125 days after the initial closure. All cases were managed endoscopically - metallic stent (n = 3), argon-plasma coagulation (n = 6), nasoenteric tube (n = 3) and TTS clip (n = 1). In 3 cases there was closure in a median of 27 days after the diagnosis.
In 12 patients the overall endoscopic approach failed and surgery was needed in 8 patients and percutaneous drainage in 4.
The observed complications were: stent migration (n = 10), upper GI bleeding (n = 2). There was no need for surgery in any case or death for a procedure related complication.
CONCLUSION: The use of esophageal stents seems to be a safe and effective therapy for esophageal leaks.
Disclosure of Interest: None declared

P0813 TREATMENT OF POSTOPERATIVE LEAKS OF THE UPPER GASTROINTESTINAL TRACT WITH COLONIC SELF-EXPANDABLE METAL STENTS: SINGLE CENTRE EXPERIENCE

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INTRODUCTION: The use of self-expandable metal stents (SEMS) for the treatment of postoperative leaks of the upper gastrointestinal tract is already established. However, there are discrepancies between the relatively small caliber of the esophageal stents available in our center and the post-surgical luminal size, which may determine an inadequate juxtaposition. As colonic stents have a bigger diameter, they might be more adequate. Additionally, stents with a larger diameter might have a lower risk of migration.
AIMS & METHODS: The aim of this study was to evaluate the efficacy and complications associated with the use of colonic SEMS in the treatment of postoperative leaks in critical patients. All patients with postoperative leaks of the upper gastrointestinal tract treated with colonic stents (Hanarostent® CCI) between 2010 and 2013 were retrospectively included.
RESULTS: Four patients with postoperative leaks treated with colonic SEMS were identified (3 men, 1 woman) with a mean age of 63. The underlying surgeries were a gastric bypass, an esophagogastrectomy for Boerhaave syndrome, a primary repair of esophagopleural fistula due to Boerhaave syndrome and an esophagectomy due to squamous cell cancer of esophagus. The leaks were detected on average 17 days after the initial surgery, and surgical resolution wasn't possible. In this way, the four cases were of difficult management, and in need of urgent care. They were all admitted to the intensive care unit.
Stent placement was technically feasible in all patients. There were no cases of stent dislocation. The median residence time of the stent was 7 weeks, and no complications were verified when they were removed. The treatment was successful in all patients, with complete healing of the leaks. On follow-up, one of the patients needs periodic endoscopic dilation due to esophagogastric stenosis. Another patient died 15 days after stent removal, due to septic shock not related to the procedure.
CONCLUSION: The placement of colonic SEMS seems to be successful and safe in the treatment of postoperative leaks of the upper gastrointestinal tract.

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P0814 TIPS BEYOND THE CLASSICALLY RECOMMENDED: IN SEVERE HYPERTENSIVE GASTROPATHY

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INTRODUCTION: In addition to variceal hemorrhage, upper gastrointestinal bleeding due to hypertensive gastropathy may also occur in liver cirrhosis with portal hypertension, contributing to the poor prognosis of these patients. The portal decompression achieved by transjugular intrahepatic portosystemic shunts (TIPS) has shown positive results in the treatment/secondary prophylaxis of variceal hemorrhage, and in that sense, the analysis of their value in other complications of portal hypertension becomes relevant.
AIMS & METHODS: The aim of this study was to evaluate the efficacy and safety of TIPS in patients with severe hypertensive gastropathy.
Retrospective study including patients undergoing TIPS for severe hypertensive gastropathy in a hospital in the period between 2000 and 2013, evaluating: demographic characteristics (age, gender), liver disease (cirrhosis etiology, prior therapy, Child-Pugh, MELD), episode of decompensation (clinical and analytical parameters) and outcome (effectiveness, complications after TIPS, liver transplantation, death at 30 days and at 1 year).
RESULTS: Of the 8 patients with severe hypertensive gastropathy with recurrent medical therapy undergoing TIPS, 62.5% were male with a mean age of 53 ± 15 years. In terms of the underlying liver disease: 37.5 % had alcoholic cirrhosis, average MELD of 17 and Child-Pugh stage C in 50%. TIPS has proved effective in only 28.6% of the patients. Portosystemic encephalopathy was recorded in 57.4% of the cases. Mortality: 1 case at 30 days and 28.6% at year, both Child-Pugh C. No other feature was implicated in the prognosis of patients after TIPS placement. Two patients underwent liver transplantation. The mean follow-up was 773 days (0-3534 days).
CONCLUSION: Given the low rates of efficacy and high morbidity and mortality rates, TIPS should be carefully weighed in patients with severe hypertensive gastropathy, especially in those with more advanced liver disease.
Disclosure of Interest: None declared

P0815 TIPS IN REFRACTORY HYDROTHORAX – A CONTRIBUTION TO AN INCREASED RELEVANCE

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INTRODUCTION: Hepatic hydrothorax (HHT) is a relatively rare complication of portal hypertension, but potentially severe. Although conservative therapy may be effective, it is not without risk and refractory cases are not rare. The portal decompression achieved by transjugular intrahepatic portosystemic shunts (TIPS) have shown positive results in the treatment of refractory ascites, and in that sense, the analysis of their value in other complications of portal hypertension becomes relevant.
AIMS & METHODS: The aim of this study was to evaluate the efficacy and safety of TIPS in patients with HHT.
Retrospective study including patients with HHT undergoing TIPS in a hospital in the period between 2000 and 2013, evaluating: demographic characteristics (age, gender), liver disease (cirrhosis etiology, prior therapy, Child-Pugh, MELD) episode of decompensation (clinical and analytical parameters) and outcome (effectiveness, complications after TIPS, liver transplantation, death at 30 days and 1 year).
RESULTS: 15 patients with HHT underwent TIPS, most previously underwent multiple thoracenteses and all with hypoalbuminemia, 60% > male, mean age 63 ± 9years, 73% with cirrhosis of alcoholic etiology, mean MELD-16 and 53% with Child-Pugh B. TIPS was effective in 50% of cases. Portosystemic encephalopathy was recorded in 66.6% of the cases. Mortality: 20% at 30 days and 40% at year with septic complications or progression of liver disease. Two cases underwent liver transplantation. In the univariate analysis, only the hematocrit value had prognostic value ($p = 0.016$). The mean follow-up was 443 days (1-2250 days).
CONCLUSION: TIPS appears to be a relatively efficient method of control HHT, making it a valid option in refractory cases despite the high risk of portosystemic encephalopathy and mortality. Low hematocrit levels seem to imply a worse prognosis of patients to be considered for TIPS for refractory HHT.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
SURGERY II – POSTER EXHIBITION – HALL XL

P0816 DIFFERENCES IN MORTALITY BETWEEN ARTERIAL, VENOUS AND NON-OCCLUSIVE MESENTERIC INFARCTION. A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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INTRODUCTION: Acute mesenteric infarction is a rare but often lethal event. Primary vascular aetiology can be of arterial, venous or a Non-occlusive mechanism. Mortality from acute mesenteric infarction may vary with aetiology. The aim of this study is to determine whether there are differences in mortality between arterial, venous and non-occlusive mesenteric infarction.
AIMS & METHODS: A literature search was performed via PubMed, Ovid and Google Scholar. Studies that had reported comparative mortality between arterial, venous and Non-occlusive mesenteric infarction (NOMI) were included. Odds ratios of mortality were calculated using a Mantel-Haenszel, random effect model. Meta-regression was attempted, however due to lack of adequate information in studies, it was not possible.
RESULTS: A total of 1,207 articles were screened. Of which, 20 were suitable for data synthesis for arterial vs. venous infarction, 16 for NOMI vs. venous infarction and 15 for Arterial vs. NOMI. When compared with venous infarction, patients who had arterial infarction were significantly more likely to die during primary hospital admission (OR 3.47, CI 2.43-4.96, $p = < 0.001$). Similarly, patients with NOMI were over three times more likely to die during hospital admission compared with those with venous infarction (OR 3.2, CI 1.83-5.6, $p = < 0.001$). There was no difference in mortality rates between arterial infarction and NOMI (OR 1.08, CI 0.57-2.03, $p = 0.82$)
CONCLUSION: Patients with arterial infarction or NOMI are over three times more likely to die from mesenteric infarction during primary hospital admission.
Disclosure of Interest: None declared

P0817 A SCORING SYSTEM TO DISTINGUISH SIMPLE FROM PERFORATED APPENDICITIS BASED ON CLINICAL PLUS IMAGING FEATURES

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INTRODUCTION: During the last decade, conservative management is suggested to be a safe and effective alternative to appendectomy for selected patients with non-perforated (simple) appendicitis. However, preoperative selection of patients with uncomplicated appendicitis is proven to be a challenge. Computed tomography (CT) is generally accepted as the most accurate test for the diagnosis of acute appendicitis, but the performance of CT in distinguishing simple from perforated appendicitis is by far not accurate enough.
AIMS & METHODS: The aim of this study was to analyse clinical and CT features associated with perforation and to develop a scoring system for the selection of patients with simple appendicitis.
All patients with a final diagnosis of acute appendicitis were selected from a prospective database including adult patients with acute abdominal pain. The final diagnosis was assigned by an expert panel based on perioperative data, histopathology and at least 3-months of follow-up. Predefined clinical and imaging features were recorded in a structured online case record form. Only patients in whom CT was performed were included in the present analysis. Medical literature was searched and several clinical and imaging features suggested to be associated with perforated appendicitis were selected. Stepwise backward elimination ($p < 0.05$) was used to construct a multivariable regression model with independent predictors of perforation. The discriminatory capacity of the model was expressed as the area under the curve (AUC). The model was transformed into a clinically applicable scoring system and a cut-off analysis was performed to illustrate the consequences in our cohort.
RESULTS: A total of 333 patients with a final diagnosis of acute appendicitis were identified. A CT was performed in 281 patients of whom 65 (23%) had perforated appendicitis. The final model for clinical and CT features included; age > 45 years (OR 2.726; 95%CI 1.363-5.452), temperature >37.2 (OR 6.066; 95%CI 2.632-13.978), white blood cell count > 10 x 10^9/L (OR 4.786; 95%CI 1.532-14.952), c-reactive protein 45 > mg/L (OR 4.761; 95%CI 2.263-10.016), appendicolith on CT (OR 2.309; 95%CI 1.142-4.661), destruction of appendiceal wall on CT (OR 2.370; 95%CI 1.028-5.467) and free extraluminal air on CT (OR 4.026; 95%CI 1.172-13.829). The model had a discriminative value of 0.850 (95%CI 0.801-0.898). A scoring system was constructed and points were assigned for every variable, with a maximum score of 27 points. Using this score in the study cohort, 134 (48%) patients were identified with a score of 12 or less of whom 7 (5%) had perforated appendicitis, resulting in a negative predictive value of 95%.
CONCLUSION: Using this simple scoring system, a subgroup of patients with simple appendicitis can be identified based on clinical and CT features with a low percentage (5%) of false negatives (i.e. patients with perforated appendicitis). These patients can be considered for treatment options other than appendectomy.
Disclosure of Interest: None declared

P0818 SURGICAL META-EVIDENCE AND ITS CURRENT CHALLENGES

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INTRODUCTION: The aim of this study was to compare the methodological quality and input paper characteristics of systematic reviews and meta-analyses done in the medical and surgical literature by performing a systematic "overview of reviews". Ulcerative colitis (UC) and Crohn's disease (CD) were used as the framework for this comparison as they are relatively common, serious conditions with medical and surgical therapy options.
AIMS & METHODS: MEDLINE, Embase, CINHAL and the Cochrane Database were searched to November 2013. Eligible papers were systematic reviews or meta-analyses that considered a question of therapy in either CD or UC. Two independent reviewers selected the papers, extracted the data and scored their methodology using the AMSTAR scoring system. The papers were categorized into medical therapy (M), surgical therapy (S), or surgical and medical therapy (MS) groups.
Following retrieval of the sample of meta-evidence papers, the original input studies used in their creation were identified and a search of MEDLINE, Embase, CINHAL and the Cochrane Database was performed. A team of researchers then examined this collection of papers for bibliographic and financial information.
RESULTS: 500 papers were identified in the meta-evidence search. 114 were deemed eligible. There was a significant difference in the AMSTAR-rated average quality of the papers (S 7.36, M 8.87, MS 8.11, ANOVA $p=0.016$). On average S papers were published in journals with a lower impact factor (S 3.26, M 5.13, MS 5.32, $p<0.001$). S papers also showed more heterogeneity (I^2: S 37%, M 24%, MS 10%, $p<0.001$). Some 25% of S meta-analyses used data-sets with significant heterogeneity ($I^2 > 75\%$), compared to 8% of M meta-analyses and 3% of the MS group. Some 5% of S papers were done on data sets that had I^2 values $> 90\%$.
There was no significant difference in the average number of papers assessed in each group (S 15.5, M 12.33, MS 15.2, p 0.38), the average number of patients per meta-paper (S 1,304, M 1,757, MS 2,576, $p=0.2$), the average time over which the reviews covered (S 16.1yrs, M 15.2yrs, MS 14.8yrs, $p=0.93$), the average number of papers considered within each meta-analysis (S 5.7, M 5, MS 3.8, $p=0.45$), or the average number of patients considered within each meta-analysis (S 632, M 689, MS 473, $p=0.12$). Considering the conclusions of each meta-analysis, S meta-evidence was 50% more likely than M meta-evidence to be unable to make recommendations for practice.
1,443 original input papers were identified, of which 469 were duplicates. Within the non-duplicate papers ($n=974$) the average impact factor within the S group was lower than that of the M and the MS groups (3.805 vs 10.241 & 7.062, ANOVA $p<0.001$). When compared with S papers, M papers had higher rates of pharmaceutical sponsorship (M 51% vs S 1%) and twice the level of government support (M 14% vs S 7%). Of note, 21% of M papers had corporate sponsorship but did not list any conflict of interest.
CONCLUSION: Compared to medical meta-analyses, surgical meta-analyses, in the UC and CD domain, are more likely to be of poorer methodological quality, are of a greater degree of heterogeneity, and less often offer a positive conclusion. The input papers used to generate meta-evidence in medical papers have a greater degree of corporate and government sponsorship, and are more likely to come from journals with higher impact factors.
Disclosure of Interest: None declared

P0819 ALTERED CORTICAL PROCESSING IN RESPONSE TO RECTAL STIMULI IN PATIENTS SUFFERING FROM IDIOPATHIC FECAL INCONTINENCE

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INTRODUCTION: The role of intact sensory function of both the rectum and the anal canal has been recognized to be essential for fecal continence. We hypothesized that a cause of idiopathic fecal incontinence is related to changes in the afferent sensory pathways and that this would be reflected in cortical potentials evoked by mechanical stimulation of the rectum.
AIMS & METHODS: Nineteen healthy women (mean age 54±12, mean Wexner score 1.5) and 20 women suffering from ideopathic fecal incontinence (mean 61±13, mean Wexner score 14.5) underwent repeated rapid balloon distensions of the rectum at the level of discomfort/ urge to defecate under simultaneous recording of cortical evoked potentials. Single sweep spectral band analysis was conducted to obtain the relative EEG amplitude within each frequency band.
RESULTS: The latency of the cortical evoked potentials generated in the vertex electrode of idiopathic fecal incontinence patients was longer than in healthy subjects ($p<0.001$), but there were no differences in location or strength of electrical sources in areas involved in the cerebral processing (insula, secondary somatosensory cortex and mid-cingulate gyrus bilaterally).
Analysing spectral contents of single sweeps, we found a significant increase in the alpha (8 - 12 Hz) and beta (12-32 Hz) bands ($p<0.001$) and a significant decrease in the gamma (32-70 Hz) band ($p<0.0001$) whereas low frequency bands did not differ. The changes in the gamma band were negatively correlated to the anal resting- and squeeze pressure as well as the first urge to defecate.
CONCLUSION: Our study indicates that idiopathic fecal incontinence is associated with abnormal rectal sensory perception and cortical processing of the afferent activity.
Disclosure of Interest: None declared

P0820 ENDOSCOPIC INTERNAL DRAINAGE FOR TREATMENT OF LEAKS FOLLOWING SLEEVE GASTRECTOMY

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INTRODUCTION: The most common complications of sleeve gastrectomy (SG) are gastric line leaks (GLL). Standard management protocol for GLL is not yet established. We report our experience about endoscopic internal drainage (EID) using double plastic pigtails stent changed between 4 and 6 weeks until healing.
AIMS & METHODS: 34 pts (26 F), 43.6 y (23 – 70) presented GLL 12.8 days (1 – 97) from surgery. 8 patients underwent single port and 26 laparoscopic SG. 25 patients underwent a second surgery at 10.6 (0 – 97) days from SG. 9 out 34 patients presented peri-gastric collections and fever. One, two or three plastic pigtail stents (AdvanixÒ, Boston Scientific®), according to orifice's size and collection, were delivered with the one end in the collection and the other one in the stomach. In 26 patients a naso-jejunal feeding tube was inserted and kept NPO. 2 presented jejunostomy, and 4 kept to eat normal. Endoscopic control was performed systematically between 4 - 6 weeks, with either re-stenting (if the leak was still present), or removal (if no extravasation of contrast medium in the peritoneal cavity was detected), or closure with an OTSC® (if contrast material passed through the crossing stent without concomitant detection in the peritoneal cavity).
RESULTS: EID was possible in 97% (33/34) of patient. 1 (3%) was perforated during stenting deliver. 13 patients were healed at first control, 32.3 days (26 – 54) from stenting, 2 needed OTSC®. At a second control, 61.6 days (48 – 87) by first EID, 10 patients respected criteria of good outcome, 4 presented a sealed fistula, 6 needed OTSC®. Three patients healed as follows: three changes at 84 days, fourth change at 135 days, and at 180 days follows 7 changes respectively. 1 patient died, 24h later EID for pulmonary embolism. Overall, 6 out 32 patients (18.8 %) are still under treatment, and 26/32 (81.2 %) were healed with an average time of EID treatment of 57.4 days (26 – 180), they are now symptom-free, on a normal diet at a median follow up of 129 days (2 – 276).
CONCLUSION: EID is a promising therapeutic mini invasive approach for the treatment of leaks following SG, well tolerated by patients, despite the need of multiple endoscopic sessions. It allows draining peri-gastric collections and promotes tissue regrow, permitting to avoid re-surgery.
Disclosure of Interest: None declared

P0821 PERINEAL WOUND PROBLEMS AFTER ABDOMINOPERINEAL RESECTION FOR RECTAL CANCER; A TWO-INSTITUTIONAL EXPERIENCE IN THE ERA OF INTENSIFIED ONCOLOGICAL TREATMENT

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INTRODUCTION: Intensified treatment for distal rectal cancer has improved oncological outcome but at the cost of more perineal wound problems in patients undergoing an abdominoperineal resection (APR). The aim of this study was to analyse perineal wound healing after APR with primary perineal wound closure over time.
AIMS & METHODS: All patients undergoing APR for primary rectal cancer with primary wound closure between 2000 and 2013 were included and analysed in three consecutive time periods. Both early (<30 days postoperatively) and late perineal wound complications were determined. Independent risk factors of perineal wound complications were identified using multivariable analysis.
RESULTS: In total 136 patients were identified, of whom 129 patients underwent primary perineal wound closure. The use of neo-adjuvant (chemo)radiotherapy increased from 58% to 91% and the use of an extralevator approach increased from 9% to 19%. The rate of complicated perineal wound healing increased from 18% to 31%. An extralevator approach (OR 3.17; 95% CI 1.16-8.66) and intra-operative perforation (OR 3.35; 95% CI 1.06-10.57) were independent predictors for perineal wound complications. No differences in oncological outcome were found in patients with and without perineal wound complications. During a median follow-up of 28 months (IQR 14-56), 3% developed a perineal fistula, in 8% a persistent presacral sinus was diagnosed, and in 8% of the patients a perineal hernia occurred.
CONCLUSION: The increased use of an extralevator approach significantly increased the perineal wound complication rate over time. Intra-operative perforation was also an independent predictor of perineal wound problems.
Disclosure of Interest: None declared

P0822 SEALING BOWEL DEFECTS WITH TISSUE ADHESIVES: A COMPARATIVE ANALYSIS OF THE CLINICAL, MECHANICAL AND HISTOPATHOLOGICAL EFFECTS OF 7 SURGICAL ADHESIVES

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INTRODUCTION: The use of tissue adhesives (TA) in bowel surgery is gaining popularity. Sealing bowel defects with TA may be a quick and safe alternative to suture closure. This study provides information on the sealing capability of several TA, as well as their histopathological effects on colonic tissue, providing a tool for the selection of the optimal TA.
AIMS & METHODS: 160 rats received a 0.5 cm incision in the proximal and distal colon which was then sealed with 1 of the following TA: Histoacryl Flex, Bioglue, Dermabond, Evicel, Duraseal Xact, Gelatin-Resorcinol-Formaldehyde and Glubran 2. A control group without TA was also included. Follow-up was 3 or 10 days. Leakage related complications were noted, bursting pressure (BP) and histopathological analysis were performed.
RESULTS: At 3 days leakage rates were highest in the control group and for Bioglue, Duraseal Xact and Tissucol. Glubran 2 and Tissucol showed the lowest Leakage rates. BP was highest in Duraseal Xact, Tissucol and Omnex. Histopathologically Tissucol, Omnex and the control group showed highest inflammation scores. At day 10 Controls, Bioglue and Duraseal showed the highest leakage rates and Tissucol and Omnex the lowest. BP was highest in Tissucol, Glubran 2 and Histoacryl Flex. Histopathological analysis showed highest inflammation for Bioglue, Omnex and Tissucol.
CONCLUSION: Sealing of colonic defects with TA is a safe and effective way to prevent leakage-related complications while maintaining high mechanical strength. However, large differences exist between the safety and effectiveness of the available TA. In this study, the cyanoacrylates Histoacryl Flex, Omnex and Glubran 2 as well as the fibrin glue Tissucol showed lowest leakage rates and the most inert histopathological profile while maintaining sufficient mechanical strength.
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Disclosure of Interest: None declared

P0823 CASE CONTROL STUDY OF USEFULNESS OF INTRA-GASTRIC BALLOON BEFORE BARIATRIC SURGERY IN MORBID OBESITY

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INTRODUCTION: Bariatric surgery has an important morbidity with a scarce number of reports using intragastric- balloons (IGB-BIB®) before surgery trying to lose weight and subsequently to reduce postoperative complications.
AIMS & METHODS: In the setting of an on-going randomized study of (IGB-BIB® for 6 months before Bariatric surgery [sleeve resection (SR) or gastric bypass (GB)]) to reduce postoperative complications. We present an interim case-control study comparing with patients came from our historic surgical group "gr2" and operated by the same surgical team. We matched cases, by gender, age (± 5 years) and type of surgery (1:1). The study protocol was approved by the H. Ethical Committee. All patients provided their informed consent OBJECTIVE: to evaluate if morbidity (medical and surgical) and hospital stay will decrease after IGB-BIB treatment, and to check if there was any relationship between patient (pt) weight before surgery and morbidity
RESULTS: The historic group included 47 pts, 21.7% were male, with a mean age of 45.9 y-o (SD 10.33), a weight before surgery of 125.05 kg (SD 21.25) and BMI of 47.42 (SD 6.77). 50% of pts were ASA III. 61% of these pts were operated with GB. All in all the surgical complications rate was 32.6% (57.1% of them severe,15pts). The hospital stay was 8 days (P25-75: 6-9). ***The case-control study*** included 48 pts, 24 in each group matched by sex (58.3% women), type of surgery (66.7% GB and 33.3% SR) and age (***gr1***, 41.5 y-o, SD 10.04, ***gr2***, 44.4 y-o,SD 10.04, p 0.261). When we compared the age, sex, weight before surgery, surgical morbidity, hospital stay and ASA score between ***gr2*** and the pts left in the historic group, we did not find statistical differences. The rate of IGB-BIB failure was 20,9% in ***gr1.*** The ***gr1*** had a lower ASA score than the ***gr2*** (ASA III, 25% vs. 54.2%, p 0.04). The mean weight loss before surgery was greater in ***gr1*** than ***gr2***: 16.7 kg (SD 9.7) vs. 1.6 (SD 6.1), p 0.0001. the morbidity related to the balloon was 8,3% in ***gr1.*** Surgical complications rate was 29.2% in ***gr1*** (38,5% of them severe) vs 33.3% in ***gr2***(58.8% severe). The reoperation rate was 8,3% in both groups. The hospital stay was 7 days (p25-75: 5.2-8) in ***gr1*** and 8 d (p25-75: 7-9.2) in ***gr2***, p 0.061. One patient died in ***gr2*** representing a 2.1% rate of mortality in the historic group. We did not find any significative differences either in surgical morbidity (p 0.781) or in total morbidity [surgical plus balloon morbidity (p 1)] in the case-control analysis. There was also not difference in morbidity classified as severe (p 1) in this case control-study. **Multivariable** logistic **Regression Analysis** in all the cohort patients of the study (***gr1+historic group***) did not find that weight before surgery,type of surgical procedure, age of sex were predictors of morbidity.
CONCLUSION: 20.9% of pt with IGB-BIB failed to lose weight. It has not been found yet a decrease in morbidity or hospital stay in the IGB-BIB® group compared with their matched control group in spite of the fact that that the case group had a lower ASA score. Case control and Multivariate analysis have not proven any relationship between patient weight before surgery and morbidity.
Disclosure of Interest: None declared

P0824 ROUTINELY CRP QUANTIFICATION AFTER APPENDECTOMY DUE TO ACUTE APPENDICITIS – A WASTE OF MONEY?

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INTRODUCTION: Appendectomy is the most frequent non elective surgical procedure in general surgery. Until now, indication is generally based on clinical findings. However, laboratory results such as leukocyte count and C-related Protein (CrP) are usually determined before and after the surgical procedure, and clinicians are not infrequently confronted with the question, if a patient can be discharged with an increasing inflammatory laboratory parameter. A clear evidence for a prospective value of the parameters and their trend regarding complications is missing.
AIMS & METHODS: Between November 2004 and April 2010, nine hundred sixty-nine patients underwent a surgical procedure due to clinically suspected acute appendicitis. All clinical, laboratory and histopathological data were obtained from the clinical and pathological records and a quality control data base containing information 0 ($n = 243$). Laboratory results were correlated with clinical and histopathological data (t-test, Chi-square test, regression analysis, ROC curve, respectively).
RESULTS: Eight hundred ninety-two (92%) patients had a histological confirmed acute appendicitis; median hospitalisation was 3 days (range 1-38 days). Overall morbidity was 6.2%; 60 (5.7%) patients suffered from infectious complications. Strongest predictive parameter for complications was a CrP value of more than 108 mg/l on the first postoperative day with an odds ratio of 16.6 (96% CI 6.4/42.8, $p < 0.001$). ROC analysis revealed an AUC of 0.821 with a Specificity of 88% and Sensitivity of 69%. Patients with below the threshold suffered from complications in 1.1% in contrast to the patients above with 16.8% ($p < 0.001$). In patients without acute appendicitis Operative trauma causes a CrP increase from less than 5 mg/l up to a median of 30 mg/l (25^{th} percentile: 8mg/l and 75^{th} percentile 100mg/l) on POD 1 to 47 mg/dl (25^{th} percentile: 23mg/l and 75^{th} percentile 125mg/l) on POD 2.
CONCLUSION: Operative trauma due to a non-acute inflamed appendectomy causes a significant increase of serum CrP, which must be taken into account for clinical assessment after appendectomy. Therefore, a moderate elevation of CrP values postoperatively is no general contraindication for discharge. However, postoperative determination of CrP serum values after appendectomy seems to be an effective predictor for complications and should therefore be measured in the clinical routine.
Disclosure of Interest: None declared

P0825 ENDOSCOPIC ELECTROCAUTERY IN PATIENTS WITH IMPLANTABLE CARDIAC DEVICES

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INTRODUCTION: Patients with implantable cardiac devices who undergo endoscopic electrosurgery are at risk of potentially harmful electromagnetic interference (EMI). However, few reports on the association between the two exist.
AIMS & METHODS: We aimed to analyze the effects of endoscopic electrosurgery in patients with implantable cardiac devices. The medical records of patients who underwent endoscopic procedures requiring the use of electrosurgery, such as snare polypectomy, endoscopic submucosal dissection (ESD), and endoscopic retrograde cholangiopancreatography (ERCP) with endoscopic sphincterotomy (EST), were analyzed retrospectively. Patients with implantable cardiac devices had their medical records reviewed, which included postprocedural patient symptoms, demographic data, and outpatient follow-up data. Electrical data, including preprocedural and postprocedural arrhythmia records, such as pacemaker interrogation, 24 h Holter monitoring, and electrocardiogram, were also reviewed.
RESULTS: Forty-nine patients who underwent 59 procedures were analyzed. Fifty procedures were performed in 43 patients with pacemakers, and nine procedures were performed in six patients with implantable cardioverter-defibrillators. There were 44 colon snare polypectomies, one colon ESD, one gastric snare polypectomy, five gastric ESDs, and eight ERCPs with EST. Fifty-five cases of electrical follow-up were observed, with two postprocedure changes noted that were not caused by electrosurgical EMI. Thirty-one pacemaker interrogations

had recordings of the procedure, with two cases of asymptomatic tachycardia events. All patients were asymptomatic, and no adverse events after the procedure were reported.
CONCLUSION: Our study reported no adverse events from endoscopic electrosurgery in patients with implantable cardiac devices, which suggests that this procedure is safe. However, because of the possibility of EMI, recommendations regarding endoscopic electrosurgery should be followed.
Disclosure of Interest: None declared

P0826 RISE IN TROPONIN T AFTER MAJOR GASTROINTESTINAL SURGERY IS ASSOCIATED WITH OCCURRENCE OF NEW MAJOR CARDIOVASCULAR EVENTS

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INTRODUCTION: A risk in Troponin T is associated with myocardial infarction, cardiovascular death and heart failure. Recently, an international prospective cohort study recently suggested a significant association between peak postoperative Troponin T (TnT) within three days after surgery and 30-day mortality. However, there is no study to investigate the long term risk of cardiovascular events among those with elevated troponin T level after surgery. This study aimed to investigate elevated Troponin after gastrointestinal surgery and 3 year outcomes.
AIMS & METHODS: This is a prospective cohort study including patients age above 45 years who underwent either elective or emergency upper or lower GI surgery under general anesthesia. Those recruited had measurement of peak troponin T (TnT) levels by fourth generation TnT assay. The data for assessing perioperative mortality and cardiovascular diseases were collected, including baseline demographics, smoking status, history of cardiovascular disease, type of surgery performed as well as clinical outcomes. The primary outcome was 3 year mortality after surgery. Secondary outcomes included new major cardiovascular events (which were defined as myocardial infarction, stroke, deep vein thrombosis and pulmonary embolism), new use of anti-platelet medication (e.g. aspirin, clopidogrel) and new use of anti-coagulation drugs (e.g. warfarin) within 3 years after surgery.
RESULTS: A total of 213 patients were recruited including 128 male and 85 female. 53 patients underwent upper gastrointestinal surgery and 152 underwent lower gastrointestinal surgery. 28 patients (13.1%) had elevated peak troponin T level (>0.01ng/mL) in at least one measurement within 3 days after surgery. 5 out of 213 patients drop out of the study with 97.7% of patients completed 3-year follow-up. There was no difference in 3 year mortality between those with and without elevation of TnT after surgery. Those in the elevated TnT group sustained significantly higher rate of cardiovascular events (57.1% vs 10.4%; $p < 0.001$) and also higher use of anti-platelets agents (30% vs8.2%; $p = 0.009$) within 3 years after surgery when compared to the normal TnT group. There was no difference in 3 year cancer recurrence between the two groups.

	Elevated Troponin T group (TnT) (n = 28)	Non-elevated Troponin T group (non-TnT) (n = 185)	P value
Age	75 (51-99)	68 (45-90)	0.002†
BMI	22.70 (15.36-30.03)	22.10 (14.91-29.29)	0.426
Gender M:F	15/13	113/72	0.450
Upper GI Surgery	6 (22.2%)	47 (26.4%)	0.644
Lower GI Surgery	21 (77.8%)	131 (73.6%)	
History of coronary artery disease	8 (28.6%)	7 (3.8%)	<0.001†
History of Diabetes	8 (28.6%)	41 (22.2%)	0.453
Occurrence of new cardiovascular events in 3 years	16 (57.1%)	19 (10.4%)	<0.001†
New use of aspirin / Clopidogrel in 3 years	6 (30%)	14 (8.2%)	0.009†

CONCLUSION: Patients with elevated TnT after major gastrointestinal surgery had significantly higher risk of cardiovascular events in 3 years after surgery.
Disclosure of Interest: None declared

P0827 DEFUNCTIONING ILEOSTOMY DOES NOT PREVENT ANASTOMOTIC LEAKS AFTER RESTORATIVE PROCTOCOLECTOMY; A MULTICENTER EVALUATION OF CLINICAL AND SURGICAL RISK FACTORS

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INTRODUCTION: Anastomotic leakage (AL) is a serious complication after restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) that could lead to pelvic sepsis and ultimately to pouch failure. Previous studies have shown significantly decreased leak rates in diverted patients with less severe clinical consequences. The last decade, a trend has been seen towards more extensive medical treatment in IBD patients, leaving refractory patients in a worse condition when it comes to surgery. Since timely identification of high-risk patients could influence surgical decision-making and diminish the risk for complications, the aim of our study is to identify clinical and surgical parameters associated with AL and to analyse whether a defunctioning ileostomy should be considered as standard care in patients undergoing IPAA.
AIMS & METHODS: In a retrospective study, 691 patients undergoing IPAA for IBD, dysplasia, or FAP were identified from prospectively maintained databases of three large IBD centres. The creation of an ileostomy was left at the discretion of the surgeon. AL was defined as any leak confirmed by either contrast extravasation on imaging or by re-laparotomy. Multivariable regression models were developed to identify risk factors for AL.
RESULTS: In 305 IBD patients (49.1%), an ileostomy was created during IPAA. A comparable overall leak rate was found in the stoma group when compared to non-diverted patients (16.7% vs 17.1%, $p = 0.92$). This unexpected finding of high leak rates despite stoma formation could probably be explained by the increased use of anti-TNF (12.6% versus 4.6%, $p < 0.001$), steroids (33.0% vs 12.1%, $p < 0.001$), and weightloss (>5% of bodyweight) (14.6% vs 8.5%, $p = 0.02$) when compared to non-diverted patients. Despite having a stoma, a high leak rate (40.0% vs 15.1%, $p = 0.02$) was found in patients treated with a combination of anti-TNF and steroids. This was also emphasized by the fact that patients undergoing subtotal colectomy with IPAA at a later stage (weaned of medication) had a significantly decreased leak rate when compared to patients undergoing primary IPAA (11.6% vs 20.7%, $p = 0.003$). Multivariable regression models demonstrated, long-term disease course (OR 2.01, 95%CI 1.27–3.19), high ASA score (OR 1.94, 95%CI 1.09–3.47) and a combination of anti-TNF and steroid treatment (OR 5.61, 95%CI 1.71–18.48) as independent risk factors for AL.
CONCLUSION: These results imply that in daily practice surgeons perform ileostomy in more fragile and disease affected patients. This strategy seems ineffective in the prevention of AL in these series implicating that a staged procedure, that is subtotal colectomy followed by completion proctectomy and IPAA after weaning of the medication, is more appropriate when preoperative risk factors are identified. Long-term disease course, high ASA score, and a combination of anti-TNF and steroid treatment within 3 months before IPAA were all independent risk factors for AL.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
IBD II – POSTER EXHIBITION – HALL XL

P0828 DIFFERENTIAL EXPRESSION OF TRPM6 AND TRPM7 FOLLOWING INTESTINAL INFLAMMATION EMERGING NEW PATHWAYS OF CHRONIC INFLAMMATION AND DIARRHEA

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INTRODUCTION: IBD patients display a variety of nutritional deficiencies because of decreased nutrient intake or absorption and/or increased losses. Magnesium (Mg) is a critical cofactor for numerous enzyme systems and its deficiency may result in several clinical manifestations. Recent evidence showed that Mg participates in immune system regulation. Intestinal mucosa and kidneys, are the natural access routes for magnesium into the blood stream which involves cation channels and transporters, like TRPM-6 and -7. Few information exist on Mg in IBD pathogenesis.
AIMS & METHODS: The aim of the study is to assess whether Mg receptors TRPM-6 and -7 are involved in an experimental model of colitis. DSS colitis was induced in C57BL/6 mice. 5 Mice received 2.5% DSS in tap water for 5 days and then sacrificed, while controls received only water. 5 further mice received 2.5% DSS for 5 days and then exposed to water for further 7 days to observe recovery. At the sacrifice plasma was collected from each animal, stored at -80°C and then assessed for Mg content by atomic absorption spectroscopy; a first section of liver, kidney and bowel were snap frozen and then analized by Real Time (RT)-PCR for TRPM-6 and -7; a second section of each was fixed in 4% formalin and embedded in paraffin for immunohistochemistry (IHC).
RESULTS: As expected mice exposed to DSS for 5 days developed a mild colitis, which was associated to lower Mg plasma concentration (mean value 0.64mM) compared to healthy controls (mean value 0.77 mM). At IHC and RT-PCR analysis TRPM-6 and -7 expression did not differ in liver and kidney among healthy and colitic mice. On the contrary, their expression in bowel decreased drastically in colitic mice. By IHC, we observed a decrease of TRPM6 expression and a change of localization of TRPM7 within enterocytes from apical to basolateral position. In recovered mice, the intestinal expression of
TRPM-6 and -7 was restored.
CONCLUSION: Mg plasma concentration decrease during active colitis. This observation paralleled the decrease of intestinal TRPM-6 and -7 expression. Further experiments are required to show the immunological consequences of this observation.
Disclosure of Interest: None declared

P0829 HIRSUTENONE AMELIORATES EPITHELIAL BARRIER DISRUPTION THROUGH CONVERGENCE OF EGFR/AKT AND ERK1/2 PATHWAYS ON HEME OXIDASE-1 INDUCTION IN HUMAN INTESTINAL EPITHELIAL CELLS

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INTRODUCTION: Oxidative stress-induced disruption of epithelial tight junctions (TJ) plays a critical role in the pathogenesis of intestinal disorders, including inflammatory bowel disease (IBD).
AIMS & METHODS: The current study investigated the protective effect of diarylheptanoid hirsutenone against disruption of the intestinal barrier *in vitro* and in a mouse model of colitis. Caco-2 cells were stimulated with *tert*-butyl hydroperoxide (*t*-BH). Monolayer permeability was assessed by measuring the transepithelial electrical resistance and inulin flux. Colitis was induced in mice by intrarectal administration of trinitrobenzene sulfonic acid (TNBS). The mRNA and protein levels were analyzed by real-time polymerase chain reaction (PCR) and immunoblotting, respectively.
RESULTS: Hirsutenone prevented the *t*-BH-induced increase in permeability by inhibiting the reduction in zonula occludens-1 (ZO-1) expression, and rapidly stimulated tyrosine phosphorylation of the epidermal growth factor receptor (EGFR). Hirsutenone-mediated protection against the loss of ZO-1 depends on the activation of both ERK1/2 and Akt signaling pathways. Interestingly, hirsutenone-mediated activation of Akt, but not ERK1/2, signaling was EGFR-dependent. Hirsutenone increased heme oxygenase-1 (HO-1) expression through both EGFR/Akt- and ERK1/2-dependent pathways, contributing to the protective effects against TJ dysfunction. Hirsutenone administration improved the clinical parameters and tissue histological appearance, stimulated HO-1 expression, attenuated reduction of ZO-1 and occludin mRNA, and promoted BrdU incorporation in the colonic epithelium of TNBS-treated mice.
CONCLUSION: Hirsutenone reversed disordered intestinal permeability by activating EGFR/Akt and ERK1/2 pathways, which are involved in HO-1 expression regulation. These findings highlight the potential of hirsutenone for clinical applications in the treatment of IBD.
Disclosure of Interest: None declared

P0830 DIFFERENTIAL EXPRESSION IN ALPHA7 NICOTINIC RECEPTOR IN MUCOSAL MACROPHAGES OF IBD PATIENTS: A ROLE FOR NICOTINE MODULATION OF INFLAMMATION?

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INTRODUCTION: It is well accepted that in animal models of intestinal inflammation nicotine activates a cholinergic counter-inflammatory mechanism through the alpha7 nicotinic acetylcholine receptors (α7nAChR). However in inflammatory bowel diseases (IBD) nicotine shows opposing effects on intestinal inflammation: it's beneficial in ulcerative colitis (UC) while it increases risk of surgery and relapse in Crohn's disease (CD).
AIMS & METHODS: In this study we measured α7nACh expression on peripheral and intestinal mucosa-derived macrophages from patients with UC, CD and healthy controls (HV) and evaluated the effect of nicotine on LPS-induced cytokines production in macrophages. Peripheral blood derived macrophages (MΦc) were obtained by supplementing blood monocytes from UC and CD patients (in clinical remission) and HV with M-CSF (7 days). α7nAChR mRNA and protein levels were evaluated by qRT-PCR and FACS analysis using α-bungarotoxin (αBgt)-FITC. MΦc were pre-incubated with nicotine (1mg/ml 30min) and then stimulated with LPS (1μg/ml 24 hrs). TNFα levels were measured on supernatant using ELISA. Colonic mucosa macrophages (MΦi) were isolated from biopsies of UC (n = 12), CD (n = 11) and HV (n = 17) and α7nAchR expression was evaluated by FACS analysis using αBgt-FITC. Macrophages were incubated for 24 hrs with LPS (1μg/ml) in presence or absence of nicotine (1mg/ml) and TNFα and IFNγ assessed by staining with specific antibodies and cytofluorimetric analysis.
RESULTS: MΦc from UC showed greater α7nAchR mRNA levels then cells from CD ($p = 0.006$), while no differences were found with HV. FACS analysis confirmed greater α7AChR expression in UC patients than in CD (90.75 Gmean in UC Vs 15.62 Gmean in CD, p 0.031) but not in HV. Although nicotine significantly decreased LPS-stimulated TNFα release in MΦc from HV, CD and UC, no differences were observed among groups. Indeed, in UC derived MΦi α7nAChR levels were significantly higher than in CD and HV cells ($p < 0.01$ vs both). Furthermore, nicotine significantly specifically reduced LPS-induced TNFα upregulation in MΦi from UC patients (from 18.91±2.57 to 10.81±1.99 %fluorescence, $p = 0.013$) but not in CD and HV whereas nicotine had no effect on LPS-induced IFNγ upregulation in MΦi in the different experimental groups.
CONCLUSION: The selective α7nAchR upregulation in MΦi from UC patients and their responsiveness to the anti-inflammatory effects of nicotine may explain nicotine's protective effects in UC but not in CD patients.
Disclosure of Interest: None declared

P0831 NOTCH SIGNALING AND TNF-A SYNERGISTICALLY PROMOTES INTRACELLULAR PROTEIN ACCUMULATION OF OLFM4 IN THE INFLAMED MUCOSA OF ULCERATIVE COLITIS

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INTRODUCTION: The intestinal epithelium is maintained by the stem cell residing at the bottom of the crypt. Olfactomedin-4 (OLFM4) is one of the specific marker genes of the human intestinal stem cell. The gene encodes secretory-type, as well as intracellular-type, OLFM4 proteins. Reports have shown that secretory-type OLFM4 facilitates cell adhesion and may take part in mucosal defense, whereas intracellular-type OLFM4 can exhibit anti-apoptotic property. Also, it has been shown that the expression and secretion of OLFM4 is upregulated in the inflamed mucosa of ulcerative colitis (UC), where Notch signaling is highly activated. However, the expression of the intracellular-type OLFM4 protein in the inflamed mucosa, or the mechanism regulating its expression, remains unclear.
AIMS & METHODS: We aimed to identify the expression of intracellular-type OLFM4 in the normal and inflamed mucosa of the human colonic tissue, and also to clarify the molecular mechanism regulating its expression in the inflamed mucosa. Expression of intracellular-type OLFM4 in colonic tissues of normal and UC patients was analyzed by immunohistochemistry (IHC). Human colonic epithelial cell lines, Ls174T and DLD1, were employed to analyze the expression of OLFM4 in response to various inflammatory stimuli. Involvement of Notch signaling in OLFM4 protein expression was examined by using a sub-line of Ls174T cells (Ls174T-NICD cells) in which Doxycycline-dependent activation of Notch signaling can be induced. Using those cell-lines, the expression of secretory-type OLFM4 protein was quantified by ELISA, whereas that of intracellular-type OLFM4 protein was examined either by immunoblot analysis or by immunocytochemistry.
RESULTS: IHC analysis of the normal human colon tissues showed that OLFM4 is expressed mostly at the apical surface of epithelial cells residing at the lower crypt, indicating dominant expression of secretory-type OLFM4. However, in the inflamed mucosa of UC patients, an increased number of colonic epithelial cells clearly expressed OLFM4 in their cytoplasm, indicating high-level expression of intracellular-type OLFM4. In vitro analysis using human colonic epithelial cell-lines showed that, among various pro-inflammatory cytokines, TNF-α significantly upregulates secretion of OLFM4, but do not promote accumulation of the intracellular-type OLFM4. In contrast, forced activation of Notch signaling never induced secretion of OLFM4, but induced accumulation of intracellular-type OLFM4. Upon addition of TNF-α under forced activation of Notch signaling, those stimuli synergistically up-regulated the accumulation of intracellular-type OLFM4 protein to a remarkably high-level, but did not give any additional change to secretion of the OLFM4 protein. Immunocytochemistry clearly confirmed the cytoplasmic accumulation of OLFM4 protein by the synergistic effect of TNF-α and Notch activation.
CONCLUSION: Notch signaling and TNF-α synergistically promotes accumulation of intracellular-type OLFM4 protein in human colonic epithelial cells. As it has been suggested that those type of OLFM4 protein can exhibit anti-apoptotic function, such an accumulation may contribute to protect human colonic epithelial cells in the inflammatory environment.
Disclosure of Interest: None declared

P0832 PPAR-GAMMA EXPRESSION IN THE COLON IS REGULATED BY THE MIR27A UNDER HYPOXEMIC CONDITION

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INTRODUCTION: The peroxisome proliferator-activated receptor-γ (PPARγ) is a key factor of mucosal homeostasis and the pharmaceutical target of 5-aminosalycilates. Thus, understanding of the primarily decrease expression of PPARγ during UC remains challenging and of therapeutic interest. Mucosal hypoxemia has been well described during UC. The aim of the study was to assess and to study the link between hypoxia and PPARγ expression in intesintal epithelial cell during UC.
AIMS & METHODS: *In Vitro*, PPARγ mRNA and protein were quantified in various epithelial cell lines 1) during exposure to hypoxia (1%O2) at several time points 2) after chemical induction of HIF-1α 3) after transfection of miR-27a or knockout of miR-27a (a microRNA induced by hypoxia and with high affinity to PPARγ *in silico*) and 4) after stimulation by sildenafil (a phosphodiesterase type 5 inhibitor used for blood vessel dysfunction). *Ex vivo*, PPARγ and miR27a expressions were quantified from mucosal biopsies of surgical specimens from controls or patients with UC.
RESULTS: *In vitro*, exposure of Caco-2 and HT29 cells to hypoxia (1% O2) decreased significantly mRNA and protein expression of PPARγ (at least 50%) as compared to normoxic condition (21% O2) at days 2. To assess the link between hypoxia and the decreased expression of PPARγ, we first induced HIF-1α expression, a key factor of cells response under hypoxic condition, by chemical treatment of cultured cells lineages (deferoxamine, cobalt chloride and dimethyloxaloylglycine). No effect was observed either on PPARγ expression neither on miR27a expression. Regarding this result suggesting an independent HIF-1α way that controls PPARγ expression during hypoxia, we focused on

miR-27a. MiR-27a was induced by hypoxia in epithelial cells. When miR-27a was overexpressed by transfection in caco-2 cells during normoxic condition, PPARγ expression was decreased. Conversely, PPARγ was not affected by hypoxia after knockout for miR27a of caco-2 cells by transfection of miR-27a inhibitors. *Ex vivo*, we confirmed a decreased of PPARγ expression in colonic mucosa of patients with UC and higher miR-27a expression as compared to controls. In order to affect the variation of PPARγ expression during hypoxia we used the sildenafil. The sildenafil raised PPARγ expression in caco-2 cells exposed to hypoxia. Furthermore the use of sildenafil resulted in the absence of overeexpression of miR-27a expression during hypoxia.
CONCLUSION: A direct relationship was observed between hypoxia and PPARγ expression. Mir-27a which is overexpressed during hypoxia and in patients with UC might be the key factor involved during hypoxia to control PPARγ expression. These results open new insight into the pathophysiology of UC and the role of hypoxia as well as new therapeutic strategy such as the use of sildenafil.
Disclosure of Interest: None declared

P0833 MECHANISMS UNDERLYING THE EFFECTS OF CALCITONIN GENE-RELATED PEPTIDE IN A RAT COLITIS MODEL

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INTRODUCTION: Calcitonin gene-related peptide (CGRP), a vasodilative neuropeptide, is involved in potent tissue repair and anti-inflammatory actions. Previous studies have shown that the administration of CGRP prevents colonic injury. However, the mechanism of action responsible for the effect of CGRP on colitis remains unknown.
AIMS & METHODS: Colitis was induced by the oral feeding of 3% dextran sulfate sodium to rats for up to 7 days. After the induction of colitis, CGRP (200 μg/μL/day) was administered via the tail vein twice a day for 7 consecutive days. Disease severity was assessed by clinical and endoscopic evaluation, and histologic scoring. The tissue levels of pro-inflammatory cytokines (interleukin [IL]-1α, IL-6, and tumor necrosis factor [TNF]-α) and CGRP receptors (receptor activity-modifying protein-1 [RAMP1] and calcitonin receptor-like receptor) were determined using real time-PCR. Bone marrow cell induction and colonic blood flow were also investigated. Additionally, the cytokine response in peripheral blood mononuclear cells stimulated by lipopolysaccharide with or without CGRP was examined in vitro.
RESULTS: The administration of CGRP, but not a control vehicle, improved the clinical disease activity ($P=0.009$) and the endoscopic disease activity ($P=0.009$). CGRP decreased the mRNA levels of IL-1α ($P=0.032$), IL-6 ($P=0.032$) and TNF-α ($P=0.016$) and increased the mRNA level of RAMP1 ($P=0.001$). CGRP increased the colonies of CFU-GM in the bone marrow ($P=0.016$) and the number of endothelial progenitor cells in the peripheral blood ($P=0.040$) and enhanced the colonic blood flow ($P=0.032$). The mRNA and protein levels of the inflammatory cytokines in lipopolysaccharide-stimulated peripheral blood mononuclear cells were significantly reduced after the addition of CGRP in vitro.
CONCLUSION: The administration of CGRP effectively suppresses colonic injury through the down-regulation of pro-inflammatory cytokines and the up-regulation of protective events, including bone marrow-derived cell induction, in addition to promoting colonic blood flow. Consequently, CGRP is an attractive and novel therapeutic target for the treatment of inflammatory bowel disease.
Disclosure of Interest: None declared

P0834 SERUM IL-23 DIFFERENTLY CORRELATES WITH COLONIC MMP-9/TIMP-1 AND MMP-9/TIMP-2 IN CROHN'S DISEASE, BUT NOT ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: Intestinal alterations in IBD are triggered and sustained by over-expression of pro-inflammatory cytokines. Cytokine quantification may become a non-invasive tool to monitor the disease progression and effectiveness of therapy, or assist in understanding disease etiology. Currently, there are limited non-invasive biomarkers for monitoring IBD progression; however, the role of selected cytokines like IL-23 and IL-17, or proteolytic proteins like matrix metaloproteinases (MMP) or their tissue inhibitors (TIMP), is under consideration.
AIMS & METHODS: The aim of this study was to evaluate if IL-17 and IL-23 correlate with MMP-9/TIMP complexes in IBD and if those parameters differ in affected and unaffected colon mucosa.
Serum and biopsy specimens from affected and unaffected colonic mucosa of 19 patients with IBD (9 with ulcerative colitis, UC and 10 with Crohn's disease, CD) and 8 controls were included in our study. Serum and tissue cytokines, and tissue MMP-9/TIMP-1 and MMP-9/TIMP-2 were quantified at the protein level by ELISA.
RESULTS: The UC subjects had significantly lower serum IL-23 ($p=0.002$) and slightly higher serum IL-17 level ($p=0.09$) compared with control. In unaffected tissues, there was a significant decrease in IL-23 content ($p=0.002$ vs. control). In CD patients no difference in serum IL-23 or IL-17 content was measured; however, both IL-23 and IL-17 were significantly decreased in unaffected colon tissues ($p=0.00003$ and $p=000002$ vs. control). The levels of IL-23 or IL-17 in affected tissues from UC and CD groups were comparable.
As IL-17/IL-23 axis directly influences MMP-9 activity, we measured the concentration of MMP-9 in complex with TIMP-1 or TIMP-2. The UC group had significantly higher MMP-9/TIMP-1 level in unaffected tissue compared with control ($p=0.001$), while in CD an opposite tendency was observed. Regarding MMP-9/TIMP-2, there was a decrease in unaffected tissue in both UC and CD groups compared with control ($p=0.07$ and $p=0.08$, respectively). Further analysis revealed that IL-23 correlates with MMP-9/TIMP-1 in UC and with MMP-9/TIMP-2 in CD. In the UC group serum IL-23 negatively correlated with MMP-9/TIMP-1 in unaffected tissue ($r=-0.903$), but positively in affected colon sections ($r=0.72$). In CD subjects, there was a strong negative correlation between serum IL-23 and MMP-9/TIMP-2 in unaffected tissue ($r=-0.94$); and positive correlations between tissue IL-23 and MMP-9/TIMP-2 in both unaffected and affected areas ($r=0.66$ and $r=0.62$, respectively).
CONCLUSION: It is believed that higher IL-23 levels decrease the content of MMP-9/TIMP complexes, which in turn may lead to elevated MMP-9 levels and MMP-9-induced tissue damage. The correlations between serum and tissue IL-23 and MMP-9/TIMP-1 in UC or MMP-9/TIMP-2 in CD, in particular in unaffected mucosa, may therefore be an indicator of an ongoing inflammatory process. However, further studies are necessary to explain the interaction between cytokines, especially IL-23 and pro- and anti-proteolytic proteins in inflamed and non-inflamed areas in IBD subjects.
Disclosure of Interest: None declared

P0835 CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE E. COLI INDUCE SECRETION OF EXOSOMES WITH PRO-INFLAMMATORY ACTIVITY BY INTESTINAL EPITHELIAL CELLS

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INTRODUCTION: Crohn's disease (CD) is a chronic inflammatory bowel disease of which the etiology involves environmental, genetic and microbial factors. Our group and others have shown a high prevalence of the invasive E. coli strains, designated adherent-invasive E. coli (AIEC), in the intestinal mucosa of CD patients. Exosomes are small endosomal-derived vesicles involved in cell to cell communication and have been implicated in various diseases including cancer and infectious disorders. It has been reported that mammalian cells infected with pathogens can release exosomes containing microbial compounds.
AIMS & METHODS: Here, we investigated the capacity of CD-associated AIEC bacteria to induce secretion of exosomes by intestinal epithelial cells and to determine the inflammatory characteristics of the released exosomes. Human intestinal epithelial T84 cells cultured on transwell filters were infected with an AIEC reference strain LF82. Exosomes were purified using the ExoQuick exosome precipitation reagent. Exosomes released into the apical or basolateral compartments of LF82-infected T84 cells were tested for their ability to promote a pro-inflammatory response in naïve macrophagic cells.
RESULTS: Electron microscopy and immunogold-labeling for an exosomal marker, CD63, analyses showed that differentiated T84 cells infected with AIEC LF82 secreted an increased amount of exosome compared to uninfected cells. This was confirmed by increased levels of four exosomal markers (CD63, CD81, CD9 and Hsp70) as assessed by Western blot. Exosomes apically secreted by infected T84 cells but not from uninfected cells significantly induced production of the pro-inflammatory cytokines TNF-α and IL-6 in human macrophages, and this was not due to the presence of lipopolysaccharide, known to induce a pro-inflammatory response.
CONCLUSION: In conclusion, our study shows that upon infection with CD-associated AIEC bacteria, differentiated intestinal epithelial cells release exosomes that can trigger pro-inflammatory responses in naïve macrophagic recipient cells.
Disclosure of Interest: None declared

P0836 DIAGNOSIS AND PERSISTENCE OF HISTOLOGICAL CHANGES IN LYMPHOCYTIC COLITIS

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INTRODUCTION: The topographic distribution of histological changes in microscopic colitis (MC) remains controversial. The main conception has been that in order to detect or rule out MC, biopsies from the right colon is necessary. However this has to some extent been proposed on the basis of a selected population of patients included in randomised trials with collagenous colitis (CC). A sigmoideoscopy is more gentle with the patient, cheaper and often more accessible and thus would be preferred if sufficient in detecting MC.
AIMS & METHODS: Aims: To access the topography of histological changes in the colon diagnostic of lymphocytic colitis (LC) in a complete series of consecutive, non-selected patients and to provide the sensitivity of left- and right-side biopsies respectively. Furthermore to analyse the persistence of changes in repeated endoscopies.
Methods: Retrospective review of the pathologic descriptions in the Danish National Pathology Database in patients diagnosed with lymphocytic colitis in the coverage area of Køge Hospital from 2000 through March 2014. Biopsies from the rectum were excluded.
RESULTS: LC was diagnosed in 238 patients; in 81 (34%) by sigmoideosopy and in 136 (57%) by colonoscopy. A medical history of watery diarrhoea could be retrieved in 196, 1 did not have diarrhoea. The median number of biopsies

taken was 6 (mean 7.6). Biopsies were taken from both right and left colon in 122 (51%) and showed LC in both left and right colon of 119 (98%). At the diagnostic endoscopy 3 patients (2%) had changes in the left colon only and no one had changes in the right colon only. The histological diagnosis in the right colon were: normal (1), chronic inflammation (1) and incomplete LC (1). The sensitivity of left sided biopsies for the primary diagnosis of LC were 100% (95% CI: 97-100%) and right sided 98% (94-100%). A second endoscopy following the diagnostic one was performed in 50 (21%) of the 238 patients after a median of 13.5 months (mean 27.2) with a median of 6.5 biopsies (mean 7.1). LC was reconfirmed in 28 (56%). Other histological changes found were: normal (4), chronic inflammation (2), incomplete LC (2), CC (2) and non specific changes (10). In 3 patients histological changes diagnostic of collagenous colitis were found in one or more of the endoscopies following the diagnostic one. Looking at the total number (161) of colonoscopies diagnostic of LC (with biopsies from both right and left colon) done in the population, 1 patient (1%) had changes in the right colon only and 3 patients (2%) had changes in the left colon only. Prior non-diagnostic endoscopies were performed in 22 patients (9%) with a median of 4 (mean 5) biopsies. In these histological changes were: normal (4), chronic inflammation (10), incomplete LC (4) and non specific changes (4).
CONCLUSION: While a full colonoscopy can be necessary in order to exclude other diagnoses, biopsies from the left colon are suffice for diagnosing or excluding LC in patients with chronic watery diarrhoea. The histological findings are not permanent and can change from one type of microscopic colitis to another suggesting that the different types of microscopic colitis are closely related.
Disclosure of Interest: None declared

P0837 METABOLIC PROFILING OF FECAL VOLATILE ORGANIC COMPOUNDS IN ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: Ulcerative colitis (UC) is an inflammatory bowel disease characterized by chronic inflammation of the colonic epithelium. The exact etiology of the disease is not fully understood, but the microbiota is implicated in the initiation and the propagation of the disease. Through bacterial fermentation of carbohydrates and proteins a plethora of luminal compounds is produced in the colon, which might interact with the host's physiology. In the present study, the metabolic activity of the microbiota was compared between healthy controls and UC patients with both active and quiescent disease.
AIMS & METHODS: Fecal samples were collected from healthy control subjects (HC; n = 19, 11 female/8 male, age range 20-61 years) and UC patients with active disease (UC-A; n = 45, 14 female/31 male, age range 20-84 years) and during remission (UC-R; n = 40, 15 female/25 male, age range 19-78 years). Active disease was defined as a partial Mayo score $\geq$3. Fecal water (FW) was derived from these samples by ultracentrifugation at 50.000 x g at 4°C for 2h and was sterile filtered. Profiles of volatile organic compounds (VOCs) were determined in the FW samples using GC-MS (single quadrupole), coupled on line to a purge-and-trap sample preparation system. All VOCs were relatively quantified versus an internal standard and classified according to chemical class. Partial least squares (PLS) analysis was applied to cluster samples with similar metabolite profiles and to identify VOCs accounting for discrimination between HC and UC patients.
RESULTS: A total of 201 different VOCs were identified in the FW samples, with an average of 61$\pm$8 VOCs per sample. Cluster analysis of the metabolite profiles revealed complete separate clustering between HC and UC patients. Samples from UC-A and UC-R patients were not completely separated. FW samples from UC patients were associated with a higher prevalence of alcohols, phenols and benzene-like VOCs. The two latter groups are suggested to arise from protein fermentation. UC-A patient samples were associated with the presence of primary alcohols (ethanol, 1-propanol and 1-butanol) and low levels of short and medium chain fatty acids (SCFA and MCFA) and other acids. SCFA (acetate, propionate and butyrate) are generally recognized to be beneficial for the host's health and mainly originate from carbohydrate fermentation. Similar reductions of SCFA in UC patients were previously observed by the use of proton NMR [1]. These carboxylic acids are the oxidized counterparts of the primary alcohols, which suggests an imbalance in reduction-oxidation (redox) reactions in the colonic lumen.
CONCLUSION: The metabolite profiles of fecal samples allowed to differentiate HC from UC patients, partly due to the increased presence of alcohols, phenols and benzene-derivatives in UC patient samples. We identified primary alcohols, SCFA and MCFA as the most discriminatory metabolites in UC-A patients compared to HC and UC-R patients. The role of the observed shift in intestinal redox balance in UC-A patients (more primary alcohols, less SCFA) needs to be further investigated.
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Disclosure of Interest: None declared

P0838 THE ASM MUCINASE IS INVOLVED IN ILEAL COLONIZATION BY CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE ESCHERICHIA COLI

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INTRODUCTION: Mucins are secreted by the intestinal epithelium and constitute an efficient component of innate immune defenses to promote homeostasis and protect against bacteria. Enteric pathogens, such as *Shigella* and *Vibrio cholerae,* can produce proteases designated mucinases that are capable of cleaving mucins. Ileal lesions of patients with Crohn's disease (CD) are abnormally colonized by adherent-invasive *Escherichia coli* (AIEC).
AIMS & METHODS: Genome analysis of the AIEC strain LF82 revealed the presence of a chromosomal gene, designated *asm,* similar to the *Hbp* gene of the avian pathogenic *E. coli* strains (79% of homology). Hbp has a mucinolytic activity. To determine whether the Asm protein cleaves mucins, we generated the LF82Δ*asm* isogenic mutant and transcomplemented this mutant with the cloned *asm* gene.
RESULTS: Concentrated supernatants from LF82 strain and transcomplemented LF82D*asm*/*asm* yielded zones of clearing on mucin gels, whereas LFD*asm* did not exhibit mucinolytic activity. We showed, by using a simple column penetration assay, that Asm promoted mucus penetration of LF82. No difference in adhesion and invasion between LF82 and LF82Δ*asm* was found in the colonic epithelial HT29 cells, which are not mucin hyperproducing. However, a significant difference between these strains was observed in the mucin hyperproducing cell line HT29-16E, suggesting a role for Asm in mucus penetration. These results were also obtained by confocal and electronic microscopy. To evaluate the involvement of Asm in LF82 colonization *in vivo*, CEABAC10 transgenic mice were orally challenged with LF82 or LF82D*asm* strains. The numbers of bacteria counted in the feces and of intestinal mucosal-associated bacteria were increased in mice infected with LF82 compared to those infected with LF82D*asm*. Quantification of *asm* mRNA levels showed that bile salts act as an activator of Asm transcription as well as ileal pH.
CONCLUSION: In conclusion, Asm has a mucinolytic activity that promotes mucus penetration of AIEC strains and enhances adhesion and invasion to epithelial cells. Asm contributes to gut colonization of AIEC in murine model. Thus, mucinases could be one of the key factors of AIEC implantation in CD patients.
Disclosure of Interest: None declared

P0839 HYPERBARIC OXYGEN THERAPY AMELIORATES TNBS-INDUCED ACUTE DISTAL COLITIS IN RATS

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INTRODUCTION: This study investigated the therapeutic effects of hyperbaric oxygen (HBO) in experimental acute distal colitis focusing on its effect on cytokines and HIF-1α.
AIMS & METHODS: Twenty-eight *Wistar* rats were divided into four groups (each group had 7 rats): I (Saline); II (Saline/HBO); III (TNBS); and IV (TNBS+HBO). Colitis was induced with a rectal infusion of 150 mg/kg of trinitrobenzenesulfonic acid–ethanol (TNBS) under anesthesia with Ketamine (50 mg/kg) and Xylazine (10 mg/kg). Control animals received only rectal saline. After induction, the colitis animals were subjected to two sessions of HBO and were then euthanized. The distal intestine was resected for macroscopic analysis, myeloperoxidase activity (MPO) measurements, Western-blot analyses of nitric oxide synthase activity (iNOS) and Cicloxygenase-2 (COX-2) and immunohistochemical analysis of HIF-1α and COX-2. Cytokines levels (IL-1β, CINC-1, IL-10 and TNF-α) in the distal intestine were measured using an enzyme-linked immunosorbent assay (ELISA).
RESULTS: HBO therapy attenuated the severity of acute distal colitis, with reduced macroscopic damage score and reduced cytokine expression. HBO therapy inhibited the acute distal colitis-induced up-regulation of HIF-1α and its downstream iNOS and myeloperoxidase activity, as well as producing diminished COX-2 levels
CONCLUSION: The results indicate that HBO therapy attenuates the severity of acute distal colitis through the down-regulation of the expression of HIF-1α and pro-inflammatory cytokines
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Disclosure of Interest: None declared

P0840 DIFFERENCES IN EXPRESSION OF G PROTEIN-COUPLED RECEPTOR 55 IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS

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INTRODUCTION: G protein-coupled receptor 55 (GPR55) is a newly discovered cannabinoid (CB) receptor, which has been qualified as a part of the endogenous CB system along with "classical" receptors CB1 and CB2. There is a growing interest in the possible use of CB receptor agonists in the treatment of inflammation and abdominal pain. Here we attempted at establishing the levels

of GPR55 expression in inflammatory bowel disease (IBD) patients and healthy controls and potential implication in IBD treatment.
AIMS & METHODS: The study aimed at identifying whether GPR55 is expressed in colonic tissue of IBD patients and if so, whether the GPR55 levels differ between Crohn's disease (CD) and ulcerative colitis (UC) patients and between IBD patients and controls. Twenty five adult patients with IBD (UC: n = 11; CD: n = 14) were enrolled in the study. The control group consisted of 6 healthy subjects. The GPR55 mRNA and protein expression were measured using RT-PCR and immunoenzymatic (Western blot) assay, respectively. Each assay was performed in triplicate.
RESULTS: GPR55 mRNA was detected in all samples tested. The level of GPR55 mRNA was strongly (2.7 fold) increased in CD, but only moderately in UC patients vs. controls. In CD, GPR55 mRNA expression was 3.5 fold higher in biopsies from inflamed compared to non-inflamed tissues. In contrast, GPR55 mRNA level in inflamed and non-inflamed tissues in UC was comparable. Similar results were observed for GPR55 expression at protein level. The changes in GPR55 expression were unrelated to patient age or gender.
CONCLUSION: Different patterns of expression of GPR55 at mRNA and protein levels were observed in IBD patients. We speculate that GPR55 is crucial for the inflammatory processes in IBD, in particular in CD and may affect disease severity, as well as response to treatment depending on disease type. The GPR55 receptors may become an attractive target for novel therapeutic strategies in the treatment of IBD.
Disclosure of Interest: None declared

P0841 HYPERACTIVITY OF THE ENDOGENOUS OPIOID SYSTEM PROTECTS AGAINST ACUTE, BUT NOT CHRONIC STRESS-INDUCED EXACERBATION OF COLITIS IN MICE

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INTRODUCTION: The endogenous opioid system plays an important role in the maintenance of homeostasis in the gastrointestinal tract. Recent studies suggest that the impairment of EOS function may be crucial in the pathogenesis and progression of inflammatory bowel diseases (IBD). However, this has not been confirmed due to the lack of relevant models.
Recently, two mouse lines - with high (HA) and low (LA) opioid system activity – were developed based on the expression of swim stress-induced analgesia. The aim of our study was to characterize the role of the endogenous opioid system and stress in the development of IBD symptoms in HA and LA mouse lines.
AIMS & METHODS: Mice were bred using bidirectional selection and classified as HA or LA line based on the measurement of analgesia with the hotplate and tail-flick tests. Colitis was induced by instillation of trinitrobenzenesulfonic acid (TNBS) in 30% EtOH/saline. After 3 days, the macroscopic score was assessed and the samples for biochemical, molecular and histological studies were collected. To evaluate the influence of stress on development of colitis, we used chronic mild stress (exposure to stress stimuli for 2 and 5 weeks) and acute stress (short restraint over 3 days) models.
RESULTS: We observed a significant difference in the development of colitis between non-stressed HA and LA mice, as indicated by the macroscopic score (3.08±0.06 vs. 6.50±0.79 for HA and LA, respectively) and ulcer score (0.30±0.31 vs. 2.10±0.31 for HA and LA, respectively). Chronic mild stress had no influence on colitis in both mouse lines. Colitis was improved in HA mice exposed to acute stress in comparison with non-stressed animals (1.77±0.12 vs. 4.60±1.60), but did not change the inflammation score in LA line.
CONCLUSION: Our studies strongly support the hypothesis that the activity of the endogenous opioid system may be crucial in IBD development and affect the success rate in IBD treatment. We also evidence that acute, but not chronic stress influence significantly the exacerbation of IBD symptoms depending on the endogenous opioid system activity.
Disclosure of Interest: None declared

P0842 ENTERIC GLIAL CELLS FROM CROHN'S DISEASE PATIENTS MISPRODUCE 15-DEOXY-Δ12,14-PROSTAGLANDIN J2: DEFECT IN INTESTINAL EPITHELIAL BARRIER RESISTANCE

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INTRODUCTION: Enteric glia, the major constituent of the enteric nervous system, plays a key role in the control of intestinal epithelial barrier (IEB) functions. Under physiological conditions, enteric glial cells (EGC) inhibit intestinal epithelial cells (IEC) proliferation, enhance IEB repair and increase its resistance to pathogens. All these mechanisms are altered during inflammatory bowel disease (IBD), such as Crohn's Disease (CD). EGC lesions have also been observed in this pathological context, and we investigated here the possible link between CD EGC and IEB dysfunctions.
AIMS & METHODS: First, we have characterised EGC isolated from CD and cancer patients (considered as control EGC) by real time Q-PCR and immunostaining. Next, we studied EGC functional impact on IEB using an indirect co-culture model with human intestinal epithelial cell (IEC; Caco-2) cell line seeded on Transwell filters, measuring transepithelial resistance (EVOM), IEC spreading (ZO1 immunostaining) and IEC proliferation (DAPI cell counting). EGC-derived soluble factors (IL6, TGFβ, proEGF, GSH) and thirty polyunsaturated fatty acid (PUFA) metabolites were quantified in EGC supernatants. 15dPGJ2, PPARγ agonist (Rosiglitazone) and PPARγ antagonist (GW9662) functional impacts were then measured on IEC spreading and IEB resistance.
RESULTS: EGC isolated from CD and cancer patients (considered as control EGC) expressed the same level of glial markers (GFAP, S100beta, Sox10). Whereas control EGC increased significantly IEC transepithelial resistance, IEC spreading and decreased IEC proliferation, CD EGC had no significant effect. EGC supernatants showed a severe decrease in 15dPGJ2 and 11betaPGF1alpha production but no change in others EGC-derived soluble factor expression. 15dPGJ2 also induced a decrease in IEC proliferation but also an increase in IEC spreading and IEB resistance. In addition, PPARγ agonist reproduced these effects and PPARγ antagonist abrogated them.
CONCLUSION: All together, these results show that human EGC from Crohn's disease patients have lost their protective properties on IEB integrity among the regulation of IEB resistance, IEC spreading and proliferation. This could be due to a defect in the 15dPGJ2 pathway in CD EGC.
Disclosure of Interest: None declared

P0843 HOMOCYSTEINE EXACERBATED DSS-INDUCED COLITIS BY ACTIVATION OF TH17 CELLS VIA P38 SIGNALING PATHWAY

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INTRODUCTION: It is well knownz that homosysteine is a pro-inflammatory molecule and contributes to the chronic inflammation of cardiovascular and cerebral disorders. Hyperhomocysteinemia (HHcy) is a common phenomenon observed in patients with inflammatory bowel disease (IBD). The influence of HHcy on the colonic inflammation of IBD has never been explored.
AIMS & METHODS: The aim of this study is to investigate the effect of HHcy on Dextran sulfate sodium (DSS) induced-colitis. Rats were randomly divided into 5 groups (n = 6 per group): control, HHcy, DSS, HHcy+DSS and HHcy+DSS+p38 inhibitor. HHcy was induced by giving rats rodent food containing 1.7% methionine for three weeks. Colitis was induced by giving water containing 5% DSS. The p38 inhibitor (5μmol SB203508/kg) was given twice daily beginning 60h after DSS treatment. The plasmatic concentration of IL-17 was measured by ELISA. The mRNA and protein expressions of inflammatory mediators were detected by RT-PCR and Western-blot, respectively.
RESULTS: The rats of HHcy+DSS group had scientifically higher body weight loss, MPO activity, DAI score, and histological score compared to the rats of DSS group. HHcy significantly increased the plasmatic concentration, the colonic mRNA and protein levels of IL-17, as well as the protein levels of phosphorylated-p38 MAP kinase, phosphorylated cytosolic phospolipaseA2, cyclooxygenases 2 and RORγt. The increased protein expressions of these inflammatory mediators were suppressed by p38 inhibitor.
CONCLUSION: HHcy aggravated DSS-induced colitis by the activation of Th17 cells via p38 signaling pathway. The p38 inhibitor may represent a novel approach to treatment the chronic intestinal inflammation exacerbated by HHcy in patients with IBD.
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Disclosure of Interest: None declared

P0844 MICRORNA-612 REGULATES AQUAPORIN 8 EXPRESSION AND IS UP-REGULATED IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: MicroRNA (miRNA) plays an important role in the pathogenesis of many diseases by regulating the gene expression at the post-transcriptional level and control crucial physiological processes. Altered levels and functions of miRNAs have been associated with ulcerative colitis (UC), although little is known about their roles in UC.
AIMS & METHODS: We screened different genes from UC tissues and healthy subjects by using genome-wide and miRNA microarray in colon samples from 20 patients with UC and 16 healthy subjects undergoing diagnostic colonoscopy. AQP8 expression and miR-612 were measured by real-time polymerase chain reaction analysis. Regulation of gene expression by miRNAs was assessed by luciferase reporter construct assays and transfection of specific miRNA mimics and inhibitor.
RESULTS: We identified that 1596 genes and 33 miRNAs were increased, 1301 genes and 35 miRNAs were decreased in UC patients compared to healthy subjects. Among them, aquaporin 8 (AQP8) was decreased in patients with UC compared with control tissues ($P < 0.01$). We searched candidate target miRNAs of AQP8 through bioformatics and the luciferase report assay analysis

indicated that miR-612 which has complementary site in the 3-untranslated region (UTR) of AQP8 could decrease the relative luciferase activities by 45% and transfection of HT29 cells with the miR-612 mimic resulted in inhibition of the basal AQP8 protein.
CONCLUSION: miR-612 appears to regulate the expression of AQP8. Increased levels of miR-612 in colon tissues of active UC appear to decrease expression of AQP8, which could involved in the pathogenesis of UC.
Disclosure of Interest: None declared

P0845 HEPATOBILIARY, PANCREATIC AND RENAL MANIFESTATIONS IN GREEK INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Inflammatory bowel disease (IBD) patients often exhibit common manifestations, which are not characterized as ''classic'' extra-intestinal manifestations, posing clinical dilemmas.
AIMS & METHODS: The aim of our study was to investigate the prevalence and characteristics of certain common manifestations from the liver, biliary tree, pancreas and kidneys in IBD patients followed-up in tertiary centers. Data from 1741 IBD patients (females: 43.5%, Crohn's disease: 53.9%, median [IQR] age at IBD diagnosis: 32.9 [23.0-48.4] and IBD duration until 1st EIM diagnosis: 3.0 [0.2-8.0] years) have been retrospectively retrieved and registered according to a pre-defined protocol. Positive results were based on imaging findings and/or pre-existing compatible clinical diagnosis. The impact of certain demographic and IBD characteristics on results was studied.
RESULTS: Cholelithiasis was present in 113/1489 (7.6%) patients mainly in females ($p<0.0001$) with Crohn's disease ileitis or extensive ulcerative colitis ($p=0.042$), concomitant nephrolithiasis ($p<0.0001$) and those having undergone a major IBD surgery ($p=0.031$), appendectomy or tonsillectomy ($p<0.0001$). Non-alcoholic fatty liver disease was detected in 159/1489 (10.7%) patients mainly in females ($p<0.0001$) with ulcerative colitis ($p=0.014$) and concomitant nephrolithiasis ($p<0.0001$). Pancreatitis was diagnosed in 46/1656 (2.8%) patients. In particular, autoimmune IgG4-related pancreatitis was observed in 5/46 (10.9%), drug-induced in 34/46 (73.9%) and lithiasic in 6/46 (13%) patients. Pancreatitis was more frequent in smokers ($p=0.004$) with concomitant nephrolithiasis ($p=0.002$) and in patients with an ileal-anal pouch anastomosis ($p=0.049$). Nephrolithiasis was present in 140/1592 (8.8%) patients less frequently in those with perianal Crohn's disease ($p=0.019$).
CONCLUSION: One tenth or less of our IBD patients exhibited at least one hepatobiliary, pancreatic or renal manifestation. A different pattern of appearance was observed between Crohn's disease and ulcerative colitis patients. Nephrolithiasis often accompanies the other manifestations.
Disclosure of Interest: None declared

P0846 RENAL CELL CARCINOMA PATIENTS HAVE A BETTER SURVIVAL IN A NATIONWIDE INFLAMMATORY BOWEL DISEASE COHORT COMPARED WITH THE GENERAL POPULATION

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INTRODUCTION: Patients with inflammatory bowel disease (IBD) frequently undergo abdominal imaging. This may result in an increased number of incidentalomas including renal cell carcinoma (RCC). A high percentage of incidentally found RCCs might improve cancer outcome; however, immunomodulators and biological agents, as used in the treatment of IBD, may also impact cancer outcome. In this study we aimed to compare the outcome of RCC between IBD patients and the general population. Next we evaluated the impact of IBD therapy on RCC outcome.
AIMS & METHODS: Using the Dutch National Pathology Registry (PALGA) we identified all IBD patients diagnosed with RCC in The Netherlands from January 1991 until May 2013. Cases were confirmed using anonymized medical records and clinical and demographic variables were collected. The control group was derived from the Eindhoven Cancer Registry (1991-2010) which provided the cancer registration for approximately 2.3 million people in The Netherlands. RCC characteristics like TNM stage, age at RCC diagnosis and treatment were compared univariately between cases and controls. Survival analyses were made with Kaplan Meier curves and confounder correction was performed with Cox regression.
RESULTS: We included 160 patients from 69 academic and non-academic hospitals with a confirmed IBD diagnosis who developed RCC. 64/160 (45.1%) IBD patients used thiopurines or biologicals during their disease course of IBD. 73/160 (51.8%) RCC cases in IBD patients concerned incidentalomas. The control group consisted of 4388 patients with RCC. Upon comparison, IBD patients had a statistically significant lower age at RCC diagnosis (median 62.0 versus 66.0; $p<0.005$), lower N-stage (5.8% N+ versus 11.4% N+; $p=0.030$) and lower M-stage (10.7% M1 versus 20.0% M1; $p<0.005$). Furthermore IBD patients underwent more frequently surgical treatment for RCC (96.2% versus 75.6%; $p<0.005$). A Kaplan Meier curve showed better overall survival in IBD patients (log rank $p<0.005$). Age at RCC diagnosis, T, and M-stage, and surgical treatment emerged as confounders. Adjusted for these confounders, a protective effect of IBD on overall survival was still present ($p=0.015$; hazard ratio 0.690; 95% CI 0.512-0.932). Comparing IBD patients with and without thiopurines and/or biologicals, overall survival was significantly better in the group who did use immunosuppression (log rank $p=0.012$). However, a Cox model adjusted for TNM stage and age at RCC diagnosis completely abolished the protective effect of immunosuppression ($p=0.949$).
CONCLUSION: Patients with IBD who develop RCC have a significantly better overall survival compared to the general population with RCC, which may partially be explained by an earlier diagnosis of RCC with a subsequent lower disease stage. Immunosuppression does not adversely affect overall survival.
Disclosure of Interest: None declared

P0847 INFLUENCE OF COPING ON THE CLINICAL COURSE OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE COHORT STUDY

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INTRODUCTION: Coping strategies are used to manage conflicts and illnesses, and may have both adaptative or maladaptative effects on health status. Coping strategies have not been well studied in patients with Inflammatory Bowel Disease (IBD), and their influence on the clinical course of the disease and the use of health resources is unknown
AIMS & METHODS: The aim of the study was to evaluate the influence of the use of different coping strategies on the number of emergency or unscheduled visits and hospitalisations in IBD patients.
Methods: A prospective observational cohort study was designed. The cohort consisted of consecutive out-patients with IBD (Crohńs disease (CD) and ulcerative colitis (UC)) who attended our monographic IBD Unit. A basal demographic and clinical questionnaire was completed by all patients. Coping strategies were assessed with the Spanish version of the COPE scale. It consists of 60 items that participants rated themselves using the dispositional response format, and indicating how frequently they engaged in each coping behaviour on a 4-point Likert scale. The scale had 3 different global strategies: Problem-focused coping, avoidance coping and emotion-focused coping. All emergency and unscheduled visits and hospitalisations related to IBD over a follow-up period of 18 months were recorded. The influence of coping on clinical course was analysed by Multiple Regression analysis.
RESULTS: 776 patients were included (364 male (46.9%), mean age 45 years, age ranging from 18 to 86 years). 317 (40.9%) patients had CD and 459 (59.1%) UC. At the baseline evaluation, the most frequently used coping strategies by IBD patients were problem-focused coping (mean: 2.72 standard deviation, SD: 0.45) and avoidance coping (mean: 2.60, SD: 0.37), and the least frequently used was emotion-focused coping (mean: 2.36, SD: 0.57). The mean number of unscheduled or emergency visits was 1.05 (SD: 1.68, range 0-14) and the mean number of hospitalizations was 0.35 (SD: 0.94, range 0-9). After a follow up of 18 months, the use of avoidance coping strategies was a risk factor for a higher number of emergency or unscheduled visits in the multivariate analysis ($B=0.027$, CI95%: 0.009-0.045; $p<0.005$). However, coping strategies did not influence the need of hospitalisations.
CONCLUSION: The coping strategies mostly used by IBD patients are the problem-focused coping and avoidance coping. A frequent use of avoidance coping strategies appears to be a risk factor for requiring a higher number of emergency visits in the following months. Therefore, these patients would probably benefit from psychological support.
Disclosure of Interest: None declared

P0848 SEXUAL DYSFUNCTION IN INFLAMMATORY BOWEL DISEASE: DO GASTROENTEROLOGISTS OVERLOOK THIS ISSUE?

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INTRODUCTION: Inflammatory bowel disease (IBD) is a condition associated with high morbidity and poor quality of life (QoL). This population is usually young and sexually active. Studies addressing sexual dysfunction (SD) in IBD patients are scarce and their results are controversial. Moreover, little is known about how often gastroenterologists discuss this matter with IBD patients.
AIMS & METHODS: Our primary objective was to estimate SD frequency among IBD patients in the ambulatory setting. Secondary objective was to estimate how often SD is addressed by gastroenterologists. A self-administered anonymous questionnaire was delivered to adult ($\geq$ 18 years) IBD patients

who assisted the IBD ambulatory clinic between August and September 2013. The survey had two parts. The first one assessed QoL by the EuroQol scale and SD by the Female Sexual Function Index (FSFI) and the International Index of Erectile Function (IIEF-15) in women and men, respectively. Patients were asked about whether gastroenterologists inquiry about their sexual function and if they considered this to be relevant. The second part was filled out by the gastroenterologist who was blinded to the first one. It included the Mayo and Harvey-Bradshaw Scores, IBD treatment in the previous month and IBD phenotype according to the Montreal Classification.
RESULTS: Response rate was 74.5%. Seventy five patients were recruited, 61% (n = 46) had ulcerative colitis, 37% (n = 28) had Crohn's disease and one had undetermined colitis. Median age was 37 years (IQR = 30-55) and 56% (n = 42) were women. SD prevalence in women was 69.7% (n = 30). In men, the most affected domains were overall satisfaction 64.5% (n = 20), sexual desire 38% (n = 12) and intercourse satisfaction 35% (n = 11). SD was not addressed in 84% (n = 63) of IBD patients. In this subgroup, 57% (n = 36) answered that the main reason was that the gastroenterologist did not ask them and 41% (n = 26) answered that it would had been important to be asked about it. QoL was good or very good in 97% (n = 73) of the subjects. None of the patients was consuming antidepressants.
CONCLUSION: SD was very frequent in both genders. Above 50% of our IBD patients had impaired sexuality, whereas in the general population SD is considered to be lower, around 35%. Notably, men had lower overall satisfaction and sexual desire rather than orgasmic and erectile dysfunction. Gastroenterologists did not assess SD in the majority of IBD patients, while a considerable proportion of them found discussing this topic with their physician to be relevant. Therefore, this issue should be addressed. Even though QoL was satisfactory in the vast majority, SD was prevalent and it should be included in the assessment of QoL in this population. The small sample size did not allow us to estimate associations. This is the first study in Latin America that addresses SD in IBD patients.
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P0849 INCREASED RISK OF WORK DISABILITY IN INFLAMMATORY BOWEL DISEASE PATIENTS AFTER SEVEN YEARS OF FOLLOW-UP – A POPULATION-BASED COHORT STUDY

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INTRODUCTION: Inflammatory bowel disease (IBD) often affects younger persons and may have considerable impact on the ability to maintain connected to the labour market.
AIMS & METHODS: We aimed to evaluate the occurrence and risk of sick leave (SL) and work disability (WD) in incident patients with IBD after 7 years of follow-up compared to a population-based control group and look for associations of social, phenotypic and clinical characteristics.
A subgroup of 379 IBD patients aged 18-67 years from an IBD-inception cohort (513 patients) registered Jan 1 2003 to Dec 31 2004 in a well-defined Copenhagen area were our IBD study population. Clinical data were collected from the medical records. Data on eucational level, sick leave and work disability was retrieved from national registers. A random subset of the general population (n = 1435) were matched on sex, age and residency to IBD cases. Survival curves displaying the cumulative probabilities of work disability and sick leave were derived with the Kaplan-Meier method. Cox proportional hazard regression analyses were performed to identify possible independently associated predictive factors.
RESULTS: After 7 years of follow-up the cumulative risk of SL and WD was 47.8% and 5.8% in UC respectively and 55.8% and 6.3% in CD respectively. The overall hazard of SL was 2.01 (95% CI 1.66-2.43) and 2.03 (95% CI 1.18-3.49) of WD in IBD patients. Male IBD patients (HR 2.38 (95% CI 1.10-5.14)) and patients aged 55-67 years at diagnosis (HR 4.36 (1.65-11.53)) were at increased risk of receiving WD compared to the general population. Both women (HR 1.83 (1.43-2.35)) and men (HR 2.29 (1.71-3.08)) were at increased risk of SL as well as patients aged 18 to 55 had a significantly higher risk of SL compared to the background population. Age above 55 years increased the risk of WD in patients with CD (HR 17.49 (95% CI 1.92-159.01) but WD in CD was not explained by sex, educational level, behaviour and localisation of disease, smoking or surgery after mutually adjustment. Educational level ($HR_{>\ 13\ years\ of\ schooling}$ 1.79 (95% CI 1.02-3.15)), stricturing disease behaviour (HR_{B2} 0.33 (95% CI 0.14-0.83) and surgery ($HR_{1\ resection}$ 4.09 (95% CI 2.17-7.71), $HR_{2+\ resections}$ 8.96 (95% CI 2.86-28.03)) were predictors of SL in CD. Smoking ((former (HR 0.22 (95% CI 0.02-2.16) or current (HR 6.02 (95% CI 0.95-37.99)) compared to never (p = .04)) was a predictor of WD in UC and female gender (HR 1.73 (95% CI 1.10-2.72)) and surgery (HR 4.19 (95% CI 2.09-8.38)) were predictors of SL in UC.
CONCLUSION: In this population-based study of incident Danish IBD patients we found that after 7 years of follow-up IBD patients are at increased risk of WD and SL compared to the background population and that educational level, disease behaviour and surgery were predictors of SL in CD, while high age was a predictor of WD in CD. Female gender and surgery were predictors of SL in UC, while smoking status was a predictor of WD in UC. Continuous attention early after diagnosis should be made on reducing the risk of WD in IBD patients.
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P0850 PHENOTYPIC CHARACTERISTICS AND USE OF THERAPEUTIC RESOURCES IN ELDERLY-ONSET INFLAMMATORY BOWEL DISEASE: A MULTICENTRE, CASE-CONTROL STUDY

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INTRODUCTION: It has been reported that IBD onset occurs at old age in up to 10% of cases. Elderly patients have more comorbidities and, therefore, a potential increased risk of drug adverse effects, increased likelihood of hospital admissions and postoperative complications.
AIMS & METHODS: To evaluate the phenotypic characteristics and use of therapeutic resources in patients with elderly–onset IBD.
Methods: Retrospective, case-control, multicentre study. All those patients diagnosed with IBD over the age of 60 years (*cases*) since 2000 and with a follow-up > 12 months were identified from the IBD databases of each centre. Cases were compared with *controls,* who were diagnosed with IBD between 18 and 40 years of age, and matched by year of diagnosis, gender, and type of IBD.
RESULTS: A total of 1,374 cases and 1,374 matched controls were included, of whom 43% women, 62% ulcerative colitis (UC), 36% Crohn's disease (CD) and 2% unclassified IBD. The mean age at diagnosis was 68 years (range, 60-87) within cases and 28 years (range, 18-45) within controls. 59% of the cases (but only 3% of controls) had at least one cardiovascular risk factor (arterial hypertension, dyslipidemia or diabetes). The proportion of active smokers at the time of IBD diagnosis was 25% among controls and 13% among cases. Phenotypically, elderly-onset patients had a lower proportion of extensive UC ($p < 0.0001$), and a higher proportion of stenosing and a lower proportion of penetrating pattern ($p < 0.0001$) and exclusive colonic location ($p < 0.0001$). Elderly-onset patients had a lower rate of IBD-related complications ($p = 0.009$) but a higher prevalence of thrombotic events ($p < 0.0001$). Regarding the use of therapeutic resources, there was a significantly lower use of corticosteroids ($p < 0.0001$), immunomodulators ($p < 0.0001$) and biological agents ($p < 0.0001$) in elderly-onset patients as compared to controls, but a similar rate of surgeries. Finally, elderly-onset patients had a higher rate of hospitalizations ($p < 0.0001$), neoplasms ($p < 0.0001$) and deaths ($p < 0.0001$). In the multivariate analysis, elderly-onset of IBD was independently associated to a decreased need of immunomodulators and biological agents, and an increased need of hospital admissions.
CONCLUSION: Elderly-onset IBD is associated to a less severe/complicated phenotype and the lesser use of immunosuppressive therapies, which probably accounts for a non-increased IBD-related morbidity. Age at diagnosis might explain the increase in the rate of hospitalizations among elderly patients.
Disclosure of Interest: None declared

P0851 C. DIFFICILE COLONISATION AND INFECTION RATES ARE NO LONGER RAISED IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: While several studies in the last 10 years have reported higher rates of C. difficile colonisation (CDC) and C. difficile infection (CDI) in IBD than in non-IBD patients, the overall incidence of CDI in the UK is now falling. We have therefore reassessed the incidence of CDC and CDI in diarrhoeal patients with and without IBD.
AIMS & METHODS: All stool samples tested for C. difficile by our laboratory in the 3-month period ending October 2012 were identified using the microbiology database (Barts Health NHS Trust). A 2-step, ELISA algorithm for C. difficile testing was applied to liquid stools only: the first was a test for CDC (presence of glutamate dehydrogenase[GDH] – a C. difficile-specific enzyme); if GDH was positive, a second step was performed to look for CDI (presence of toxin in stool). Electronic patient records (EPR) were then reviewed to see if patients whose stool was tested had a known diagnosis of IBD (Crohn's or ulcerative colitis) when the sample was sent.
RESULTS: 927 stool samples were tested, EPR data was not available for 22 (2%) cases (excluded from analysis). 88 (10%) patients had IBD. Mean age (SEM) in years was 42.1 (2.1) for IBD and 58.2 (0.8) for non-IBD patients, respectively ($p < 0.0001$). With the groups combined: 109 (11%) patients had CDC and 27 (3%) had CDI. CDC was found in 4 (5%) IBD and 105 (12%) non-IBD patients ($p = 0.02$). There were no CDI cases in IBD patients and 27 (3%) in non-IBD samples ($p = 0.1$). None of the non-IBD CDC patients went on to develop IBD (EPR review to March 2014) after their samples were analysed.

CONCLUSION: In our diarrhoeal patients, CDC is now less common in IBD than in non-IBD patients. We also found no CDI in our 88 IBD samples. Although the period studied was short and the numbers of samples limited, our results suggest that the recent 'epidemic' of CDI in IBD patients may now be on the wane.
Disclosure of Interest: None declared

P0852 RECENTLY-DIAGNOSED CROHN'S DISEASE PATIENTS DEMONSTRATE MIXED COPING SKILLS TO CONTROL THEIR PSYCHOLOGICAL DISTRESS

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INTRODUCTION: The general psychopathology and coping processes of Crohn's disease (CD) patients are incompletely understood. Since these elements are expected to impact on quality of life, it is necessary to define their relationships precisely. The social constructionist perspective has become a useful framework for understanding coping strategies of men and women. This study examines emotional distress and coping strategies between the genders.
AIMS & METHODS: 158 consecutive CD patients undergoing clinical assessment at the IBD Clinic completed a series of questionnaires: Brief Symptom Inventory (BSI) which measures psychological distress (range: 0 = "not at all" to 4 = "extremely distressed"), Ways of Coping (WAYS) that measures thoughts and actions that people use to handle stressful encounters (range: 1-8, greater value = higher use), and IBDQ (disease-specific quality of life). Appropriate univariate analysis was performed. Data given as mean ± SD.
RESULTS: 135 patients (85%) completed the questionnaires, 62 men (age 39.1 ± 14.9 years, Harvey-Bradshaw Index (HBI) 7.1 ± 3.7, disease duration 2.2 ± 0.3 years) and 73 women (age 43.5 ± 17.2, HBI 7.9 ± 4.4, disease duration 2.4 ± 0.8). BSI scores for somatization (1.15), obsessive-compulsive behavior (1.10), interpersonal sensitivity (0.83), depression (0.81), anxiety (1.08), hostility (0.79), phobic anxiety (0.65), paranoid ideation (0.81) and psychoticism (0.59) revealed low levels of psychological distress and did not differ significantly between men and women. WAYS scores without gender differences were: range >6: acceptance, self-blame, active coping; range 5-6: self-distraction, planning, positive reframing; range 2-4.9: humor, religion, denial, behavioral disengagement, substance use. WAYS scores with gender differences were: use of emotional support (men 4.03, women 4.80, $p<0.02$), use of instrumental support (3.92, 4.64, $p<0.03$), venting (3.48, 4.32, $p<0.005$). BSI depression correlated with WAYS instrumental support ($p=0.01$), behavioral disengagement ($p<0.03$), and self-blame ($p<0.02$). IBDQ scores were men 49.2 ± 14.9; women 48.6 ± 12.6. Significant correlations were found between IBDQ and the WAYS scores of self-distraction, denial, behavioral disengagement, venting, self-blame and religion; and HBI with the BSI scores of somatization, positive symptom total and positive symptom distress index. IBDQ correlated with HBI ($p<0.001$).
CONCLUSION: In this recently-diagnosed CD cohort, men and women had similar levels of disease activity and psychological distress. The most prominent positive coping mechanisms were acceptance and active coping, and negative trends of self-blame and self-distraction. Women practiced more emotional support, instrumental support and venting. These findings need attention in clinical practice. [Supported by a generous grant from the Leona M. and Harry B. Helmsley Charitable Trust].
Disclosure of Interest: None declared

P0853 PREVALENCE OF ALCOHOL CONSUMPTION AND ITS INFLUENCE ON DISEASE COURSE IN SWISS IBD PATIENTS

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INTRODUCTION: Little is known about the prevalence and influence of alcohol consumption on the disease course in patients with IBD. Pathophysiologically alcohol might have an impact on disease course by increasing intestinal permeability, disrupting gut barrier function, inhibiting intestinal immune system and favouring bacterial overgrowth. Otherwise, low to moderate alcohol consumption might have an anti-inflammatory effect by lowering IL-6 and TNF-α levels.
AIMS & METHODS: We aimed to estimate the prevalence of alcohol consumption and its influence on disease course within the Swiss IBD cohort. Frequency of alcohol consumption was assessed in a screening question provided in the enrolment questionnaire of the Swiss IBD cohort. According to the given answers patients were distributed in 3 categories: non-drinkers (abstainers or rarely), light-to-moderate drinkers (1-2x per week to daily alcohol consumption), heavy drinkers (> = 2x daily). At enrolment socio-demographic variables and disease characteristics were compared cross-sectionally to identify risk factors for increased alcohol consumption and to evaluate a possible influence of alcohol consumption on disease course. During follow-up need for surgeries and occurrence of abscesses and fistulas were compared prospectively between the 3 groups.
RESULTS: 2019 patients, who had answered the question about alcohol consumption at enrolment in the Swiss IBD cohort between July 2006 and May 2013, were included in the analysis. 870 patients (43%) drank regularly alcohol: 818 low-to-moderately, 52 heavily. Drinkers were older, by the majority male, had a higher body mass index and smoked more often. The proportion of Crohn's disease patients was lower in non-drinkers (59%) compared to low-to-moderate drinkers (52%). Drinkers reported less extraintestinal manifestations than non-drinkers (32% vs. 39%, $P<0.01$). Low-to moderate drinkers (31%) with ulcerative colitis have a lower ($p=0.03$) proportion of pancolitis than non-drinkers (41%). However heavy drinkers with ulcerative colitis had to be hospitalized less often before enrolment,which, after stratification, seems to be due to the known protective effect of smoking. Generally heavy drinkers received significantly less immunomodulators (AZA, MTX) and anti-TNF-inhibitors. During follow-up (6925 patient-years) the need for surgery was similar among non-drinkers and low-to-moderate drinkers. However heavy drinkers with Crohn's disease had to undergo less surgeries and developed fewer abscesses and fistulas.
CONCLUSION: The prevalence of regular alcohol consumption within the Swiss IBD cohort was 43%, whereof 94% drank low-to-moderately. Patients with higher alcohol consumption were older, preferably males with a higher body mass index and more often smokers. Heavy drinkers received less treatment with immunosupressants. In ulcerative colitis low-to-moderate drinking seemed to favour a shorter extent and heavy drinkers were less hospitalized. In Crohn's disease heavy drinking seemed to reduce the development of abscesses and fistulas and the need for surgeries during follow-up. A prospective project nested within the Swiss IBD cohort for a better understanding of alcohol on disease course is ongoing.
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P0854 IS HOSPITALIZATION PREDICTING THE DISEASE COURSE IN UC? PREVALENCE AND PREDICTORS OF HOSPITALIZATION AND RE-HOSPITALIZATION IN ULCERATIVE COLITIS IN A POPULATION-BASED INCEPTION COHORT BETWEEN 2000-2012

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INTRODUCTION: Limited data are available on the hospitalization rates in population-based studies. This is a very important outcome measure.
AIMS & METHODS: The aim of this study was to analyze prospectively if early hospitalization is associated with the later disease course as well as to determine the prevalence and predictors of hospitalization and re-hospitalization in the population-based UC inception cohort in the Veszprem province database between 2000 and 2012. Data of 347 incident UC patients diagnosed between January 1, 2000 and December 31, 2010 were analyzed (m/f: 200/147, median age at diagnosis: 36, IQR: 26-50 years, duration: 7, IQR 4-10 years). Both in- and outpatient records were collected and comprehensively reviewed.
RESULTS: Probabilities of first UC-related hospitalization and first re-hospitalization were 28.6%, 53.7%, 66.2% and 23.7%, 55.8% and 74.6% after 1, 5 and 10 years of follow-up in Kaplan-Meier analysis. Main reasons for first hospitalization were diagnostic procedures (26.7%), disease activity (22.4%) or UC related surgery (4.8%), but the majority of the hospitalizations were unrelated to UC (44.8%). In Kaplan-Meier and Cox-regression analysis disease extent at diagnosis (HR: 1.35, $p=0.018$, $HR_{extensive}$: 1.79, $p=0.02$ vs. proctitis) or at last follow-up (HR: 1.56, $p=0.001$), need for steroids (HR: 1.98, $p<0.001$), azathioprine (HR: 1.55, $p=0.038$) and anti-TNF (HR: 2.28, $p<0.001$) were associated with the risk of UC-related hospitalization. Early hospitalization was not associated with a specific disease phenotype, however 46.2% of all colectomies were performed in the year of diagnosis.
CONCLUSION: Hospitalization and re-hospitalization rates are relatively high in this population-based UC cohort. Early hospitalization was not predictive for the later disease course.
Disclosure of Interest: None declared

P0855 FAECAL CALPROTECTIN IS AN ACCURATE PREDICTOR OF ENDOSCOPIC AND HISTOLOGICAL DISEASE ACTIVITY IN IBD

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INTRODUCTION: Assessment of disease activity in Inflammatory Bowel Disease (IBD) is challenging as the gold standards of endoscopy and histology are invasive, expensive and impractical for regular use. Faecal calprotectin (FC) is increasingly being used as a biomarker of intestinal inflammation but its role in predicting endoscopic and histological changes in IBD is limited. We explore the role of FC to assess histological disease in IBD patients, in comparison to C-reactive protein (CRP), in the largest series of IBD patients to date.
AIMS & METHODS: Retrospective analyses of 407 IBD patients who had a colonoscopy with FC (mg/g) and CRP (mg/L) measurements. The most severe histological inflammation found was graded according to the simplified histology score (0-normal, 1-mild, 2-moderate, 3-severe). Spearman's correlation coefficient (r) was used to measure correlation between the groups. Receiver operating

characteristic (ROC) curves were used to differentiate patients with normal/mild disease (histology scores 0-1) from patients with moderate/severe disease (histology scores 2-3).
RESULTS: In 203 Crohn's disease (CD) patients, the median FC values for the histology scores; 0, 1, 2, 3 were; 113, 238, 645 and 3075, respectively (graph). The corresponding medians for CRP were; 2.5, 9.8, 14.6 and 54.6. Both FC (ρ 0.59, $p<0.0001$) and CRP (ρ 0.30, $p<0.0001$) showed very strong correlations to histology scores. Using a cut-off value of 250μg/g, FC showed an 88% sensitivity and 62% specificity for predicting moderate / severe disease (AUC 0.82). CRP >6 mg/L was less sensitive and specific (70%, 44%, respectively, AUC 0.64).
In 204 ulcerative colitis (UC) patients, the median FC values for the histology scores; 0, 1, 2, 3 were; 38, 296, 520 and 1468, respectively (graph). The corresponding values for CRP were; 2.5, 5.4, 8.2 and 9.7. There was a very strong correlation between the FC values to histology scores (ρ 0.37, $p<0.0001$), compared to CRP (ρ 0.21, $p=0.003$). Using a cut off value of 222 μg/g, FC had a 71% sensitivity and 51% specificity (AUC 0.66) for predicting moderate / severe histological disease. The corresponding figures for CRP>6 mg/L were 54% and 59%, respectively (AUC 0.59).

Histology score	n (CD)	CD - Calpro (Median)	95% CI		n (UC)	UC - Calpro (Median)	95% CI	
0	42	113.0	53.0	to 161.0	25	38.0	25.0	to 66.0
1	87	238.0	175.0	to 330.0	94	295.5	205.0	to 481.0
2	65	645.0	517.0	to 955.0	73	520.0	280.0	to 770.0
3	9	3075.0	452.0	to 5575.0	12	1468.0	122.0	to 4655.0

CONCLUSION: In the largest IBD series to date, FC was strongly predictive of histological disease activity in both CD and UC patients, and with a cut off level of 220-250μg/g gave high sensitivity and moderate specificity for predicting moderate to severe disease activity. FC showed greater accuracy in CD than in UC and also performed better than CRP. This study highlights the importance of FC as a valuable, non-invasive biomarker of disease activity in IBD, which can help direct treatment and reduce the need for invasive endoscopic procedures.
Disclosure of Interest: None declared

P0856 THE ROLE OF CONFOCAL LASER ENDOMICROSCOPY IN THE MANAGEMENT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASES: A CONSENSUS REPORT BASED ON LITERATURE

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INTRODUCTION: Confocal Laser Endomicroscopy (CLE) allows microscopic imaging of the colonic mucosal layer during endoscopy. Clinical studies published during the past years have enhanced the potential of this technique to accurately assess the mucosa at the microscopic level and to provide accurate information either for the assessment of inflammation or for the detection of neoplasia. Those findings have the potential to improve patient management by tailoring both diagnostic and treatment approaches.
AIMS & METHODS: The aim of this study is to develop evidence-based consensus statements for the assessment of the role of CLE in the management of patients with IBD.
Initial statements on the use of CLE in the assessment of IBD were developed by a single CLE expert based on the available clinical literature. Those preliminary statements were edited and submitted by an external group of 8 GI physicians experts in CLE, using a modified Delphi approach. After two rounds of votes based on current literature and strength of recommendation, statements were adopted if the threshold of agreement was higher than 75%.
RESULTS: Out of 17 proposed statements, 11 were adopted and 6 rejected. CLE can identify Crohn's disease (CD) and ulcerative colitis (UC) associated histological changes in vivo. CLE can be used to acquire targeted biopsies for surveillance of IBD patients. Targeted biopsies should be preferably used instead of random four quadrant biopsies for surveillance in IBD. CLE can identify IBD associated histological changes in macroscopically non-inflamed mucosa. CLE provides dynamic in vivo live information about intestinal barrier function and vascular permeability. CLE provides dynamic in vivo live information about intestinal barrier function and vascular permeability. Surveillance in IBD by using CLE should be performed in macroscopically non-inflamed mucosa. CLE can redefine the term "mucosal healing" in vivo. The ultimate goal of CLE for IBD patients is to predict response to anti-tumour Necrosis Factor (anti-TNF) antibody therapy and may help to initiate an individualised therapy of IBD patients to reduce drug associated side effects, morbidity and costs for the health care system. Step-down and step-up approaches should be replaced by an individualized, adapted approach, including microscopic evaluation of the mucosa.
CONCLUSION: 11 consensus statements on the use of Confocal Laser Endomicroscopy for the management of IBD were adopted by a panel of 8 clinical experts. These statements were established based on published literature and consensus opinions, suggesting that Confocal Laser Endomicroscopy has the potential to play an important role in the management of IBD patients by assessing mucosal healing and individualizing approach with biologics. Further clinical studies are necessary to support these ideas.
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P0857 NEGATIVE PREDICTIVE VALUE OF TRANSABDOMINAL ULTRASOUND FOR SHORT-TERM OUTCOMES OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Transabdominal ultrasound is considered a useful tool for the assessment of inflammatory bowel disease (IBD) activity but its negative predictive value for gold standards diagnostic methods, such as endoscopy, is limited. Therefore, usefulness of transabdominal ultrasound in monitoring of disease activity has been questioned. However, the diagnostic value of ultrasound has not been tested with regards to short or long-term outcomes of IBD.
AIMS & METHODS: The aim of our study was to assess the negative predictive value of transabdominal ultrasound in IBD for short –term disease complications. We retrospectively evaluated all IBD patients with clinical suspicion of disease flare who underwent an intestinal ultrasound performed by one sonographist at a single tertiary IBD Center. Disease activity and the presence of disease complications were evaluated according to standard parameters for intestinal ultrasound. Findings of colonoscopy performed within 2 months of the ultrasound were compared to the ultrasound findings for each respective bowel segment. For correlation of categorical findings at ultrasound and colonoscopy a chi-square test was used. The changes in therapy were noted as well as clinical remission and surgical intervention at respective month 3 and 6 following the ultrasound and negative predictive value of ultrasound was calculated for each of the outcomes.
RESULTS: In total, sixty five ultrasounds were performed in 61 IBD patients (mean age 39, range 18 to 94 years; 41% of males; 45/16 Crohn's disease/ ulcerative colitis) were evaluated. Overall, there were 45 cases (70%) of disease activity detected by ultrasound, in 18 cases (28%) no abnormalities were found and 2 cases (3%) were inconclusive. Complications of IBD, such as abscess and fistulas were found in 10 cases (15%). Colonoscopy was performed in 39 cases. Ultrasound correlated well with endoscopy in assessment of disease activity in terminal ileum ($p=0.049$) as well as in colonic disease ($p<0.0001$). The positive and negative predictive values (NPV) of ultrasound for disease activity as assessed by endoscopy were 90% and 78%, respectively, for terminal ileum disease localisation; and 100% and 75%, respectively, for colonic disease. None out of 18 cases with no abnormalities found on ultrasound needed a therapy adjustement nor surgery during the six months following the ultrasound; all these patients were in remission at respective months 3 and 6 (NPV of relapse 100%).
CONCLUSION: Transabdominal intestinal ultrasound has a high negative predictive value for short-term complications of inflammatory bowel disease.
Disclosure of Interest: None declared

P0858 HERPES FAMILY VIRUSES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND IMMUNOSUPPRESSION

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INTRODUCTION: Herpes family viruses (herpes simplex virus 1 and 2 (HSV1 and HSV 2), Epstein Barr Virus (EBV), cytomegalovirus (CMV)) are prevalent in the adult population.
AIMS & METHODS: Aim: Study the primary infection in an adult population with inflammatory bowel disease and infection reactivation under immunesuppression.
Patients-Methods: 56 patients (40 with Crohn's disease, 13 with ulcerative colitis, 3 with indetermined inflammatory bowel disease) were evaluated before immunosuppression initiation (infliximab 36 patients, immunosuppressant 9, infliximab+immunosuppressant: 11). Serology was evaluated before treatment (anti-HSV IgG/IgM antibodies, anti-CMV IgG/IgM antibodies, IgG/IgM antibodies against EBV viral capsid antigens and nuclear antigen). Patients were follow-up for 3 years with serologic evaluation every 3 months and tissue sampling in case of disease flare ups for PCR.
RESULTS: In patients aged 17-20 years 3/3 (100%) were HSV 1,2 (+), 3/3 (100%) EBV (+), 2/3 (66%) CMV (+); in those aged 21-25: 6/8 (75%) were HSV 1 (+), 5/8 (63%) HSV2 (+), 8/8 (100%) EBV (+), 7/8 (88%) CMV (+); in patients aged 26-30 years: 6/7 (86%) were HSV1 (+), 5/7 (71%) HSV2 (+), 4/7 (58%) EBV (+), 6/7 (84%) CMV (+); in patients aged 31-40: 9/11 (81%) were HSV 1,2 (+), 9/11 (81%) EBV (+), 9/11 (81%) CMV (+); in patients aged 41-50: 11/11 (100%) were HSV 1 (+), 10/11 (91%) 10/11 (91%) EBV (+), 7/11 (64%) CMV (+); in patients aged over 60: 10/12 (84%) were HSV 1,2 (+), 12/12 (100%) EBV (+), 9/12 CMV (+). During follow-up 3 patients presented HSV2 seroconversion, while HSV1 was positive, 3 EBV seroconversion and 3 CMV seroconversion. All of them were reported to be asymptomatic. 3 patients presented HSV flare-ups treated with topical and systematic treatment, while immunosuppression was temporally withheld. No flare-ups reported for EBV and CMV.

CONCLUSION: Herpes family viruses are prevalent in patients with inflammatory bowel disease. Flare-ups under immunosuppression are rare while seroconversions are rather asymptomatic.
Disclosure of Interest: None declared

P0859 ACIDITY OF INTESTINAL CONTENTS IN THE DISTAL PARTS OF THE COLON IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: It is nececcary to determine the possibility of using mesalazine-delivering drugs with different release mechanisms depending on the pH value in patients with UC relapse.
AIMS & METHODS: To evaluate the acidity of intestinal contents in the distal parts of the colon in patients with ulcerative colitis (UC) relapse. 43 patients with left-sided UC and 24 patients with extensive UC having mild or moderate relapse were evaluated. The evaluation of the pH of the chymus with use of a universal indicator test strip, as well as analysis of changes in the pH of intestinal contents depending on clinical, laboratory and endoscopic indicators of ulcerative colitis activity, were carried out in all these patients. The control group consisted of 16 healthy volunteers.
RESULTS: On the whole, there was a trend towards acidification of chymus in patients with left-sided UC as compared to healthy volunteers ($pH = 6.76 \pm 0.21$ *vs.* $pH = 6.94 \pm 0.2$, respectively); however, this difference was not statistically significant. In the group of patients with extensive UC, a decrease in pH to below 6.0 (20.8%) was noted significantly more often as compared to the patients with left-sided UC (4.7%, $p < 0.05$) or control group subjects (0%, $p < 0.05$). Statistically significant correlation between the pH of the intestinal contents with ulcerative colitis activity index (correlation coefficient (CC) = -0.23), fecal calprotectin value (CC = -0.25), UC duration (CC = -0.21) or duration of UC treatment (CC = 0.35) was not revealed.
CONCLUSION: In patients with left-sided UC, acidity of the intestinal contents in the distal parts of the colon did not differ from that in the healthy volunteers and did not depend on disease activity or duration of ulcerative colitis. Decrease in the pH of the intestinal contents to below 6.0 was noted significantly more often in patients with extensive UC as compared to patients with left-sided UC or healthy volunteers. In the treatment of patients with decreased intraluminal pH levels, preference should be given to drugs with pH-independent release of active ingredient.
Disclosure of Interest: None declared

P0860 IT'S ALL IN THE STOOL. FAECAL CALPROTECTIN TO HELP GUIDE ANTI-TNF THERAPY; A RETROSPECTIVE STUDY

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INTRODUCTION: Faecal calprotectin (FC), a protein derived mainly from neutrophils and monocytes, is detected in increased quantities in the stool of patients with inflammatory bowel disease (IBD). Recently, the National Institute of Clinical Excellence (NICE) in the United Kingdom (UK) has recommended its use as a biochemical test to differentiate between IBD and functional bowel disease; furthermore, it can also be used to evaluate disease activity or response to treatment. We routinely assess patients' symptoms and biological markers including FC at least annually once established on anti-TNF therapy. This assessment is brought forward if there is a suspicion of ongoing disease activity.
AIMS & METHODS: We sought to assess the impact of FC testing on our clinical management, specifically for our patients with Crohn's disease receiving anti-TNF therapy. We interrogated our pathology database to collect FC results from all patients at Gloucestershire Hospitals NHS Foundation Trust who were established on anti-TNF therapy for Crohn's disease. FC samples had been obtained either as part of annual assessment or earlier due to ongoing symptoms. We then reviewed the patient's notes to determine what actions, if any, had been taken as a consequence of the FC results.
RESULTS: FC results were available from 28 of 31 patients collected during 2011 and 2012. Results were subdivided based on the FC level into four groups. 1) < 50ug/g (n = 9, 32.1%); 2) 50-100ug/g (n = 7, 25%); 3) 100-200ug/g (n = 5, 17.9%) and 4) >200ug/g (n = 7, 25%).
Across all four groups anti-TNF therapy was unaltered in 14 patients (50%) and stopped in 3 (11%). The dose was increased but frequency of treatment maintained in 2 (7%), and frequency increased in a further 2 (7%). Frequency was reduced in one patient from 8 weekly to 10 weekly (3.5%). Two patients were lost to local follow up.
More specifically, in group 1, 34% had their anti-TNF therapy unaltered and 22% had their therapy stopped with consequent significant cost savings. In contrast; 43% of patients in group 4 had their anti-TNF therapy altered, either by increasing dose or frequency of administration. Regarding further investigations no patient with a FC result >100ug/g went on to have a colonoscopy compared with 33% of patients with an FC <50ug/g.
CONCLUSION: FC is a useful tool when judging clinical response to anti-TNF therapy in patients with Crohn's disease. Once treatment is established it allows identification of patients for whom anti-TNF therapy can be further optimised or stopped. It also helps guide the need for further investigation, if either to re-stage disease extent and severity or if considering alternative diagnoses.
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Disclosure of Interest: None declared

P0861 INFLAMMATORY LOAD MEASURED BY SPECT-CT RELIABLY CORRELATES WITH HISTOLOGY AND FECAL CALPROTECTIN IN ULCERATIVE COLITIS

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INTRODUCTION: Assessing inflammatory activity is essential in therapeutic decision making in Ulcerative Colitis (UC). Novel scintigraphy techniques including SPECT-CT are promising to measure inflammatory load in chronic inflammatory conditions such as UC. Leukocyte scintigraphy therefore needs to be validated using other established markers of inflammation.
AIMS & METHODS: We aimed to prospectively validate leukocyte SPECT-CT as a tool to measure and quantify inflammatory load in patients with different extent and severity of UC.
UC patients with an indication for full colonoscopy were included. Within 1 week and without any changes in therapy both colonoscopy (Mayo score, UCEIS) with biopsies (Geboes score) and leukocyte scintigraphy were performed. In addition, serum CRP and fecal calprotectin (Bühlmann ELISA) were measured and clinical questionnaires (CCAI, Mayo) were collected. Patients' peripheral blood leukocytes were isolated and labelled with 200 MBq technetium-99m HMPAO. SPECT combined with a low-dose CT was performed 60 min after reinjection of labelled cells. To quantify inflammation in each colon segment the uptake of leukocytes was calculated as a ratio to the mean uptake in bone marrow of 4 lumbar vertebrae and expressed as SPECT inflammation score in each colon segment and a Summed Activity Score (SAS) for the inflammatory activity in all 5 colonic segments together.
RESULTS: Twenty-six UC patients were studied. 3/26 were using anti-TNF, 4/26 thiopurines, 3/26 prednisone and 20/26 5-ASA at inclusion. At endoscopy 6/26 (23%) of patients had proctitis, 8/26 (31%) left-sided and 12/26 (46%) pancolitis. According to endoscopic Mayo score, 1/26 (4%) of patients had inactive, 5/26 (19%) mild, 8/26 (31%) moderate and 12/26 (46%) severe disease. The median (IQR) full Mayo score was 7 (5-10), CCAI: 6 (2-9), serum CRP 4.1 mg/L (1.7-12.5) and fecal calprotectin 449 ug/g (245-1142). According to SPECT-CT patients were classified as having 9/26 mild, 12/26 moderate and 5/26 severe disease in their most affected segment. At the level of individual segments, significant correlations (Spearman) were observed between the SPECT inflammation score and endoscopic Mayo: r 0.54 ($P < 0.01$), UCEIS r 0.56 ($P < 0.01$) and histologic Geboes score r 0.59 ($P < 0.01$). The Summed Activity Score correlated much better with fecal calprotectin r 0.55 ($P < 0.01$) than with CRP: r 0.24 ($p = 0.24$), CCAI: r 0.43 ($P < 0.05$) or clinical Mayo: r 0.54 ($P < 0.01$).
CONCLUSION: SPECT-CT assessment of UC disease severity in the most inflamed colon segment is correlated with both endoscopic and histologic scores. The total inflammatory load in UC at SPECT-CT is better reflected by fecal calprotectin than by serum CRP.
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P0862 A "COCOON" IMMUNISATION STRATEGY AMONG HOUSEHOLD CHILDREN OF ADULTS PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: In order to protect patients with inflammatory bowel disease (IBD) against serious infections, vaccination of their household children is recommended.
AIMS & METHODS: The aim of our study was to assess the not mandatory and not reimbursed vaccination coverage including pneumococcal, rotavirus, influenza, and varicella vaccines among household children of adult patients with IBD as the "Cocoon Strategy". A self-designed survey was conducted in 138 IBD patients hospitalised in the Department of Gastroenterology and Hepatology at Wroclaw Medical University from November 2013 to March 2014. The survey comprised questions about household children vaccination coverage and the reasons of its refusal as well as the history of infectious diseases in the patients. Randomly, patients completed the survey with a physician present to determine questions comprehension. In order to provide test-retest reliability a group of ten patients completed it twice. Fisher exact test was used for cross-classification tables.

RESULTS: The survey data from 52 IBD patients having household children (25 women, 27 men, mean age: 36 years) were analysed. Two patients declared refusing one obligatory vaccination of their children, while 40% of the patients reported at least one not reimbursed vaccine administration. Most frequently, children obtained pneumococcal (31%), rotavirus (23%), varicella (14%), and influenza (10%) vaccines. The most common reasons for non-immunisation was unawareness of the existing recommendations (46%), fear of adverse effects of the vaccines (18%) and not believing in vaccines efficacy (10%). In one case a medical health care worker discouraged from immunisation. There was statistically significant association between not reimbursed vaccines coverage and educational level of the patients ($p<0.001$). Despite the fact that 28% of IBD patients could not definitively recall varicella infection, none of their household children nor they were vaccinated against chickenpox.
CONCLUSION: The use of not mandatory vaccines recommended in Poland in IBD patients' family members is insufficient. Frequently, patients have serious doubts concerning safety and efficacy of vaccinations. Therefore, further vaccines promotion and education of patients as well as their health care providers are needed. A particular concern is associated with not vaccinating against influenza and varicella, which pose a high risk of infection. Non-immunised and VZV seronegative IBD patients should be vaccinated, and in case of their immunosupression, vaccination of household children is required.
Disclosure of Interest: None declared

P0863 THE ROLE OF PET-CT IN THE CHARACTERIZATION OF THE ACTIVITY OF CROHN'S DISEASE

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INTRODUCTION: Crohn's disease is an immune-mediated disorder with unknown etiology, characterized by segmental, transmural inflammation of the gastrointestinal tract and extraintestinal inflammatory symptoms. The diagnosis is based on endoscopy, imaging examinations, the disease activity is characterized by Crohn's disease activity index (CDAI), which includes subjective, objective sympthoms and laboratory parameters. PET-CT is a global, non-invasive, highly sensitive method to determine the location and activity of some malignant and inflammatory lesions. Former studies showed 85% sensitivity and 87% specifity of 18F-FDG-PET-CT in IBD.
AIMS & METHODS: The aim of the study was to evaluate the role of PET-CT in patients with active Crohn's disease (CDAI >300) before and after biological therapy and comparing with endoscopic index (SES-CD), CDAI and biochemical parameters. Twelve patient were examined: 5M/6F, age between 18 and 39, average age: 25 years. The evaluation of the PET-CT activity was determined considering the activity of the small intestine and the four colon segments. The SUVmax (Standardized Uptake Value) of the intestinal segment was correlated to the SUVmax of the liver, which was chosen as a reference for normal tissue activity. To get the global PET-score, the activity scores of the five intestinal segments were summed.
RESULTS: The PET-score showed correlation with CDAI ($R^2=0.1441$) and CRP ($R^2=0.0512$), but not with SES-CD ($R^2=0.0041$). After one year biologic therapy CDAI ($R^2=0.1622$), CRP ($R^2=0.0815$) and SES-CD ($R^2=0.1699$) correlated well with the PET-score. In active disease, the PET-CT was more sensitive than the endoscopy to indicate the extent of the inflammation. Examining new patients, PET-CT was the most informative on the activity and extent of the disease (small intestine involvement). In one case, the terminal ileum stenosis with high CDAI score associated with negative PET-CT score, which was a fibrotic stenosis as it turned out after the surgery. Patients with negative PET-CT score after biological treatment remained in remission during a two year follow-up period.
CONCLUSION: The PET-CT results correlated well with the activity of the Crohn's disease. In the future, this should be a promising, non-invasive method in the diagnosis of Crohn's disease and in the planning the treatment and follow-up. Negative PET-CT proved to be a good indicator of deep remission.
Disclosure of Interest: None declared

P0864 THE ROLE OF DOUBLE BALLOON ENDOSCOPY FOR CROHN'S DISEASE

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INTRODUCTION: Deep enteroscopy has been widely used for various small bowel diseases. One of the most common diseases that affected the small bowel is Crohn's disease. The idea is being accepted that the mucosal healing is important parameter for the better outcome of Crohn's disease. However the efficacy and safety of the DBE is not fully understood.
AIMS & METHODS: We conducted a retrospective case series study to elucidate the efficacy of DBE in Crohn's disease. We enrolled the consecutive 40 patient who underwent the 95 DBE examinations since 2003. Patients' characteristics, indications of the deep enteroscopy, duration of procedures, therapeutic interventions and complications were assessed.
RESULTS: Subjects were 7 females and 33 males, mean age was 38±13 years old. The indications of DBE were mucosal evaluation for known Crohn's disease, obscure gastrointestinal bleeding, small bowel obstruction, removal of the retained small bowel capsule endoscopy (SBCE), suspicious of Crohn's disease and further evaluation of protein-losing enteropathy in 17, 10, 7, 3, 2, 1 case, respectively. The mean number of DBE examination per patient was 2.4±1.4. Types of scope were type T, type P (thin type), and type B (short type) in 49, 41 and 5 cases. The choice of the scope had depended on the therapeutic capability or the facility of deeper insertion. The insertion roots were antegrade (from mouth) in 31 patients and retrograde (from anus) in 64 patients. The mean insertion time was 65±31 minute. The antegrade vs. retrograde was 45±25 vs. 34±40 minutes ($p=0.005$). The mean total examination time was 83±34 min. The antegrade vs. retrograde was 83±34 vs. 56±26 min. ($p<0.0001$). The mean insertion depth was 95±93 cm. The antegrade vs. retrograde was 178±75 vs. 55±70 minutes ($p<0.0001$). Balloon dilation therapies were performed in 18 procedures in 8 patients. In 10 patients, the prior SBCE had been done and 6 patients were retained. All the retained SBCE were removed by double balloon endoscopy. In only one out of 10 patients, DBE had not shown any severe stricture and SBCE was used for the mucosal evaluation repeatedly. No complication was encountered in diagnostic and therapeutic DBE.
CONCLUSION: DBE showed that ileal lesions were more common and oral DBE was time-consuming in Crohn's disease. The evaluation with DBE also can pick out the patient who can undergo the SBCE. The dilation therapy may delay the timing of the surgical interventions. DBE, especially the retrograde DBE, have a potential to improve the outcome of Crohn's disease.
Disclosure of Interest: None declared

P0865 USE OF INTERVAL ULTRASOUND TO PROSPECTIVELY MONITOR PATIENTS WITH CROHN'S DISEASE ON ADALIMUMAB

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INTRODUCTION: Accurate, non-invasive methods of evaluating treatment response in patients with Crohn's disease (CD) are important in a treat to target paradigm. The aim of this study is to prospectively evaluate the ability of sonography to monitor patients on adalimumab (ADA), correlated with endoscopy as a gold standard.
AIMS & METHODS: This is an IRB-approved, single-center, prospective study, evaluating patients with CD treated with adalimumab for at least 6 months. Baseline clinical score (Harvey Bradshaw/HBI), C-reactive protein (CRP), ileocolonoscopy and transabdominal ultrasound were completed within 2 weeks at time zero and 12 months (if clinically indicated), with intervening scans at 4 and 8 months. Standard sonographic assessment included bowel wall thickness, color Doppler signal, presence of inflammatory fat and lymph nodes. Endoscopy was scored using validated simple endoscopic score (SES) and/or Rutgeert's score (Ri) in post-operative patients. Endoscopic responsiveness was defined as mucosal healing (SES-CD$\leq$5 and/or Ri$\leq$1) and sonographic responsiveness as bowel wall thickness ($\leq$6mm) with minimal inflammatory fat and Doppler signal. The aim of this study is to prospectively evaluate sonographic and endoscopic maintenance of remission in patients on adalimumab.
RESULTS: 50 patients have been recruited to date with $n=34$ included in this analysis ($n=16$ excluded given drop out, missing data or in progress). At time zero, 34 patients had endoscopy and 19/34 (56%) patients underwent follow-up endoscopy at 1 year, those who did not were deemed in clinical and serologic remission without indication for endoscopy. There were (3/34) strictures limiting endoscopic visualization of disease at time zero, and one had proximal disease. The agreement between the remaining US and endoscopy ($n=30$) at time zero was excellent (complete agreement in 26/30), as was the correlation at twelve months. Table 1 shows endoscopy and US findings for 17/19 at 12 months. Final endoscopies were limited given proximal disease in 2/19 and thus were not included. Patients with endoscopically active disease at 12 months showed active sonographic disease as early as 4 months.

	Mucosal Healing (SES-CD$\leq$3 and/or Ri$\leq$1)	Endoscopically Active (SES-CD$>$3 and/or RI$>$1)
Absence of US disease	11	0
Presence of US Disease	1	4 (+1 pouch case)

CONCLUSION: US is an accurate, non-invasive modality useful in evaluating maintenance of response to therapy, which correlates with mucosal healing on endoscopy. Thus, US may be a surrogate for endoscopy and a repeatable, objective target for treatment.
Disclosure of Interest: None declared

P0866 QUALITY OF LIFE IN ULCERATIVE COLITIS – ASSOCIATION BETWEEN THE SHORT INFLAMMATORY BOWEL DISEASE QUESTIONNAIRE (SIBDQ) AND THE SHORT HEALTH SCALE (SHS) AND THEIR RELATIONSHIPS WITH CLINICAL AND ENDOSCOPIC DISEASE ACTIVITY

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INTRODUCTION: Health Related Quality of Life (HRQoL) is an important part of Inflammatory Bowel Disease (IBD) assessment, and is affected by both disease activity, psychological, and social factors. Several HRQoL questionnaires

have been developed, but are primarily used in the setting of clinical trials. Little is known about the relationship between HRQoL and disease activity and between the different HRQoL questionnaires. We aimed to assess the association between the SIBDQ and the SHS and their associations with clinical and endoscopic disease activity.
AIMS & METHODS: Prospectively, 110 patients with ulcerative colitis underwent sigmoidoscopy and completed the SIBDQ and the SHS. The SIBDQ is a validated 10-question tool measuring physical, social, and emotional status (score 10-70, poor-good). The SHS is a four-part visual analogue scale questionnaire measuring bowel symptoms, activities of daily life, worry, and general well-being (score 0-40, good-poor). Clinical disease activity was assessed using the Mayo score (0-12) and was divided into remission (≤2), mild (3-5), moderate (6-9), and severe (10-12) activities. The endoscopic grade of inflammation was assessed using Mayo Endoscopic Score (MES, 0-3).
RESULTS: The median age was 37 years (19-80), and 56 % were female. The median disease duration was 4.5 years. 29 % had mucosal healing, 20 % active proctitis, 16 % active proctosigmoiditis, 18 % active left-sided colitis and 18 % pancolitis. According to the MES, 29 % had mucosal healing, 26 % had mild, 31 % moderate and 14 % severe inflammation. According to the Mayo score, 37 % were in clinical remission, 21 % had mild, 31 % moderate and 11 % severe disease activity.
HRQoL significantly decreased with increasing clinical disease activity (Mayo score) when assessed with both SIBDQ ($\chi^2 = 51.9$, $p < 0.0001$) and SHS ($\chi^2 = 56.2$, $p < 0.0001$). HRQoL also significantly decreased with increasing endoscopic disease severity (MES) when assessed by both SIBDQ ($\chi^2 = 33.1$, $p < 0.0001$) and SHS ($\chi^2 = 40.3$, $p < 0.0001$). Overall, we found a significant difference in HRQoL between patients with mucosal healing (MES = 0) and active inflammation (SIBDQ, inactive/active, 59.1/45.6, $p < 0.0001$ and SHS, inactive/active, 6.8/19.7, $p < 0.0001$). Moreover, we found a strong association between SIBDQ and SHS using linear regression (SHS = -0.73×SIBDQ+52.1, $p < 0.0001$).
CONCLUSION: In this study we demonstrate that HRQoL is not only strongly associated with clinical disease activity, but also with the endoscopic disease severity. We also demonstrate that SIBDQ and SHS are strongly associated with each other.
Both SIBDQ and SHS show significantly decreasing HRQoL with increasing clinical disease activity as well as with increasing endoscopic disease severity. The study also shows significant difference in HRQoL between patients with mucosal healing and endoscopic active disease. Both questionnaires seem equally adequate in determining the disease impact on HRQoL.
HRQoL is from the patients' perspective one of the most important parts of IBD management. SIBDQ and especially SHS can be completed quickly during regular visits, and can be used as an easy tool for HRQoL monitoring. Significant changes must be followed by exploration of the possible causes including assessment of disease activity.
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P0867 IS THE TUBERCULIN SKIN TEST ALONE ACCURATE IN MODEATE-TO-SEVERE BCG VACCINATED PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH IMMUNOSUPPRESSIVES TO TEST FOR LATENT TUBERCULOSIS?

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INTRODUCTION: There are few data available on effect of immunomodulator/biological therapy on the accuracy of tuberculin skin test (TST, Mantoux skin test) and interferon-gamma release assay (IGRA) in BCG vaccinated immunosuppressed IBD patients.
AIMS & METHODS: Our aim was to define the accuracy of the TST and IGRA tests in a BCG vaccinated referral IBD cohort treated with immunosuppressives and/or biologicals. Data of 135 consecutive moderate-to-severe IBD (98 CD, 37 UC) patients were analyzed (male/female: 64/71, median age at diagnosis: 24.0; IQR: 18-31 years, duration: 7.0; IQR: 4-13 years). Patients were treated with immunosuppressives (azathioprine, steroids) and/or anti-TNF therapy. Blood samples for IGRA were collected during routine laboratory testing parallel with TST. The result of TST was determined according to international guidelines. Both in- and outpatient records were collected and comprehensively reviewed.
RESULTS: TST positivity rate was 21.6%, 20.1%, 13.4% or 12.7% with cut-off values of 5, 10, 15 and 20mm. IGRA positivity rate was 7.7% with indeterminate result in 1.2%. The correlation between TST and IGRA was significant, with moderate-to-good kappa values if TST results were >15mm (kappa: 0.32-0.34, $p < 0.001$). In addition, a TST of 14 and 17mm was also identified as best cut-off value in a ROC analysis (AUC: 0.70, $p = 0.04$). There was no association between the type and number of immunomodulators used or any disease phenotype characteristics and the TST or IGRA results. Importantly, smoking was identified as a risk factors for TST but not IGRA positivity (OR: 3.80, 4.88, 9.87 and 8.98, $p < 0.002$, for $TST_{cut\text{-}off}$ 5, 10, 15 and 20mm).
CONCLUSION: The TST and IGRA are partly complimentary methods and accuracy is acceptable also in BCG vaccinated and immunosuppressed IBD patients. A TST of >15mm should be used as a cut-off to identify patients at risk for latent TB in these patients. Smoking is a risk factor for TST positivity.
Disclosure of Interest: None declared

P0868 INCREASED EXTRACELLULAR MATRIX PROTEINS TURNOVER IN PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: Ongoing inflammation in Crohn's disease (CD) may lead to development of intestinal fibrosis and patients may present with stenosis. Inflammation is a dynamic process with a permanent remodeling of the extracellular matrix (ECM). Small fragments of the ECM generated during this process, so called neoepitopes, are released into the circulation and could be used as biochemical markers of disease activity or markers of fibrosis.
AIMS & METHODS: This study investigates a panel of these novel developed markers in patients with suspected or known CD.
106 patients referred for evaluation of CD had serum samples drawn. Patients were evaluated with colonoscopy, small-bowel imaging (capsule endoscopy, MR enterography, and CT enterography), fecal calprotectin, and C-reactive protein. 35 patients had newly diagnosed CD, 26 had CD with active inflammation or stenosis, 11 had known CD without inflammation or complication, and 34 had no evidence of Crohn's disease. The following neoepitopes were measured by competitive ELISAs; MMP-mediated of type I, III, IV collagen (C1M, C3M, C4M), N-terminus pro-collagen type I (P1NP), and MMP-degraded, citrullinated vimentin (VICM).
Data were not normally distributed and Kruskal-Wallis one-way analysis of variance was used for comparison. ROC-curve analysis were used to test the biomarkers ability to discriminate CD from non-CD.
RESULTS: Serum levels of C3M were significantly elevated in patients with CD compared to patients without CD (median 24.4 and 19.1, respectively; $P = 0.01$). C3M discriminated CD from non-CD with an AUC of 0.66. Concentrations of C1M and C4M were also elevated but statistical significance was not reached (C1M: median 68.9 and 62.9; $P = 0.12$. C4M: median 70.5 and 67.2; $P = 0.15$). In patients with CD, C1M and C3M concentrations were higher in clinically active disease (CDAI > 150) compared to quiescent disease (C1M: median 75.0 and 63.2; $P = 0.02$. C3M: median 24.5 and 22.7; $P = 0.10$), and C3M concentrations were higher in CD involving the colon compared to small bowel CD (median 26.2 and 22.1; $P = 0.05$). C1M, C3M and C4M correlated with CRP (Spearman's rho 0.76, 0.40, and 0.45, respectively; $P < 0.001$) but not with fecal calprotectin. Concentrations of ECM degradation markers were not significantly increased in patients with stricturing CD compared to patients without CD. In subgroup analysis of patients with diagnosed CD and elevated CRP compared to non-CD and normal CRP C1M, C3M and C4M discriminated CD from non-CD (AUC of 0.95, 0.88 and 0.90).
CONCLUSION: Turnover of ECM proteins is increased in patients with CD. These neoepitopes may distinguish between patients with CD and patients without CD and between active CD and disease in remission. Further studies of these promising markers of the ECM are warranted.
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P0869 INTESTINAL EPSTEIN- BARR VIRUS IS ASSOCIATED WITH MUCOSAL LYMPHOPROLIFERATION AND SUBSEQUENT INTESTINAL SURGERY IN INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Thiopurine therapy increases the risk of (Epstein- Barr virus associated) lymphomas for Inflammatory Bowel Disease (IBD) patients up to four times. Epstein- Barr virus (EBV) can cause a wide spectrum of lymphoproliferative reactions, ranging from morphologically benign with normal B lymphocytes (BL) and lymphoplasmacytic infiltrate in the lamina propria (LI) to aggressive lymphomas with atypical BL and LI.
EBV can be detected in colonic mucosa in up to 60 % of the IBD patients, but there is no consensus on when to perform EBV testing on intestinal mucosa. We hypothesized that EBV testing can be guided by histological features including morphology of BL and LI.
AIMS & METHODS: The aim of this study was to determine the value of the histology of the inflammation in predicting EBV presence in intestinal mucosa and to correlate EBV positivity with clinical endpoints such as intestinal surgery and development of lymphoma.
All IBD patients who underwent EBV testing by EBV-encoded RNA – in situ hybridization (EBER) in intestinal biopsies between January 2005 and October 2013 in our centre were identified. All biopsies were revised by a blinded, expert gastro-intestinal pathologist and scored on three histological features: number of EBV positive cells per high power field (HPF); normal or atypical LI and normal or atypical BL. Demographic and clinical data were collected from patient charts. Adverse events that were registered included intestinal surgery and lymphoma.

We used the Chi square test or Fisher's exact test to identify an association with EBV positivity.
RESULTS: 58 IBD patients were included, 28 were EBV positive and 30 were EBV negative. Ulcerative colitis was more frequent in the EBV positive group (82,1 % versus 56,7 %; p = 0.052)
EBV positive patients had significantly more frequent atypical LI (57.1 % versus 3.3 %; p = <0.001). The specificity for predicting EBV presence of the atypical LI is high (96.7 %), just as its positive predictive value (94.1 %). At time of biopsy, EBV positive patients used more often combinations of two or more anti-inflammatory drugs (5-aminosalicytes excluded; 50 % versus 16.7 %; p = 0.007) Eighteen EBV positive patients (64.29 %) had 20 pre-defined complications (18 colectomies, 2 lymphomas). Within the group of EBV positive patients, those who developed complications had a significantly higher EBV load (50 % versus 10 %; p = 0.048), expressed as the frequency of ≥ 10 EBV positive cells per HPF. 11 patients had atypical LI and BL, including 2 lymphomas: those were treated with chemotherapy. In the other 9 patients at least one immunosuppressive drug was stopped. In all patients the atypical LI showed resolution. 8 of the 9 patients became EBV negative and 1 patient had reduction of EBV positive cells.
CONCLUSION: In the present study, atypical LI was associated with mucosal EBV in IBD patients. A high EBV load is correlated with adverse events. Reduction of immunosuppression may decrease intestinal EBV associated lymphoproliferation.
Disclosure of Interest: None declared

P0870 SCREENING OF NOVEL PLASMA MICRORNAS ASSOCIATED WITH DISEASE PROGRESSION IN ULCERATIVE COLITIS

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INTRODUCTION: New biomarkers are required to monitor patients with Ulcerative Colitis (UC) and predict complications such as dysplasia and colitis associated cancer (CAC). Accurate plasma based biomarkers would allow physicians to make clinical decisions, thereby avoiding unnecessary invasive tests.
AIMS & METHODS: This feasibility study aimed to identify novel microRNAs (miRNAs) in the plasma of patients with Ulcerative Colitis related to disease progression.
RESULTS: Primary analysis of the array data identified the differential expression of several miRNAs from which the following miRNAs 122,125b, 139-3p, 331-5p, 375, 383-3p, 409-3p, 720, 1274B were chosen for validation. Analysis of variance was used to assess differences between groups. MiR-375 was shown to be significantly up-regulated in the CAC cohort (p = 0.002) when compared to UC and PSC. MiR-375 was found to be an effective biomarker of disease progression over disease duration, with Cox-regression analysis showing a Cox hazard ratio of 1.91 (p = 0.01).
CONCLUSION: Peripheral plasma miRNAs have the potential to act as biomarkers of disease progression in Ulcerative colitis. This study provides the first evidence that miRNA-375 is up regulated in cases of CAC. This finding needs to be extended to a larger validation cohort.
Disclosure of Interest: None declared

P0871 THE "INS" AND "OUTS" OF MRI AND ENDOSCOPY IN THE EVALUATION OF DISEASE ACTIVITY AND SEVERITY IN CROHN'S DISEASE

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INTRODUCTION: Endoscopy is the gold standard for activity assessment in luminal Crohn's disease (CD) but, due to the full thickness involvement of the bowel wall, or presence of complications, CD activity is the result of an integration of endoscopic, clinical, laboratory, and imaging data. Recently, a radiological score which integrates both mural and extramural involvement has been validated for a global disease evaluation (1).
AIMS & METHODS: to examine the relationships among MRI, laboratory inflammatory markers, clinical activity scores and endoscopy in a series of CD patients.
45 consecutive patients with endoscopically proven CD underwent at the time of enrollment MRI enterography, performed utilizing a 1.5 T system, for the staging of disease at diagnosis and activity assessment. Endoscopic activity was measured by a quantitative score (Simple Endoscopic Score for Crohn's Disease, SES-CD (2), range 0-40) with active disease being present for a >3 score and mild, moderate ad severe disease for ranges of respectively 4-10, 11-19 and >20. MRI activity was measured by a previously validated quantitative score (Magnetic Resonance Enterography global score, MEGS, range 0-296), with active disease being present for a >0 score. For all participants the *Crohn's Disease Activity Index* (CDAI) was completed and CRP and fecal calprotectin (FC) were measured (positivity cut-off respectively > 0.50 mg/dl and >150 μg/gr).
RESULTS: We enrolled 19 males and 26 females, mean age 37±14 years, mean disease duration 5 years. According to Montreal disease classification the phenotype was L1 in 47%, L2 in 6% and L3 in 47%; the behavior was B1 in 24%, B2 in 56%, B3 in 20% and perianal disease in 2%; resectional surgery related to CD was observed in 20%. According to SES-CD, 91% of patient had active disease and 9% had inactive disease (64% mild, 20% moderate and 7% severe disease). Mean MEGS was 20±18, with 82% having active disease and 18% inactive disease (p < 0.01 in comparison to endoscopy, sensibility 88%, specificity 75%, VPP 97%, VPN 38%). MEGS, was significantly higher in penetrating than in non-penetrating and non-stricturing disease (respectively 35±9 vs 7±11, p < 0.001). MEGS was significantly correlated with SES-CD (p < 0.01), in particular for the ileal (p < 0.01) and ceacum-ascending colon subscores (p < 0.05). Severity of the disease at endoscopy did not correlate to severity at MEGS (p = 0.7). Both MEGS and SES-CD show significant correlations with CDAI (p < 0.01) and CRP (p < 0.05), yet SES-CD only correlated significantly with FC (p < 0.001). The extramural involvement subscore, observed in half of patients, regardless of the behavior and severity at endoscopy, was associated to CRP positivity (p < 0.05), not with fecal calprotectin (p = 0.67). Increasing staging of grading at endoscopy was significantly correlated to the risk of extramural involvement (p = 0.008)
CONCLUSION: MRI is capable of identifying disease activity, although it results less accurate in the assessment of severity as measured at endoscopy. The presence of positive CPR suggests the need of MRI for the staging of patients with active luminal disease.
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Disclosure of Interest: None declared

P0872 ASSAY SPECIFIC DIFFERENCES IN CONSECUTIVELY MEASURED F-CALPROTECTIN IN PATIENTS WITH IBD FOLLOWED OVER TIME

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INTRODUCTION: Faecal calprotectin (FC), an abundant neutrophil protein, has recently been introduced as a non-invasive marker for monitoring of disease activity in inflammatory bowel disease (IBD). However, it has been difficult to define a definite threshold to discriminate between remission and active disease.
AIMS & METHODS: We, aimed to compare the results of different FC-assays in a well-characterized cohort of patients with IBD, followed over time. Patients (n = 13) with established IBD provided faecal samples and reported clinical activity every third months prospectively for a two year period. Relapse was defined as increasing symptoms and intensified treatment. FC was measured with three different assays; Calprotectin Elisa Buhlmann Laboratories AG, Basel, Switzerland; Phadia Elia Calprotectin, ThermoFischer Scientific, Freiburg, Germany; and PhiCal Calprotectin Elisa, Immundiagnostik AG, Bensheim, Germany. Disease status, defined as clinical remission or relapse, i.e. active disease, was determined at the time of collection of each fecal sample in each patient. Samples were grouped as corresponding to clinical remission or active disease. However, samples collected three months after a relapse were excluded to reduce possible bias due to prolonged intensified therapy, steroid dependent disease or ongoing subclinical inflammation.
RESULTS: In total, the 13 patients prospectively provided 91 faecal samples during the two year period. The median (IQR) concentration of FC was 187 (57 – 582) μg/g, 52 (15 – 415) μg/g and 55 (9 – 158) μg/g using the Bühlmann-, Phadia- and Immundiagnostik assay, respectively (p < 0.0001). Based on the cut-off provided by the manufactures, i.e. >50 μg/g, the FC assay was positive in 74 (81 %), 47 (52 %) and 50 (55 %) of the 91 samples when analyzed by the Bühlman-, Phadia- and Immundiagnostik assay, respectively. Modest to fairly good correlations were observed between the Bühlmann- and the Phadia assay, the Bühlmann- and the Immundiagnostik assay and the Phadia- and the Immundiagnostik assay ($R^2 = 0.70$, $R^2 = 0.80$ and $R^2 = 0.86$, respectively). However, Bland-Altman plots revealed overall poor agreement between the assays. Assay specific sensitivity, specificity and predictive values for defining clinical remission *vs.* active disease for each assay based on different cut-offs are shown in table 1.
Table 1. Assay specific sensitivity, specificity and predictive values for defining clinical remission *vs.* active disease for each assay based on different cut-offs

FC cut-off (μg/g)	Bü ≥50	Ph ≥50	Im ≥50	Bü ≥100	Ph ≥100	Im ≥100	Bü ≥150	Ph ≥150	Im ≥150
Sensitivity	86%	71%	86%	86%	64%	36%	79%	50%	14%
Specificity	26%	66%	62%	50%	72%	78%	56%	76%	80%
NPV	87%	89%	94%	93%	88%	81%	90%	84%	77%
PPV	24%	37%	39%	32%	39%	31%	33%	37%	17%

Bü; Bühlmann assay, Ph; Phadia assay, Im; Immundiagnostik assay, NPV; negative predictive value, PPV; positive predictive value
CONCLUSION: By cross-comparisons pronounced inter-assay differences were revealed. Although moderate to fairly good correlations between the FC assays were observed, Bland-Altman plots showed overall poor agreement.
Disclosure of Interest: None declared

P0873 RESIDUAL ABNORMALITIES AFTER MAYO ENDOSCOPIC SUBSCORE DEFINED COMPLETE MUCOSAL HEALING DEMONSTRATED BY NOVEL ISCAN ENDOSCOPIC AND REFINED HISTOLOGICAL GRADINGS

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INTRODUCTION: High definition(HD)- iSCAN endoscopy can characterize in details the mucosa in patients with ulcerative colitis (UC) and may provide more information about inflammation and mucosal healing (MH). However, the gold standard of mucosal healing is still histological diagnosis. More refined histologic and high definition iSCAN endoscopic criteria may redefine mucosal healing.
AIMS & METHODS: 78 patients (40 male, median age = 42y, range = 19-90y) with UC were assessed by HD–iSCAN colonoscopy (Pentax EC-3490Fi; Pentax, Japan) as well as by white light endoscopy (WLE). Mayo endoscopic subscore and UC endoscopic index of severity (UCEIS) score were assigned to patients according WLE findings. Mucosal pattern on iSCAN was graded as 1 = normal, 2 = mosaic pattern, 3 = tubular-gyrus, 4 = nodular rosette. The vascular pattern was graded as 1 = normal, 2 = spiral isolated vessels, 3 = crowded tortuous vessels, 4 = Irregular vessels. A histological grading and scoring system that assesses all changes possibly seen in IBD was developed for a detailed and comprehensive evaluation. This system (GUI-ECAP system) was designed to reflect all histologic changes in IBD categorized as 1) Extent of inflammation (focal, multifocal, diffuse), 2) Chronicity (crypt architectural alteration, Paneth cell metaplasia), 3) Activity (surface epithelium changes, neutrophilic cryptitis, crypt abscess, crypt destruction, lamina propria mononuclear cellularity, lamina propria neutrophil infiltration, and basal plasmacytosis), and 4) Plus additional findings, including eosinophilia and lymphoid follicles/aggregates. An established histologic grading system, New York Mount Sinai score was used to validate the grading of inflammation.
RESULTS: In this cohort of 78 patients with UC, 23 (29%) patients had Mayo endoscopic subscore of 0. Of these 23 patients with complete MH, 18 patients (78%) had abnormal vascular pattern on iSCAN and 7 (30%) had abnormal mucosal pattern on iSCAN. By using ECAP histologic scoring all 23 patients (100%) showed various histologic abnormalities including crypt architectural alteration [19, (83%)], surface epithelium abnormality [16, (70%)], crypt destruction [3, (13%)], increase in lamina propria mononuclear cells [15, (65%)], basal plasmacytosis [11, (48%)], lamina propria neutrophilic infiltration [5, (21%)] and other additional findings [19, (83%)].
CONCLUSION: The subtle histologic abnormalities underlying the apparently healed mucosa with Mayo endoscopic subscore of 0 can be detected by using refined histological scoring system (GUI-ECAP) in combination with iSCAN. Sensitive endoscopic techniques such as iSCAN and histologic scoring such as ECAP can detect residual abnormalities in the majority of patients with seemingly complete MH in UC.
Disclosure of Interest: None declared

P0874 COLORECTAL CANCER IN IBD PATIENTS TREATED OR UNTREATED WITH ANTI-TNFS: A RETROSPECTIVE MATCHED-PAIR STUDY IN A 13 YEARS FOLLOW UP

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INTRODUCTION: In murine models, blocking TNF-alpha showed efficacy in colitis-associated colon cancer. Chronic inflammation in Inflammatory Bowel Disease (IBD) colitis has been associated with colorectal cancer (CCR).
AIMS & METHODS: In a monocentric retrospective matched-pair study, the frequency of colon cancer was compared in a cohort of IBD patients treated or untreated with anti-TNFs. In a matched-pair study, the role played by clinical characteristics of IBD in determining the frequency of colon cancer was also evaluated. Clinical records of all IBD patients in follow up from 2000 to 2013 at our tertiary IBD referral center developing cancer of the lower GI tract (IBD-K)(small intestine, appendix, CCR, anal canal) were reviewed. Each IBD-K patient was retrospectively matched with 2 IBD patients with no cancer of the lower GI tract (IBD-C), for IBD type (MDC/RCU), gender, age (±5yrs). Anti-TNFs (Infliximab or Adalimumab≥1 dose) and IMM (≥6mos) use was reported. Data expressed as median (range). Student's T test and Chi squared test used as appropriate.
RESULTS: From 2000 to 2013, the study population included 2387 IBD patients: anti-TFNs use in 384 (16%). Cancer of the lower GI tract developed in 15/2387 (0.62%) patients (9CD,6UC), including 12 CCR, (6UC,6CD), 1 ileal adenocarcinoma (1CD), 1 carcinoid of the appendix (1CD), 1 anal canal carcinoma (1CD). In the 15 IBD-K patients, age at diagnosis of cancer was 51 (28-73) yrs, IBD duration 19yrs (1-47): there were 9 CD of the ileum (I) (n = 4), colon (C) (n = 2), ileum-colon (IC) (n = 3) and 6 UC distal (n = 3), left-sided (n = 1) or total (n = 2). Among the 15 IBD-K patients, 3 (20%) received anti-TNFs and/or IMM (combined in all 3). In these 3 patients, cancer included CCR (n = 2) or carcinoid (n = 1) in 2CD (2F,age 40 and 54yrs, CD duration 28 and 26 yrs; I-C, fistulizing) and 1UC (1F, CCR, age 30, duration 19yrs; pancolitis). Among the 384/2387 (16%) IBD patients treated with anti-TNFs, CCR developed in 3 (0.78%)(combined IMM in 3). Among the 2003/2387 (84%) patients anti-TNFs naïve, 12(0.6%) developed cancer of the lower GI tract,including CCR in 10 (0.5%) (p = ns *vs* anti-TNFs treated patients). IBD-C included 30 patients (18CD,12UC;14 M/16 F, age 54,range 37-75), with CD (13 I;2 C;3 I-C) or UC (distal 11, left-sided 1). Anti-TNFs use was reported in a comparable proportion of IBD patients developing or not cancer (IBD-C n = 6/30; 20% *vs* IBD-K n = 3/15; 20%). In IBD-C, IMM were used in 10 (33%)(combined anti-TNFs in 2;6.7%).
CONCLUSION: In a retrospective matched-pair study, a comparable low frequency of colon cancer was observed in IBD patients treated or untreated with anti-TNFs.
Disclosure of Interest: None declared

P0875 IS THERE A ROLE FOR THE NEW SEROLOGICAL MARKERS IN PREDICTING DISEASE COURSE IN AN IBD POPULATION COHORT? LESSONS LEARNT FROM A PROSPECTIVE IRISH POPULATION

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INTRODUCTION: Crohn's disease and Ulcerative colitis are the two main forms of inflammatory bowel disease. There are different disease phenotypes within those groups and yet another 10-17% of patients may not have either diagnosis and can be then be classified as indeterminate colitis until later on in their disease course when they are reclassified into either main group as symptoms progress. Furthermore, some patient with gastrointestinal symptoms may not have IBD initially, but develop it in future. Several antibodies have been linked to CD and different IBD subtypes.
AIMS & METHODS: The aim of our study was to determine the prevalence of the new anti-glycans antibody panel in a prospective homogenous IBD cohort to help differentiating those with IBD from healthy controls. We aimed to assess panel's role in discriminating between CD and UC with their different phenotype and their predictive value for disease course and treatment stratification in the future.
Antibodies against a mannan epitope of Saccharomyces cerevisiae (gASCA), laminaribioside (ALCA), Chitobioside (ACCA), mannobioside (AMCA) were tested in serum samples of 103 IBD patients, 199 healthy matched controls. Antibody response was matched to disease type and course. A backward step multiple-regression analysis was performed along with 2- sample t-test for univariate biomarker analysis.
RESULTS: The anti-glycans antibody panel was useful in differentiating IBD patients from healthy matched controls. Overall, 72% of IBD patients tested positive for anti-glycans antibodies and of those 64% were positive for gASCA, compared to 49% for ACCA antibody. gASCA was highly sensitive and specific in CD patients.
CONCLUSION: From applying the anti-glycans antibody panel, combination of gASCA IgA**,** Anti-L and Anti-C antibodies were statistically very significant in differentiating CD from UC (with a $p < 0.0001$). gASCA was very specific to CD and correlated with severe disease course requiring surgery or fistulas, requiring anti -TNF therapy in the lateral years.
Disclosure of Interest: None declared

P0876 CLINICAL OUTCOMES IN PATIENTS WITH INTERMEDIATE RAISED FAECAL CALPROTECTIN LEVELS

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INTRODUCTION: Calprotectin is a calcium binding protein of the S100 family associated with inflammation. A recent systematic review has confirmed its value in distinguishing between organic (inflammatory bowel disease - IBD) and non-organic gastrointestinal disease (irritable bowel syndrome - IBS). Those with FC levels below 50 mcg/g have a negative predictive value of >92% to exclude organic gastrointestinal disease. Conversely, FC levels greater than 250mcg/g, correlates with endoscopic disease activity in those with IBD; sensitivity of 90%. The aim of our study was to determine the clinical outcome in patients presenting with an intermediate raised level of FC between 50-250 mcg/g.
AIMS & METHODS: FC test results from July 2012 to October 2013 were reviewed. FC testing was performed using the PhiCal ELISA method. 482 patients were identified from the UHCW pathology database: 390 normal (<50mcg/g), 51 intermediate (50-250mcg/g) and 41 high (>250mcg/g). Excluding paediatric patients (under 16), left 47 intermediate and 35 high results. Where possible clinical information was obtained from the UHCW Clinical results and reporting system. If no information was found then general practitioners (GPs) were contacted for further details (long term clinical data could not be found for 5 intermediate and 9 high patients).
RESULTS: We studied a subset of 50 of the 390 normal FC values (<50mcg/g) which served as a comparator group. Of these, 9 (18%) were referred to secondary care gastroenterology, with 3 (6%) still in secondary care 6 months post FC. None were diagnosed with IBD.
Of the 26 patients with high FC (>250mcg/g), 8 did not have details provided by their GPs, 8 (31%) were known IBD patients and 3 (12%) were not investigated - declining referral or patient mortality. 6 (23%) had a new diagnosis of IBD and 1 (4%) with post infective IBS. 15 (58%) were still in secondary care 6 months after FC testing.
Of the 42 intermediate (50-250mcg/g) patients, 17 did not have information provided by their GPs and 2 (5%) were known IBD patients. 8 patients (19%) were diagnosed with colon cancer or were still under investigation. 3 (7%) had a new diagnosis of IBD and 12 (29%) with non IBD conditions (e.g. BAM,

Diverticular disease and IBS). 13 (31%) patients were still in secondary care 6 months after initial FC –see table 1.
Within the intermediate group, 10 patients had FC < 100mcg/g, none were diagnosed with IBD and 20% remained in secondary care 6 months post FCP. Of the 16 available patients with FC of 100-250, 3 (23%) had a new diagnosis of IBD and 7 (54%) were still in secondary care 6 months after FC.

Groups	<50mcg/g (subset n = 50)	50-250mcg/g (n = 42)	>250mcg/g (n = 26)
Managed in primary care	41(82%)	5 (12%)	3 (12%)
Undergoing investigations	9 (18%)	17 (40%)	6 (23%)
New diagnosis of IBD	0	3 (7%)	6 (23%)
Existing diagnosis of IBD	0	2 (5%)	8 (31%)
Still under follow-up at 6 months (from FC testing)	3 (6%)	13 (31%)	15 (58%)

CONCLUSION: 1) The majority (81%) of FC requested were normal with a similar proportion managed in primary care without any new diagnosis of IBD. 2) New diagnosis of IBD is three times more common in those with FC values > 250mcg/g and 3) A third (31%) with intermediate FC levels remain under secondary/tertiary care at 6 months but still half compared with those having high FC levels.
Disclosure of Interest: None declared

P0877 LONG-TERM EFFECTIVENESS, PATIENT SATISFACTION & COST-BENEFIT ANALYSIS OF A SELF-MANAGEMENT PROGRAMME FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A FIVE YEAR FOLLOW-UP STUDY

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INTRODUCTION: Self management programmes enable patients with Inflammatory Bowel Disease to play a greater role in monitoring and treating their illness, allowing them to be discharged from hospital follow up. Short-term studies have shown reduced health service utilization, without compromising health outcomes[1].
AIMS & METHODS: The aim of our study was to evaluate the long-term effectiveness of a self-management programme for patients with IBD and assess patient satisfaction and health care cost benefits. Over a 12 month period in 2007, 157 patients with IBD (122 with Ulcerative colitis (UC), 31 Crohn's disease (CD) and 4 indeterminate colitis were recruited to our IBD self management programme. Stable patients on first line therapy met with a specialist IBD nurse and were provided with specific information about their diagnosis, relapse recognition and medication. A personalised written self management programme was provided with an escalation plan in the event of symptoms. The first 70 patients recruited to the study were sent a patient satisfaction questionnaire 1 year post-recruitment. A cost-saving analysis over the 5 year period was performed based on the premise of avoiding 2 hospital follow-up appointments per year and the local tariff (£103). After 5 years, the case notes of all patients re-referred were reviewed to establish the reason for re-referral and interval between discharge & re-referral.
RESULTS: Over the 5 year period 22 (14.0%) patients (22 = UC, 2 = CD) had been re-referred to our service with a flare of their IBD. Five patients required azathioprine & one patient with Crohn's disease was started on biologics. One patient was admitted as an emergency, initially responding to cyclosporine but required a colectomy 1 year later. The remainder were treated with increased 5-ASA, topical therapy or oral steroids. Median time from discharge to re-referral was 31 months (range 11-60 months). 62/70 (88.6%) patients completed their patient satisfaction surveys; 58 (93.5%) being satisfied with the programme and 58 (93.5%) feeling involved in their treatment decisions. Over the 5 year period, there was an estimated health-care cost saving of £147290. (Table 1)

Year	No. of patients in self-management programme at start of year – No. of patients re-referred to service in each year	Local follow-up appointment tariff x estimated appointments per year	Estimated Cost-savings
Year 1	157- 2 = 155	£103 x 2	£31930
Year 2	155- 6 = 149	£103 x 2	£30694
Year 3	149- 7 = 142	£103 x 2	£29252
Year 4	142- 6 = 136	£103 x 2	£28016
Year 5	136- 3 = 133	£103 x 2	£27398
Overall savings			**£147290**

CONCLUSION: This study shows that self-management is an effective long term strategy for selected stable patients with IBD and is acceptable to patients. Few patients are re-referred and the substantial 5-year cost savings could be re-invested in developing specialist IBD services.

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Disclosure of Interest: None declared

P0878 SERUM HEPCIDIN LEVELS PREDICT INTESTINAL IRON ABSORPTION IN IBD PATIENTS

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INTRODUCTION: Circulating hepcidin is proposed to regulate iron absorption by modulating iron export by ferroportin at the basolateral membrane of the duodenal mucosal cells and/or uptake into the cells at the apical membrane by DMT1. To date, no data have shown a relationship between plasma hepcidin concentrations and iron absorption in IBD patients.
AIMS & METHODS: We used stored samples from a human iron absorption study to further test the hypothesis that plasma hepcidin may explain interindividual variation in iron absorption in IBD patients. Serum ferritin (SF) and serum markers of inflammation [high-sensitivity C-reactive protein (hsCRP) and IL-6] were measured in stored samples from a human iron absorption study using commercially available immune-assays. Hepcidin-25 concentrations were determined in fasting samples from 71 adult subjects with IBD (31 UC, 40 CD) and 26 healthy controls. Hepcidin was measured by LC-MS.
RESULTS: There was a positive correlation between hepcidin (mean: 2.3; range: 0.1–7.8nmol/L) and hsCRP ($p < 0.005$), but not between hepcidin and serum ferritin ($p > 0.05$). Whereas iron absorption was negatively correlated with serum ferritin only in patients with inactive disease (hsCRP < 5md/dl; $p < 0.001$), a negative correlation was observed with serum hepcidin in both active and inactive disease ($p = 0.006$), independent of IBD phenotype. Multiple linear regression models showed that serum hepcidin in isolation significantly predicted the interindividual variation in iron absorption.
CONCLUSION: Concentration of serum hepcidin, but not serum ferritin, was highly correlated with intestinal iron absorption in IBD patients.
Disclosure of Interest: None declared

P0879 LONG TERM OUTCOME OF CROHN'S DISEASE ACTIVITY – A PROSPECTIVE STUDY-

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INTRODUCTION: Crohn's Disease (CD) is a chronic and heterogeneous inflammatory bowel disease affecting the gastrointestinal tract; its etiology is unknown and its outcome is unpredictable
AIMS & METHODS: To analyze the long term outcome of the disease activity, we studied a cohort of 226 consecutive cases of CD hospitalized from 01/01/2000 to 31/12/2004. These patients, enrolled at diagnosis, underwent initial complete investigation. CD diagnosis was based on international criteria. All patients were included in a prospective study and followed-up from 01/01/2005 to 31/12/2009 during at least 5 years or until the first surgical resection. A systematic clinical control was performed every 6 or 12 months and on demand; complete investigation comprising endoscopy was done when needed. Statistical study: Student – Fisher's t test and Mann Withney U test.
RESULTS: The cohort included 103 males and 123 females (mean age was 30, 3 years at diagnosis); 41 patients were smokers (18.1%). At the end of follow-up: 1/ The overall annual activity which was defined as the percentage of active disease per year has showed a progressive decrease (from 59.3 % the first year to 46.5% the last year $p < 0.05$) associated with a decrease of the number of severe flares (from 34.7% to 15% $p < 0.05$). 2/the age at onset of the disease didn't influence the disease activity: 62%; 59.3%; 59.7% at diagnosis and 50%; 45.3%; 45.4% at the end of follow- up in patients aged <20 years, 20-40 years, >40 years respectively ($p > 0.05$).3/ the rate of activity tends to decrease over time when lesions were located in both small intestine and colon (59.5% to 46.5% $p < 0.05$) whereas it remained stable when lesions were located exclusively in the colon (from 48.8% to 44.1%;$p > 0.05$). 4/decrease of activity was more often observed in inflammatory type lesions (from 50% to 41.3% $p < 0.05$). 5/smoker (S), non smoker (NS) and previous smoker (PS) statutes didn't influence activity outcome (from:S = 60%;PS = 60%; NS = 57.6% to S = 45.4%; PS = 43.4%; NS = 47%: $p > 0.05$).6/ however, the need for surgery increased progressively over the time (from 4% the first year to 7% the last year).
CONCLUSION: This prospective study showed that the overall Crohn's Disease activity decreased and became less severe over time, which probably expresses a slight tendency to a disease extinction. The course of disease hasn't been significantly influenced neitherby the age at onset of disease, nor by tobacco consumption. The outcome of initial inflammatory type lesions was more favourable than stricturing or penetrating lesions.
Disclosure of Interest: None declared

P0880 PREVALENCE OF ANAEMIA IN A COHORT OF PATIENTS WITH IBD AND ITS RELATIONSHIP TO FAECAL AND SERUM BIO-MARKERS OF INFLAMMATORY BURDEN, AND MARKERS OF IRON STATUS

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INTRODUCTION: Anaemia is common in IBD and usually due to either iron-deficiency or anaemia of chronic disease. Serum ferritin is a frequently used marker of iron status in patients with IBD. It is influenced by inflammatory status with CRP commonly used in clinical practice to aid in determining the presence or absence of iron deficiency. However, the correlation of ferritin with markers of mucosal disease activity such as faecal calprotectin (FC) is unknown and may have important implications in determining the effect of inflammation on the diagnosis of iron deficiency. The aim of this study was to investigate the prevalence of anaemia and its relationship to markers of iron stores and faecal and serum markers of inflammation in IBD.
AIMS & METHODS: We performed a computer database search of all IBD clinic patients who had paired blood tests (including Hb, mean cell volume, CRP, ferritin) and FC in the last 12 months. Blood and faecal samples were accepted as paired if taken within 7 days of each other. Anaemia was defined using WHO criteria, with a ferritin of <30ng/ml taken to indicate iron-deficiency. An FC of <50 ug/g was taken to indicate inactive disease, an FC of 50-200 ug/g a borderline result and an FC >200 ug/g as active disease. Results were analysed to assess for prevalence of anaemia and iron deficiency and their correlation with faecal and biochemical markers of disease activity.
RESULTS: 124 patients (79 Crohn's disease, 45 Ulcerative Colitis) with a diagnosis of IBD and paired blood tests and faecal inflammatory markers were identified and their data analysed. 30/124 (21%) of the whole cohort were anaemia, and 34% were iron-deficient. There was a clear negative correlation between disease activity and both haemoglobin and ferritin levels. 20/30 (66%) of the anaemic patients had a ferritin of <30 and could clearly be classified as iron-deficient. The average CRP in this group was 11.4mg/l and calprotectin 686ug/g. 9/30 (30%) of patients had a ferritin of >30 with one patient having a ferritin of >100. The average CRP in this group was 17.8 and calprotectin 832ug/g. 40% of anaemic patients with a ferritin >30 had a CRP <5 and would not be classified as iron deficient. All these patients had a raised calprotectin (av 1030). Use of a raised Calprotectin of >500ug/g as a marker of inflammatory burden rather than CRP would have resulted in half these patients being classified as iron deficient which was supported by other markers of iron stores.
CONCLUSION: Anaemia (21%) and iron deficiency (34%) were common in this cohort of patients with IBD. There was a clear negative correlation between markers of anaemia and iron deficiency and faecal calprotectin. There was a closer correlation between calprotectin and anaemia than CRP and anaemia. Calprotectin may be a more effective marker of inflammatory burden than CRP in the assessment of IDA in patients with active IBD.
Disclosure of Interest: None declared

P0881 UTILITY OF FAECAL CALPROTECTIN IN PREDICTING RELAPSE IN INFLAMMATORY BOWEL DISEASE: A META-ANALYSIS

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INTRODUCTION: Faecal calprotectin (FCP) is a non-invasive marker of gastrointestinal inflammation. Its utility in the clinical management of inflammatory bowel disease (IBD) is still under evaluation. We aimed to perform a meta-analysis of prospective studies in assessing the ability of baseline FCP for predicting disease relapse with 12 months in patients with Crohn's disease (CD) and ulcerative colitis (UC) in clinical remission.
AIMS & METHODS: Multiple electronic databases were searched including Pubmed, Embase and Ovid looking for studies providing data on relapse prediction in IBD using FCP. Pooled sensitivity, specificity, negative (LR-) and positive (LR+) predictive value diagnostic odds ratio (DOR) and pooled area under the receiver operating characteristic (AUROC) was calculated using MetaDiSc ver1.4 software. A random effects model was used and publication bias was assessed using Funnel plots and Egger's test and heterogeneity was assessed using Cochran's Q and the I^2 test.
RESULTS: 8 studies involving 507 patients with CD and 8 studies involving 587 patients with UC were included. The predictive value for a relapse within 12 months for baseline FCP in patients with CD was sensitivity 73%(64-80), specificity 78% (74-82), LR+ 2.9 (1.9-4.5), LR- 0.4 (0.2-0.6), DOR 10.1 (4.5-22.6) and AUROC 0.83 ($\pm$0.04). The cut off for baseline FCP used for the CD studies ranged from 130-340 µg/g. The predictive value for a relapse within 12 months for baseline FCP in patients with UC was sensitivity 72%(65-77), specificity 78% (74-83), LR+ 3.0 (2.3-4.0), LR- 0.4 (0.2-0.6), DOR 9.2 (5.4-15.7) and AUROC 0.82 ($\pm$0.03). The cut off for baseline FCP used for the UC studies ranged from 130-250 µg/g. There was significant heterogeneity ($I^2 > 50\%$) for all the analysis likely because of the differences in relapse rates and FCP cut off values used.
CONCLUSION: FCP is a simple non-invasive marker with the potential to predict relapse in CD and UC. With pooled sensitivity and specificity under 80% for both CD and UC but with a likelihood ratio of a negative test being 0.4, its value may be mainly to identify low risk patients. However wide variations in the cut off values for FCP used in these studies makes it difficult to apply this to routine clinical practice. Serial measurements of FCP to check for a rise from baseline may be the way forward for future studies.
Disclosure of Interest: None declared

P0882 IS THERE ANY RELATION BETWEEN RED BLOOD CELL DISTRIBUTION WIDTH AND MUCOSAL REMISSION IN ULCERATIVE COLITIS?

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INTRODUCTION: A higher red blood cell distribution width (RDW) has been shown as an indicator of disease activity in ulcerative colitis (UC). However, the relation of mucosal remission with RDW has not been investigated. We aimed to determine if RDW level as a categorical variable (high or normal) could be used as a parameter for predicting mucosal remission in UC.
AIMS & METHODS: This study was conducted prospectively at a university hospital with high volume of inflammatory bowel disease patients. C-reactive protein (CRP), RDW value and colonoscopic findings were analyzed in UC patients. The endoscopic procedures were performed by a dedicated IBD endoscopist. Mucosal remission was defined as a Mayo score of 0 for UC. The groups were compared using chi-square test. SPSS version 16 was used for statistics.
RESULTS: A total of 178 patients (102 male, 76 female; age range: 19 to 82 years) were included in the study. The number of patients with mucosal-remission was 57 (normal or inactive disease). No correlation between CRP levels and mucosal remission was found. Of the patients in mucosal remission, 46 had normal RDW level. Of the 121 patients with no mucosal remission, 75 had normal RDW level. RDW was found as a significantly useful parameter for identifying mucosally active UC patients ($p<0.005$).
CONCLUSION: This study shows that categorical RDW value is a useful parameter for identifying mucosally active UC patients and could be used as a marker for non-invasive monitoring of mucosal activity in UC patients.
Disclosure of Interest: None declared

P0883 PREVENTION OF OPPORTUNISTIC INFECTIONS IN PATIENTS ON BIOLOGICAL AGENTS FOR MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Patients with inflammatory bowel disease are at increased risk of infection; this is especially true of the 20% on biological agents. ECCO guidelines recommend the following vaccines: Influenza (annual), Pneumococcal, Hepatitis B, Varicella, HPV (women under 26). The guidelines also highlight the need to exclude latent TB; local policy is to perform an interferon gamma release assay. Within the UK vaccination services are provided by primary care.
AIMS & METHODS: The measures taken to prevent opportunistic infection in patients prescribed anti-TNFs for IBD at Chelsea and Westminster Hospital in 2013 were audited against the ECCO OI Guidelines. The following were retrieved from electronic records: age, sex, anti TNF prescribed, pneumococcal antibodies, hepatitis B core and surface antibodies, varicella IgG, Elispot®. Attempts were made to retrieve vaccination history from General Practice.
RESULTS: 60 patients were prescribed infliximab and 15 patients were prescribed adalimumab. 46 GPs were able to provide vaccination history.
Influenza: 50% (23/46) patients received vaccination against influenza within the past year.
Pneumococcus: 55% (47/85) patients demonstrated immunity. 6% (5/85) were not immune and the remainder were not tested. The vaccination history of 26 patients who were not immune or not tested was retrieved. 27% (7/26) had since been vaccinated.
Hepatitis B: No patients were core Ab positive. Surface Ab levels demonstrated immunity in 7% (6/85). 53% (45/85) were not immune, and the remainder were not tested. Vaccination history of 44 patients who were not immune or not tested was retrieved. Of these, 25% (11/44) had since been vaccinated.
HPV: 4 patients were women under 26 years old. 25% (1/4) had confirmed HPV vaccination.
Varicella: 21% (18/85) patients demonstrated immunity to varicella. 2% 2/85 were not immune.
Elispot: 65% (55/85) patients had a nonreactive assay. 1% (1/85) had a positive result and the remainder were not tested.
CONCLUSION: The standards set out by ECCO to protect patients from opportunistic infection are not being met.
Problems obtaining accurate vaccination history from GP records include incorrect surgery details, lack of availability of staff able to review records and incomplete records. HPV vaccination usually takes place at school and is not routinely recorded by primary care.
Potential service improvements include provision of vaccines at clinic, improved patient education regarding the importance of vaccination and a check list to review bloods at first anti-TNF prescription.
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Disclosure of Interest: None declared

P0884 EFFICACY, SAFETY, AND DEMOGRAPHICS FACTOR OF ORAL TACROLIMUS THERAPY IN 666 JAPANESE PATIENTS WITH REFRACTORY ULCERATIVE COLITIS

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INTRODUCTION: Ulcerative colitis (UC) is a form of chronic inflammatory bowel disease and is characterized by periods of remission and episodes of relapse. The pathogenesis of UC remains unclear. This study aims to evaluate the efficacy and safety of tacrolimus (TAC).
AIMS & METHODS: Aims: To evaluate the safety and efficacy of oral TAC in Japanese patients with refractory (corticosteroid-resistant or -dependent) active UC in a real clinical setting.
Methods: The observation period of this study was 6 months. Six hundred and sixty-six UC patients were enrolled between 2009 and 2011 in 145 medical institutions. Efficacy was evaluated using the Disease Activity Index (DAI) score (1), clinical remission and endoscopic remission. DAI score improvement was defined as either a reduction in DAI of more than 4 points with improvement of all categories (Stool frequency, Rectal bleeding, Mucosal appearance, Physician's global assessment) or complete resolution of all categories (2). Clinical remission was defined as stool frequency ≤ 3 per day and no rectal bleeding. Endoscopic remission was defined as mucosal appearance ≤ 1.
RESULTS: Mean DAI score was 8.9 ± 1.97 at baseline. Adverse drug reactions (ADRs) occurred in 39% of the patients. The most frequent ADRs were Nervous system disorders (serious: 2 patients, non-serious: 71 patients) such as finger tremor (50 patients), and the most frequent serious ADRs were infections and infestations (20 patients) such as cytomegalovirus-related events (7 patients) and pneumonia-related events (5 patients). In 18 out of 20 patients, serious infections and infestations were resolved or became mild during the observation period. When serious infections and infestations occurred, 6 patients discontinued the TAC treatment and 11 patients continued after they occurred. One patient had discontinued before the event. In another 2 patients, one patient (age 81) developed sepsis and died 2 days after it occurred. One patient (age 56) developed herpes zoster and didn't improve during the observation period. TAC treatment was continued after it occurred. Serious renal and urinary disorders were reported in 8 patients. Seven out of 8 patients were resolved or became mild during the observation period. One patient (age 62) developed renal impairment and didn't improve during the observation period. All of the 8 patients discontinued the TAC treatment when serious renal and urinary disorders occurred. DAI score improvement was observed in 63% of the patients during the observation period. Sixty-seven percent of the patients had clinical remission during the observation period. The endoscopic remission rate increased with time during the observation period (17% after 3 months, 31% after 6 months).
CONCLUSION: Oral TAC therapy, with monitoring of blood trough concentration was well tolerated and induced clinical and endoscopic remission with time in Japanese patients with refractory active UC.
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P0885 WITHDRAWAL OF AZATHIOPRINE IN PATIENTS WITH CROHN'S DISEASE IN STABLE CLINICAL REMISSION: A DOUBLE-BLIND, PLACEBO-CONTROLLED 2 YEARS TRIAL

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INTRODUCTION: Many patients with quiescent Crohn's disease are maintained on long-term treatment with azathioprine (AZA), but controlled data are limited. The aim of the present study was to evaluate the efficacy of AZA therapy for more than 4 years to maintain clinical remission.
AIMS & METHODS: We performed a randomized double-blind placebo-controlled AZA withdrawal trial with a follow-up period of 24 months. Patients had to have continuous AZA therapy for a minimum of 4 years without exacerbation of disease during the previous 12 months before enrollment, and a Crohn's disease activity index <150 at baseline. Patients were randomized to continue on AZA ($n=26$) or switch to placebo ($n=26$). The primary endpoint was time to clinical relapse during follow-up.
RESULTS: During the 2-year follow-up clinical relapse occurred in 4 patients on continued AZA and in 8 patients on placebo. Time to clinical relapse averaged 22.3 months (95% CI 20.6-24.0) in the AZA group, and 19.2 months (95% CI 16.4-22.1) in the placebo group ($p=0.20$). According to life-table analysis, the proportion of patients in remission after 12 and 24 months was $96\pm4\%$ and $86\pm7\%$ in patients receiving AZA versus $76\pm8\%$ and $68\pm9\%$ in patients receiving placebo (month 12, $p=0.035$; month 24, $p=0.30$). A higher AZA dose at enrollment was an independent predictive factor for relapse ($p<0.05$).
CONCLUSION: In patients with clinically inactive Crohn's disease on maintenance therapy with AZA for $>$ 4 years discontinuation of AZA resulted in a numerically higher relapse rate compared to further AZA treatment. Our results are in line with previous observations.
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P0886 COST-EFFECTIVENESS OF ADALIMUMAB IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS (SUB-ACUTE) IN THE UK

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INTRODUCTION: The objective was to compare the cost-effectiveness of adalimumab (ADA) versus standard of care (SOC) for the treatment of patients with moderately to severely active ulcerative colitis (UC) (sub-acute) who have an inadequate response to SOC in the UK. The base case was conducted for a UC patient population including patients who are naïve to the cytokine inhibitors affecting tumour necrosis factor alpha (anti-TNF-α) and patients who have previously been exposed to anti-TNF-α agents other than ADA.
AIMS & METHODS: A Markov model was constructed to simulate the treatments and disease course of adults with moderately to severely active UC (including both anti-TNF-α naïve and experienced patients) who had an inadequate response to conventional therapies receiving ADA therapy, or receiving SOC. SOC refers to conventional treatments including anti-inflammatory drugs or immunosuppressants. The model estimated the direct health care costs and quality-adjusted life years (QALYs) over a 10-year time horizon. The model was conducted from the perspective of the U. K. National Health Service. Only direct costs were considered. Eight health states were defined in the Markov model, including three pre-surgery states (i.e. remission, mild, and moderate-to-severe), surgery state, and four post-surgery states (i.e. post-surgery without complication, transient complication, chronic complication, and surgery-related death). The transitional probabilities of the pre-surgery states were primarily derived from the randomized, controlled clinical trials of ADA in the treatment of moderately to severely active UC patients [the Ulcerative Colitis Long-term Remission and Maintenance with Adalimumab M06-827 (ULTRA 2) trial and M10-223 (the ULTRA 1/2 extension trial)]. The transitional probabilities for the surgery and post-surgery states were derived based on published literature. Utility values were specified for each disease state, and were based on published literature. The model considered drug costs, disease states costs, hospitalization costs, surgery costs, surgery-related complication costs, and costs associated with surgery-related death. These costs inputs were derived from published literature. Results were expressed in the incremental cost-effectiveness ratio (ICER) per QALY gained. The impact of uncertainty of model parameters was examined using deterministic sensitivity analyses (DSA) and probabilistic sensitivity analyses (PSA).
RESULTS: The ICER per QALY gained for ADA vs. SOC was £34,417 over a 10-year time horizon in the base case (in 2013 GBP pounds). DSA varying key model inputs produced ICER per QALY gained in the range of £29,437 to £38,073. The probability for ADA to be cost-effective at the willingness-to-pay threshold of £30.000 was 30%.
CONCLUSION: With no NICE recommended biologic options, there is currently a high unmet need for patients in England and Wales with moderately to severely active UC (sub-acute) who have failed on standard of care. This economic evaluation demonstrated that when compared to SOC, the ADA therapy has a reasonable cost-effectiveness ratio. The cost-effectiveness result of the ADA strategy was shown to be robust in a range of sensitivity analyses.

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P0887 MAINTENANCE OF REMISSION OF ULCERATIVE COLITIS: PREBIOTICS AND DIETARY FIBER

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INTRODUCTION: Butyrate enemas may be effective in the treatment of active distal ulcerative colitis (UC). Colonic fermentation of Plantago Ovata seeds (dietary fiber) yields butyrate. UC patients have an altered intestinal flora which can be modified by administration of prebiotics such as fructo-oligosaccharides, and probiotics like bifidobacterium longum w11, which promote selective growth of saccharolytic bacteria with low inflammatory potential.
AIMS & METHODS: We conducted an open-label, parallel group, randomized clinical trial. A total of 36 patients with ulcerative colitis who were in remission for over 3 months (4 < C. A. I. Rachimilewitz) were randomized into 3 groups to receive oral treatment with mesalamine (group A), Plantago Ovata (Colon help) + mesalamine (group B) and fructo-oligosaccharides/bifidobacterium longum w11 + mesalamine (group C). All patients were 18-65 years old. At day 0 and weeks 12 and 24 we determined the clinical activity index (C. A. I.) and the endoscopic index. Clinical safety was monitored using the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire every 4 weeks.
RESULTS: After 6 months, treatment failure was 35% in group A, 28% in group B ($p = 0.02$) and 30% in group C ($p = 0.05$). Probability of continued remission was similar (Mantel Cox test, $p = 0.76$; Breslow test, $p = 0.52$). Mean times to treatment failure were 4.34±0.44, 4.57±0.76 and 4.62±0.81 months, respectively for groups A, B and C. It was shown that patients with total colitis as compared to those with left-sided colitis had an increased probability of relapse during the 1 year follow-up. Patients of group B experienced more asymptomatic nights (90% vs 77% in group C vs 58% in group A, $p = 0.0011$) during the first 3 months. Fecal calprotectin was lower in group C vs A and B ($p < 0.05$).
CONCLUSION: Plantago Ovata seeds and the combination of fructo-oligosaccharides/bifidobacterium longum w11 maintain UC remission and increase the response to mesalamine.
Disclosure of Interest: None declared

P0888 DRUG SURVIVAL AND REASONS FOR DISCONTINUATION OF ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE (IBD) IN CLINICAL PRACTICE

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INTRODUCTION: Since its introduction, anti-TNF therapy has shown to be effective for the treatment of IBD in several clinical trials. However, its long-term effectiveness and reasons for discontinuation in clinical practice might be different from those observed in clinical trials
AIMS & METHODS: Aims: To evaluate the drug survival and reasons for discontinuation of the first anti-TNF therapy in IBD patients in clinical practice.
Methods: IBD patients under anti-TNF therapy from 2000 to 2012 in our center were included. Data regarding the first anti-TNF treatment were extracted from clinical records fulfilled prospectively. Kaplan-Meier method was used to estimate the long-term drug survival of the treatment.
RESULTS: 160 IBD patients were included: 130 with Crohńs disease (mean age 42±14 years; 47% male) and 30 with ulcerative colitis (mean age 45±17 years; 63% male). The distribution of first biologic in Crohn's disease was 76 (58%) adalimumab and 54 (42%) infliximab, while in ulcerative colitis it was 1 (3%) adalimumab and 29 (97%) infliximab. Time to a probability of 50% discontinuation was 3.94 years in Crohńs disease compared with 0.97 years in ulcerative colitis ($p < 0.001$). The reasons for discontinuation of the drug, respectively in Crohn's disease and ulcerative colitis, were: intolerance (20% and 19%), lack of response (30% and 24%), loss of response (22% and 19%), remission achievement (17% and 29%), and others (11% and 10%). The probability of maintaining (retention rate) the anti-TNF treatment in Crohn's disease was 69% at 1 year, 59% at 2 years, 52% at 3 years, 50% at 4 years, 45% at 5 years, and 41% at 10 years. The corresponding figures for ulcerative colitis were 48% at 1 year, 41% at 2 years, 36% at 3 years, 31% at 4 years, and 15% at 5, 6 and 7 years
CONCLUSION: The probability of maintaining the first anti-TNF drug in Crohn's disease patients is around 50% after 5 years of treatment. Discontinuation rate was even higher in ulcerative colitis, with only 15% of patients maintaining anti-TNF therapy at 5 years. The most frequent reasons for discontinuation of anti-TNF therapy were lack of response, loss of response, remission achievement and intolerance
Disclosure of Interest: J. P. Gisbert Other: Dr. P. Gisbert has served as a speaker, a consultant and advisory member for, and has received research funding from MSD and Abbvie., M. Arredondo: None declared, M. Chaparro Other: Dra. M Chaparro has served as a speaker and has received research funding from MSD and Abbvie, I. Cañamares: None declared, E. Daudén: None declared, G. Fernández-Jiménez: None declared, V. Meca: None declared, A. Morell: None declared, J. Aspa: None declared, L. Carmona: None declared, J. M. Alvaro-Gracia: None declared

P0889 CLINICAL BENEFIT OF ADALIMUMAB DOSE ADJUSTMENT FOR PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE IN EXTEND

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INTRODUCTION: Weekly dosing was shown to have a clinical benefit for adalimumab (ADA)-treated patients with Crohn's disease enrolled in the clinical trial CHARM who had flares or lost response to every other week (EOW) ADA dosing[1]. The clinical outcomes of dose escalation in patients enrolled in the EXTEND[2] trial are evaluated.
AIMS & METHODS: EXTEND was a 52-week double-blind (DB) trial in which patients received open-label (OL) ADA 160/80 mg at weeks 0/2. At week 4, patients were randomized to placebo or ADA 40 mg EOW. Patients with flares/non-response could move to OL ADA 40 mg EOW beginning at week 8, followed by escalation to 40 mg weekly (EW) for continued flare/non-response. Week 52 clinical remission (CDAI < 150), clinical response (decrease in CDAI ≥ 70 from baseline), and mucosal healing (absence of mucosal ulceration) were assessed in patients who moved to and remained on OL ADA EOW and in those who moved to OL ADA EW. Endpoints are reported using non-responder imputation (NRI) for patients with missing data and as observed for patients remaining in the study at week 52. Logistic regression analysis was used to determine predictors of moving to OL EW ADA.
RESULTS: In EXTEND, 42.2% (27/64) of patients randomized to DB ADA moved to OL ADA, and 23.4% (15/64) escalated to EW dosing. The only significant predictor of dose escalation was week 4 non-response (odds ratio 24.2, 95% CI 1.6, 365.2, $p = 0.021$). Week 52 outcomes for patients who completed the study on OL ADA (EOW or EW) are shown in the table. Increased adverse event rates were not observed with OL EW dosing.
Table. Week 52 efficacy in patients randomized to ADA who completed the study on OL EOW or EW ADA dosing

	NRI		Observed	
	OL EOW n/N (%)	OL EW n/N (%)	OL EOW n/N (%)	OL EW n/N (%)
Remission	3/12 (25.0)	3/15 (20.0)	3/6 (50.0)	3/9 (33.3)
Response	6/12 (50.0)	6/15 (40.0)	6/6 (100)	6/9 (66.7)
Mucosal healing	1/12 (8.3)	2/15 (13.3)	1/7 (14.3)	2/7 (28.6)

CONCLUSION: Escalation to weekly ADA dosing demonstrated clinical benefit in patients who met protocol criteria for dose escalation. No new safety risks were observed with EW ADA dosing.
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2. Rutgeerts P, et al. *Gastroenterology* 2012; 142: 1102-1111.
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P0890 CLINICAL OUTCOMES IN CONTINUOUS CLINICAL RESPONDERS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: SUB-ANALYSES FROM THE PURSUIT-SC MAINTENANCE STUDY

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AIMS & METHODS: The objective was to evaluate long-term clinical outcomes in patients with moderately to severely active UC who achieved complete continuous response (CCR) compared with patients who did not achieve CCR (non-CCR) through Wk54 of SC golimumab (GLM) maintenance therapy. During PURSUIT-Maintenance, GLM induction responders (464 patients) were randomized to receive PBO, SC GLM 50mg, or SC GLM 100mg at baseline (Wk0) and q4wks through Wk52. The primary endpoint was clinical response through Wk54 (CCR). Clinical remission, mucosal healing, corticosteroid use, and IBDQ outcomes and fecal markers at Wk54 among CCR versus non-CCR were assessed. All sub-analyses are based on patients randomized at Wk0 of maintenance (n = 456).

RESULTS: On all of the selected endpoints evaluated, CCR patients had better results when compared with non-CCR patients (Table). Among patients receiving corticosteroids at baseline, a greater proportion of CCR patients were not receiving corticosteroids at Wk54 versus non-CCR patients. Greater proportions of CCR patients were also in clinical remission versus non-CCR patients. Additionally, mean decreases in fecal lactoferrin and fecal calprotectin at Wk54 from Wk0 of maintenance were greater for CCR patients compared with non-CCR patients. Data between the GLM groups were similar and thus were pooled in the table.

Table: Clinical outcomes based on continuous clinical response at Wk54 in the PURSUIT-SC maintenance study*
Table to abstract P0890

Clinical endpoints	Non-CCR: PBO	Non-CCR: Combined GLM	CCR: PBO	CCR: Combined GLM
Randomized pts receiving concomitant steroids at Wk 0 (n)	60	87	27	73
Pts not receiving corticosteroids at Wk54(%)	1.7	4.6	66.7	75.3
Remission: Randomized pts(n)	106	156	48	146
Pts in clinical remission at Wk54(%)	0.9	1.9	68.8	67.1
Mucosal healing:Randomized pts(n)	106	156	48	146
Pts with mucosal healing at Wk54 (%)	1.9	2.6	87.5	90.4
IBDQ score:Randomized pts (n)	105	156	48	144
Change from Wk0 through Wk54 [mean(SD)]	-38.9(32.1)	-36.9(37.6)	10.6(18.2)	11.3(28.1)
Pts with IBDQ score >170 at Wk54 (%)	18.1	24.4	81.2	75.0

CONCLUSION: These data continue to support that patients induced into clinical response who maintain a clinical response through Wk54 are more likely to have better clinical outcomes.

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P0892 INTRA-ABDOMINAL ABSCESSES IN CROHN'S DISEASE: OUTCOMES FOLLOWING INFLIXIMAB THERAPY

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INTRODUCTION: Crohn's disease (CD) may be complicated by a sealed-off perforation that results in the development of an abscess typically located next to adjacent loops of bowel. Traditional treatment has been antibiotics, surgical or CT-guided drainage of drainable collections, bowel rest, and, ultimately, in some patients, resection of the affected bowel segment. Most gastroenterologists avoid immune suppression in this setting because of the potential for disseminated and systemic infection. Data regarding use of anti-tumor necrosis factor (TNF) in this situation are scarce. The aim of this study was to examine outcomes for patients with CD who developed an abdominal abscess that was subsequently treated with infliximab without initial drainage in order to evaluate its safety and efficacy in a larger number of patients than previously reported.

AIMS & METHODS: We retrospectively reviewed the records of all CD patients attending the Mount Sinai Medical Center in New York City, between 2000 and 2013, with an intra-abdominal abscess who were treated with infliximab in order to evaluate its safety and efficacy.

RESULTS: There were 18 patients with CD complicated by an intra-abdominal collection treated with antibiotics and infliximab at our center between 2000 and 2013. The median age was 25.5 (18-46) years and eleven patients were males. Seventeen patients had ileal disease. Fourteen patients developed an intra-abdominal abscess (size ranging from 1.1 cm to 7.9 cm) and four had a phlegmon only. In addition to anti-TNF therapy, all patients were treated with broad-spectrum antibiotics. No complications following infliximab therapy were reported including sustained fever or sepsis. None required a surgical drainage but four patients required abscess drainage by interventional radiology. Eight patients underwent surgery within 6 months after initiating anti-TNF therapy.

CONCLUSION: Penetrating CD complicated by intra-abdominal abscess formation may be safely and effectively managed with a combination of antibiotics and infliximab therapy without drainage. Prospective trials are required to confirm these findings.

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P0893 HIGH SERUM CRP PREDICTS FASTER CLEARANCE OF INFLIXIMAB AND POOR OUTCOME IN MODERATE-SEVERE ULCERATIVE COLITIS

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INTRODUCTION: Insufficient serum concentrations have been suggested as a cause of lack of response to infliximab (IFX) in Ulcerative Colitis (UC) and may be associated with a high inflammatory load. Early pharmacokinetics (PK) of IFX related to inflammatory markers and response to induction therapy have been poorly studied.
AIMS & METHODS: We studied the PK of IFX induction therapy and markers/predictors for response in patients with moderate-to-severe UC (endoscopy Mayo 2 or 3) in a multicenter prospective study. Serum IFX concentrations and antibodies to IFX (Radioimmunoassay, Sanquin Laboratories, Amsterdam), serum CRP and albumin and fecal samples (for calprotectin and IFX concentrations) were collected at 10 serial time points during the first 6 weeks of therapy. Endoscopic response was defined as improvement by at least 1 Mayo point at week 6-8.
RESULTS: Twenty patients were included, all but one receiving IFX according to standard induction regime (5mg/kg at week 0.2,6). 11/19 patients showed endoscopic improvement. The median IFX serum concentration at week 6 was 2.9 (0.01-5.8) ug/ml for endoscopic non-responders versus 8.1 (3.0-13.7) ug/ml for responders ($p=0.03$). Serum IFX$\leq$7ug/ml at week 6 was defined as a predictive cut-off (OR:18.67, 95%CI 1.56-223.1, $p=0.02$) for endoscopic non-response. The presence of antibodies to IFX at week 6 ($n=4$) was associated with a 2.93 fold increased clearance of the drug. Fecal IFX concentrations at day 1 were 4.1 (1.3-20.1) ug/ml in non-responders compared to 1.3 (0-5.8) ug/ml for responders (P[GD1]$=0.10$). Median area under the curve (AUC), IFX concentration versus time, was 1229 mg/L/day in the endoscopic non-responders compared to 1352 mg/L/day for the responders ($p=0.65$). Patients with a baseline CRP$>$50mg/l had a significantly smaller AUC than those below 50mg/l (578 vs. 1361 mg/L/day, $p=0.001$), with IFX clearance 1.63 fold increased ($P<0.001$, multivariate analysis).
CONCLUSION: Ulcerative Colitis patients with a high baseline serum CRP have increased clearance and lower serum IFX concentrations during IFX induction therapy, predicting poor outcome as early as week 6. These patients can be selected for more intensive induction regimens.
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P0894 PULMONARY INVOLVEMENT AND THE EFFECT OF TNF-ALPHA-INHIBITORS ON PULMONARY FUNCTION IN IBD-PATIENTS

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INTRODUCTION: Extraintestinal manifestations are a frequent complication in patients with Inflammatory-Bowel-Disease (IBD). Pulmonary involvement is commonly recognized but describe as a rare manifestation. Of note, increased mortality from respiratory diseases was observed in patients with ulcerative colitis. This may be due to an overlap between genetic causes in IBD and various chronic inflammatory lung diseases. Therefore, pulmonary involvement may be overlooked in IBD patients.
AIMS & METHODS: The aim of this prospective study was to assess pulmonary-function-abnormalities in IBD patients in comparison to healthy controls and investigate the effect of TNF-a-inhibitors on pulmonary-function-test (PFT). 90 consecutive patients with IBD (51 Crohńs disease (CD), 39 UC) were included. 47 patients were in remission and 43 had active disease. Out of these, 25 patients were seen for initiating anti-TNF therapy. 40 matched healthy controls were included. Pulmonary function was evaluated using the Medical Research Council (MRC) dyspnea index and a standardized spirometry. IBD activity was assessed using Harvey-Bradshaw index for CD and partial-Mayo-score for UC. In patients treated with anti-TNF all parameters were reevaluated 6 weeks later. Data are presented as Median/25thpercentile/75thpercentile.
RESULTS: Patients with active IBD showed significantly reduced parameters in their PFT. Tiffeneau index-values (FEV1%) were significantly reduced in IBD patients with active disease (78,9/73,7/85,1) compared to controls (86/81,8/88,3; $p=0.001$) and IBD patients in remission (84,5/81,2/89,4; $p=0.0002$). No difference was found between IBD patients in remission and controls ($p>0.05$). Parameters of peripheral airway obstruction (MEF 75-25%) showed comparable changes (MEF75: IBDactive vs. controls $p=0.01$; IBDactive vs. IBDremission $p=0.002$). Clinically significant peripheral airway obstruction was seen in 19.1%, obstructive dysfunction in 12.8% and restrictive dysfunction in 2.1% of IBD patients with an active disease (IBDremission: 4.6%/2.3%/6.9%; Control: 5%/0%/0%). Patients treated with anti-TNF showed a significant improvement of obstructive parameters ($p=0.003$ FEV1%) compared to baseline levels.
CONCLUSION: IBD patients with active disease showed significant abnormalities in their obstructive PFT-parameters in comparison to healthy controls and IBD patients in remission. Anti-inflammatory therapy with anti-TNF improves obstructive abnormalities. Pulmonary obstruction and chronic broncho-pulmonary inflammation might be the cause of reduced exercise levels during active disease and may be overlooked in the majority of patients. Further studies are necessary to determine whether chronic obstruction should be treated and whether it contributes to the observed mortality from lung problems in IBD.
Disclosure of Interest: None declared

P0895 THE EFFECT OF ANTI-TNF TREATMENT ON FISTULAS IN CROHN'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Peri-anal fistulas are an incapacitating complication of Crohn's disease affecting approximately 25% of patients in population-based estimates. Since the introduction of anti-TNF agents (infliximab and adalimumab), the treatment for Crohn's fistulas has changed from almost exclusively surgical to placing a much larger emphasis on medical therapy.
AIMS & METHODS: The purpose of this systematic review is to provide an overview of the literature evaluating the success rate of perianal fistula treatment with anti-TNF. PubMed, Embase and Biosis were searched. Randomized controlled trials on the effect of anti-TNF treatment on Crohn's perianal fistulas were included. Studies assessing perianal fistulas in children, rectovaginal fistulas and costs were excluded. The primary outcome of interest was complete fistula closure with partial closure as a secondary outcome parameter. A subgroup analysis for complete fistula closure was performed based on studies with a follow-up longer than 4 weeks.
RESULTS: Four studies comparing placebo with anti-TNF therapy regimens were included in the meta-analysis: one study on infliximab (ACCENT study) and three studies analysing adalimumab (CLASSIC, CHARM and GAIN trial). All patients with fistulising disease were included in the trials (peri-anal, entero-cutaneous and entero-enteral fistulas). In total, 179 patients were treated with anti-TNF medication whereas 109 patients received placebo. All studies assessed complete closures rates and three studies reported partial closure rates. The mean follow-up time was 13 weeks (range 4-26). In the anti-TNF group, 54 of 179 (30%) patients responded to treatment with complete fistula closure, whereas complete healing was seen in 13 of 109 (12%) patients in the placebo group. Partial fistula closure was seen in 48 of 109 (44%) patients in the anti-TNF treatment group and in 15 of 62 (24%) patients in the placebo group. There was no significant difference in complete or partial closure rates between the two groups (RD 0.12, -0.06-0.30, I^2 74% and 0.09, 95% CI -0.23-0.41, I^2 78%, respectively). The subgroup analysis showed a significant advantage for complete fistula closure with anti-TNF in the two trials with follow-up longer than 4 weeks (ACCENT: 46% versus 13%, $p=0.003$ and CHARM: 30% versus 13%, $p=0.03$) when compared to the placebo group.
CONCLUSION: Meta-analysis of 4 randomized controlled trials did not show a significant advantage for (partial) fistula closure with anti-TNF treatment as compared to placebo. However, subgroup analysis showed an advantage of anti-TNF treatment on complete fistula closure rates in the two trials with a follow-up longer than 4 weeks.
Disclosure of Interest: None declared

P0896 SAFETY AND EFFICACY OF BUDESONIDE MMX IN REMISSION OF ULCERATIVE COLITIS: A META ANALYSIS

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INTRODUCTION: Significance
Budesonide MMX is a novel drug developed for the treatment of ulcerative colitis using multi-matrix system. The effects on remission of disease would help to form recommendations for efficacy and safety profile. Most of these trials conducted have relatively small size, limited data and a meta-analysis for this drug could have stronger conclusion.

AIMS & METHODS: Manual search through MEDLINE & PUBMED using "ulcerative colitis" and "Budesonide MMX" were merged yielding 9 studies. Six studies were shown which was limited to human. Excluded were two reviews and a comment. Three multicenter, randomized, placebo-controlled trials were included & Cochrane Review Manager Software Version 5 was used.
RESULTS: There was a significant remission of symptoms in patients using the combined Budesonide MMX 9 & 6 mg with a p-value of 0.02. Sensitivity analysis using Budesonide MMX 9 mg is effective in the remission compared to Budesonide 6 mg alone and placebo with p-value 0.0005 at 95% confidence interval. Adverse effects showed no significant difference between Budesonide MMX group and the placebo group with a p value of [illegible].
CONCLUSION: Budesonide MMX, [illegible] meta-analysis, is beneficial in assessing the response to treatment in remission of symptoms. The adverse effects have no significant difference with placebo thus further study is needed to assess the safety profile of the drug.

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Disclosure of Interest: None declared

P0897 PHLEGMONOUS CROHN'S DISEASE: A REVIEW OF OUTCOMES AT A TERTIARY CENTRE

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INTRODUCTION: Penetrating Crohn's disease (CD) can be complicated by sealed-off perforation resulting in the development of an inflammatory mass or phlegmon. This typically involves the mesentery and adjacent bowel loops, and can be further complicated by an abscess or a fistula. The optimal management strategy and long-term outcomes of phlegmons in CD remains unknown.
AIMS & METHODS: Patients with CD and confirmed phlegmons on MRI/CT between January 2009 and December 2012 were identified retrospectively. Radiographic evidence of co-existing strictures, abscess, fistula and/or perforation was recorded. Medical records were reviewed and demographic data, CD phenotype, CD therapy prior to and following presentation, requirement for abscess drainage or surgical resection, and clinical status at most recent follow-up were recorded. Clinical remission was defined as a Harvey -Bradshaw index of <5. Repeat imaging was evaluated to assess phlegmon resolution.
RESULTS: 13 patients (7 male) were identified with median follow up of 40 months (range 33-61 months). 3 had ileal and 10 had ileocolonic CD. 11 had co-existing strictures, 5 had co-existing abscess, and 4 had co-existing enteroenteric fistula. 4 patients were receiving a thiopurine at presentation with phlegmon. 12 patients reported significant abdominal pain with 8 requiring admission. In 4 of these, imaging studies confirmed perforation. 2 patients required short-term parenteral nutrition and 6 were managed with exclusive liquid diet.
7 patients were treated primarily with medical management (2 with prolonged courses of antibiotics, 5 with thiopurine and corticosteroids, and subsequently 2 escalated to an anti-TNF agent) and this led to phlegmon resolution in 4 patients, and clinical remission in 3 patients. 2 patients have subsequently required surgery, and 2 persist with low grade obstructive symptoms treated conservatively. 6 patients were managed with primary surgery. All received a thiopurine as post-operative prophylaxis, of whom 3 escalated to an anti-TNF agent for significant post-operative recurrence. Repeat surgical resection or abscess drainage was not required subsequently.
2 of 4 patients presenting with perforation and phlegmon at presentation were treated surgically, 2 of 4 patients with enteroenteric fistula and phlegmon at presentation were treated surgically, and 3 of 5 patients with abscess and phlegmon at presentation were treated surgically. All 4 patients on thiopurine at presentation required surgery.
CONCLUSION: Phlegmonous disease remains challenging to treat. Medical and surgical management are both viable options, however phlegmon resolution was more likely in the surgically treated group. Medically treated patients remain at risk of need for future surgery. Surgically treated patients require aggressive medical treatment post-operatively, to limit recurrence of CD.
Disclosure of Interest: None declared

P0898 COMBINED USE OF AZATHIOPRINE/6-MERCAPTOPURINE ARE ASSOCIATED WITH DECREASED RISK OF ANTI-TNF INDUCED SKIN LESIONS

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INTRODUCTION: Anti-tumor necrosis factors (anti-TNF) agents are given for treating patients with moderate to severe active inflammatory bowel disease (IBD). Among various adverse events during anti-TNF therapy, skin lesions such as psoriasis or eczema could be a reason for discontinuation of anti-TNF therapy.
AIMS & METHODS: We aimed to identify the risk factors for skin lesion occurrence and compared the cumulative incidence of skin lesions in relation to concomitant use of azathioprine/6-mercaptopurine during being treated with anti-TNF agents in IBD patients. Methods: Between June 2002 and July 2013, 500 patients (404 Crohn's disease and 96 ulcerative colitis) were treated with anti-TNF at Asan Medical Center. Among them, new skin lesions occurred in 47 IBD patients at the department of dermatology. We retrospectively reviewed the medical records. To identify risk factors for skin lesions, we compared 47 patients with skin lesions to 443 patients without any skin disease or history.
RESULTS: The incidence of skin lesions during anti TNF therapy was 9.4%. The skin lesions were listed in Table 1. Face was the most common involved site ($n=21$, 45%), followed by trunk ($n=18$, 38%) and upper extremities ($n=18$, 38%). Thirty three (70%) patients were treated with topical steroids with or without antihistamine and showed good response. Four subjects (9%) discontinued anti-TNF because of eczematiform ($n=2$), psoriasiform ($n=1$), linear IgA dermatosis ($n=1$). On univariate analysis, skin lesion occurred more in female (HR: 1.794, 95% CI: 1.011-3.181, $p=0.046$) than in male. Also, combined use of azathioprine/6-mecaptopurine was associated with decreased risk of the occurrence of skin lesions (HR: 0.452, 95% CI: 0.251-0.814, $p=0.008$). However, only combined use of azathioprine/6-mercaptopurine (HR: 0.437, 95% CI: 0.242-0.790, $p=0.006$) decreased the risk of occurrence for skin lesions on multivariate analysis. Thus, we compared the cumulative incidence of skin lesions according to the use of azathioprine/6-mercaptopurine. Combined use of azathioprine/6-mercaptopurine at the time of starting anti-TNF agents tended to be lower cumulative incidence of skin lesions ($p=0.009$ by log rank test) during follow-up period.
Multivariate analysis of factors associated with skin lesion occurred during treatment of anti-TNF agents in patients with inflammatory bowel disease

Variables		HR	95% CI	p-value
Sex	Male	1		
	Female	1.741	0.978-3.105	0.059
Age				0.129
Concomitant use with IMM (azathioprine / 6-mecaptopurine)	No concomitant use	1	0.941-1.008	
	Continue to concomitant use during follow-up period	0.441	0.215-0.905	0.025
	Stop IMM during follow-up period	0.433	0.214-0.879	0.020
IBD group	CD	1		
	UC	0.672	0.230-1.961	0.467

HR, hazard ratio; CI, confidence interval; IMM, immunomodulator; IBD, inflammatory bowel disease
CONCLUSION: Combined use of azathioprine/6-mercaptopurine may reduce the occurrence of skin lesions on anti-TNF therapy at the time of starting anti-TNF agents.
Disclosure of Interest: None declared

P0899 COSTS DRUG SAVINGS USING A TEST-BASED STRATEGY VERSUS AN EMPIRIC DOSE ESCALATION IN PATIENTS WITH CROHN'S DISEASE LOOSING RESPONSE TO ANTI-TNF THERAPY

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INTRODUCTION: Pharmacokinetics of anti-TNF therapy is increasingly used to treat inflammatory bowel disease (IBD). Whether this approach is associated with significant cost savings beyond one year in a large cohort of patients with IBD has yet to be determined (1,2).
AIMS & METHODS: We compared two cohorts of patients with Crohn's disease treated with anti-TNF therapy (infliximab and then adalimumab in case of infliximab failure) and presenting loss of response. The first cohort followed a process management based on current practice, with drug optimization (increasing dose and/or shortening the interval) not taking into account pharmacokinetics of anti-TNF. In the second cohort, results of trough levels and antibodies against anti TNF were integrated when patient was not responding for the first time to an anti TNF agent. We used a selected mathematical model to describe the trajectories of Crohn's disease patients in the management of their disease based on a discrete event system. This allows tracking over a given period (1, 3 or 5 years) a double cohort of patients (10.000 patients) who move randomly and asynchronously from one state to another while keeping the whole information on their entire trajectory. Both cohorts were modeled by a state diagram parameters where transition probabilities from one state to another are derived from literature data. A stochastic sensitivity analysis on the transition probabilities was conducted in order to assess the stability of results. In the second analysis, we used the cost of an Elisa test from Theradiag (France, 100 euros) and no other indirect costs were included in this test based strategy. The costs of anti TNF therapy integrated in this model were reported by the French healthcare system.

RESULTS: There was a dramatic decrease in overall costs within the cohort of Crohn's disease patients benefiting from a test-based strategy (table 1)

	Decrease in total costs (n = 10.000)	Percentage of decrease in direct costs	Decrease in costs per patient
One year	**23 847 619 €**	**14.1%**	**2 385 €**
Three years	**88 588 892 €**	**22.4%**	**8 859 €**
Five years	**131 300 293 €**	**24.6%**	**13 130 €**

For this simulation, the mean decrease in costs was similar when testing a population of 3 000 or 10 000 patients. At 5 years the mean decreased costs were 12 899 (95% CI:11820 - 13977) for 3 000 patients and 13 130 euros (95% CI:12535 - 13725) for 10 000 patients. After a stochastic sensitivity analysis (30 simulations with random choice of transition probabilities and a bootstrap analysis), these results were comparable with a decreased costs at 5 years for each patient using tests with a 95CI [13 251,74 € - 13 565,05 €]. The impact of the direct cost of test is not significant and our results were similar using cost of test of 2.000 euros.
CONCLUSION: A test-based strategy is associated with major cost savings among Crohn's disease patients treated with anti-TNF strategy. These findings should be taken into account to guide decision making in clinical practice and also by French healthcare system.
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P0900 LONG-TERM OUTCOME IN PATIENTS WITH CHRONIC ACTIVE ULCERATIVE COLITIS STARTED ON INFLIXIMAB: A RETROSPECTIVE SWEDISH MULTICENTER STUDY

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INTRODUCTION: Infliximab has been shown to be effective in acute severe ulcerative colitis (UC) reducing the risk of colectomy. The ACT studies proved efficacy for IFX in patients with a more chronic type of UC, However, long-term data on clinical outcome of anti-TNF therapy are scarce. We assessed long-term outcome in patients with chronic UC started on IFX.
AIMS & METHODS: METHODS: Retrospective data capture from local registries at 9 Swedish IBD centers from November 2004 to December 2011. Inclusion criteria were: a) IFX treatment on an ambulatory basis. b) age ≥18 years, c) 8 weeks or more on continuous steroid use or more than 12 weeks during the last 6 months, d) steroid intolerance, e) insufficient response to, or intolerance to thiopurine therapy. Patients were eligible if followed at least 12 months or until colectomy.
RESULTS: 243 patients (145 males, 98 females) were included; median age 26.3 years (8-71.7) at diagnosis and a median disease duration of 5.0 years (0.2-39.5 years). 114/243 patients (47%) were on steroids and 116/243 (48%) were on concomitant thiopurines, 25/243 (10%) started a thiopurine together with IFX at inclusion and 90/243 (37%) patients had a previous thiopurine exposure. Median follow-up was 3.3 years (0.1 –8.9 years) during which a median of 6 (1-41) infusions were given. At 12 months 114/243 (46.9%) patients were in steroid-free remission and 46/243 (18.9%) had a steroid-free response. Lack of response was noted in 39/243 (16%) and 32/243 (13.2%) underwent colectomy. The corresponding figures at a median follow-up of 3.3 years were steroid-free remission: 114/243 (46.9%), steroid-free response 31/243 (12.8%), no response 14/243 (5.8%) while 75/243 (30.9%) had undergone colectomy. Of non-responders at 1 year, 21/39 (53.8%) had a colectomy during follow-up compared to 22/172 (13%) patients with response or remission at 12 months. At last follow-up, 44 patients were on IFX maintenance treatment with a median of 24 (11-54) infusions. The remaining 199 patients had a first course of IFX treatment with a median of 4 (1-41) infusions, 41 patients had a second course with a median of 5 (1-29) infusions, 9 patients a third course with a median of 5 (1-14) infusions and one patient a fourth course with 4 infusions. The main reasons for stopping IFX at the first course was remission in 32%, loss of response 28%, non-response 18% and adverse events 10%. Overall 62 (25,5%) patients were switched to adalimumab.
CONCLUSION: Anti-TNF is an efficacious long-term treatment in chronic active UC with 47% of patients in steroid-free remission at 12 months and sustained at 3.3 years. 66% had at least a clinically significant steroid-free response at 12 months with a slight decrease to 60% at 3.3 years. In contrast, non-response at 12 months was associated with a high risk of subsequent colectomy.
Disclosure of Interest: None declared

P0901 INFLIXIMAB POPULATION PHARMACOKINETIC MODELLING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: ESTIMATION OF INDIVIDUAL PHARMACOKINETIC PARAMETERS AND TROUGH LEVELS PREDICTION

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INTRODUCTION: Infliximab (IFX) trough levels (TLI) vary greatly between inflammatory bowel disease (IBD) patients. This variability is relevant because there is a relationship between IFX concentration and clinical response.
AIMS & METHODS: Main objective: estimate individual pharmacokinetic parameters and predict trough IFX levels. Secondary objective: evaluate the association between IFX exposure and covariates that could modify trough levels.
(a) Observational and prospective study of patients on IFX treatment from July 2013 to March 2014. TLI and antibodies toward infliximab (ATI) were measured by ELISA at steady-state. Variables recorded: demographic, disease location C-reactive protein levels (CRP), serum albumin concentrations (SAC), immunomodulatory treatment (IMM) and smoking. Individual pharmacokinetic parameters were estimated and TLI were predicted using population PK modelling (Nonmem® 7.2).
RESULTS: 55 patients (49% women) were included. 93 TLI and ATI were measured. Mean age: 43 yr (18-75); weight: 74 kg (IC95%: 71-77.5). Diagnose: 58.5% CD and 41.5% UC. 70 % received IMM. 27% patients were under intensified IFX doses. Mean CRP: 6.45 mg/L (IC95%: 4.56-8.35), mean SAC: 4.70 g/dL (IC95% 2.55-6.84).
Mean TLI: 3.34 mg/L (CD: 3.62. UC: 2.49) (IC95%:2.66-4.02). TLI: <3: 56 % and 3-7: 31.2%. ATI status: 4.3% of patients tested positive. All patients who developed ATI had undetectable trough levels. 68.5% of patients with trough levels<3 were in remission. Mean estimated peak levels: 114.35 mg/L (IC95%: 107.37-121.305); mean estimated AUC: 27105.77 mg/h/L (IC95%: 24835-29376.54).
Fasanmade et al (2011) population PK model for CD was used in both CD and UC patients. Mean predicted TLI: 3.1 mg/L (IC 95%: 2.49-3.69). Bias –5.55% (IC95 %: -7.98-(-3.129)) and precision 10.4% (IC95 %: 8.85-11.95). Fasanmade et al (2009) population PK model for UC was not precise enough.
Individual estimated PK parameters (mean): central clearance (Cl) 5.65 ml/kg/day (IC95%: 5.13-6.16), volume of distribution (central) (Vd) 50.59 ml/kg (IC95%: 49.97-51.21), half-life ($t_{1/2}$): 11.7 days (IC95%: 10.7 -12.7). Population PK parameters: Cl 5.42 ml/kg/day, Vd 52.4 ml/kg. Difference between individual and population PK parameters: 4% in Cl and 3.4% in Vd. Comparison of exposures achieved showed that patients with positive ATI, SAC< 3.9 g/dL, non receiving IMM and smokers had significant lower trough IFX levels, higher Cl and lower $t_{1/2}$. Patients with PCR>6 mg/L and ileo-colonic CD had lower IFX levels.
CONCLUSION: High interindividual variability in IFX PK and trough levels exists in IBD patients. The influence of IMM, SAC, smoking and inflammation on infliximab clearance suggests that individual adjustment of infliximab doses according to disease activity may be useful in IBD.
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Disclosure of Interest: None declared

P0902 MESENCHYMAL STEM CELL TREATMENT DOES NOT INCREASE COLITIS-ASSOCIATED COLON CANCER RISK

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INTRODUCTION: Mesenchymal stem cells (MSCs) are potent immune regulators, proposed for local and systemic use in human IBD. Recent studies reported that MSCs can promote tumorigenesis, warning their use in clinical condition associated to increased cancer risk, such as IBD.
AIMS & METHODS: To evaluate the cancer risk associated to the therapeutic effect of MSCs in murine model of colon cancer associated to chronic colitis.
MSCs were isolated from adipose tissue of C57BL/6 mice, and analyzed for MSCs markers and for adipocyte and osteogenic differentiation. An MTT assay was used to explore the direct effects of MSCs on tumor intestinal epithelial cells proliferation and vitality. CT26 cells were incubated with TNF-a for 48 h and then exposed to the surnatant of TNF-alfa pre- treated AMSC. C57BL/6 mice were injected intraperitoneally with azoxymethane (AOM) and exposed to 3 weekly cycles of 2.5% DSS.1 million of MSCs were injected intra-peritoneally at day 3 of each DSS cycle, control (CT) mice received saline. Body weight, occult blood test and stool consistency were used to calculate the Disease Activity Index (DAI). Mice were sacrificed at week 10 and colon was analyzed macroscopically and microscopically for number of cancer and degree of inflammation. Nude mice were subcutaneously engrafted respectively with murine (CT26) or human

(HCT116) tumor cells lines alone or in combination with MSCs to evaluate their role in tumor cell growth. CT nude mice received MSCs alone.
RESULTS: MSCs differentiated into adipocytes and osteocytes, and expressed low levels of CD31, CD34, LIN and cKIT markers, and highlevels of SCA-1, CD44 and CD106. MSCs proliferation was increased when stimulated with TNF. Their surnatant leaded to a not significant reduction of CT26 growth. MSCs injection significantly reduced DAI in treated mice vs. CT. MSCs treated mice showed lower body weight loss and better survival rate. Treated mice had a not significant reduced rate of colon cancer development vs. CT. In nude mice, there was no significant difference in tumor size between groups. No lesions were found in CT mice.
CONCLUSION: MSCs did not increase cancer risk in this colitis model and did not affect the progression of pre-existing tumor lesions. MSCs exerted an immune-modulatory effect in vivo, by decreasing the severity of colitis in mouse, suggesting that their anti-inflammatory effects may contra-balance their pro-carcinogenetic potential, even in pre-cancer condition such as chronic colitis. Further analyses are required to define mechanisms of action underlying these findings.
Disclosure of Interest: None declared

P0903 INCREASED FREQUENCY OF ENDOSCOPIC MUCOSAL HEALING AND REDUCED INTESTINAL RESECTION IN PATIENTS WITH SEVERE IBD BY LONGTERM AZATHIOPRINE THERAPY, BUT NEGATIVELY AFFECTED BY MALE GENDER

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INTRODUCTION: Currently, safety and economic issues have increasingly raised concerns about the long term use of biologics as maintenance therapies.
AIMS & METHODS: To evaluate the role of azathioprine (AZA) on mucosal healing in patients with inflammatory bowel disease (IBD). Two thousand seven hundred patients with IBD were evaluated from January 1995 to April 2014. The searching criteria were as follows: (1) endoscopic records before the AZA and during the AZA therapy; (2) AZA naïve patients with severe IBD. The data included patients and disease demographics and the efficacy of AZA. Patients with a minimum duration of 4 months of AZA were included in this study.
RESULTS: A total of 120 patients treated with AZA for IBD were enrolled. AZA therapy reduced the number of the surgical interventions in patients with IBD* (*: $p<0.05$). Male gender had a negative impact on the efficacy of AZA therapy*. IBD patients with responce were older than the nonresponder*. There was no difference between the operated CD patients and nonoperated for the AZA responce rates (32% vs 34%, $p> 0.05$ respectively). Then, 33 AZA non-responder patients with CD were put on biologics. Responce rate was 30%. Of the nonresponders, intestinal resection performed in 35% .

	number	mucosal healing by AZA	Nonresponce %
Patients with IBD	120	37 %	63%
UC	38%(45p)	42%	58%
CD	62%(75p)	33%	67%
Male	60%	25%	67%*
Operated after AZA	13%	4.5%	18.4*
AZA used (months)	31.5±24.7 (4-113)	31.2±25.7 (4-90)	31.6±24.3 (4-113)
Age at IBD diagnose (years)	36.8±12.3 (11-72)	38.1±12.3 (17-58)	36.1±12.3 (11-72) *
Period (AZA started-IBD diagnosed (months)	39.8±52.5 (0-264)	56±69 (0-264)	30±37 (0-204)

CONCLUSION: In this study, we showed that AZA therapy increased endoscopic mucosal healing rates and decreased the frequency of the surgical interventions in AZA naïve patients with severe IBD. We believe that there is still room for the AZA therapy in the management of severe IBD patients. Of the 33 CD patients with no previous AZA responce, biologics failed in 70%.
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P0904 EFFICACY OF ADALIMUMAB TREATMENT IN STEROID-DEPENDENT ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: Steroid dependency develops frequently (more than 30%) with regards to ulcerative colitis (UC) patients. Limited data exists concerning adalimumab (ADA) administration in steroid-dependent UC patients.
AIMS & METHODS: Our aim was to evaluate the clinical efficacy of ADA in steroid-dependent UC patients.
We designed an open-label, retrospective, consecutive, and multicentre study. Inclusion criteria were patients over 18 years old with UC and ECCO criteria of steroid-dependency: Patients who are either unable to reduce corticosteroids below the equivalent of prednisolone 10 mg/day within three months of starting corticosteroids, without recurrent active disease or who have a relapse within three months of stopping corticosteroids. All patients received ADA treatment for induction (160/80 mg) at weeks 0 and 2 and 40 mg every 2 weeks thereafter. In the event of loss of response patients received higher doses of ADA. The main endpoint evaluated was clinical remission without steroids during all the treatment. Clinical response, mucosal healing and varying levels of C-reactive protein (CRP) and calprotectine were also evaluated. Results are shown in percentages; associations were analyzed by Cox regression whenever appropriate.
RESULTS: 37 steroid-dependent UC patients were treated with ADA: 67% female, mean years since UC diagnosis being 11 years, 40% presenting extraintestinal manifestations and 65% with extensive colitis (E3). 12 patients (32%) were naïve to anti-TNF and 25 (68%) had previously received infliximab. Mean follow-up was 25.9 months. 83% received concomitant treatment with immunosuppressive drugs. 43% needed higher doses of ADA treatment due to loss of response. After induction 35% of patients were in remission and after 12 months. 40% of patients were in remission without steroids. The mean partial mayo score was 6.89 basal, 3.13 at month 6 and 2.33 at month 12 ($p<0.001$). Mucosal healing was achieved in 48% of patients. Mean calprotectine decreased from 563 basal to 218 at month 6 ($p<0.05$) and to 61 at month 12. CRP decreased from 19.13 to 6.13 at month 12 ($p<0.001$). Only 3 patients (8%) needed a colectomy during the first year. We did not observe any association between concomitant treatment with immunosuppressive drugs and response to ADA, but after Cox regression patients with need of intensification with ADA (HR = 48.1 95%IC:1.46-1589.1; $p=0.03$) and with previous IFX (HR = 12.8; 95%CI: 2.24-73.54, $p=0.004$) had a lower remission rates.
CONCLUSION: Adalimumab can be effective for clinical remission without steroids and mucosal healing in steroid-dependent UC. Previous IFX or need of intensification are predictive factors of poorer efficacy.
Disclosure of Interest: None declared

P0905 ONE HOUR INFLIXIMAB INFUSIONS DO NOT AFFECT ANTIBODIES ANTI-INFLIXIMAB AND TROUGH LEVELS IN IBD PATIENTS

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INTRODUCTION: Infliximab therapy in patients with inflammatory bowel disease (IBD) requires intravenous administration in over 2 hours, with a further 1 hour of post-infusion observation. Recent studies demonstrated the safety and the tolerance of a shortened 1-hour infusion in IBD patients under scheduled maintenance infliximab treatment. We report our experience in order to evaluate if repeated 1-hour infliximab infusions could affect the antibodies to infliximab (ATI) and the infliximab trough levels (TL).
AIMS & METHODS: This was a prospective cohort study on patients with IBD receiving infliximab with shortened 1-hour infusions. All patients were treated with scheduled maintenance infliximab therapy, after at least 5 well tolerated 2-hours infusions before enrolment. For each patient we recorded diagnosis, vital signs. All patients were routinely premedicated with 20 mg i.v. methylprednisolone and oral antihistaminics. We analyzed serum samples collected before starting the first shortened infusion and after one year of maintenance scheduled infliximab treatment for ATI and TL by a commercial ELISA kit according to the manufacturer instructions (DRG Diagnostics GmbH, Marburg, Germany). All samples were analyzed simultaneously at the end of the collection period. Statistical analysis was performed by Wilcoxon test for paired samples and Fisher's exact test.
RESULTS: Fifty-seven IBD patients (28 Crohn's Disease, 29 Ulcerative Colitis) were treated at our IBD Outpatient clinic with 1-hour infliximab infusion protocol: out of them 24 (42%) at the dose of 10 mg/kg and 18 (31.6%) with a shortened interval of 6 weeks. Eleven patients (19.3%) were on concomitant immunosuppressants. In total, 396 maintenance 1-hour infliximab infusions were administered. Adverse reactions were reported in 2 out of 396 (0.5%) 1-hour infusions: these reactions were considered as severe, resulting in infliximab discontinuation. Both patients had elevated ATI at the time of the first 1-hour infusion. No significant difference was found between median ATI (17.5 AU/ml versus 17.7 AU/ml) and TL (3.1 mcg/ml versus 2.26 mcg/ml) measured before and after 1 year of shortened infliximab infusions. The percentage of patients with ATI positive (scoring higher than 10 AU/ml) and of patients with undetectable TL were unchanged after one year of 1-hour infusions. We found no correlations of ATI positivity and detectable TL measured after one year of shortened infusions with the infliximab dose (5 mg/kg or double dose 10 mg/kg), the dose interval (every 8 or 6 weeks) and the concurrent immunosuppressive therapy. Five out of 55 patients (9%) changed their ATI status from negative to positive, while 10/55 (18%) from positive to negative, at the end of the study period ($p=$ n.s.).
CONCLUSION: In our experience, shortened 1-hour infliximab infusions were safe and well tolerated in IBD patients under scheduled maintenance therapy also with dose and interval optimisation and did not affect ATI and TL.
Disclosure of Interest: M. Marzo: None declared, A. Armuzzi Lecture fee(s) from: AbbVie, MSD, Chiesi, Ferring, Nycomed, Takeda and Otsuka, Consultancy for: AbbVie, Lilly, MSD and Takeda, B. Tolusso: None declared, D. Pugliese: None

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P0906 TUBERCULOSIS INFECTION IN INFLAMMATORY BOWEL DISEASE PATIENTS AFTER ANTI-TNF THERAPY IN A HIGH TUBERCULOSIS PREVALENCE RATE AREA

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INTRODUCTION: Galicia is a region located in the north west of Spain. It has an estimated incidence of 27 new cases of tuberculosis per 100000 population, that is higher than the Spanish average rate of 15.5/100000. On the other hand cases of active tuberculosis have been reported worldwide with the use of therapeutic agents that inhibit tumor necrosis factor (TNF) alpha. Our aim was to study the prevalence of latent tuberculosis infection and active tuberculosis in inflammatory bowel disease (IBD) patients before and during TNF therapy in this geographical area.
AIMS & METHODS: We conducted a retrospective study collecting clinica data of IBD patients on anti TNF therapy from January 2000 to December 2012, identifying the cases with latent tuberculosis and active tuberculosis infection. Latent tuberculosis was defined as a positive tuberculin cutaneous test (TCT) or Booster re-test (> 5 mms). Active tuberculosis infection was confirmed by positive culture to Mycobacterium tuberculosis.
RESULTS: 225 patients received TNF alpha drugs, 136 male (60.4%), 173 (76.9%) Crohńs disease. Nine patient had suffered from previous lung diseases. Tuberculin cutaneous test was done in 190 patients, and Booster re-test in 100. Latent tuberculosis was diagnosed in 20 and 1 patients whether TCT or Booster were > 5 mms respectvely and all of them received oral isoniacide prophylaxis (9.3%). Seven patients suffered from active tuberculosis infection (3.1%): 4 male (57.1%) mean age 49.6 years 57.1% ulcerative colitis. Four of them had negative TCT and Booster but they were on inmunosuppresant but no corticosteroids when these tests were performed, and the other 3 patients had received oral quimioprofilaxis (3-6 months) because TCT was positive. Time from last TNF dose to symptoms and from symptoms to tuberculosis diagnose were and days respectively. Active tuberculosis were generally disseminated (85.5%) and required hospitalization until diagnose and clinical stabilization. Multidrug therapy was continued for 6-8 months but one patient eventually died. Anti TNF-alpha was no restarted in these patients.
CONCLUSION: Active tuberculosis in IBD patients on antiTNF therapy in a high prevalence area was 3.1%. The infection was generally disseminated, required hospitalizations and even caused death.
TCT test and previous oral quimioprofilaxis failed to eliminate risk of active infection in these patients, so any other tests or preventive measures should be develop.
Disclosure of Interest: None declared

P0907 COMBINATION THERAPY WITH LOW DOSE THIOPURINE AND ALLOPURINOL IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Thiopuine is used as a second line therapy in patients with ulcerative colitis (UC) failing 5-ASA treatment. However up to 50 % of patients treated with thiopurine fail this treatment due to intolerance or to lack of efficacy. A high ratio between Methylmercaptopurine (MeMP) and the active metabolite 6-Thioguanine-nucleotide (6-TGN) can be the explanation for intolerance and thiopurine-faliure in some patients.
Adding Allopurinol to a low dose of thiopurine changes the ratio between MeMP and 6-TGN, thereby decreasing the risk of some adverse events and at the same time increasing the efficacy.
AIMS & METHODS: To determine the tolerance and efficacy of combination therapy with low dose of thiopurine and allopurinol in patient with UC.
A retrospective analysis of patient with CU starting combination therapy between October 1th 2010 and October 1th. 2013 in a single IBD-center in Denmark.
36 UC patients were identified. 21 males and 15 females. Disease duration was mean 7 years (range 2 – 28 years). 2 patients had proctitis, 22 patients had left-sides colitis and 12 patients had pancolits.
The reason for starting combination therapy was: abnormal liver test in 8 patients, high MeMP/6-TGN ratio in 24 (14 were proven to fail mono-treatment with thiopurine), 3 other adverse events and 2 patient failing thiopurine treatments, but without a high MeMP/6-TGN ratio.
When starting combination therapy 20 patients had active disease despite of treatment with systemic steroid in 2 patient, anti-TNFa treatment in 5, steroid and anti-TNFa treatment in 3 patients. 16 patients had inactive disease, but 3 patients were receiving steroid and 7 anti-TNFa treatment.
RESULTS: Six (17 %) patients were intolerant to combination therapy and had to stop treatment. 5 patients had the same adverse event as in mono-therapy and 1 patient had an unspecific event not thought to be related to treatment.
The active metabolite increased from mean 130 pmol/nmol Hgb (range 62-220) to mean 243 pmol/nmol Hgb (range 115-434) and MeMP decreased from 4158 pmol/nmol Hgb (range 487-12150) to mean 134 pmol/nmol Hgb (range: 0-419) and ratio between MeMP and 6TGN decreased from 31 to 0, 55 upon changing from thiopurine mono-therapy to combination-therapy.
Four (11 %) patients had no or poor response to combination therapy, 2 had a colectomy and 2 started treatment with anti-TNFa.
Twenty-six (70 %) patients responded to combination treatment and have since start of treatment been in steroid and anti-TNFa free clinical remission.
CONCLUSION: Combination therapy with low dose thiopurine and allopurinol is well tolerated, cheap and a highly effective treatment in patients with CU and a high MeMP/6-TGN ratio experience intolerance or having poor or no response to thiopurine mono-therapy.
Disclosure of Interest: None declared

P0908 CAN MINDFULNESS-BASED COGNITIVE THERAPY IMPROVE THE QUALITY OF LIFE FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)?

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INTRODUCTION: Around 30% of patients with IBD report depression and anxiety and require psychological support. A prolonged effect of such comorbidities has been associated with poorer quality of life (QoL) and exacerbation of IBD symptoms. Mindfulness-Based Cognitive Therapy (MBCT) is a psychological intervention successful in improving depression and anxiety scores in depressed patients, but no previous randomised controlled trial has tested its possible effects on IBD patients.
AIMS & METHODS: The aim of this study was to evaluate the feasibility and acceptability of MBCT with IBD patients and assess its possible effect on QoL, depression, anxiety, disease activity and dispositional mindfulness.
IBD patients (n = 44) recruited from outpatient gastroenterology clinics in two Scottish NHS Boards were randomised to receive MBCT (intervention group n = 22) or allocated to a wait-list (control group n = 22). The intervention was 16 hours of structured group MBCT training over 8 consecutive weeks plus guided home practice and an hour of monthly follow up session for four months. Primary outcome was feasibility and acceptability of MBCT assessed by a self-complete questionnaire. Secondary outcomes included: QoL, depression, anxiety, disease activity and dispositional mindfulness assessed at three points: baseline, post intervention and six month follow up.
RESULTS: 24 patients completed the trial. All patients described the MBCT program as a feasible and useful method and 100% would recommend MBCT to other IBD patients. Dispositional mindfulness significantly improved ($p = .03$) in the intervention group at post intervention and follow up. QoL, depression, anxiety and disease activity scores also showed promising improvement in the intervention group.
CONCLUSION: A larger randomised controlled trial of MBCT for patients with IBD is feasible and pilot data suggests that MBCT significantly improved dispositional mindfulness in IBD patients and also has the potential to improve QoL, depression, anxiety and disease activity scores. MBCT offered in combination to standard care holds a potential to benefit IBD patients.
Disclosure of Interest: M. Schoultz: none, I. Atherton: none, R. Kyle: none, A. Watson: none

P0909 ARE HIGH INFLIXIMAB TROUGH LEVELS ASSOCIATED WITH IMPAIRED QUALITY OF LIFE IN IBD PATIENTS IN CLINICAL AND BIOCHEMICAL REMISSION ON INFLIXIMAB MAINTENANCE THERAPY?

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INTRODUCTION: Preliminary evidence suggests a therapeutic window for infliximab (IFX) trough levels (TLs) in patients with inflammatory bowel disease (IBD). It remains unknown if higher or presumably 'supra-therapeutic' TLs are associated with adverse effects. The aim of this study was to identify a possible association between high TLs, side effects of IFX treatment and quality of life.
AIMS & METHODS: We performed a cross-sectional study in IBD patients in clinical and biochemical remission whilst receiving IFX maintenance therapy. Clinical remission was defined as HBI < 5 for Crohn's disease (CD) and CCAI < 5 for ulcerative colitis (UC). Biochemical remission was defined as a fecal calprotectin < 250 ug/g. IFX TLs and biochemical markers (Hb, Ht, TSH, CRP and vitamin D) were assessed to rule out alternative diagnoses for fatigue. Patients were excluded in case of pregnancy or diseases such as cancer, infections or rheumatologic disorders. Quality of life was assessed by IBDQ and SF-36. Fatigue and joint pain were measured by visual analogue scores (VAS) and for skin lesions a skin questionnaire was completed. The patient cohort was separated in groups consisting of patients with 'therapeutic' (IFX TL 3-7 ug/ml) and 'supra-therapeutic' (IFX TL > 7 ug/ml) TLs. Patients and investigators were unaware of TL results when completing the questionnaires and during the assessment of clinical and biochemical remission. In total 115 patients on IFX maintenance treatment (5 or 10 mg/kg) were approached of which 46 patients (CD n = 33, UC n = 13) were deemed fit for inclusion.
RESULTS: We did not find a significant correlation between the severity of side-effects and IFX TLs. Moreover, no correlation was observed between quality of life and IFX TLs. Patients with supra-therapeutic TLs had lower median scores (although not significant) compared to the therapeutic TL group on several SF-36 domains: e.g. SFphysical, SFsocial, SFpain, SFrole-physical and SFperception. The supra-therapeutic group scored lower on the physical

component score (PCS) (43.9 vs. 49.7; p = 0.18) while both groups scored equally on the mental component score (MCS) (47.2 vs. 48.3; p = 0.98). The supra-therapeutic TL group had lower scores on the IBDQ (178 vs. 183; p = 0.35) and joint pain VAS (10 vs. 6; p = 0.67) compared to the therapeutic TL group. Skin problems were more often seen in the therapeutic group versus patients in the supra-therapeutic TL group, but this difference did also not reach statistical significance, Skin score (4 vs. 6; p = 0.097).

CONCLUSION: CD and UC patients who were in clinical and biochemical remission with supra-therapeutic IFX TLs did not show an increase in side-effects nor impaired quality of life compared to patients with therapeutic IFX TLs.

Disclosure of Interest: None declared

P0910 THE RELATIONSHIP BETWEEN REMISSION STATUS AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MILD-TO-MODERATE ULCERATIVE COLITIS RECEIVING SHORT-TERM AND LONG-TERM DAILY THERAPY WITH MULTIMATRIX MESALAZINE

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INTRODUCTION: Studies of patients with ulcerative colitis (UC) have found an inverse relationship between disease activity and health-related quality of life (HRQL): Decreases in disease severity predict improvement in HRQL. The current analysis examines whether this association holds at various levels of disease activity by testing whether HRQL differs among patients in complete clinical and endoscopic remission, in partial remission, or not in remission after treatment with multimatrix mesalazine.

AIMS & METHODS: Data were from a multinational, open-label, prospective trial of multimatrix mesalazine (ClinicalTrials.gov ID: NCT01124149). In the initial (acute) treatment phase, patients with active mild-to-moderate UC received 4.8 g/day of multimatrix mesalazine once daily (QD) for 8 weeks. Patients in complete or partial remission at Week 8 were eligible to receive 12 months of maintenance treatment with 2.4 g/day of multimatrix mesalazine QD. Remission status at Week 8 and Month 12 was determined using a modified UC-Disease Activity Index (UC-DAI). Complete remission was defined as UC-DAI $\leq$1 with scores of 0 on both rectal bleeding (RB) and stool frequency (SF) components and $\geq$1-point reduction from Baseline in the endoscopy component. Partial remission was defined as UC-DAI $\leq$3, RB+SF $\leq$1, and not in complete remission. At Baseline, Week 8, and Month 12, patients completed measures of generic HRQL (12-item Short-Form survey [SF-12v2]) and disease-specific HRQL (Shortened Inflammatory Bowel Disease Questionnaire [SIBDQ]). Analysis of variance models tested whether HRQL scores at Week 8 and Month 12 differed by remission status. Repeated-measures mixed-effects models (RMMM) tested if changes in HRQL scores across Baseline, Week 8, and Month 12 visits varied by remission status. Analyses of each phase included only patients who fully completed treatment during that phase.

RESULTS: The numbers of patients in complete, partial, and no remission, respectively, were 186 (30.0%), 282 (45.4%) and 153 (24.6%) at Week 8 for acute phase completers, and 159 (50.6%), 103 (32.8%) and 52 (16.6%) at Month 12 for maintenance phase completers. At both Week 8 and Month 12 visits, patients in complete or partial remission scored better on all SF-12v2 and SIBDQ domains than those not in remission (all Bonferroni-adjusted $P < 0.001$). At Week 8, scores on most HRQL domains (all but the SF-12v2 pain domain, and social functioning domains on both instruments) did not statistically differ between patients in complete vs. partial remission. HRQL scores also did not differ between complete and partial remission groups at Month 12 (all Bonferroni-adjusted $P \geq 0.130$). Estimated parameters and means from RMMM models indicated that patients who achieved or maintained complete or partial remission showed similarly larger improvements and better maintenance of HRQL than patients not in remission.

CONCLUSION: Patients with UC in complete or partial remission who completed short-term and long-term daily treatment with multimatrix mesalazine had similar HRQL. Both groups had better HRQL than completers not in remission. These results indicate that achievement of partial remission of UC provides advantages comparable to those of complete remission with respect to improvement and maintenance of HRQL.

Disclosure of Interest: M. K. Willian Shareholder of: Shire, Other: Employee of Shire, A. Yarlas Other: Employee of Optum, which received funds from Shire Development LLC to conduct these analyses, A. Joshi Shareholder of: Shire, Other: Employee of Shire

P0911 DISEASE BURDEN AND TREATMENT IMPACT IN PATIENTS WITH MILD-TO-MODERATE ULCERATIVE COLITIS: A COMPARISON OF RESULTS FROM TWO OPEN-LABEL TRIALS

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INTRODUCTION: Data addressing the burden of ulcerative colitis (UC) on health-related quality of life (HRQL) and the impact of multimatrix mesalamine treatment on HRQL and work-related outcomes (WRO) of patients with UC were compared across 2 similarly-designed clinical trials. The objective of this comparison was to examine the robustness and relative magnitudes of these effects among multiple samples.

AIMS & METHODS: Trials 409 (ClinicalTrials.gov ID: NCT01124149) and 404 (NCT00446849) were each multicenter, open-label, prospective studies of multimatrix mesalazine treatment for adults with active mild-to-moderate UC. Both trials included an 8-week acute treatment phase followed by a 12-month maintenance treatment phase. This analysis includes acute phase data only. Patients received 4.8 g/day (Trial 409) or 2.4 to 4.8 g/day (Trial 404) of multimatrix mesalazine once daily for 8 weeks. At Baseline and Week 8 visits, all patients completed 3 patient-reported outcomes (PRO) instruments, measuring HRQL (the 12-item Short-Form survey [SF-12v2] and the Short Inflammatory Bowel Disease Questionnaire [SIBDQ]) and WRO (Work Productivity and Activity Impairment Questionnaire: UC [WPAI:UC]). Within each trial, burden of UC on HRQL was estimated as the deficits in patients' SF-12v2 scores relative to scores from a US general population sample (USGPS). Analysis of variance (ANOVA) models compared the magnitude of pre-treatment disease burden, and differences in Baseline PRO scores, between trials. ANOVA models also tested between-trial differences in burden at Week 8 for patients who completed treatment. Analysis of covariance (ANCOVA) models tested for between-trial differences in PRO scores at Week 8, controlling for Baseline scores for treatment completers.

RESULTS: In Trial 404, 42.4% (56/132) of patients completed treatment at 8 weeks, compared to 89.1% (639/717) in Trial 409. Patients in Trial 409, compared to Trial 404, showed greater burden on several SF-12v2 domains (general health, limitations due to emotional problems, social functioning, and mental health; $P < 0.05$ for differences). Comparisons of Baseline PRO scores between trials found worse scores for Trial 409 than Trial 404 on several domains of the SF-12v2 (general health, limitations due to emotional problems, and mental health), SIBDQ (social and emotional function), and WPAI:UC (presenteeism and overall work impairment); $P < 0.05$ for differences. Comparison of burden at Week 8 for treatment completers found no trial differences for any SF-12v2 domains (all $P > 0.05$); burden at Week 8 was similarly small for each trial, with most domain scores at least equivalent to those scores of the USGPS. Direct comparisons of Week 8 post-treatment scores between trials found no significant differences for any PRO measure (all $P > 0.05$).

CONCLUSION: Patients in Trial 409 entered treatment with a larger disease burden on HRQL and with generally worse HRQL and WRO than patients in Trial 404. At Week 8, there were no between-trial differences in burden on HRQL or for direct comparisons of all HRQL and WRO measures for treatment completers. Further, for patients in both trials, Week 8 scores on most SF-12v2 domains were not below scores from the USGPS, indicating that patients with UC achieved near-normal levels of most aspects of HRQL following 8 weeks of daily multimatrix mesalazine treatment.

Disclosure of Interest: M. K. Willian Shareholder of: Shire, Other: Employee of Shire, A. Yarlas Other: Employee of Optum, which received funds from Shire Development LLC to conduct these analyses, A. Joshi Shareholder of: Shire, Other: Employee of Shire

P0912 EFFICACY AND SAFETY OF INFLIXIMAB SALVAGE THERAPY IN PATIENTS WITH ULCAERATIVE COLITIS AFTER FAILURE OF TACROLIMUS INDUCTION THERAPY

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INTRODUCTION: Tacrolimus and anti-TNFα therapy like infliximab have been shown to be effective for the treatment of patients with moderate to severe corticosteroid-refractory/dependent ulcerative colitis. However, currently, there are no guidelines pertained to the order or the timing of these medications.

AIMS & METHODS: In our hospital, tacrolimus precedes infliximab as a second-line therapy for patients of ulcerative colitis. This study was to investigate the efficacy and safety of infliximab in patients with moderate to severe corticosteroid-refractory/dependent ulcerative colitis who failed to respond to tacrolimus induction therapy. We enrolled twenty-nine patients (16 male, 13 female; mean age 43.9) treated with tacrolimus between January 2010 and January 2014, and 11 (4 male, 7 female; mean age 47.6) out of these patients were treated with infliximab because of refractoriness or loss of response to tacrolimus, or no tolerance. We assessed therapeutic outcomes at baseline, 8, and 30 weeks for 11 patients treated with infliximab using Lichtiger index, a score of which less than or equal to 4 was defined as clinical remission.

RESULTS: Mean Lichtiger index was significantly decreased to 11.6, 6.7, and 5.1 at baseline, 8, and 30 weeks, respectively ($P < 0.05$). Five patients (45%) showed clinical remission at 8 weeks and six (54%) showed clinical remission at 30 weeks. Three patients who did not respond to infliximab were all over 60 years old, and finally underwent colectomy. Rates of clinical remission at 8 and 30 weeks were 42.4% and 53.1% in tacrolimus responders (2 loss of response; 4 no tolerance), 46.3% and 56.4% even in tacrolimus nonresponders (4 patients). There was no significant difference in clinical remission rate between tacrolimus responders and nonresponders. No serious adverse events were encountered.

CONCLUSION: Infliximab salvage therapy following tacrolimus appeared to be efficacious in both tacrolimus responders (loss of response or no tolerance) and in nonresponders (refractoriness), and 8 (72.7%) of 11 patients could avoid colectomy. Infliximab salvage therapy is considered to be useful and well tolerated.

Disclosure of Interest: None declared

P0913 PATIENT PERCEPTION TOWARDS FAECAL MICROBIOTA TRANSPLANTATION FOR TREATMENT OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Faecal microbiota transplant (FMT) is a novel highly effective treatment for Clostridium difficile infection (CDI).* Initial clinical trials and case reports suggest that this may be a promising therapy for patients with inflammatory bowel disease (IBD).** As part of a patient audit regarding our FMT treatment for CDI we performed a survey to evaluate patient attitudes to potentially receiving FMT as treatment for IBD and gauged attitudes towards participation in a future clinical trial evaluating the effectiveness of FMT in IBD.
AIMS & METHODS: We conducted a structured survey on patients attending gastroenterology clinics to assess perceptions of effectiveness, tolerability, safety and thresholds for considering FMT as a treatment.
RESULTS: We collected 105 responses (M:F 46:59, Median age 36 years) including 80 (76%) from patients with IBD. 91% (96/105) felt that this treatment would be effective and 56% (59/105) did not consider it unpleasant. 96% (101/105) patients perceived it to be safe. 72% (76/105) and 82% (86/105) would be comfortable with having FMT via an NG tube or rectal enema route respectively. 78% (82/105) did not have any concerns regarding the faecal transplant being obtained from a screened unrelated donor. 74% (78/105) of the patients would be willing to have FMT as a first line treatment of CDI. 50% (40/80) of IBD patients surveyed would consider FMT as a first line treatment of their IBD, 85% (68/80) if steroid resistant or dependant, 89% (71/80) if failing on biologics and 94% (75/80) as a salvage treatment option prior to surgery. Importantly 75% (60/80) would consider taking part in a clinical trial evaluating faecal microbiota transplantation for treatment of their IBD.
CONCLUSION: In this survey of patient attitudes to FMT amongst patients from the UK, we found that patients perceived FMT as a potentially effective, safe, tolerable treatment and were inclined to consider this as part of conventional medical therapy for IBD. In our cohort we did not discover reluctance to take part in a trial of FMT for treatment of IBD.

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P0914 ADALILMUMAB SERUM CONCENTRATION AS A PREDICTOR FOR CLINICAL EFFICACY - ROC ANALYSES

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INTRODUCTION: The relationship between adalimumab trough concentration and efficacy (clinical remission and response) in patients with ulcerative colitis has been previously characterized[1]. The purpose of this analysis was to explore whether an adalimumab concentration threshold is predictive of adalimumab efficacy in ulcerative colitis.
AIMS & METHODS: Data from 242 patients with moderate to severe ulcerative colitis enrolled in the adalimumab treatment arm in ULTRA2 were included in the analysis. Patients received 160/80 mg adalimumab at Week 0/ 2 and 40 mg eow thereafter. Adalimumab trough concentration at Week 8 was used to predict clinical remission and response per Full Mayo scores at Week 8, 32 or 52. In case of dropouts or missing Week 8 concentrations, values were imputed using last-observation-carried-forward method. For Week 8, 32 and 52, efficacy, non-responder imputation was implemented such that subjects were considered not in remission/response if they were discontinued or moved to open-label prior to the time point of efficacy assessment or if they had a missing Mayo score at the time point of efficacy assessment. Receiver operating characteristic (ROC) curves were constructed and area-under the ROC curves (AUC) were calculated using R Ver 3.0.3. Determination of predictive adalimumab trough concentration thresholds was based on the choice of corresponding specificity and sensitivity pair determined from the ROC curves.
RESULTS: Mean (range) adalimumab trough concentrations at Week 8 were 8.7 (0-22.8 mcg/mL). ROC curves showed AUC values ranging from 0.64 to 0.67 for remission and 0.55 to 0.63 for response at Week 8, 32 and 52. No concentration threshold exhibited a combination of specificity and sensitivity that was highly predictive of remission or response at Week 8, 32 or 52. The highest value for AUC (0.67) was associated with Week 52 remission, for which the algorithm-determined threshold showed a specificity and sensitivity of 0.52and 0.78, respectively.
CONCLUSION: ROC analyses were conducted and did not identify an adalimumab trough concentration threshold that predicts clinical remission or response at Week 8, 32 or 52 in UC.

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P0915 EFFICACY OF CONCOMITANT MESALAMINE SUPPOSITORY IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS WHO SHOWED INADEQUATE RESPONSE TO ORAL 5-AMINOSALICYLIC ACID PREPARATIONS: A PROSPECTIVE STUDY

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INTRODUCTION: Oral 5-aminosalicylic acid (5-ASA) preparations have been widely given as first-line medications for inducing and maintaining remission in patients with mildly to moderately active ulcerative colitis (UC). Further, for distal UC, topical salicylate preparations as enema or suppository have been applied. However, up to now, there is no widely accepted evidence for efficacy of concomitant mesalamine suppository in patients with active UC who do not respond well to oral 5-ASA preparations.
AIMS & METHODS: We were interested to evaluate the efficacy of concomitant Pentasa suppository as remission induction therapy in patients who had active UC while on oral mesalamine preparations for at least 4 weeks. In a single-centre prospective setting, 114 consecutive patients with mildly to moderately active UC with rectal inflammation who had shown inadequate response to oral 5-ASA preparations were included. All patients received concomitant Pentasa 1g suppository rectally once a day for 4 weeks together with the ongoing oral 5-ASA preparations. No patient received corticosteroid or immunosuppressant. At week 4, clinical efficacy for Pentasa suppository was evaluated by the UC-Disease Activity Index (UC-DAI), including the 3 sub-scores. Clinical remission was defined as the bleeding sub-score = 0.and a decrease of $\geq$ 3 in the UC-DAI score, while clinical response meant a decrease of $\geq$ 1 in the UC-DAI score.
RESULTS: Of the 114 patients, 41 (36.0%) achieved clinical remission, 37 (32.4%) achieved response level. The UC-DAI fell from 3.2±0.8 at entry to 1.6±1.7 at week 4 ($n = 114$, $P < 0.001$). The bleeding sub-score fell from 1.0±0.2 to 0.4±0.5 ($P < 0.001$). Regarding the response rate vs extent of UC, the UC-DAI fell from 3.2±0.8 to 1.5±1.7 in patients with proctitis ($n = 101$, $P < 0.001$), and from 3.0±0.6 to 1.8±1.5 in patients with left-sided colitis ($n = 12$, $P < 0.05$), and one patient with pancolitis worsened. Further, by concomitant Pentasa suppository, the bleeding sub-score in patients who did not respond well to oral 5-ASA preparations alone ($n = 60$) fell from 1.0±0.1 to 0.4±0.5; in sulphasalazine-treated subgroup ($n = 21$), mean dose 3.7±1.2g/day, range 1.5-6.0/day fell from 1.0 ± 0.0 to 0.4±0.5 ($P < 0.01$); in Pentasa ($n = 7$) 1.7±0.6g/day, range 1.5-3.0/day fell from 1.0 ± 0.0 to 0.3±0.5 ($P < 0.05$); in Asacol ($n = 32$) 3.5±0.3g/day, range 2.4-3.6/day fell from 1.0 ± 0.2 to 0.4±0.6 ($P < 0.001$), reflecting significant efficacy for concomitant Pentasa suppository in patients who did not respond well to high dose oral 5-ASA preparations alone. No serious adverse events were observed.
CONCLUSION: This is the first study in Japan that has investigated the efficacy of Pentasa suppository in patients who did not respond well to oral 5-ASA preparations. Based on the outcomes of the present investigation, we believe that patients with distal UC who remain with active UC while on oral 5-ASA preparations alone should benefit from receiving concomitant Pentasa suppository.

Disclosure of Interest: None declared

P0916 PREDICTORS AND FREQUENCY OF ANTI-TNF DOSE ESCALATION AND DE-ESCALATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The role of anti-TNF therapy in patients with Inflammatory Bowel Disease (IBD) is well established; however in some patient dose needs to be intensified in order to maintain remission. We aimed to determine predictors and frequency of anti-TNF dose escalation and de-escalation in patients treated with infliximab or adalimumab for ulcerative colitis (UC) or Crohn's disease (CD).
AIMS & METHODS: Since September 2010, all consecutive patients treated with infliximab or adalimumab for active Crohn's disease or ulcerative colitis at the IBD clinics of the two participating centers (both tertiary referral hospitals) were prospectively included in this cohort study. All patients were anti-TNF

naïve, while concomitant azathioprine was administered for 6 months. The outcome of anti-TNF therapy was consequently evaluated every 2 months throughout the follow up period. Secondary loss of response was defined in those patients who initially responded to anti-TNF therapy and subsequently lost clinical response. Patients were considered to initially respond to anti-TNF therapy if they experienced a clear improvement in symptoms and drop in CRP if elevated at baseline at week 6 through week 14. Absence of primary response precluded the patient from further analysis. Patients were considered to lose response if symptoms reappeared and CRP re-elevated at any time period after the first 14 weeks of anti-TNF therapy. For patients losing response, anti-TNF dose escalation was scheduled. During the follow up period and after 1 year of intensified administration, anti-TNF was de-escalated in patients in remission (absence of symptoms, normal CRP).
RESULTS: During the study period 161 IBD patients (CD = 133, UC = 28) were started on infliximab (n = 96) or adalimumb (n = 65) in the participating centers; however 29 (18.0%) did not respond to therapy (absence of primary response) and were excluded from further analysis. From the remaining 132 patients (CD = 113, UC = 19, infliximab = 77, adalimumab = 5), 31 (23.5%) needed a dose escalation for maintenance of remission (CD = 30, UC = 1), during the median follow up period of 26 months (range 2 to 36 months). Factors associated with the need for anti-TNF dose escalation were azathioprine discontinuation earlier than 6 months in all patients and smoking in CD patients. Most patients achieved clinical remission (n = 25, 80.6%) without any other intervention and among them, 16 (64%) were successfully de-escalated to the standard maintenance infliximab or adalimumab dose schedule, after 1 year of intensified anti-TNF administration.
CONCLUSION: A substantial number of UC and CD patients (23.5%) initially responding to anti-TNF therapy required dose escalation to maintain disease remission. Factors associated with anti-TNF loss of response were discontinuation of azathiorpine co-administration earlier than 6 months in all patients and smoking in Crohn's disease patients. Dose escalation was successful in 80.6% of the patients studied and among them dose de-escalation was possible in 64%, after 12 months of intensified anti-TNF administration
Disclosure of Interest: None declared

P0917 THE IMPACT OF ANTI-TNF THERAPY AND SURGERY ON PERIANAL CROHN'S FISTULAS

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INTRODUCTION: The management of perianal Crohn's fistulae represents a significant challenge. Combination medical and surgical therapy, guided by radiology is often required. The aim of this systematic review and meta-analysis is to assess healing rates between medical treatment (anti-TNF-a therapies +/- immunomodulators) or surgical treatment alone compared to combined medical and surgical treatment in fistulating Crohn's Disease (CD).
AIMS & METHODS: This review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent reviewers searched PubMed (January 1966 to January 2014), the Cochrane Database, and EMBASE (January 1980 – January 2014). All studies investigating anti-TNF-α therapy combined with surgery as a treatment for Crohn's perianal and rectovaginal fistulas were included. Meta analysis was carried out using a random effects model. Odds ratios and confidence intervals were generated.
RESULTS: A total of 24 articles were included. Six were amenable to quantitative data synthesis and were meta-analysed. The total population was 1138 patients; 460 (40.4%) received single treatment with either biological or surgical therapy, and 682 (60%) received combined biological and surgical therapy. Forty four percent of the patients were male (n = 503) and 48.6% were female (n = 553). Across the studies, the mean age ranged from 28 years to 46 years of age. Similarly the median age reported, ranged from 25 years to 43 years old. The mean follow up ranged from 2.5 to 68.8 months whilst the median was 8 to 62.5 months.
Within the six studies, the total population was 686 patients (single therapy, n = 382, combination therapy n = 304). In the single therapy group (either biologics alone or surgery), out of 382 patients, 184 patients were in complete remission (48.2%). This was lower than the healing rate of the combined therapy group 170/304 (56.0%). Patients who had single therapy were less likely to go into complete remission when compared with the combination therapy group (OR 0.69, CI 0.50-0.95, p = 0.02).
CONCLUSION: Combined surgical and anti-TNF-a therapy has an additional beneficial effect on perianal fistula healing in patients with Crohn's disease, compared with surgery or medical therapy alone. A well-designed Crohn's perianal fistula clinical trial is required in a multidisciplinary medical and surgical setting with clearly defined end points of clinical and radiological healing.
Disclosure of Interest: None declared

P0918 LONG TERM OUTCOMES OF ANTI-TNF THERAPY FOR FISTULISING PERIANAL CROHN'S DISEASE

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INTRODUCTION: Fistulising perianal Crohn's disease (CD) is a challenging condition to treat and a multidisciplinary approach to treatment is required. Little is known regarding long-term efficacy of anti-TNF therapy for this group of patients.
AIMS & METHODS: We evaluated the clinical and radiological outcomes and the effects of biological therapy on our cohort of CD patients.
A database of 173 consecutive patients with Crohn's disease treated at our institution between 2005 and 2014 was established. Data on patient demographics and relevant outcomes were collated from medical, electronic and radiological reports. Chi-Squared, Cox regression and binary logistic analysis were used for statistical analyses.
RESULTS: Patients received Infliximab therapy (61%), Adalimumab therapy (6%) or switched between the two (33%) for the treatment of perianal fistulas. Forty-five percent of the patients were male and 55% female, with 13.5% being current smokers and 68% previous smokers. A fistula diagnosis and treatment occurred in 8% of patients prior to Crohn's diagnosis with a 10-year gap between a diagnosis of fistula and a diagnosis of CD in 65% of patients. Montreal classification identified that 40% of patients had L1 disease, 76% L2, 28% L3 and 2% L4, and 3.5% had perianal disease only. Proctitis was noted in 36% of patients.
At the start of anti-TNF therapy, 32% of patients had a simple fistula, 68% had a complex fistula at the baseline MRI. Combined therapy with thiopurines was observed in 58% of patients. Seton drainage was performed for 51% of patients at the start of anti-TNF therapy.
Overall, after a median follow-up period of 52 months (range 1-163), 32% of patients were in clinical remission, 74% of patients had a clinical response to treatment and the recurrence rate after remission was 12%. Radiological remission was noted in 14% of patients, response in 62% of patients and recurrence of 4.7% over a median of 37 months (range 3-101) MRI follow-up.
With regards to complexity of fistula, Cox Regression analysis demonstrated that clinical remission was seen in 47% of patients with a classification of a simple fistula, and 22% of those with a complex fistula ($p < 0.01$). Radiological remission however was noted in 28% of patients with a simple fistula and 5% of those with a complex fistula ($p < 0.01$). Factors influencing the time to clinical response were fistula duration ($p = 0.03$), and the concomitant use of immunomodulators ($p = 0.02$).
Multivaraite binary logistic regression revealed that patients who have a Montreal classification of L1 disease are 64% less likely to achieve clinical remission (OR = 0.36, CI = 0.17-0.79 p = 0.01), and those who have L3 disease are 60% less likely to achieve remission (OR = 0.40, CI = 0.17-0.93, p = 0.03). Having proctitis at the start of biological therapy predicts a 60% decrease in the likelihood of clinical remission in this group of patients (OR = 0.40, CI = 0.16-0.98, p = 0.04).
CONCLUSION: About three-quarters of patients with fistulising perianal Crohn's disease had clinical response to biological therapy, whereas two-thirds had a radiological response. Fistula complexity and the presence of ileal and ileocolonic disease were predictors of a worse clinical and radiological outcome. Radiological remission is an important outcome measure to assessment in predicting sustained fistula healing.
Disclosure of Interest: None declared

P0919 ANAEMIA DEVELOPS IN PATIENTS FOLLOWING ILEOANAL POUCH ANASTOMOSIS (IPAA): A SINGLE CENTRE STUDY REVIEW OF IPAA PATIENTS

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INTRODUCTION: Anaemia is reported in 17% of patients following IPAA[1]. However, few studies specifically report the prevalence of iron deficiency anaemia (IDA) following IPAA: One small study of 18 patients report 56% developed IDA[2]. There are no specific guidelines on investigating IDA in IPAA.
AIMS & METHODS: Retrospective demographic and pre and post-operatively medical data from IPAA patients at the Royal Free Hospital was collected to analyse the frequency of anaemia, specifically IDA, and its subsequent investigation and treatment. Anaemia was defined as Haemoglobin (Hb) < 13g/dL for males or <12g/dL for females; iron deficiency defined using CRP adjusted ferritin.
RESULTS: 80 patients (51% [41] male), median age 38 years (range 19 to 74) were included. Pre-operatively all 80 had a diagnosis of ulcerative colitis (UC), although subsequent histological analysis was most consistent with Crohn's Disease in 5% [4/80] and Indeterminate Colitis in 2.5% [2/80]. Median age at diagnosis 17.5 years, and median age at pouch formation 28 years.
16% [13/80] were anaemic pre-operatively, while 64% [51/80] developed anaemia within a 6 month period post-operatively. 53% [42/80] patients were iron deficient and 21% [17/80] patients had IDA post-operatively. Most (76% [13/17]) were treated with either oral or parenteral iron. 82% [14/17] were investigated with sigmoidoscopy, 29% [5/17] with OGD, 65% [11/17] had a TTG checked and 29% [5/17] with video wireless capsule endoscopy. 94% [16/17] had pouchitis.
CONCLUSION: We report that anaemia develops many months post IPAA in a large proportion of patients. Many patients are iron deficient and some have IDA. IDA was well treated, but investigated predominantly with only sigmoidoscopy; invariably pouchitis was discovered and felt to be the aetiology of IDA. We suggest that there is a need for further research into the mechanisms of anaemia following IPAA. IDA, even when pouchitis is discovered, should still be investigated following BSG guidelines, given 20% of patients will have dual pathology.
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Disclosure of Interest: None declared

P0920 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR DYSPLASTIC LESIONS IN LONG-STANDING ULCERATIVE COLITIS: LESION DEFINITION AND CURATIVE RESECTION

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INTRODUCTION: Long-standing inflammatory bowel diseases (IBD) are associated to an increased risk of dysplasia and cancer, and proctocolectomy is recommended for flat dysplasia and dysplastic lesions associated with dysplasia in the surrounding flat mucosa (DALM) due to the risk of synchronous / metachronous advanced cancer. Contrary to resection by snare, endoscopic submucosal dissection (ESD) achieves curative resections with wide margins of normal mucosa regardless lesion size and submucosal (SM) fibrosis.
AIMS & METHODS: To assess ESD feasibility of curative resection of IBD dysplastic lesions and differentiate DALM from sporadic adenomatous-like mass (ALM). From May 2011, consecutive patients with long-standing (>8 yrs) extended ulcerative colitis (UC) and a superficial dysplastic lesion within the colitic mucosa were prospectively enrolled. Dysplastic lesions were characterized by chromoendoscopy (CE) with indigo-carmine 0.4% and acetic acid 1%, and narrow band imaging (NBI) with no magnification. ESD was performed according to the standard technique. Mucosal incision was planned at >5 mm from lesion margins. SM fibrosis was graded from 0 to 2. Follow-up with pan-CE colonoscopy was planned every 6 months after curative resection (low-risk for lymph node metastasis after en bloc R0 resection).
RESULTS: Five patients with 6 lesions were included. Patient mean age was 63 (55-69), UC duration 13 yrs (9-22). Lesion morphology was LST-G homogeneous type in 3, LST-NG flat type in 3. Lesions were located in the right, left colon, and rectum in 3, 2, and 1, respectively. Median diameter was 28 mm (20-40). The rectal lesion had a wide scar from previous transanal endoscopic microsurgery. Acetic acid CE permitted to better delimitate lesion margins; peripheral markings were used in two cases. SM fibrosis was observed in 3 cases during dissection. ESD achieved en bloc, R0 and curative resection in 5 (83%) cases, and failed in the rectal case. Histology showed a T1 cancer with SM-slight invasion in 1 case. Wide margins of normal mucosa were achieved in all successful ESD cases with no flat dysplasia. No complication occurred. No advanced cancers or flat dysplasia on random biopsies were observed within a follow-up of 20 months (16-36).
CONCLUSION: Delineation of IBD dysplastic lesion margins is difficult and requires a multimodal CE approach. The ESD en bloc R0 resection of IBD dysplastic lesions with wide margins of normal mucosa is feasible and permits to accurately differentiate DALM from ALM with important clinical implications.
Disclosure of Interest: None declared

P0921 INTESTINAL SURGERY FOR CROHN'S DISEASE: ROLE OF PREOPERATIVE THERAPY IN POST OPERATIVE OUTCOME

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INTRODUCTION: Patients affected by Crohn's disease (CD) require life-long medical therapy but they can also often require abdominal surgery. The effect of CD therapy on postoperative course is still unclear. The aim of this study was to evaluate the effect of preoperative medical therapy on the outcome of intestinal surgery in these patients.
AIMS & METHODS: Data from a consecutive series of 186 patients with CD operated on at the University of Padova Hospital form 2000 to 2013 were retrieved. Data of their preoperative therapy during the 6 months before surgery were available for 146 patients who were enrolled in this retrospective study. Clinical data and surgical details were retrieved and postoperative complications and reoperation were considered outcome measures. Univariate and multivariate analysis were performed.
RESULTS: No significant difference was observed between patients without data about their preoperative therapy and those with them. Eight patients underwent reoperation in the first 30 postoperative days: two of them for anastomotic leak, three for bleeding, one for obstruction and two for abdominal wound dehiscence. At multivariate analysis preoperative adalimumab and budesonide resulted to be an independent predictor of reoperation (OR = 7,67 (95%CI = 1,49-39,20), p = 0.01 and OR = 6,7749 (95%CI = 0.98-46,48), p = 0.05, respectively). At multivariate analysis neither pharmacological nor clinical variables resulted to predict anastomotic leak.
CONCLUSION: In our series, adalimumab but not infliximab seemed to be associated to early reoperation after intestinal surgery. This may be due to a worst disease severity in patients who needed surgery in spite of biological therapy. Preoperative tapering of budesonide dose seems a safe option before elective abdominal surgery for CD.
Disclosure of Interest: None declared

P0922 LONG-TERM OUTCOME OF TERMINAL ILEOSTOMY IN CROHN'S DISEASE (CD) PATIENTS AT THE ERA OF BIOLOGICS. A RETROSPECTIVE SINGLE CENTRE STUDY

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INTRODUCTION: Anti-TNF antibodies (mAbs) significantly changed CD treatment strategy. However, despite their efficacy, several patients failed all available medical therapy and require surgery, in some cases coloproctectomy with terminal ileostomy. By contrast to ileocolonic resection with ileocolonic anastomosis where postoperative relapse risk factors are known, for terminal ileostomy - often considered as at low risk of recurrence, such factors have not been clearly identified.
AIMS & METHODS: We aimed to analyze the long-term outcome of CD patients with terminal ileostomy and to try to find predictive factors of relapse, since anti-TNF mAb were largely used.
All patients with coloproctectomy/terminal ileostomy performed between 1995 and 2010 were considered for this single center study (to ensure homogeneity of the studied group, with a same treatment and follow-up strategy). The following items were recorded: demographic, clinical, biological and therapeutic patients characteristics, frequency and characteristics of disease relapse after ileostomy (defined by the association of clinical symptoms, at least one endoscopic or radiologic result confirming CD relapse, and the need to introduce/change a medical treatment), factors potentially predictive of relapse (including anti-TNF mAb use previous to surgery). Statistical significance was set at $p < 0.05$.
RESULTS: The charts of 1414 patients were reviewed. 51 CD patients with terminal ileostomy were found. Nine were excluded from analysis (5 lost for follow-up, 4 with discharge ileostomy). Among the remaining 42 patients, 23.8% relapsed. Recurrence at 5 and 10 years was of 21.7 and 30.7% respectively, with a mean delay between ileostomy and the first recurrence of 36±37 months (mean follow-up: 8±5 years). 42.9% of patients needed at least one new surgical procedure (for ileostomy complications or CD relapse). Anti-TNF mAb treatment before terminal ileostomy (n = 20/42) did not change the risk to need terminal ileostomy despite ileostomy was performed at a younger age in these patients (40.6±10.6 vs. 51.5±10.6 years; p = 0.01). Multivariate analysis showed that age at ileostomy [Hazard ratio (HR): 0.92 - 95% confidence interval (95% CI): 0.84-1; p = 0.05), presence of granuloma at resection (HR: 6.31 - 95% CI: 1.49-26.75; p = 0.01) and ongoing smoking after ileostomy (HR: 9.11 - 95%CI: 2.19-37.83); p = 0.01) were independent factors associated to CD relapse after ileostomy.
CONCLUSION: In conclusion, despite an increasing use of anti-TNF mAb for CD treatment, long-term CD relapse after terminal ileostomy occurred in 24% of patients. We identified three factors being predictive of risk of recurrence. Among those, presence of granulomas on resected tissue at the time of ileostomy and continuing smoking after ileostomy may allow to identify patients at high relapse risk. These patients are susceptible to need a close long-term postoperative surveillance.
Disclosure of Interest: R. Akrimi-Molière: None, V. Juif: None, L. Dupont-Kazma: None, N. Herraney: None, J.-M. Reimund: None, B. Duclos: None

P0923 ENDOSCOPIC BALLOON DILATION OF STRICTURES IN CROHŃS DISEASE PATIENTS: SAFE AND EFFECTIVE ALTERNATIVE TO REPEATED SURGERY

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INTRODUCTION: Endoscopic balloon dilation is frequently used to avoid repetitive surgery in patients with Crohńs disease.
AIMS & METHODS: The aim was to evaluate efficacy and safety of endoscopic balloon dilations in patients with Crohńs disease-related strictures. This was a retrospective study in patients who underwent endoscopic balloon dilation between May 2007 and December 2013 at a single tertiary IBD center. We assessed both short- and long-term efficacy and safety of this procedure as well as relationship between efficacy and specific disease and patients´characteristics.
RESULTS: We performed 220 dilations in 108 patients with Crohńs disease (49 women, median age 37 years, range 13-75), majority of procedures (85%) were performed in anastomotic strictures. Obstructive symptoms preceded only 53% of dilations, remaining procedures were either coincidental, or resulted from regular endoscopic check-up. Technical success (passage with endoscope through the stricture after dilation) was achieved in 77% of procedures, 75% of dilations were effective clinically (relief of obstructive symptoms). Median duration of symptomatic relief was 10 months (range 1-59). Significantly more patients with end-to-end anastomosis lost their obstructive pain after dilation as compared to those with end-to-side anastomosis (89% vs. 61%, resp., p = 0.01, Fisheŕs exact test). In contrary, patients with end-to-side anastomosis had significantly longer clinical effect (median duration 17 months, range 3-55) compared to patients with end-to-end anstomosis (median duration 10 months, range 1-38, p = 0.006, Mann-Whitney test). Technical success was associated with longer duration of symptomatic relief. We have not found any relationship between age, smoking or medical therapy at the time of procedure, and clinical efficacy of dilation. Mild bleeding occured after 9% of dilations, it was stopped

endoscopically in all cases. Serious complications, such as delayed bleeding or perforation were rare (2%), and no patient died.
CONCLUSION: Endoscopic balloon dilation is highly effective and safe therapeutic modality of Crohńs disease-related strictures, especially when the passage of the scope is achieved. Effectiveness of dilation seems not to bee associated with medical treatment.
Acknowledgement: The study was supported by IBD-COMFORT Foundation.
Disclosure of Interest: None declared

P0924 FACTORS AFFECTING THE INCIDENCE OF AN EARLY ENDOSCOPIC RECURRENCE AFTER ILEOCOLONIC RESECTION FOR CROHN'S DISEASE: A MULTICENTRE STUDY

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INTRODUCTION: An early endoscopic recurrence is frequently observed in patients following resection for Crohn's disease (CD). However, factors affecting the incidence of an early endoscopic recurrence have not been fully determined.
AIMS & METHODS: The aim of this study was to evaluate risk factors for an endoscopic recurrence after ileocolonic resection for CD. This was a retrospective, international multicentre study. All consecutive patients who underwent ileocolonic resections for CD in 7 IBD referral centres from 3 countries (Japan, Brazil, Italy) were initially included in our MULTIPER database. In this study, 127 patients with the first ileocolonoscopy conducted between 6 and 12 months after resection were included. The endoscopic activity score at the proximal site of the ileocolonic anastomosis was determined according to Rutgeerts, and an endoscopic recurrence was defined as a Rutgeerts sore of $\geq$ i2. The following variables were investigated as potential risk factors for an early endoscopic recurrence: sex, age at surgery, location and behaviour (perforating vs non-perforating) of CD, smoking, concomitant perianal lesions, preoperative use of steroids, immunosuppressants and biologics, previous resection, blood transfusion, surgical procedure (open vs laparoscopic), length of resected bowel, type of anastomosis (side-to-side vs end-to-end), postoperative complications, granuloma, and postoperative biologic therapy. To identify risk factors for an endoscopic recurrence, both univariate and multivariate analyses were conducted.
RESULTS: Forty-three patients (34%) developed an endoscopic recurrence which was confirmed at the time of ileocolonoscopy between 6 and 12 months after resection. In the univariate analysis, only preoperative steroid use was significantly associated with a higher rate of an early endoscopic recurrence. Twenty-one of 45 patients (47%) on steroids and 22 of 82 patients (27%) without steroids developed an endoscopic recurrence ($p = 0.04$). In the multivariate analysis, no factors were associated with the incidence of an endoscopic recurrence.
CONCLUSION: This study failed to find any significant factors associated with an endoscopic recurrence after ileocolonic resection for CD. However, prospective studies are necessary to precisely evaluate the impact of perioperative medications on an early endoscopic recurrence.
Disclosure of Interest: None declared

P0925 HAND-ASSISTED LAPAROSCOPIC VERSUS OPEN COLECTOMY FOR ULCERATIVE COLITIS: SAFETY AND FEASIBILITY

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INTRODUCTION: Laparoscopic surgery is now becoming widely used in the management of colorectal cancer. However, safety and feasibility of laparoscopic colectomy for ulcerative colitis (UC) have not been fully evaluated.
AIMS & METHODS: Since 2005, we have introduced hand-assisted laparoscopic surgery (HALS) for patients with UC and extensive Crohn's colitis. This study was to assess safety and feasibility of HALS for UC. Seventy UC patients were treated with HALS (HALS group). The outcomes of HALS were compared with those of open surgery conducted for 70 age-, sex- and disease severity-matched patients (OPEN group).
RESULTS: In both groups, 37 elective patients were treated with a total proctocolectomy and ileal pouch-anal (canal) anastomosis with a loop ileostomy, and 33 emergency patients with a total colectomy (rectal closure) with an end-ileostomy. In the HALS group, intra-operative complications were experienced in two patients (duodenal injury 1, colonic perforation 1). None of the patients required conversion to open procedure, and laparoscopic procedure was successfully completed in all patients. In the HALS group, the mean operative time was 293 minutes, which was significantly longer than 258 minutes in the OPEN group. The mean intra-operative blood loss was not significantly different between the groups. Eighteen patients (26%) in the HALS group and 20 patients (29%) in the OPEN group experienced postoperative complications (not significant). Six patients in the HALS group and 7 patients in the OPEN group required laparotomy for postoperative complications (not significant).
CONCLUSION: Although HALS takes longer time as compared with open surgery, it can be safely conducted without conversion to open procedure. HALS is a feasible option in the surgical management of UC.
Disclosure of Interest: None declared

P0926 URGENT LOWER GASTROINTESTINAL BLEEDING: IS THERE A PLACE FOR COLONOSCOPY WITHOUT ORAL PREPARATION IN ELDERLY PATIENTS? – A SINGLE CENTRE EXPERIENCE

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INTRODUCTION: In urgent lower gastrointestinal bleeding (LGIB), bowel preparation for colonoscopy is highly influenced by logistic factors, patient tolerance and adverse reactions, particularly in elderly patients. In these cases a colonoscopy can be performed without preparation (WP) or after a cleansing enema (CE).
AIMS & METHODS: The aim of this study was to compare diagnostic accuracy of urgent colonoscopy WP and after CE in elderly patients. It was performed a retrospective study involving patients aged over 70 years with acute LGIB, submitted to colonoscopy WP and after CE, according to the gastroenterologist option, for a 6-month period. Cases with known inflammatory bowel disease or recent polipectomy were excluded. Data related with demographics, clinical information, colonic segment reached in the exam and diagnostic findings in the two groups were compared.
RESULTS: Seventy-four patients (mean age 81.6±6.6 years, 54.4% male) were included. Chronic medication: antiaggregants - 50.0%, anticoagulants - 10.8% and nonsteroidal anti-inflammatory drugs - 4.1%. Mean hemoglobin value at admission was 11.1±2.9g/dl and red blood cell transfusion was required in 24.3% patients. Colonoscopy was performed WP in 70.3% and after CE in 29.7%. Colonic segment reached: cecum - 5.4%, ascending colon - 2.7%, transverse colon - 12.2%, descending colon - 23.0%, sigmoid colon - 52.7% and rectum - 4.1%. Diagnostic findings: ischemic colitis - 29.7%, diverticula - 20.3%, hemorrhoids - 10.8% and neoplasia - 6.8%. There were no statistically significant differences between WP and CE colonoscopies regarding the colonic segment or diagnostic findings. Globally, including the diagnosis considered as definitive by the gastroenterologist, the diagnostic yield of colonoscopy without oral preparation, (WP and after CE) was 56.8%. Transfusion requirement at admission was an independent risk factor for absence of diagnosis, in both groups (OR 11.5; $p < 0.001$).
CONCLUSION: Comparing WP and post CE colonoscopy, there were no differences in the colon segment achieved or in endoscopic findings. Colonoscopy without oral bowel preparation showed to have a limited diagnostic yield. In more severe LGIB (with transfusion requirement) should be considered diagnostic colonoscopy after oral preparation ab initio.
Disclosure of Interest: None declared

P0927 PREDICTIVE FACTORS OF RECURRENCE AND MORTALITY IN LONG-TERM IN PATIENTS WITH COLONIC ANGIODYSPLASIA BLEEDING

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INTRODUCTION: Data on rates of recurrence and mortality throughout the course of colonic angiodysplasia are limited. The aim of this study is to determine rates and risk factors for recurrence and mortality in long-term in a cohort of patients.
AIMS & METHODS: In 2007, data from 2462 patients with lower gastrointestinal bleeding were collected prospectively in 102 french general hospitals; 79 patients (3.2%) bled on colonic angiodysplasia. We retrospectively studied in 2013 the follow up of these patients. Collected data were: rates of death and reccurence, taking anticoagulant and antiplatelets treatments, comorbidity Charlson's score, ischemic and valvular diseases. Data were obtained by contacting the referent gastroenterologist, the general practitionner and sometimes the patient. Predictive factors of recurrence and mortality were studied by univariate analysis.
RESULTS: Data of 46 patients (58.2% of the initial population) were collected; it was 22 women (47.8%). Six patients were excluded because of an early death, 13 patients were lost to sight and in 14 cases no data were available. The median duration of follow up was 3.3 years (OQR 25-75% :1.5-5.4 years). The average age of patients at the end of follow up was 76.8 +/- 9 years; 8 (17.4%) had a valvular disease. Twenty-three patients died (50%), including 4 from bleeding recurrence. Mortality rates at 1 year, 3 years et 5 years were respectively 19.6%, 34.8% and 43.5%. Eighteen patients (39.1%) had at least a bleeding recurrence. Reccurence rates at 1 year, 3 years and 5 years were respectively 19.6%, 34.8% and 39.1%. These reccurences were complicated by 4 deaths. One patient has needed an hemostatic colectomy. Seven patients (38.8% of recurrences) had to stop anticoagulant and antiplatelet treatments because of a recurrence, and 3 have developed after that an ischemic disease (2 strokes and one myocardial infarction). No risk factors of recurrence and mortality was found, especially taking anticoagulant and antiplatelets treatments or a valvular disease. Charlon's score was not higher in dead patients.
CONCLUSION: Bleeding colonic angiodysplasia are a rare cause of lower gastrointestinal bleeding and concern an elderly population. In this study, after a

median follow-up of 3.3 years, the cumulated rate of recurrence was 39.1% and the mortality rate was 54.3%. The continuation of antiplatelet and anticoagulant treatment is not associated with a higher risk of recurrence and conversely stopping aspirin may increase the risk of death because of ischemic diseases.
Disclosure of Interest: None declared

P0928 LONG-TERM FOLLOW-UP AND PREDICTIVE FACTORS OF REBLEEDING AND MORTALITY IN PATIENTS WITH DIVERTICULAR BLEEDING

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INTRODUCTION: Data on rates of recurrence and mortality in patients with diverticular bleeding (DB) are limited. The aims of this study were to determine rates and risk factors for recurrence and mortality in a large cohort of patients with previous DB.
AIMS & METHODS: In 2007, data from 2462 patients with lower GI bleeding were collected prospectively in 102 French general hospitals, 789 (32%) had DB. We retrospectively studied in 2013 the follow up of these patients. The following data were collected: recurrence and mortality rates, drug intake (anticoagulants, antiplatelet agents, NSAIDs), rate of surgery and comorbidities (evaluated by the Charlson's score). These data were obtained by contacting the gastroenterologist, the attending physician and sometimes the patient himself. Predictive factors of recurrence and mortality were studied by univariate and multivariate analyses.
RESULTS: Data of 365 patients (47.3 % of the initial population) were collected, including 181 women (49.6 %). Mean age of patients was 84.7±9.7 years. Median duration of follow-up was 3.9 years. Hundred forty eight patients died (40.5%) nine of them after bleeding. Mortality rate at 1, 3 and 5 years were 22 %, 36 % and 52 % respectively. Sixty-nine patients (19.2%) had at least one recurrent bleeding. Recurrence rate at 1, 3 and 5 years were 11 %, 21% and 30% respectively. Among patients with recurrence, 9 died (12.8 % mortality of recurrences) and 3 (4.3%) had surgical hemostasis procedure. Anticoagulation or antiplatelet therapy were discontinued in 17 (19.2%) cases.
Risk factors for mortality by multivariate analysis were: age > 80 years ($p < 0.001$) and a Charlson comorbidity score > 2 ($p = 0.003$). Discontinuation of anticoagulation or antiplatelet therapies was not associated with an excess risk of death by cardiovascular events.
No risk factors for rebleeding were identified in particular taking antiplatelet or anticoagulant therapy. A past history of DB was almost significant ($p = 0.078$).
CONCLUSION: In this population, cumulative recurrence rate was 19.2 % after a median follow up of 3.9 years, and the mortality rate of 40.5 %. The majority of deaths were not related to bleeding. Continuation of anticoagulant and antiplatelet treatment was not associated with an excess risk of rebleeding conversely discontinuation did not significantly increased mortality from ischemic injury.
Disclosure of Interest: None declared

P0929 OUTCOMES OF URGENT COLONOSCOPY IN PATIENTS WITH LOWER GASTROINTESTINAL BLEEDING

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INTRODUCTION: Early endoscopy is the standard of care in upper gastrointestinal bleeding. However most patients with lower gastrointestinal bleeding (LGIB) have favorable outcomes and majority will stop bleeding spontaneously. Therefore the role of urgent colonoscopy in LGIB remains controversial.
AIMS & METHODS: We wanted to study, diagnostic yield and clinical outcome of urgent colonoscopy in patients with Lower gastrointestinal bleed. We prospectively enrolled 140 consecutive patients who presented to our facility with lower gastrointestinal bleed. Study was conducted from January 2012 to December 2012. All patients who had malena, upper GI endoscopy was normal (was not source of bleed) were considered eligible for this study.
RESULTS: 120 urgent colonoscopies were performed for LGIB during study period. 70 (59%) were male. Mean age was 56.5 years and median age was 56.6 years (range 18:8 to 90.0 years). Caecal intubation rate was (60% n 70). 10% (n 12) of patients needed repeat colonoscopy due to inadequate visualization of bowel for definite clinical decisions. (25.0% n 30) had an endoscopic therapy done. 40% (n 12) of them altered the immediate clinical management. Causes were found in (60%n 70) of patients. However only 40% (n - 24) of them had endoscopic therapy and (60% n 46) had no clinical impact on immediate management of patients though the cause was identified. The causes were colorectal ulcers (n 30, 25%), diverticular disease (n 40, 34%), hemorrhoid (n 20, 17 %), colitis (n 20, 17 %), carcinoma (n 10, 8%).
CONCLUSION: Urgent colonoscopy for LGI bleed results in high rate of incomplete examinations. Even when causes were found, only half of them had an impact on the clinical management in terms of endoscopic intervention or change in immediate clinical decision. Therefore, decision to perform urgent colonoscopy for LGIB should be individualized, taking into consideration relative importance of timing of intervention versus colonic preparation and overall impact on Clinical management of patients.
Disclosure of Interest: None declared

P0930 ENDOSCOPIC BAND LIGATION FOR COLONIC DIVERTICULAR HEMORRHAGE: A LARGE CASE SERIES

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INTRODUCTION: Endoscopic band ligation (EBL) has been performed for haemostasis in colonic diverticular haemorrhage[1]. However, the number of the patients who have colonic diverticular haemorrhage and have been treated by EBL is not sufficient, and the safety and efficacy of EBL in the colon have not been fully established.
AIMS & METHODS: The aim of this study is to evaluate the safety and efficacy of EBL for colonic diverticular haemorrhage. EBL was applied as an initial treatment in 91 consecutive patients (67 males and 24 females; age range: 34-93 years) who presented between June 2009 and March 2014 with definitive colonic diverticular haemorrhage. This type of haemorrhage involves the diverticula with stigmata of recent haemorrhage (SRH) such as active bleeding (AB), non-bleeding visible vessels (NBVV), or adherent clots (AC). We retrospectively evaluated these patients to determine the success rates of EBL and the rates of early re-bleeding (re-bleeding within 30 days of the initial EBL) and to outline any complications such as perforation and abscess formation. Informed written consents for EBL were obtained from all the patients.
RESULTS:

Location in colon (right / left), no	68 / 23
SRH (AB / NBVV / AC), no	33 / 22 / 36
Success rate of EBL (%)	93 (85/91)
Median procedural duration (range) (min)	36 (15-101)
Rate of early re-bleeding after EBL (%)	15.3 (13/85)
Median time to early re-bleeding (range) (days)	2 (0-21)
Complications (%)	0 (0/85)

The results of performing EBL for colonic diverticular haemorrhage are presented in the table. The success rate of EBL was 93% (85/91). Five lesions that had a small orifice and large dome and one lesion with an orifice that was too large could not be adequately suctioned into the suction cup of the endoscopic ligator, and EBL was not successful. Endoscopic clipping or epinephrine injection was performed in these cases, and in one of the cases interventional radiology was also performed for haemostasis. The rate of early re-bleeding after EBL was 15.3% (13/85). Re-bleeding was managed conservatively and/or endoscopically (repeat EBL or endoscopic clipping) except in one case where a right hemicolectomy was performed because of the patient's preference. There were no complications such as perforation or abscess formation after EBL.
CONCLUSION: EBL can be considered to be a safe and effective endoscopic treatment for colonic diverticular haemorrhage.
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Disclosure of Interest: None declared

P0931 GI BLEEDING IN THE MODERN ERA - A 3-YEAR REVIEW AT TALLAGHT HOSPITAL

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INTRODUCTION: Gastrointestinal bleeding is a common clinical condition accounting for up to 13% of Gastroenterology referrals. It frequently requires hospitalization with subsequent intervention and is associated with significant morbidity and mortality. Determining the origin of bleeding can be a challenge. Newly available modalities in both gastroenterology and radiology are available to address obscure bleeding cases.
AIMS & METHODS: a) To examine the role of endoscopic and radiological investigations in a cohort with GI bleeding.
b) To assess the diagnostic performance of available radiological and endoscopic techniques in cases of GI bleeding, including obscure bleeding.
Methods:
A Retrospective analysis was undertaken of patients admitted with Gastrointestinal bleeding at Tallaght Hospital from 2010-2013 via HIPE (Primary discharge diagnosis – Malaena, Haematemesis, Gastrointestinal haemorrhage or IDA due to bleeding). Discharge summaries were reviewed and patients were excluded if they were <18 yrs or had no evidence of bleeding. All radiological and endoscopic investigations were identified from cross-referencing with ''Keogh'' Radiology, Capsule Endoscopy (CE) and Unisoft Endoscopy Reporting Systems. Outpatient investigations were included if prompted by the index admission. Patient demographics, procedures and positivity rates for the various modalities were recorded
RESULTS: In all, 418 patients were identified from HIPE, 106 (25%) were excluded following discharge review. Of the 312 remaining cases the majority were male 176 (56%) with a mean age of 59 years (Range 18-97). In all 294 (94%) presented with overt bleeding vs 18 (6%) with occult bleeding. Of note 18 (6%)

underwent no investigation for bleeding. Of the 294 who had tests, 163 (55%) had either a colonoscopy or OGD and 122 (41%) had both and 39 (13%) proceeded to have additional endoscopic tests, CE and/or Enteroscopy. In all 110 (37%) had a specialized radiological test. After any investigation, 122 (41%) had negative tests with no etiology found. While 77 (26%) had obscure GI bleeding defined as a negative gastroscopy and colonoscopy. In this obscure cohort, only 26 (34%) had 2nd line GI Investigations and disregarding standard CT, only 27 (35%) had a specialized radiological test. Overall 66 (22%) remained obscure despite all investigations. The frequency of investigations by type and positivity rate is illustrated in table 1. Diagnostic yield was highest for standard endoscopy at 48% OGD and 28% Colon whilst also significant for CE (31%), Enteroscopy (50%) and Angiography (50%).
CONCLUSION: Obscure GI bleeding remains common (26%) and the diagnosis often remains elusive despite advanced endoscopic and radiological tests. The diagnostic yield for many commonly employed less specific modalities is poor and suggests changes to the diagnostic paradigm are appropriate.
Disclosure of Interest: None declared

P0932 HOW TO DETERMINE THE NEED FOR EMERGENCY COLONOSCOPY TO ACHIEVE TIMELY HEMOSTASIS OF LOWER GI BLEEDING

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INTRODUCTION: We occasionally perform endoscopic hemostasis during emergency colonoscopy for lower gastrointestinal (GI) tract bleeding, but endoscopic hemostasis is not always necessary. Making the correct decision about the need for emergency colonoscopy is very important from the perspective of preparation and examination time.
AIMS & METHODS: To investigate how to determine the need for endoscopic hemostasis in cases of lower GI bleeding, 241 cases of lower GI bleeding (excluding post polypectomy bleeding) that underwent CT and emergency colonoscopy between January 2008 and February 2014 were reviewed retrospectively. Glasgow-Blatchford scores (usually used in upper GI bleeding) and the results of CT and colonoscopy were analyzed. The indications for hemostasis were active bleeding, a visible vessel, and adherent clot.
RESULTS: High-frequency colonic bleeding sources included diverticular bleeding (122 cases, 51%), ischemic colitis (52 cases, 22%), and rectal ulcer (15 cases, 6%). Hemostasis was required in 41 (17%) cases. CT findings consisted of extravasation of contrast medium showing active bleeding (group A; 23 cases) and colonic wall thickening showing inflammation (group C; 47 cases). Group B was defined as neither extravasation nor wall thickening (171 cases). Endoscopic hemostasis was performed in 83% of group A (19/23), 13% of group B (22/171), and none of group C. The Glasgow-Blatchford scores without melena were significantly higher in hemostasis cases (7.6 ± 3.8) than in no hemostasis cases (4.3 ± 4.0) ($P<0.01$). Scores of hemostasis cases varied from 1 to 15, and 37 of 41 hemostasis cases had scores of four or more, whereas 109 of 200 of no hemostasis cases had scores of three or less ($P<0.01$). If one takes both group B cases with scores of three or less and group C cases as non emergency cases, there were 119 non-emergency cases. Of these, 116 (97%) were actually no hemostasis cases, that is, use of this criterion would avoid emergency colonoscopy in 58% of no hemostasis cases. The remaining three hemostasis cases all had slight bleeding.
CONCLUSION: CT findings and Glasgow-Blatchford scores are useful for determining the need for emergency colonoscopy to achieve timely hemostasis of lower GI bleeding.
Disclosure of Interest: None declared

P0933 LONG-TERM FOLLOW-UP STUDY ON THE RECURRENCE OF PATIENTS HOSPITALIZED FOR ACUTE LOWER GASTROINTESTINAL HEMORRHAGE

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INTRODUCTION: Long-term recurrence in lower gastrointestinal bleeding (LGIB), particularly benign diseases, has not been extensively studied. This study aimed to ascertain the rate of recurrence in LGIB and associated risk factors.
AIMS & METHODS: A cohort of 312 patients hospitalized for overt LGIB from benign sources was analyzed. All patients underwent colonoscopy. The Charlson comorbidity score and the use of non-steroidal anti-inflammatory drugs (NSAIDs), low-dose aspirin, other antiplatelet drugs, and warfarin were assessed. The Kaplan–Meier method was used to estimate the cumulative recurrence of LGIB. The Cox proportional hazards model was used to estimate hazard ratios (HR).
RESULTS: Rebleeding was identified in 84 patients with a mean (SD) follow-up of 19 (22) months. The cumulative rebleeding rate at 1 and 5 years was 21% and 51%, respectively. Associations with recurrence by univariate analysis were as follows: age ≥65 years ($p<0.01$), Charlson comorbidity index ≥2 ($p<0.05$), and the use of NSAIDs ($p=0.02$), low-dose aspirin ($p=0.03$), non-aspirin antiplatelet drugs ($p<0.02$) and warfarin ($p=0.59$). Multivariate analysis revealed age ≥65 years (HR, 1.9; $p=0.02$) and the use of NSAIDs (HR, 1.8; $p=0.03$) and non-aspirin antiplatelet drugs (HR, 2.0; $p=0.02$) as independent risk factors for rebleeding. Dual antiplatelet therapy carried a higher risk than single therapy (adjusted HR, 1.8; $p<0.05$).
CONCLUSION: There is a substantial recurrence rate among patients hospitalized for LGIB. Besides advanced age, various antithrombotic drugs increased the risk of recurrence in LGIB. Dual users of those drugs have a higher risk than single users.
Disclosure of Interest: None declared

P0934 WHAT FACTORS ARE RELATED TO DEATH FROM INTESTINAL ISCHEMIA IN THE PATIENTS WITH RENAL FAILURE UNDERGOING CONTINUOUS HEMODIALYSIS?

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INTRODUCTION: It has been reported that end-stage renal disease (ESRD) patients on hemodialysis (HD) were at risk for intestinal ischemia (II). Some severe cases of II die from transmural gangrenous necrosis of the intestine. Other mild cases develop ulceration and colitis, and can be treated with conservative management. In this study, we tried to identify factors associated with death from II in patients on HD.
AIMS & METHODS: Approximately 2,500 patients at our dialysis clinics underwent HD three times weekly from January 2009 to October 2013. The diagnosis of II, which includes mesenteric ischemia, non-occlusion mesenteric ischemia, and ischemic colitis, was made from endoscopy, pathology, computed tomography, ultrasound findings, and/or clinical condition. The subjects were divided into two groups of the fatal II group and the non-fatal II group. The latter included some who died from other causes than II. Continuous variables were compared by *t*-test, while qualitative variables by Fishers exact test.
RESULTS: Twenty-six of 2,500 longterm HD patients developed II for the first time during the study period. The fatal and the non-fatal group consisted of 7 and 19 subjects, respectively. Six of the non-fatal group died from the following causes: cerebral hemorrhage, infective endocarditis, heart failure, pneumonia, suicide, and unknown. The frequencies of those who had each of warfarin and laxative were higher in the fatal group than in the non-fatal (57.1% vs 5.26%, respectively, $p=0.01$). Two fatal cases used both of the drugs. Then, we needed avoid the effect of laxative on II, to focus on the effect of warfarin only. After removal of the two, the corresponding result still remained to be significant (66.7% in the fatal vs 5.56% in the nonfatal, $p=0.04$). Three of 4 who had warfarin suffered from atrial fibrillation (Af) in the fatal group. In the non-fatal group, 3 had Af but 1 of them took warfarin. There was no significant difference in the frequency of Af between the two groups. The fatal group more frequently underwent laparotomy than the non-fatal (42.9% vs 5.26%, respectively, $p=0.05$). Regarding the location of II, 71.4% of the fatal group developed the ischemic colitis on the right-sided, while 5.26% of the non-fatal on the right-sided ($p<0.01$).
CONCLUSION: This study showed that there was a possibility that warfarin causes the fatal II regardless of Af, as well as laxative. Therefore, considering the previous reports that warfarin provokes calciphylaxis on ESRD, warfarin could facilitate ischemia based on calcification of the feeding-artery. In addition, the fatal group involved the right-sided colon, and undertook laparotomy more frequently as the previous studied reported. Further studies with larger number of the subjects are required to confirm our results.
Disclosure of Interest: None declared

P0935 COMPARISON OF MICROWAVE COAGULATION WITH MONOPOLAR AND BIPOLAR COAGULATION IN A PORCINE MODEL

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INTRODUCTION: Intra-procedural bleeding is considered an immediate serious adverse event and a major concern for the endoscopist and the patient. Current endoscopic devices utilise monopolar or bipolar energy to treat acute bleeding vessels and/or pre-coagulate visible vessels. Monopolar/Bipolar devices have proven safe in clinical practice to control acute arteriolar bleeding but there are no ex vivo comparative studies assessing the safety profile with histology.
AIMS & METHODS: The optimal time of application for the microwave modality of a new endoscopic device "Speedboat-RS2, Creo Medical Ltd, UK" was initially assessed compared to a standard mono-polar endoscopic device, Coagrasper, Olympus, USA. After histological assessment of the optimal time range, a comparison of the Speedboat RS2 to a standard bipolar endoscopic device, Gold Probe, Boston Scientific, USA, and to standard monopolar device, Coagrasper, was performed to assess the safety profile of coagulation with histology and the endoscopic performance of pre-coagulation in the porcine colon. The Speedboat-RS2 blade delivers microwave coagulation (5.8GHz) for hemostasis, and also has an insulated hull to prevent thermal injury to the underlying muscle layer. Cold snare polypectomy (9mm) was performed to reveal the submucosal layer and video recorded on 3 consecutive 60kg pigs. The colonic resection sites were aligned in cranial-caudal direction. The following parameters were measured: histological assessment and pre-coagulation endoscopic performance. All animals were recovered for 2days, 5days and 7days.

RESULTS: In animal one, microwave bursts of 5sec, 10sec and 15sec were applied to the revealed submucosa compared to standard monopolar bursts of a 1sec. Histology showed that 5sec and 10sec of microwave has equivalent histological appearance with standard monolopar preserving the serosal integrity with mild muscle alteration. In animal 2 and 3, microwave was applied for 9 sec in 6 lesions, standard monopolar was applied for 1-2sec in 6 lesions and standard bipolar was applied for 3-4sec in 6 more lesions. Histology showed viable serosa with no muscle alterations in microwave group, viable serosa with mild muscle alterations in standard bipolar and viable serosa with mild/moderate muscle alterations in standard monopolar group. In all cases muscle layer cells were contiguous. During the pre-coagulations endoscopic assessment, all modalities were applied to coagulate vessels with median calibre of 2mm before and after dissection. Effective pre-coagulation was achieved in 3 out of the 6 visible vessels (microwave group) and in 2 out of the 6 visible vessels (standard monopolar and bipolar groups). Effective coagulation (defined when blood flow stopped) was achieved after the dissection, in all three groups.
CONCLUSION: Compared to Coagrasper (monopolar) and Gold Probe (bipolar), the microwave modality of Speedboat RS2 appears to be equivalent during the pre-coagulation phase. The safety profile of coagulation phase resembles the profile of the other two modalities but with less muscle alterations in the histological specimens.
Disclosure of Interest: Z. Tsiamoulos Consultancy for: Creo Medical Ltd, C. Hancock Shareholder of: Creo Medical Ltd, P. Sibbons Consultancy for: Creo Medical Ltd, B. Saunders Consultancy for: Creo Medical Ltd

P0936 BPREDICT: BURGENLAND PREVENTION TRIAL OF COLORECTAL DISEASE WITH IMMUNOLOGICAL TESTING

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INTRODUCTION: Colorectal cancer (CRC) is the third most common cancer and cause of cancer death in Europe and continues to be among the most severe health problems in the EU. In Austria, 4,600 new cases are diagnosed per year. Ten years ago there used to be a remarkable east west decline in CRC incidence with the highest incidence rates in Burgenland, a province in the very east of Austria, with about 300.000 inhabitants. Therefore, 2003 the screening project Burgenland PREvention trial of colorectal Disease with ImmunologiCal Testing (bPREDICT) was initiated.
AIMS & METHODS: This screening project utilizing fecal immunochemical testing (FIT) was first implemented in the district Oberpullendorf in 2003. Since 2006, the screening program has been expanded to the whole province Burgenland. Between 2003 and 2010, a qualitative fecal occult blood test was applied. Since 2010 this test was replaced by a quanitiative FIT test (OC sensor, Mast Diagnostica Germany).
Annually, 150.000 residents aged between 40 and 80 (50% of the population) receive a stool sample container and are invited to take part in bPREDICT. Stool samples are processed and evaluated in a central laboratory. Individuals with positive testing (cutoff level 50ng hemoglobin/mL) are advised to undergo colonoscopy.
RESULTS: The target group from 2003 to 2012 was 1.2 million. In this time period 100.000 colonoscopies were performed, 20,292 (25%) were triggered by the screening program. The participation rate was about 35 percent, 8.3 percent of the participants had a positive FIT. Within this group we found CRC in 314 persons, high grade intraepithelial neoplasias in 225, high risk adenomas in 2,673 and low risk adenomas in 3,379 individuals.
Age-standarized incidence rates per 100.000 decreased from 43.4 (average 1998-2000) to 25.7 (average 2009-2011) in Burgenland (Statistic Austria).
Within bPREDICT FIT positive participants are also invited to take part in the Colorectal Cancer Study of Austria (CORSA), yielding a large biobank (DNA and plasma) comprising more than 10.000 CRC patients and colonoscopy-negative controls. This biobank is the basis for several molecular epidemiology research projects.
CONCLUSION: Most recent data of "Statistic Austria" show that the incidence pattern has changed in Austria, Burgenland is now on the last but one position, this may due to the effect of bPREDICT.
Disclosure of Interest: None declared

P0937 COLORECTAL CANCER RISK IS HIGHEST IN MALE NON-SOUTH ASIAN (NSA) PATIENTS IN A REGIONAL BOWEL CANCER SCREENING (BCS) POPULATION

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INTRODUCTION: The literature on colorectal cancer screening and ethnic diversity is dominated by studies from the USA. There is no such published data from the UK BCS population. 10.3% of the Black Country BCS population are of South Asian (SA) ethnicity. We aimed to determine the effect of ethnicity and gender on the risk of polyp or cancer detection over a 5 year period (2007-11).
AIMS & METHODS: Data was collected from the BCS cohort retrospectively. SA patients were identified and compared to those of Non South Asian (NSA) ethnicity and colonoscopy outcomes were determined.
RESULTS: 3552 subjects underwent BCS colonoscopy (NSA = 3363; SA = 189). The incidence of colorectal cancer within the SA population was 7.4 per 100.000 per year compared with 36 per 100 000 per year in NSA ($p < 0.05$). The probability of colon cancer is higher (OR = 3.84; $p < 0.05$) in NSA compared with SA patients. Similarly patients in the 65-70 age group have the highest risk (OR = 1.60; $p < 0.05$) of colorectal cancer.

		95% confidence interval	
Parameter	Risk odds ratio	Lower	Upper
Male	2.26021*	1.72979	2.953527
NSA	3.846221*	1.894585	7.806838
South Staffordshire	0.517331*	0.318861	0.839457
Walsall	1.124037	0.827787	1.526534
Wolverhampton	1.130742	0.818731	1.562051
Age 65-70	1.602908*	1.18412	2.170592
Age 70-75	1.449215*	1.051271	1.997707
Intercept (SA female aged 60-65 years living in Dudley is the baseline and all groups are deviations from this estimate)	4.54E-05	3.06E-05	6.75E-05

Table: Factors predicting risk of colorectal cancer in BCSP. *denotes statistical significance ($p < 0.05$).
CONCLUSION: The colorectal cancer risk is significantly higher in the male NSA BCS population in this regional study. This is the first such study in the BCS population.
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Disclosure of Interest: None declared

P0938 OPPORTUNISTIC COLORECTAL CANCER SCREENING – HOW OFTEN DID WE FOUND PATHOLOGY IN CLINICAL PRACTICE?

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INTRODUCTION: While a population-based colorectal cancer screening program is not implemented, probably any other method of early detection of this disease is welcome.
AIMS & METHODS: The aim of our study was to assess which were the findings in regard to neoplastic pathology (polyps or colorectal cancer) of opportunistic colorectal cancer screening by colonoscopy (asymptomatic subjects in whom we performed a colonoscopy for colorectal cancer screening).
We included in our study the colonoscopies performed in asymptomatic subjects in whom the indication was screening for colorectal cancer, in 3 endoscopy centers from Timișoara and Tg. Mureș. We excluded the colonoscopies performed in patients with previous history of polyps and colorectal cancer. We studied the prevalence of polyps, significant polyps (polyp ≥1cm) and colorectal cancer, globally and in different age groups.
RESULTS: 2537 colonoscopies were performed in asymptomatic subjects in the 3 endoscopy centers between January 2008-December 2013; from these 95.9% (2433 cases) were total colonoscopies. The statistic analysis was performed only on total colonoscopies.
The 2433 total colonoscopies performed in asymptomatic subjects led to the discovery of polyps in 32.1% (783/2433) of cases, of significant polyps in only 7.2% (175/2433) of cases and of colorectal cancer in 2% of cases (50/2433). Most often we found neoplastic pathology in the 60-69 years age group: 38.5% (302/785) polyps, 8.4% (66/785) significant polyps, 2.5% (20/785) cancers.
CONCLUSION: The detection rate of significant pathology (significant polyps and cancer) in asymptomatic subjects' colonoscopy was 9.2% in the studied group, which confirms the need for colorectal cancer screening.
Disclosure of Interest: None declared

P0939 RADIATION PROCTOCOLITIS AND THE RISK OF COLORECTAL NEOPLASIA

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INTRODUCTION: A mainstay in the treatment of prostate and some gynecological cancers is the use of external beam radiation therapy. Radiation proctocolitis is a common complication of this treatment. Little is known about the association between external beam radiation, radiation proctocolitis, and the risk of colonic neoplasia.
AIMS & METHODS: The current study is a prospective analysis of patients with radiation proctocolitis referred from the Newfoundland and Labrador Bliss Murphy Cancer Centre from Jan. 2010 to Dec. 2013. The current study investigated the relationship between radiation proctocolitis at index colonoscopy and the detection of colorectal polyps. These results were then compared to data

collected for colonoscopies conducted on (i) average risk individuals and (ii) fecal immunohistochemical test (FIT) positive patients. Data was recorded on a standardized data sheet and entered into SPSS version 20.0 for analysis.
RESULTS: Data was collected on 81 individuals who had radiation proctocolitis, 130 individuals who were average risk, and 109 FIT positive individuals. At colonoscopy the adenoma detection rate (ADR) was 60.5% for patients with radiation proctocolitis, 21.5% for individuals at average risk and 55.6% for FIT positive individuals. The colon cancer rate was 6.2% for individuals with radiation proctocolitis, 0% for individuals at average risk and 1.8% for FIT positive individuals.
There was a significant difference in the ADR between the patients with radiation proctocolitis and average risk individuals 60.5% vs. 21.3 ($p<0.0001$) and the corresponding colon cancer rate was 6.2% vs. 0 respectively ($p<0.002$). There was no significant difference in the ADR or colon cancer rate in patients with radiation proctocolitis compared to FIT positive.

Histiopathology	ADR	Colon Cancer Rate
Patients with Radiation Proctocolitis (n = 81)	60.5%	6.2%
Average Risk Individuals (n = 130)	21.5%	0%
FIT Positive Individuals (n = 109)	55.6%	1.8%

CONCLUSION: Pelvic radiation exposure is known to be associated with the development of proctocolitis. This study also shows it is associated with an extremely high prevalence of colorectal neoplasia. Patients with a history of radiotherapy require screening for colonic neoplasia.
Disclosure of Interest: None declared

P0940 HEIGHT AND RISK OF COLORECTAL ADENOMA: A COHORT STUDY OF A KOREAN MEN

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INTRODUCTION: Increasing cancer risk with increasing adult height has been reported for all cancers combined and for several common site specific cancers, including colon and rectum. The underlying mechanism is unclear, but it has been suggested that increased cell turnover mediated by insulin like growth factor or increased cell number might increase cancer risk by increasing the amount of tissue available to undergo malignent transformation. Evidence is limited, however, for adenomatous polyps, precursors to colorectal cancer.
AIMS & METHODS: The aim of this study was to evaluate the associations between height and risk of colorectal adenomas at the various stages of the adenoma-carcinoma pathway.
We conducted a retrospective study using data from who had undergone a complete colonoscopy as part of a health examination at the Health Promotion Center of Samsung Medical Center between October 13, 2009 and December 31, 2011. A total of 1356 male subjects were included. Multivariable logistic regression analysis was used to evaluate the association between height and colorectal adenoma.
RESULTS: Each 5-cm increment in height was associated with 19.4% and 9.8% higher risk of advanced colorectal adenoma and high risk colorectal adenoma, after adjusting for age, BMI, metabolic syndrome, smoking, drinking, family history of colorectal cancer, and regular use of aspirin. Still, there was clearly no significant association. (p-vaule 0.4404 and 0.6852 each)
CONCLUSION: Unlike colorectal cancer, there is no clear association between colorectal adenoma and height. The difference between the patterns associated with cacner and adenoma could be explained as some cancers may not arise from an adenoma, and only a limited portion of subjects with adenomas will eventually have cancer.
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Disclosure of Interest: None declared

P0941 RECTAL NEUROENDOCRINE TUMOURS: MANAGEMENT AND SURVIVAL IN 60 PATIENTS

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INTRODUCTION: Rectal neuroendocrine tumours (rNETs) are increasing in incidence, with more found incidentally on routine colonoscopy.
AIMS & METHODS: To retrospectively analyse a cohort of rNETs to characterize diagnostic features and clinical behaviour. Patients (pts) with confirmed diagnosis of rNET were identified from a database
RESULTS: 60 pts evaluated, median age 55 years (range 23-78). Most common presentation was rectal bleeding n = 29 (48%). 29/60 pts had tumour <1cm, 7/60 pts 1-2cm, 22/60 >2cm, 2/60 size was unknown. Of patients with tumour size <1cm, 3/29 did not require endoscopic follow-up (pT1a) and of the other 26, none had evidence of recurrence on endoscopic follow-up (follow-up range 6 to 88 m). 24/60 pts had metastases at presentation, 5/60 developed metastases during follow-up (of these 29 pts 86% liver, 40% bone, 10% lung). Of 29 pts with metastases, 24/29 had somatostatin receptor imaging with 62% avid uptake. Chromogranin A available in 23/29 pts and was not elevated in 83%. Of 29 pts with metastases, 19/29 had chemotherapy, 10/29 somatostatin analogues (SST), 15/29 surgery and 10/29 peptide-receptor-radionuclide-therapy (PRRT). Chemotherapy: 1/19 pts partial response, 2/19 stable disease (SD), 12/19 progressive disease (PD) (median time to progression 4 months (m)); 4/19 no data. PRRT: 4/10 had SD (follow-up range 24 to 53m), 4/10 PD (median time to progression 4m, range 2-9), 2/10 no data. SST: 2 sustained SD (range 12-27m), 7/10 PD, (median time to progression 3m, range 2-5); 1/10 no data. During median follow-up of 20m (range 3–170m), 100% of pts with primary tumour <1cm, 86% with tumour size 1-2cm, and 25% with size >2cm are currently alive. Tumour size >2cm have poorer outcome than the other 2 groups ($p<0.001$).
CONCLUSION: Tumours larger than 2cm are associated with poor prognosis. Chromogranin A is mostly normal even in advanced disease. Prospective studies are needed to determine progression free survival data for systemic therapy.
Disclosure of Interest: None declared

P0942 CANCER INVADING THE SUBMUCOSAL LAYER: SOMETHING IS MISSING. A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Actually we don't know how long does it takes for a preneoplastic lesion to became a cancer invading the submucosal layer (pT1). We don't know, also, how long a pT1 lesion rest in the submucosal layer before going deeper to reach the muscolaris propria becoming pT2. Qualitative parameters to determinate high metastatical risk in pT1 as showed in Europeans Guidelines in Colorectal Cancer (CCR) screening[1] and Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines[2] are: high tumor grade, deep extent of invasion, vascular invasion, presence of high grade budding, polipectomy resection margin <1mm. The presence of none (low risk) or one (high risk) of these parameters involves a metstatical risk from 0.7% to 36%, and a overall average of 13%.
AIMS & METHODS: to assess the metastatical risk in pT1 lesions diagnosed during routine colonoscopies and in those found during the colorectal cancer screening program. We retrospectively enrolled in the study 15.252 consecutive patients gone for colonoscopy in our Endoscopy Unit from april 2009 to april 2014. 4.970 patients were Fecal Occult Blood Test (FOBT) positive and enrolled in the CCR screening program. pT1 patients gone for a strict follow-up with CT scan, CEA and colonoscopy. Fisher exact test and Student's T-test for unpaired data were used for statistical analysis.
RESULTS: in 5 yr 119 pT1 (67M, 52F) tumors were detected, 96 during screening colonoscopies (SC) and 23 during routine colonoscopies (RC). Overall pT1 prevalence was 1,9% in SC and 0.3% in RC. 60/119 (50.4%) patients underwent for surgery because considered at high metastatic risk, of those only 3 patients (3.3%) presented limphnode metastasis, 1/5 (20%) in RC and 2/55 (3.6%) in SC (p = ns). The mean follow-up was 132 months. During the follow-up none other patient had metastasis. Population mean age was higher in RC 71.87 vs 61.24 ($p<0.0001$). High risk pT1 were more frequent in SC (56.2% vs 26.1%, $p=0.01$). No differences were found in the two populations for: polyp dimension, tumor grading, deep/extent of invasion, vascular invasion, polypectomy resection margin (p = ns). The presence of tumor budding was higher in male (23.1% 15/65 vs 6.1% 3/49, $p=0.01$) and in RC pT1 gone for surgery (60% 3/5 vs 16% 8/50, $p<0.05$).
CONCLUSION: The probability to find a pT1 tumor is 6 times higher during SC. Colorectal pT1 lesions found during the screening colonoscopy program seams to be at less metastatic risk compared to analogue pT1 lesions found during routine colonoscopies, probably because are diagnosed at an early stage; for this reason we must find new parameters to better predict the real metststic risk for these kind of tumors. The controversial budding parameter is probably affected by gender.
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Disclosure of Interest: None declared

P0943 NATIONAL COLORECTAL CANCER SCREENING PROGRAME IN CROATIA

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INTRODUCTION: In Croatia in 2012 colorectal cancer was the second leading cause of cancer mortality in males, (1.136 or 55.0/100.000) as well as women (868 or 39.1/100.000). According to Croatian Cancer Registry in 2011 it was diagnosed in 19% of cases at the localised stage, and 61% with regional metastases or distant metastases at time of diagnosis.
AIMS & METHODS: Faecal occult blood testing (FOBT) is an evidence based, cost-effective screening approach in organised population-based colorectal cancer screening programmes throughout the world. The hypersensitive guaiac-based Hemognost (Biognost, Zagreb) card test was used to screen population age between 50-75 years in Croatia.
RESULTS: By the end of September 2012 a total of 1,419.639 persons (born between 1933-1957) were received three FOBT test cards. Among them, 15,339 persons were ineligible for testing. 288,935 (21%) sent test packages with correctly applied specimens which is in accordance to the response rate according to EU guidelines (17.2 to 70.8%) in the first round.
Within the program, more than 10.000 colonoscopy examinations were conducted (80% response rate) and 576 people with colon cancer were discovered (2.3‰ of total number of tested persons, which is consistent with the expected: EU guidelines 1.2-2,3/1000). In 4223 people polyps were found (39.7% of incurred colonoscopy) and removed. The largest number of polyps were found in the left half of the colon: 64% (19%, 37% and 8% in the rectum, sigma, and descendens, respectively). The other 36% were detected in the proximal part (17% in the transverse colon and 19% in ceco-ascending colon). Small polyps in the rectum (5-10 mm in diameter), sigmoid and descending colon were histologically found to be tubular adenomas in 60% of cases, with a low degree of dysplasia, and 40% were classified as hyperplastic. Polyps of this size in the transverse or ceco-ascending colon in almost 20% had a histologically villous component, but still had a low degree of dysplasia. Polyps sized 10-20 mm in diameter were in 43% cases tubulovillous, and among them, 32% had areas with a high degree of dysplasia, especially those polyps in the ceco-ascending or transverse part
CONCLUSION: According to first cycle results and organisational obstacles it was suggested a need for intervention strategies in order to improve compliance. A number of organizational changes are performed together with educational and promotional activities to improve awareness of CRC screening usefulness and increase participation rates.
Disclosure of Interest: None declared

P0944 RISK FOR COLORECTAL ADENOMAS AMONG PATIENTS WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS (IPMNS): A CASE-CONTROL STUDY

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INTRODUCTION: It is well documented that patients with IPMN are at the incresed risk of colorectal cancer.
AIMS & METHODS: Aim of the study was to investigate if risk of colorectal cancer development in patients with IPMN may be related to an increased propensity to harbor colorectal adenomas. A two centers case–control study. Cases were prevalent IPMN without history of colorectal cancer, who underwent screening colonoscopy for the first time in their life. Matched controls were enrolled along side between individuals who underwent colonoscopy for screening and evaluation of non specific abdominal pain.
RESULTS: During the study period, 122 IPMN cases and 246 controls were enrolled. IPMNs were more frequently branch-duct (87.7%), multifocal (67.2%) with a mean diameter of greater lesion of 16.1 mm ± 8.1. First-degree family history of colorectal cancer was more frequently among controls (14.1% vs. 37.8%, $p<0.001$), while 2nd degree family history of any cancer (18.2% vs. 10.3%, $p=0.035$), as well as pancreatic ductal adenocarcinoma (3.3% vs. 0%, $p=0.01$) was more frequent among cases. Colorectal polyps were found in 52 IPMN (42.6%) and 78 controls (31.7%). In 29 cases (23.8%) and 55 controls (22.5%) histological examination disclosed adenomatous polyps, which were multiple in 11 cases (9%) and 20 controls (8.2%). Three cases of cancer were found, 2 in IPMNs (1.6%) and 1 in controls (0.4%). We observed a significantly increased risk for harboring colorectal polyps among IPMN cases than IPMN-free controls [adjusted odds ratio (OR): 1.60, 95% confidence interval (CI): 1.10-2.59]. However, IPMN was not significant risk factor for harboring adenomatous polyps (OR: 1.05, 95% CI: 0.61-1.80). Due to the small number of discovered cancers it was not possible to conduct the same analysis for colorectal cancer as an outcome.
CONCLUSION: Increased risk of colorectal cancer in patients with IPMNs do not seem to be related to an increased propensity to harbor adenomatous polyps.
Disclosure of Interest: None declared

P0945 DIMINUTIVE POLYPS: RESECT AND DISCARD STRATEGY IS NOT ENOUGH. A DIFFERENT FOLLOW UP IS NEEDED IF THERE IS A CONCOMITANT PRESENCE OF LARGER POLYPS

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INTRODUCTION: Oncological significance of diminutive polyps alone (DPA) is controversial as the association of diminutive polyps with other types of larger polypoid or non-polypoid lesions (DPP). The resect and discard strategy for diminutive polyps appears to be cost effective but the post polypectomy follow up, that is crucial for colonoscopy screening programs, still remain uncertain[1]. Colonoscopy intervals are based on pathological assessment of all polyps detected during colonoscopy and several elements contribute to assess the risk to develop colon cancer: polyps dimension, colon side, histology, number of polyps detected at the index colonoscopy and colonoscopy quality.
AIMS & METHODS: to establish the appropriateness and safety of the ''resect and discard'' strategy in a colorectal cancer screening population undergone for index colonoscopy in 2010 and subjected at least a survaillance colonoscopy within 3 years. We retrospectively analyzed 585 patients positive for FOBT undergone for colonoscopy during a Colorectal Cancer Screening Program in Padua in 2010 and with polyps. Subsequently among this initial population were identified 387 patients with detection of DPA or with DPP. These patients were divided into two groups: DPA (184 pts) and DPP (203 pts). The number, dimension, colon side and histology of all the polyps were assessed at first colonoscopy and during the follow up. Only clean colonoscopies were considered in the study. Statistical analysis used: Fisher exact test and Student's T-test for paired and unpaired data.
RESULTS: A regular follow up was observed in 82 pts (M 60-F 22, mean age 66 y) with DPA and in 158 pts (M 113- F 45, mean age 66 y) with DPP. Quality index of colonscopy: adenoma detection rate 57.2% and coecal intubation 98%. 1150 polyps resected at index colonoscopy, 397 (34.3%) DPA and 758 (65.7%) DPP. 450 polyps were resected during the follow up, 125 (27.7%) in DPA and 325 (72.2%) in DPP. The total number of patients with advanced adenomas was higher in DPP vs DPA 108-83% vs 21-17% ($p<0.0001$) at index colonoscopy, but in the follow up colonoscopy the difference about advanced adenomas was not significant ($p=0.342$). Also the right side was predominantly in DPP at the index colonoscopy (113-59.8% vs 76-41.2%, $p<0.0001$). Finally the two group as expected are different for mean number of total polyps at index DPA 2.17 vs DPP 3.72 ($p<0.0001$) and subsequent colonoscopy DPA 1.52 ± DPP 2.06 ($p<0.05$), mean number of colonoscopies at follow up was similar 1.37 vs 1.39 ($p=$ ns). One interval cancer was found in the group of DPP in the right colon, this event was statistically consistent with literature data[2].
CONCLUSION: The ''resect and discard'' strategy appears to be safe, cost effective and adequate in the context of colorectal screening programs against data of follow up in patients with **only** diminutive polyps, in who prevails not advanced adenomas. A closer follow up program should be performed according to the presence of **non** diminutive polyps, where prevails advanced adenomas and frequently the lesions are in the right colon with consequent high risk of interval cancer.
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P0946 KRAS_G12C MUTATION: AN EFFECTIVE SCREENING BIOMARKER FOR MUTYH-ASSOCIATED POLYPOSIS DIAGNOSIS

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INTRODUCTION: *MUTYH*-associated polyposis (MAP) is an autosomal recessive inherited condition commonly showing an attenuated familial adenomatous polyposis phenotype. It represents about 1% of all CRC although is thought that it might be underdiagnosed. Apparent sporadic cases not fulfilling clinical and pathological criteria are being described, though no screening marker is widely adopted.
AIMS & METHODS: We aimed to approach the analytical and clinical validation of *KRAS*_G12C somatic mutation as screening marker for MAP diagnosis. Sensitivity, specificity, positive and negative predictive values were calculated.
A total number of 103 patients were included in this study: 75 patients with polyposis (EPIPOLIP cohort) and 28 CRC patients (EPICOLON and

Hereditary Cancer Program Comunidad Valenciana, cohorts). All patients were tested for germline mutations at *MUTYH* gene (Sanger sequencing of the whole coding region and intron-exon boundaries); and *KRAS*_G12C mutation at polyps or CRC microdisected tissues (Sanger sequencing).
RESULTS: *MUTYH* biallelic mutation was present in 13 and 19 of the polyposis and CRC patients, respectively. No *MUTYH* mutation was detected in 62 and 9 of the polyposis and CRC patients, respectively. Eleven out of 13 (84.6%) *MUTYH* biallelic carriers and 2 out 62 (3.2%) wildtype *MUTYH* polyposis patients harboured *KRAS*_G12C mutation in at least one of their polyps. In the CRC cohort, 13 out of 19 (68%) *MUTYH* biallelic mutation carriers and none of the nine *MUTYH* wildtype patients had *KRAS*_G12C mutation. Taking together these results, we found that the diagnostic value of *KRAS*_G12C for screening of MAP syndrome shows a specificity and sensibility of 0.972 and 0.75 respectively, with positive and negative predictive values of 0.923 and 0.896, respectively.
CONCLUSION: Our results suggest that *KRAS*_G12C mutation is an effective screening marker for MAP syndrome in both, polyps and tumor tissues. Larger studies are needed to confirm the clinical value of this marker for its potential use in the universal screening for MAP-syndrome.
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Disclosure of Interest: None declared

P0947 SHOULD ALL BARIUM ENEMAS BE CONVERTED TO COLONOSCOPY? ANALYSIS OF 300 BARIUM ENEMAS BY INDICATION AND OUTCOME

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INTRODUCTION: Historically in the UK barium enemas have played a greater role in clinical diagnosis than in countries where colonoscopy is more available. It is now the policy of the Department of Health and thr National Institue for Health and Care Excellence (NICE) to improve access to colonoscopy and phase out barium enemas[1]. At the Great Western Hospital 2,700 barium studies were done in 2012; to switch all of these to colonoscopy would have major implications for colonoscopy workload. Furthermore, the switch might not always be clinically appropriate.
AIMS & METHODS: We retrospectively studied the stated indications for 300 consecutive barium enemas in patients over 45 years (older age group) and those 45 years and younger (younger age group). We looked at the outcome for each age group and indication: a **Relevant Positive** examination revealed pathology considered relevant to the stated indication; a **Diagnostic Negative** was a negative result with no further colonic investigations (these 2 groups constitute **Useful Results**). A **Disbelieved Negative** was a negative result followed up with lower gastrointestinaI endoscopy. **False Positives** and **False Negative** results were based on subsequent revision of findings on colonoscopy.
RESULTS: Five indications accounted for 83% of all studies in both age groups cumulatively: altered bowel habit (ABH) 42%; Per Rectal bleed (PRB) 22%; abdominal pain (AP) 15%; anaemia (An)14% and diarrhoea (Dia) 7%.
ABH comprised the majority of indications in both age groups when combined together (42%). In the younger age group, this, together with abdominal pain, yielded mostly diagnostic negatives (63% & 78% respectively) and only 12% relevant positives, all diverticulosis. The yield of relevant positives doubled in the older age group to 25% (mostly diverticulosis but 18% neoplasms, 5% strictures, 5% rectocele).
PRB was more common than other indications in the younger age group (38%) compared with older age group (20%). In the younger age group all patients with PRB who had positive results were found to have neoplasms, whereas in the older age group, 33% were neoplasms and 67% diverticulosis. The rectal bleeding groups also provided the most disbelieved negatives (55%) prompting clinicians to request a colonoscopy.
In the older age group, anaemia and diarrhoea had low yields (6% and 18% respectively) and a significant number of disbelieved and false negatives necessitating further investigation with colonoscopy.
CONCLUSION: Colonoscopy is preferable in patients with rectal bleeding, diarrhoea or anaemia. For young patients with altered bowel habit and/or abdominal pain a negative barium result was common and accepted as reassuring; colonic investigation should therefore be used sparingly in these patients and where used, should be less invasive and expensive than colonoscopy.
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Disclosure of Interest: None declared

P0948 DISCORDANCE IN TUMOR GRADE BETWEEN PRIMARY AND METASTATIC LESIONS IN PATIENTS WITH ENTERO-PANCREATIC NEUROENDOCRINE TUMORS: IMPLICATIONS FOR CLINICAL MANAGEMENT?

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INTRODUCTION: In neuroendocrine tumors (NET), the therapeutic strategy is highly dependent on tumor grade assessed according to the WHO classification. The decision is commonly based on the histological characteristics of the primary tumor, even in the patients in whom metastatic disease developed several years after resection of the primary tumor. It is possible, however that metastatic lesions present characteristics different from the primary tumor which could have important clinical implications. The aim of the present study was to compare the tumor grade between the primary tumors and their liver metastases in patients with entero-pancreatic NETs, and to determine the consequences in terms of survival
AIMS & METHODS: Patients with entero-pancreatic NETs treated in our institution from 1995 until 2012, for whom both the samples from the primary tumor and from the liver metastases were available, were included. Clinical data were collected and 3 markers of tumor cell proliferation (reflecting the tumor grade) were evaluated: a) mitotic index (MI), measured by counting the number of mitoses in 10 HPF presenting the highest mitotic activity, b) mitotic index measured with a new metaphase specific marker: phosphohistone 3 (PPH3), assessed in the same conditions, and c) the Ki67 index, expressed as percentage of MIB1-positive cells per 2000 tumor cells in the areas of the highest proliferation activity. Statistical analyses were performed using the exact Mc Nemar test. Survival was analysed using logrank test.
RESULTS: Twenty-five patients (12 males, median age 58 years, range 33-79) were included. Primary NETs were pancreatic in 7 patients and intestinal in 18 patients. Liver metastases were synchronous in 20 patients and metachronous in 5 patients. 44% and 56% of primary lesions were of grade 1 and 2, respectively, while 20%, 68% and 8% of the metastatic lesions were of grade 1, 2 and 3, respectively. Tumor grade differed between the primary and the metastatic lesion in 12 patients (48%): out of 10 patients who had a Ki67$\leq$2% in the primary lesion, 8 had a Ki67$>$2% in the metastatic lesion, out of 22 patients who had a MI $<$ 2 in the primary lesion, 10 had a MI $\geq$ 2 in the metastatic lesion, and out of 14 patients who had a PPH3 $<$ 2 in the primary lesion, 9 had a PPH3 $\geq$ 2 in the metastatic lesion. The median Ki67 and MI in metastases were statistically higher than in primary tumors ($p = 0.01$). Ki67 of metastases, but not of primary lesions, tended to correlate with mortality: 0% of mortality if Ki67$\leq$2 % and 66% if Ki67$>$2% on metastases, vs 60% and 47%, respectively, on primary lesions, for the median follow-up of 87 months. A good correlation was found between Ki67 and PPH3 ($p = 0.0001$), but not between Ki67 and MI ($p = 0.4$).
CONCLUSION: In about half of the patients with entero-pancreatic NETs, there is a significant difference in tumor grade between the primary and the metastatic lesions. Metastatic histology seems to better correlate with the survival. The prognostic and therapeutic impact of systematic biopsies of metastatic lesions needs to be further investigated.
Disclosure of Interest: None declared

P0949 A STUDY OF HYPERPLASTIC POLYP AS THE PRECURSOR OF SSA/P IN COLON AND RECTUM

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INTRODUCTION: SSA/P (sessile serrated adenoma/polyp), the precursor of MSI positive colorectal cancer proposed by serrated pathway, has recently attracted attention. We pathologically and genetically investigated serrated lesions including SSA/P based on the findings of magnifying endoscopy. We have reported *BRAF* mutation presence in the right colon in SSA/P, CpG island methylator phenotype (CIMP)-positive and characteristic findings of magnifying endoscopy (Kimura T, et al. Am J Gastroenterology 107:460-469, 2012). It is essential to investigate the precursor of SSA/P.
AIMS & METHODS: According to the WHO classification, hyperplastic polyps (HPs) were sub-classified and pathologically and genetically investigated. The aim of this study was to investigate the precursor of SSA/P.
Subjects were 46 HPs endoscopically resected at our center. According to WHO classification proposed in 2010, microvesicular variant (MVHP), goblet cell rich variant (GCHP) and mucin poor variant (MPHP) were classified. We investigated genetic mutation and methylation from samples extracted from lesions by location.
RESULTS: Classification of 46 HPs and locations was as follows; 33 MVHPs (14 lesions in the right colon and 19 in the left colon), 13 GCHPs (3 lesions in the right and 10 lesions in the left), and absence of MPHP. In investigation of genetic mutation, 7 MVHPs were observed in *kras* mutation, 22 MVHPs in *BRAF* mutation and 4 MVHPs in wild type. Conversely, 8 GCHPs were observed in *kras* mutation, 5 GCHPs in wild type and lesions were not observed in *BRAF*

mutation. Regarding investigation of methylation, CIMP-positive was confirmed in 10 lesions out of 22 lesions indicating *BRAF* mutation in MVHPs and the other lesions were CIMP-negative. In *BRAF* mutation, CIMP-positive was observed in 8 lesions (66.7%) out of 12 lesions in the right colon and 2 lesions (20.0%) out of 10 lesions in the left colon and difference between the left and right was confirmed. On the other hand, all of the GCHPs were CIMP-negative.
CONCLUSION: The findings indicated that MVHP presence in the right colon was considered to be similar to SSA/P by clinical pathology and generic background and may be the precursor of SSA/P.
Disclosure of Interest: None declared

P0950 SERUM SCD26 AND NDK-A IN A PREDICTIVE MODEL TO IDENTIFY COLORECTAL ADVANCED NEOPLASIA IN A NEGATIVE FECAL IMMUNOCHEMICAL TEST COHORT AT FAMILIAL RISK

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INTRODUCTION: First-degree relatives (FDR) of colorectal cancer (CRC) patients have an increased CRC risk [1] and are likely to show advanced neoplasia [AN: CRC and advanced adenomas (AA)] despite a negative FIT [2]. Consequently, there is an imperative need to find new non-invasive screening tests to identify patients with AN after a false-negative FIT result. Based on our previous results we propose the proteins sCD26 and NDK-A as serum candidate biomarkers [3-4].
AIMS & METHODS: To find a risk prediction model combining serum sCD26 and NDK-A proteins, and clinical variables to identify AN in FIT negative subjects at familial risk. The studied cohort included 486 asymptomatic individuals with at least one FDR with CRC and a negative FIT result, recruited from the "Complejo Hospitalario de Ourense". All individuals underwent a colonoscopy and a blood extraction. Concentration of sCD26 and NDKA in serum was measured with ELISA kits.
RESULTS: According to the colonoscopy findings patients were classified as: 335 with no neoplasia, 116 with non-advanced adenomas and 36 with AA. The risk of AN associated with the molecular and clinical variables was evaluated with a univariate analysis (see table).
Risk factors associated with the presence of AN in a FIT negative family-risk cohort.

Variable	Odds Ratio (95% IC)	*P*
sCD26 (≤330ng/mL)	7.38 (3.57-15.28)	<0.001
NDK-A (≥66.5 pg/mL)	2.78 (1.40-5.52)	0.003
Age (≥50 years)	2.90 (1.18-7.10)	0.020
Sex (male)	2.00 (1.01-3.97)	0.047
Number of FDR (2 or more)	1.20 (0.50-2.88)	0.679
Age of younger FDR (≤60 years)	1.03 (1.00-1.07)	0.055

The variables associated with an increased risk for AN ($P<0.1$) were included in the logistic regression model. The ROC curve obtained had an AUC of 0.820 (95% IC 0.758-0.891). The proposed risk model at a 0.122 cut-off predicts the presence of AA with a sensitivity of 48.6% and a specificity of 89.4%. Accordingly, 18 cases of AA originally not detected by FIT would be identified.
CONCLUSION: The risk prediction model proposed including serum sCD26 (≤330 ng/mL) and NDK-A (≥66.5 pg/mL), and the variables sex (male), age (≥50 years) and age of younger FDR (≤60 years) has the capability to re-classify FIT negative individuals who are at risk of having AA in a family-risk population.
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P0951 DIAGNOSTIC RISK FACTORS FOR THE DETECTION OF ADVANCED SERRATED POLYPS IN ASYMPTOMATIC PATIENTS

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INTRODUCTION: Evidence has accumulated that approximately 20% of colorectal cancer (CRC) arises from a serrated polyp (SP) precursor lesion via the serrated neoplasia pathway. Therefore CRC population screening should not only focus on detecting advanced adenomas and CRC, but also on detecting advanced SPs (ASPs). Risk stratification for the detection of ASPs could contribute to target colonoscopy screening towards a population of increased risk.
AIMS & METHODS: The aim of this study was to identify diagnostic risk factors associated with ASPs in a colonoscopy screening program for CRC. Data were collected from the colonoscopy arm of a multicenter randomized trial conducted in the Netherlands comparing colonoscopy with CT-colonography for primary population screening. 6600 Asymptomatic men and women between the age of 50 and 75 years were randomly selected from a population registry and invited to undergo a screening colonoscopy. Information on patient risk factors was obtained before colonoscopy through an extensive and validated risk questionnaire. A literature review was conducted to identify possible risk factors for ASPs. For these risk factors, the diagnostic odds ratio (OR) for the detection of ASPs during colonoscopy was calculated using multiple logistic regression analysis. SPs were defined as hyperplastic polyps, sessile serrated lesions or traditional serrated lesions. ASPs were defined as SPs ≥10mm or SPs with dysplasia.
RESULTS: Of 6600 screening participants, 1426 underwent a colonoscopy; 1236 (86%) also completed the questionnaire. Of all participants, 636 (52%) were male and the average age was 60.3 (SD 6.2). Colonoscopy detected an ASP in 53 (4.3%) participants.
The evaluated diagnostic risk factors are presented in table 1. The following risk factors were significantly associated with ASPs detected at colonoscopy: current smoking (OR: 4.36; 95% CI: 2.93–7.95), BMI (OR: 1.08 per kg/m^2; 95% CI: 1.02–1.15) and fiber intake (OR: 1.02 per gram; 95% CI: 1.01–1.03).
Table 1. Association of risk factors and the detection of advanced serrated polyps

Risk factor	OR (95% CI) univariate advanced SP	OR (95% CI) multivariate advanced SP
Male gender	1.15 (0.66-2.00)	
Age (years)	1.019 (0.98-1.07)	
First degree relative with CRC	1.38 (0.68-2.79)	
BMI (kg/m^2)	**1.07 (1.01-1.14)**	**1.08 (1.02-1.15)**
Current smoking	**4.00 (1.95-8.22)**	**4.36 (2.93-7.95)**
Alcohol consumption (units/week)	1.01 (0.98-1.04)	
Fiber intake (g/week)	**1.01 (1.00-1.02)**	**1.02 (1.01-1.03)**
Calcium intake (mg/week)	1.00 (0.99-1.01)	
Aspirin/NSAID use	0.94 (0.48-1.86)	

CONCLUSION: Current smoking, elevated BMI and elevated fiber intake are diagnostic clinical risk factors for the detection of ASPs during colonoscopy in asymptomatic patients. These risk factors could be combined with risk factors for the detection of advanced adenomas and CRC to optimize targeting CRC population screening towards a high-risk population.
Disclosure of Interest: None declared

P0952 CIRCULATING GALECTIN-1 AND 90K/MAC-2BP CORRELATED WITH THE TUMOR STAGES OF PATIENTS WITH COLON CANCER

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INTRODUCTION: The simultaneous correlation of serum galectin-1,-3, 90K/Mac-2BP levels with clinical stages of patients with colon cancer has not yet been clarified.
AIMS & METHODS: To measure the serum levels of galectin-1,-3 and 90K/Mac-2BP of patients at different stages of colon cancer and analyze the correlation of these galectins with stages of colorectal cancers. One hundred ninety-eight colorectal cancer patients (62 ± 13 (range 31-85) years old, 43.6 % female) were recruited for this study. Subjects were checked blood samples for serum galectin-1, galectin-3, 90K/Mac-2BP and CEA by sandwich ELISAs. We determined the correlation between plasma concentrations with pathologic TNM stages.
RESULTS: Our study found colon cancer patients with larger cancer sizes (stage T3, 4 than T1, 2) have higher serum 90K/Mac-2BP levels ($p=0.014$) and patients with lymph node metastasis have higher serum galectin-1 levels ($p=0.002$) but there was not a significant correlation between galectin-3 levels and patients with prognosis of colon cancer patients. In colon cancer patients with normal CEA levels, serum galectin-1 levels could predict more lymph node metastasis.
CONCLUSION: We found 90K/Mac-2BP correlated with the size of colorectal cancer. Galectin-1 but not galectin-3 was associated with lymph node metastasis. Galectin-1 could predict more lymph node metastasis of colon cancer when colon cancer patients had normal serum CEA levels.
Disclosure of Interest: None declared

P0953 METHYLATED SEPTIN 9 DETECTION IN TISSUE AND PLASMA OF COLORECTAL NEOPLASIA AND THE RELATIONSHIP TO THE AMOUNT OF CIRCULATING CELL-FREE DNA

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INTRODUCTION: Methylated Septin 9 (SEPT9) was evaluated as a sensitive and specific biomarker for colorectal cancer (CRC) in plasma samples. However, it has not been investigated how methylated DNA detected in plasma relates to the occurrence of methylated DNA in colon tissue.
AIMS & METHODS: The goal of this study was to quantitatively compare levels of methylated SEPT9 in matched plasma and tissue samples of healthy, adenoma and CRC cases; and to determine the amount of circulating free DNA (cfDNA) and the expression of Septin-9 protein in tissue. Plasma and matching biopsy samples were collected from 24 patients with no evidence of disease (NED), 26 adenomas and 34 CRC. A commercial real-time PCR assay was used to determine the total amount of DNA in each sample and the portion of DNA methylated at a specific locus of SEPT9 after bisulfite conversion of DNA. In a subset of tissue samples, Septin-9 protein expression was determined using immunohistochemistry.
RESULTS: In tissue samples, percent of methylated reference (PMR) values of SEPT9 above a selected PMR threshold of 1% were detected in 4.2% (1/24) of NED, 100% (26/26) of adenoma and 97.1% (33/34) of CRC. PMR differences were found highly significant ($p<0.001$) between NED vs. adenoma and NED vs. CRC comparisons.
In matching plasma samples SEPT9 PMR values, using a cut-off level of 0.01%, were detected in 8.3% (2/24) of NED, 30.8% (8/26) of adenoma and 88.2% (30/34) of CRC cases. Significant PMR differences were observed in comparisons between NED vs. CRC ($p<0.01$) and adenoma vs. CRC ($p<0.01$).
Significant differences ($p<0.01$) in the amount of cfDNA (circulating cell-free DNA) were found between NED and CRC and a modest correlation was observed between mSEPT9 concentration and cfDNA in plasma of cancer patients ($R^2=0.48$).
Protein expression of Septin-9 in tissues determined by IHC was inversely correlated to SEPT9 methylation levels with abundant expression in normals, and diminished expression in adenomas and tumors.
CONCLUSION: Methylated SEPT9 was detected in healthy tissue samples only at low levels, but significantly elevated in adenoma and CRC tissues. In plasma samples, elevated mSEPT9 values were detected in CRC, but not in adenomas. Tissue levels of mSEPT9 alone are not sufficient to predict mSEPT9 levels in plasma. Parameters like degree of vascularisation of the lesions, the amount of cfDNA in plasma and probably additional factors seem to be equally important.
Disclosure of Interest: None declared

P0954 COMPARATIVE CLINICOPATHOLOGICAL CHARACTERISTICS OF COLON AND RECTAL T1 CARCINOMAS: A SINGLE-CENTER RETROSPECTIVE STUDY

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INTRODUCTION: The biology of colorectal carcinomas has been reported to differ by location. Although the investigation of clinicopathological diversities between colon and rectal carcinomas could provide useful information for more effective clinical treatment, there is not adequate evidence of the differences.
AIMS & METHODS: The aim was to compare the clinicopathological features of T1 carcinomas between colon and rectum and to reveal whether these carcinomas should be considered as a single entity or two distinct entities. This study was performed at Showa University Northern Yokohama Hospital in Japan (UMIN Clinical Trials Registry number, UMIN000010979). A total of 21060 colorectal neoplasms were resected endoscopically or surgically at our institution between April 2001 and September 2013. Of these, 580 surgically resected T1 carcinomas, 475 colon and 105 rectal were evaluated. Factors analyzed included patient age, gender, tumor size, morphology, recurrence, depth of invasion, histologic type, vascular invasion, lymphatic invasion, tumor budding, and lymph node metastasis.
RESULTS: Rectal T1 carcinomas were significantly larger (19.9 ± 10.9 mm vs. 23.7 ± 12.9 mm, $p<0.001$) and were accompanied by significantly higher rates of vascular invasion (30.7% vs. 47.6%, $p<0.001$) and recurrence (0.4% vs. 2.9%, $p<0.05$) than colon T1 carcinomas. None of the other clinicopathological factors, including lymph node metastasis, differed significantly.
CONCLUSION: Rectal T1 carcinomas were significantly larger in size, with a significantly higher rate of vascular invasion and recurrence, than colon T1 carcinomas. However, the tumor location was not a risk factor for lymph node metastasis. These suggest that additional surgery after endoscopic resection be recommended for rectal T1 carcinomas with high risk for lymph node metastasis as well as colon ones even if rectal surgery is more invasive and rectal T1 carcinomas need more careful management after treatment.
Disclosure of Interest: None declared

P0955 CLINICAL UTILITY OF APPLYING A SIMPLE, LOW-COST METHODIC APPROACH TO EVALUATION OF CIRCULATING TUMOR DNA (CTDNA) IN COLORECTAL CANCER PATIENTS UNDERGOING SURGICAL TREATMENT

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INTRODUCTION: Circulating tumor DNA (ctDNA) is a very promising marker for non-invasive management of patients with cancer (1). The main clinical significance of ctDNA is in monitoring of patients after tumor resection, detection of recurrence or progression of disease and predicting and monitoring of the response to treatment. Most methods for ctDNA detection and monitoring are based on highly dedicated technologies, mainly utilizing digital PCR with subsequent detection by flow cytometry or next-generation sequencing (2). The high cost of equipment as well as sample processing prevents wide application of ctDNA testing in a clinical practice.
AIMS & METHODS: In a multicentric setting consisting of seven clinical collaborators we have optimized methodology for the collection and processing of samples and isolation and detection of ctDNA by PCR followed by denaturing capillary electrophoresis (DCE). In total, we have prospectively examined presence of ctDNA in 210 patients including 186 patients with colorectal cancer (CRC) at various stages and 24 patients with colorectal adenomas. Subsequent samplings were carried at 2-6 month intervals to monitor the ctDNA dynamics. Results were correlated with clinical data of patients (stage R0/R2 surgery, tumor markers, response to treatment, recurrence or progression of the disease).
RESULTS: The overall ctDNA detection rate in cancer patients was 28% (52/186), with the highest rate of 68% (19/28) in stage IV. In subsequently monitored patients levels of ctDNA correlated with the R0/R2 resection radicality, response to (neo)adjuvant chemotherapy, recurrence or eventual disease progression. Tumor markers CEA and CA19-9 correlated with ctDNA in 62% (65/104) of cases, in 13% (13/104) of ctDNA-positive cases the markers were negative.
CONCLUSION: A routine procedure has been implemented for the ctDNA analysis applying a simple methodology available to standard molecular laboratory. The ctDNA detection rates are ca. 20% below the rates produced by dedicated techniques and at 10 – 50x lower cost per patient. Our results confirm a significant potential of ctDNA in monitoring patients after resection of the primary tumor / metastasis and prediction of the response to biological treatment. The work was supported by IGA Ministry of Health No. NT 13660.
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P0956 FAMILIAL ADENOMATOUS POLYPOSIS (FAP) IN PEDIATRIC PATIENTS. A SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Familial Adenomatous Polyposis is an autosomal dominant inherited disorder in 80% of cases, characterized by the early onset of hundreds to thousands of adenomatous polyps throughout the colon. If left untreated, all patients develop colon cancer by age 35-40 years. In children with FAP colectomy is advised at the age of 17-18 years.
AIMS & METHODS: Aim of presentation was to study the characteristics of pediatric patients with FAP from our centre.
7 patients with Familial adenomatous polyposis, aged 7.5-17 years {5 boys (B) & 2 girls (G)} were included. All patients had positive familial history of FAP. One patient has Turcot syndrome, while the rest of patients have no other pathological findings or associated conditions. They were asymptomatic, with normal growth, and normal blood tests.

RESULTS: P0956

Patients	Genetic study	Endoscopy	Histological findings
B /12.5 y	(-)	~1000-10.000 polyps	Adenomatous polyps with moderate grade epithelial dysplasia
B/7.5 y	P. Ser1213X (c3638 C>A)	~ 10-100 polyps	Adenomatous polyps
G /14 y Sdr Turcot	P. Ser1213X (c3638 C>A)	~ 100 polyps	Tubular-vilous adenoma (median grade differentiation) with high grade dysplasia & focal signs of adenocarcinoma
B /16 y	(-)	~1000 polyps	Adenomatous polyps with low to moderate grade epithelial dysplasia
G/16 y	p. Ser583X (c.1748 G>A)	~ 10-100 polyps	Adenomatous polyps with moderate grade epithelial dysplasia
B /17 y	p. Ser583X (c.1748 G>A)	~ 100-1000 polyps	Adenomatous polyps with low grade epithelial dysplasia
B/14 y	p. Ser583X (c.1748 G>A)	~ 100-1000 polyps	Adenomatous polyps with low grade epithelial dysplasia

CONCLUSION: The development of colon adenocarcinoma in patients with FAP could occur also in pediatric age even without any previous alarming symptom. Children with a positive family history should be checked regularly and in the presence of FAP an intensive follow-up & eventually early intervention should be considered.

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Disclosure of Interest: None declared

P0957 A PHASE 3 PLACEBO-CONTROLLED TRIAL OF CELECOXIB IN GENOTYPE-POSITIVE SUBJECTS WITH FAMILIAL ADENOMATOUS POLYPOSIS

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INTRODUCTION: This study was conducted to evaluate efficacy and safety of celecoxib versus placebo in paediatric subjects with familial adenomatous polyposis (FAP).

AIMS & METHODS: The standard of care for FAP has long been prophylactic colectomy, a major surgical procedure associated with up to 2% mortality. Colonoscopic polypectomy has a role in maintaining a minimal polyp burden, in order to delay surgery in the typically young (age 10-16 y) patient. Elevated levels of cyclooxygenase-2 (COX-2) in colorectal adenomas suggest that COX-2 inhibitors may help maintain the polyp burden within the limits of endoscopic management, as has been demonstrated in clinical trials.

METHODS: This was a randomised, double-blind, multicentre, placebo-controlled, 5-year study in subjects aged 10-17 years, with a confirmed diagnosis of FAP (based on mutation testing) and no more than 30 colorectal polyps at screening, all of which had to be removed such that no subjects initiated treatment with an adenoma > 2 mm. Approximately 200 subjects were to be randomized in a 1:1 ratio to the 2 treatment arms: celecoxib 16 mg/kg/d or placebo. Subjects had yearly visits, with colonoscopies at each visit. The primary end point was the time-to-treatment failure, defined as the time from randomisation to the earliest occurrence of ≥ 20 polyps (> 2 mm in size) at any colonoscopy during the study or diagnosis of colorectal malignancy.

RESULTS: The study was terminated, at the recommendation of the Data Monitoring Committee, due to lower than expected enrolment and end point accumulation rate. At the time of study termination, 106 subjects had been randomised. There were 7 (13%) subjects in the celecoxib group and 13 (26%) in the placebo group who met the primary end point. Among them, the median time to disease progression was 2.1 years in the celecoxib group and 1.1 years in the placebo group, respectively. None of the subjects in any treatment group developed colorectal malignancy. The proportion of subjects reporting all causality treatment-emergent adverse events (TEAE) was similar between the treatment groups: 40 (76%) subjects in the celecoxib group and 35 (73%) subjects in the placebo group. The proportion of subjects with treatment-related TEAEs was also similar: 18 (34%) subjects in the celecoxib group and 15 (31%) subjects in the placebo group. The most common AEs (occurring in more than 10% of subjects in a group) were abdominal discomfort, abdominal pain, diarrhoea, nausea, vomiting, fatigue, seasonal allergy, influenza, nasopharyngitis, upper respiratory tract infection, pain in extremity, headache, cough, and oropharyngeal pain.

CONCLUSION: Treatment with celecoxib in children with FAP was generally well tolerated, with a safety and tolerability profile similar to that observed in previous studies, and with no new or unexpected safety results. Although a trend toward delay in progression of adenomas was seen in the celecoxib arm, it was not statistically significant, which was likely to be related to low sample size and event rate.

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P0958 PROSPECTIVE MULTICENTER STUDY OF SELF-EXPANDABLE METALLIC STENTS FOR MALIGNANT COLORECTAL OBSTRUCTION IN JAPAN: SHORT-TERM SAFETY AND EFFICACY IN 512 PATIENTS

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INTRODUCTION: Endoscopic stenting with self-expandable metallic stent (SEMS) is a widely accepted procedure for the palliative management of malignant colonic obstruction and as a bridge to surgery, however, was not able to be performed under Japanese insurance system. We conducted prospective feasibility study, after this procedure was covered by government medical insurance in Jan. 2012.

AIMS & METHODS: Our objectives were to estimate safety and feasibility of SEMS placement for malignant colorectal obstruction in general clinical practice in Japan.

We conducted a prospective, observational, single-arm and multicenter clinical trial from Mar. 2012 to Oct. 2013. This study was registered with UMIN Clinical Trial Registry (UMIN000007953). Forty five facilities consisted of 12 academic and 33 community hospitals participated this study. Ahead of the start-up of the study, we launched a website (http://colon-stent.com/) and pronounced the standard methods based on previous published data to standardize the maneuver of SEMS placement. Each patient was treated with an uncovered WallFlex Enteral Colonic Stent (Boston Scientific Corporation). SEMS were placed under fluoroscopy and endoscopy. Technical success was defined as deployment of the stent across the entire length of the stricture on the first attempt. Clinical success was defined as a resolution of symptoms and radiological relief of the obstruction within 24 h. Patients undergoing the stenting as a bridge to surgery (BTS) were followed until surgery, and incurable patients undergoing palliative treatment (PAL) were followed until death or 12, whichever came first. The following conditions were considered to be complications: stent occlusion, stent migration, colonic erosion or ulcer, perforation, hematochezia, tenesmus, and bacteremia. Complications were categorized as early (within 7 days) or late (after 7 days).

RESULTS: We registered 518 patients. Six patients were excluded, because of loose stenosis with passed by colonoscope (3), benign stricture (1), unknown indication (1) and placement with another SEMS (1). We enrolled 512 patients for a BTS (311) and PAL (201) indication. In an intension-to-treat analysis, technical and clinical success was 98% (97% BTS, 99% PAL) and 96% (96% BTS, 95% PAL). The overall early complication rate was 8% (7% BTS, 9% PAL), including stent occlusion 1.2% (0.3% BTS, 2.5% PAL), stent migration in 1.5% (0.5% BTS, 2.3% PAL), perforation in 1.9% (2.3% BTS, 1.5% PAL).

CONCLUSION: This large multicenter, prospective study demonstrates the feasibility of SEMS placement for malignant colorectal obstruction within 7 days after SEMS placement. Despite of short period experience of this procedure in Japan, the incidence of complications including perforation was relatively low.

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P0959 EICOSAPENTAENOIC ACID (EPA) SUPPRESSES COLORECTAL ABERRANT CRYPT FOCI (ACF) AND CELL PROLIFERATION IN COLORECTAL EPITHELIUM VIA GPR120

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INTRODUCTION: Eicosapentaenoic acid (EPA), the omega-3 polyunsaturated fatty acid (ω3PUFA) that is widely used in the treatment of hyperlipidemia and

prevention of cardiovascular disease, has recently been suggested to have a suppressive effect on tumorigenesis and cancer cell growth. However, the mechanism of EPA chemopreventive effect was still unclear. Recently, G-protein coupled receptor 120 (GPR120) functions as a receptor forω3PUFA and has a critical role in various physiological homeostasis mechanisms. It is known that GPR120 is expressed abundantly in the intestinal tract and in adipocytes. However, it is unclear that the role of GPR120 in intestinal tract, especially in anti-carcinogenesis effect against EPA. In the present study, we explore the colon chemopreventive effect of EPA focused on via GPR120 pathway using GPR120 deficient mice.
AIMS & METHODS: We produced and used GPR120 deficient mice and the littermate wild type mice. Both mice were fed with normal diet or EPA containing chow. Then we investigated carcinogen-induced formation of aberrant crypt foci ACF and tumors in the colon.
RESULTS: In WT, mice fed with EPA were significantly suppressed ACF formation. On the other hand, in GPR deficient, both mice fed with normal diet and EPA containing chow were present similar ACF formation.
CONCLUSION: We demonstrated the importance of EPA/GPR120 signaling in the colon in colorectal carcinogenesis.
Disclosure of Interest: None declared

P0960 DOES THE UBIQUITIN PROTEASOME SYSTEM IS INVOLVED IN THE EFFECTS OF PAR2 RECEPTORS ACTIVATION IN THE INTESTINE?

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INTRODUCTION: The irritable bowel syndrome (IBS) is a functional disorder in which chronic digestive discomfort or abdominal pain are the primary symptoms. Dysfunction of the intestinal barrier has been observed leading to changes in the immune system and visceral hypersensitivity. Protease-activated receptor type 2 (PAR2) and ubiquitin-proteasome system might play contribute to the pathophysiology of IBS. Thus, we aimed to investigate whether ubiquitin proteasome system might be involved in the effects of PAR2 activation in human intestinal epithelial Caco-2 cells and in C57BL/6 mice.
AIMS & METHODS: Caco-2 cells were grown on microporous filters to obtain a monolayer of polarized cells and were then incubated with the agonist peptide PAR2 (PAR2-AP, 100μM) and/or IL-1β (1ng/ml) and/or a proteasome inhibitor, MG132 (10 μM). Production of proinflammatory IL-8 chemokine was measured by ELISA in apical and basolateral culture media. Proteolytic activities of proteasome, paracellular permeability and the expression of subunits of proteasome have been evaluated. C57BL/6 Mice also received intraperitoneal injection of a proteasome inhibitor MG132 (15μmol/kg) or "vehicle". After one hour, under anesthesia, mice received intracolic injection of a solution of 100μl of PAR2-AP (1mg/ml) or saline. After 4 hours, production of proinflammatory CXCL1/KC chemokine was measured by ELISA in colonic washes and in portal serum.
RESULTS: Addition of PAR2-AP alone did not influence the ubiquitin-proteasome system, both in its activity and in its composition. However, when PAR2-AP was combined with IL-1β, chymotrypsin-like and caspase-like proteasome activities were increased (2.85 and 1.37 fold changes, respectively) as well as the composition of proteasome. Indeed, the ratio β5i / β5 was significantly decreased. Production of IL-8 and its mRNA level was increased in presence of PAR2-AP ($p < 0.05$). In Caco-2 cells polarized model, production of IL -8 was apical or basolateral differentially modulated when PAR2-AP was applied in apical or basolateral media. Proteasome inhibitor, MG132, exacerbated effects of PAR2-AP on production of IL-8 and barrier function. In mice, intracolonic injection of PAR2-AP decreased production of CXCL1/KC in both luminal and portal sides. This effect was blocked by injection of MG132.
CONCLUSION: In conclusion, we have shown in a cell model that PAR2 agonist peptide alone did not affect the ubiquitin-proteasome system under basal conditions but can modify proteasome activities in presence of an inflammatory stimulus (IL-1β). Furthermore, complete inhibition of proteasome enhances effects of PAR2 activation on inflammatory response and intestinal barrier. In contrast, in mice, inhibition of proteasome blocks effects of agonist peptide PAR2 on production CXCL1/KC. Further studies are needed to explain these results.
Disclosure of Interest: None declared

P0961 LACTIC ACID BACTERIA DIFFERENTIALLY MODULATES UROCORTIN 2 MRNA EXPRESSION IN HUMAN COLON EPITHELIAL CELLS

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INTRODUCTION: It has been shown that interventions on the gut microbiota affect behaviour in rodents and healthy human volunteers. This has led to establish what is now recognized as the microbiota-gut-brain axis. However, the mechanisms of communication between microbes and nerve cells or nerve endings in the gastrointestinal tract (GIT) remain largely unknown.
The intestinal microbiota is composed by a large number of microorganisms, including gram-positive lactic acid bacteria, which are able to interact with several cell types within GIT, including epithelial cells. Due to their ability to express neuropeptides, epithelial cells might act as intermediaries capable of transducing signals from luminal bacteria to nerve cells or sensory nerve endings in the GIT wall. One candidate neuropeptide is urocortin 2 (UCN2), which is known to regulate visceral nociception and gastric emptying.
AIMS & METHODS: We aimed to evaluate whether human colonic epithelial cells (Caco-2 cell line) are able to increase UCN2 mRNA expression upon stimulation with three types of *Lactobacillus* species: *L. rhamnosus* GG, *L. casei* L54-2-33 and *L. plantarum* L46-1-12. For this, Caco-2 cells were stimulated with 10^3, 10^5 and 10^7 colony forming units (cfu) per millilitre (cfu/mL) of each *Lactobacillus* strain for 3 hours. Control Caco-2 cells were exposed to broth alone. Then, total mRNA was extracted and UCN2 mRNA expression was analyzed using RT-PCR.
RESULTS: Caco-2 cells stimulated with 10^5 and 10^7cfu/mL of *L. casei* L54-2-33 displayed increased levels of UCN2 mRNA in comparison to control Caco-2 cells. On the other hand, stimulation of Caco-2 cells with 10^7cfu/mL of *L. plantarum* L46-1-12 reduced UCN2 mRNA expression in comparison to controls, while *L. rhamnosus* GG was not able to affect UCN2 expression at any of the analyzed doses.
CONCLUSION: These findings show that lactic acid bacteria are able to modulate neuropeptide expression (i.e.: UCN2) in intestinal epithelial cells, suggesting a potential pathway of communication with the nervous system. Modulation of UCN2 expression was strain specific suggesting that alterations in the intestinal microbiota and/or interventions through the use of antibiotics or probiotic bacteria would differentially affect this communication and potentially have differential effects on the gut-brain axis.
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P0962 ACUTE PSYCHOLOGICAL STRESS INCREASES PARACELLULAR PERMEABILITY IN THE SIGMOID COLON OF HEALTHY VOLUNTEERS

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INTRODUCTION: Psychological stress (PS) has been shown to have an effect on the course of both irritable bowel syndrome (IBS) and ulcerative colitis (UC). The mechanisms behind these effects are as yet unknown. Animal studies have shown that PS increases the intestinal barrier function. Our group has previous preliminary data showing that in vivo PS increases paracellular permeability in the rectum of healthy volunteers (HV). Whether or not the same is true for the sigmoid colon is unknown.
AIMS & METHODS: 18 HV (11 women and 7 men) were stressed using the method modified dichotomous stress for 60 minutes. Stress was monitored as blood pressure (BP), pulse (HF) and subjectively using a visual analogue scale (VAS). The control session was 60 min listening to calm music and the same HV were their own controls. Immediately following the stress/control sessions biopsies were taken from the sigmoid colon. The biopsies were mounted in modified Ussing chambers and passage of the paracellular permeability marker CrEDTA was measured for 120 min.
RESULTS: VAS, BP and HF were significantly higher at the stress than at the control session. There was a significant increase in passage of CrEDTA (6.2E-06 (5.3 E-06 -8.3 E-06)cm/s vs 4.4 E-06 (3.3-6.2) cm/s (median(IQR) ($p(<0.05)$.
CONCLUSION: Vanuytsel et al have recently shown that PS increases paracelluar premability in the small intestine in HV. Our results show similar permeability results in the colon. The mechanisms should be further investigated.
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Disclosure of Interest: None declared

P0963 ROLE OF INSULAR CORTEX IN VISCERAL HYPERSENSITIVITY RAT INDUCED BY CHRONIC STRESS

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INTRODUCTION: Visceral hypersensitivity is an important pathophysiological mechanism of stress-related FGIDs. In recent years, abnormalities of brain activity are thought to play important roles in the pathogenesis of visceral hypersensitivity. The insula as one important center processing visceral sensory and regulating emotion is inferred to be closely related with the pathogenesis of visceral hypersensitivity induced by chronic stress. However, the role of insula in visceral hypersensitivity has not been clearly defined.
AIMS & METHODS: We aimed to determine if insular neuron activation plays an important role in visceral hypersensitivity induced by chronic stress. Chronic water avoidance stress (WAS) was used to establish visceral hypersensitivity rat models. Visceral sensitivity was determined by measuring visceromotor response (VMR) amplitude to graded colorectal distention (20mmHg, 40mmHg, 60mmHg CRD). The bilateral insula was stimulated electrically, and insular lesions were generated with n-methyl-d-aspartate (NMDA).
RESULTS: Compared with sham WAS (2.07±0.61) and normal rats (2.15±0.46), the VMR to graded CRD in WAS rats (4.22±0.35) significantly

increased (p = 0.000). Bilateral insular lesions caused a significant decrease of the VMR in WAS rats (2.17±0.56) comparing with that in sham-lesion (4.02±0.84) and non-lesion WAS (4.35±0.87) rats (p = 0.000). The VMR to 60mmHg in insular lesion WAS rats have no significant differences with that in normal rats (p = 0.691). Electrically stimulating (ES) the left or right insula all enhanced the VMR of WAS rats (left: ES-before 4.62±1.51, ES-after 13.59±4.27 p = 0.000; right: ES-before 4.54±0.62, ES-after 13.95±4.77 p = 0.000) and the increase level of VMR amplitude had no significant differences between bilateral insula electrically stimulated (p > 0.05)

CONCLUSION: Insula plays a critical role in the modulation of visceral hypersensitivity induced by chronic stress, without unilateral advantage phenomenon in modulating process. After insular lesions, the pathological hypersensitivity symptoms in visceral hypersensitivity rats disappearance, but it keeps "natural state" visceral sensitivity.

Disclosure of Interest: None declared

P0964 IN IBS PATIENTS WITH SEVERE POSTPRANDIAL BLOATING AND ABDOMINAL DISTENTION, COLONIC TONE IS REDUCED IN POSTPRANDIAL PERIOD

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INTRODUCTION: Bloating is a very frequent complaint, is frequently associated to IBS and, in a subgroup of patients, is accompanied by a severe, visible abdominal distention. These subgroup of patients is characterized by different clinical presentations: bloating and abdominal distention onset may be related or not to food ingestion, they may be absent on waking and progressively worsen during the day, they may occur immediately after meal ingestion. The characteristics of the onset suggest a different pathophysiology.

AIMS & METHODS: Accordingly, we studied colonic tone in fasting condition and after a meal in a group of IBS patients with bloating and abdominal distention and we compared the results of patients with a meal-related and a meal unrelated occurrence of symptoms.

A group of 38 consecutive IBS patients (mean age 38.4±9.4 years, range 21-60, IBS-C = 20; IBS-D = 5 IBS-M = 13) with severe bloating and abdominal distension, diagnosed according to Rome III criteria was enrolled. Twenty-one patients suffered from postprandial onset of bloating and severe abdominal distention and 17 had meal-unrelated symptoms. In all subjects, recto-sigmoid tone was monitored with barostat, during a 30-min fasting period and a 60-min period after meal consumption (200 Kcal, 200 ml liquid meal). Every ten minutes, the occurrence of abdominal distention was monitored by abdominal girth measurement.

RESULTS: In the subgroup of patients with postprandial occurrence of bloating and abdominal distention, meal intake induced a significant decrease of recto-sigmoid tone as mean postprandial recto-sigmoid volume modification was +26.6±4,4% in these patients; on the contrary and as expected, in the subgroup with meal unrelated symptoms, mean recto-sigmoid volume modification was -4,1±4.0% (p = 0.001). Moreover, in patients with postprandial symptoms a meal-induced increase of the balloon volume higher than 10% of the fasting value was present in 14/21 (66.7%) vs 2/17 (11.7%) of the other subgroup (p = 0.0009) and postprandial abdominal girth significantly increased (85.0 cm ± 7.7 cm) vs the other subgroup (83.4 cm ± 7.2; p < 0.01).

CONCLUSION: A reduction of intestinal tone in the postprandial period may represent an important pathophysiological mechanism for the occurrence of abdominal distention in functional patients with bloating. An inappropriate, diffuse activation of a nitrergic pathway might be responsible for this alteration.

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P0965 DIFFERENTIAL EFFECTS OF EXTRACELLULAR CYCLIC GMP (CGMP) AND THE GUANYLATE CYCLASE-C (GC-C) AGONIST, LINACLOTIDE, ON MOUSE GASTRIC VAGAL AFFERENT MECHANOSENSITIVITY

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INTRODUCTION: cGMP is a second messenger produced in intestinal epithelial cells in response to GC-C activation. GC-C is expressed in the epithelium of the stomach (1). In addition, the endogenous peptide ligand for GC-C, uroguanylin, is located in enterochromaffin-like cells within the stomach (2). These findings suggest the stomach mucosa may be capable of producing cGMP in response to a GC-C agonist. In mouse colon both extracellular cGMP and linaclotide inhibit colonic nociceptor mechanosensitivity. Vagal afferents are associated with reflexes commonly altered in diseases such as functional dyspepsia. However, little is known about the effects of GC-C receptor activation and cGMP on these afferents.

AIMS & METHODS: We aimed to determine the effect of extracellular cGMP and linaclotide on gastric vagal afferent mechanosensitivity. Single fibre *in vitro* recordings of gastric vagal mechanoreceptors from 8wk old female C57BL/6 mice were recorded (3). The response of mucosal receptors to mucosal stroking with von Frey hairs (10-1000mg) and tension receptors to circular stretch (1-5g) in the absence and presence of cGMP (30-1000μM) or linaclotide (10-300nM) was determined. An increase or decrease in response to mucosal stroking (50mg)/circular tension (3g) of ≥ 20% in the presence of cGMP or linaclotide was considered to be potentiation or inhibition, respectively.

RESULTS: The effect of cGMP and linaclotide on gastric vagal afferent mucosal and tension receptor mechanosensitivity is illustrated in the table below:

	cGMP (30-1000μM)			Linaclotide (10-300nM)		
	Inhibit	**Potentiate**	**No effect**	**Inhibit**	**Potentiate**	**No effect**
% gastric mucosal receptors	27% (n = 7)	31% (n = 8)	42% (n = 11)	36% (n = 5)	41% (n = 9)	23% (n = 8)
% gastric tension receptors	0%	44% (n = 7)	56% (n = 9)	18% (n = 6)	55% (n = 12)	27% (n = 4)

The inhibitory and excitatory effects of linaclotide occurred close to the limiting ridge in the corpus and along the lower curvature of the stomach respectively. In contrast, there was no relationship between cGMP effects on vagal afferents and the location of these afferents in the stomach.

CONCLUSION: Linaclotide and extracellular cGMP can both inhibit and enhance responses of gastric vagal afferents to mechanical stimulation. The functional significance of these effects on gastric sensory signalling remains to be determined.

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P0966 DIFFERENT SUBTYPES OF PATIENTS WITH IRRITABLE BOWEL SYNDROME HAVE DISTINCT ALTERATIONS IN THE GUANYLATE CYCLASE-C/CYCLIC GMP PATHWAY

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INTRODUCTION: Linaclotide, a guanylate cyclase C (GC-C) agonist, reduces abdominal pain and improves constipation in patients with irritable bowel syndrome with constipation (IBS-C).[1] We recently showed that linaclotide activates GC-C expressed on intestinal epithelial cells, resulting in the production and release of cyclic GMP (cGMP), which accelerates gastrointestinal transit and inhibits colonic nociceptors.[1] We have also shown that key components of the GC-C/cGMP signalling pathway are expressed within human colonic mucosa.

AIMS & METHODS: We investigated whether components of the GC-C/cGMP signalling pathway are differentially expressed in different IBS patient subtypes. Recto-sigmoid mucosal biopsies were obtained from healthy subjects (N = 10) and IBS patients (N = 14), as per Rome II criteria. We compared IBS patients with mixed (constipation and diarrhoea) bowel habits (IBS-M; N = 7) and patients with IBS-C (N = 7). RNA was extracted from biopsies and Taqman qRT-PCR used to assess mRNA expression of: GC-C (*GUCY2C*); the endogenous GC-C agonists, guanylin (*GUCA2A*) and uroguanylin (*GUCA2B*); and the cGMP transporters, MRP4 (*ABCC4*) and MRP5 (*ABCC5*). Expression of these targets was determined relative to the housekeeping genes 18S RNA and GAPDH. In separate biopsies, immunohistochemistry determined localisation of GC-C/cGMP signalling pathway components to cellular structures.

RESULTS: In mucosal biopsies from healthy controls, guanylin was the most abundantly expressed component of the GC-C/cGMP signalling pathway, followed sequentially by uroguanylin ($P < 0.01$), GC-C ($P < 0.001$), MRP5 ($P < 0.001$) and MRP4 ($P < 0.001$), respectively. In IBS-M biopsies, both of the endogenous GC-C agonists (guanylin and uroguanylin) were significantly reduced compared with healthy controls ($P < 0.05$). By contrast, in IBS-C patient biopsies, MRP4 was significantly down-regulated compared with expression in biopsies from healthy controls ($P < 0.001$). No significant change in either MRP5 or GC-C expression was observed between IBS patient subtypes and healthy controls. Immunohistochemistry revealed MRP4 expression on the apical side of colonic epithelial cells, whilst MRP5 displayed basolateral expression.

CONCLUSION: Distinct alterations in the GC-C/cGMP pathway are evident between different subtypes of IBS patients and may contribute to the pathophysiology of IBS. In IBS-M, reduced expression of the endogenous hormones guanylin and uroguanylin may contribute to alternating bowel habits. In IBS-C, a reduction in apically expressed MRP4 may result in reduced release of cGMP into the colonic lumen. Overall, these changes may help to explain some aspects of the pathophysiology associated with IBS and the differential stool frequency and symptom patterns between IBS subtypes, which are under further investigation.

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P0967 EXTRACELLULAR CYCLIC GMP, THE DOWNSTREAM MEDIATOR RELEASED IN RESPONSE TO LINACLOTIDE-INDUCED ACTIVATION OF GUANYLATE CYCLASE C, REDUCES EXCITABILITY OF MURINE AND HUMAN DORSAL ROOT GANGLION NEURONS

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INTRODUCTION: Linaclotide, a guanylate cyclase C (GC-C) agonist, reduces abdominal pain and improves constipation in patients with irritable bowel syndrome with constipation (IBS-C).[1] Cyclic GMP (cGMP) is a second messenger produced in intestinal epithelial cells in response to GC-C activation. We have recently shown that both linaclotide and exogenous extracellular cGMP inhibit colonic nociceptor mechanosensitivity with greater efficacy during chronic visceral hypersensitivity (CVH) compared with healthy nociceptors.[1] However, the effects of exogenous cGMP on sensory neuron function remain to be determined in isolation.
AIMS & METHODS: We investigated the effects of exogenous extracellular cGMP on dorsal route ganglion (DRG) neurons isolated from both mice and humans. For mouse DRG studies we performed whole-cell patch-clamp recordings in current-clamp mode from retrogradely traced colonic DRG neurons. We compared the effect of cGMP (100 nM-50 μM) on the rheobase, or threshold for action potential firing, of DRG neurons from healthy C57BL/6 mice and mice with CVH, 28 days post-trinitrobenzene sulphonic acid administration.[1] For human DRG studies we performed calcium-imaging studies and compared the effects of cGMP (10 μM-300 μM) on Ca^{2+} influx in response to hypo-osmotic stimuli of DRG neurons from healthy donors.
RESULTS: Colonic DRG neurons from CVH mice displayed a significantly reduced rheobase ($P<0.001$, n = 13-23) and fired significantly more action potentials ($P<0.05$, n = 13-23) compared with healthy mice. In a subpopulation of colonic DRG neurons, cGMP inhibited the neuronal excitability of putative nociceptors, significantly increasing the rheobase ($P<0.01$) and reducing action potential discharge ($P<0.01$). This effect was evident in both healthy and CVH DRG neurons, was most apparent in CVH DRG neurons, and occurred at concentrations as low as 100 nM cGMP. In human DRG neurons, cGMP induced an overall reduction in the number of cells responding to hypo-osmotic stimulation. In addition, in human DRG neurons cGMP caused, in a concentration-dependent manner, up to 60% inhibition of the Ca^{2+} influx induced by hypo-osmotic stimulation.
CONCLUSION: Exogenous cGMP directly decreases the excitability of sensory DRG neurons isolated from both mice and humans. These results complement our previous findings in mice, which demonstrated that cGMP inhibited the peripheral endings of nociceptors within the wall of the colon. These current findings also provide further mechanistic insight into how linaclotide, through GC-C agonism and the release of cGMP from mucosal epithelial cells, reduces nociceptive signalling from the colon.
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P0968 EFFECT OF TOLL LIKE RECEPTORS 2 AND 4 ON THE SEROTONIN INDUCED MOTOR RESPONSE MEDIATED BY 5-HT2 AND 5-HT3 RECEPTORS IN MOUSE ILEUM

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INTRODUCTION: The recognition of intestinal microbiota is in part carried out by toll-like receptors (TLR), which are responsible for initiating the innate immune response. Alterations in the intestinal microbiota may contribute to the development of intestinal inflammatory pathologies. Moreover, it has been described that the serotonergic system may result also altered in situations of intestinal inflammation. Serotonin (5-HT) has been shown to regulate gastrointestinal motility by binding to several receptors ($5\text{-}HT_{1\text{-}7}$). However, the influence of TLRs in 5-HT intestinal motor response mediated by 5-HT receptors in the intestine remains unknown.
AIMS & METHODS: The aim of this study was to investigate the role of $5\text{-}HT_2$ and $5\text{-}HT_3$ receptors in the motor response induced by 5-HT in the mouse ileum, and the involvement of TLR2 and TLR4 in this response.
Segments of ileum from male C57/BL10 wild-type (WT), TLR2 $^{-/-}$ and TLR4 $^{-/-}$ mice of 8-12 weeks old were suspended in an organ bath in the direction of longitudinal smooth muscle fibres. The effects of ritanserin ($5\text{-}HT_2$ receptor antagonist) or ondansetron ($5\text{-}HT_3$ receptor antagonist) on motor responses induced by 5-HT in the WT, TLR2 $^{-/-}$ and TLR4 $^{-/-}$ mice were studied. The gene expression (mRNA) of $5\text{-}HT_2$ and $5\text{-}HT_3$ receptors was determined in ileum from WT, TLR2 $^{-/-}$ and TLR4 $^{-/-}$ mice by quantitative RT-PCR.
RESULTS: Expression of $5\text{-}HT_{2A}$, $5\text{-}HT_{2B}$ and $5\text{-}HT_3$ receptors was found in ileum from WT mice. The contractile response induced by 5-HT 100 μM in ileum from WT mice was partially reverted by ritanserin 1 nM and ondansetron 10 nM, suggesting that $5\text{-}HT_2$ and $5\text{-}HT_3$ may be involved in this response. Expression of $5\text{-}HT_{2A}$, $5\text{-}HT_{2B}$ and $5\text{-}HT_3$ in ileum from TLR2 $^{-/-}$ mice, was not modified compared with WT mice. 5-HT-induced contractile response in TLR2$^{-/-}$ mice was partially reverted by ritanserin but not by ondansetron, indicating that $5\text{-}HT_2$ but not $5\text{-}HT_3$ may be involved in this response. In TLR4 $^{-/-}$ mice ileum, the expression of $5\text{-}HT_{2A}$, $5\text{-}HT_{2B}$ and $5\text{-}HT_3$ resulted increased compared with WT mice. The 5-HT-induced contractile response in TLR4$^{-/-}$ was blocked by ritanserin and ondansetron, suggesting that $5\text{-}HT_2$ and $5\text{-}HT_3$ may be involved in this response.
CONCLUSION: These results suggest that $5\text{-}HT_2$ and $5\text{-}HT_3$ receptors are involved in the contractile response evoked by serotonin in mouse ileum. Furthermore, TLR2 and TLR4 seem to interact with $5\text{-}HT_2$ and $5\text{-}HT_3$ receptors.
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P0969 ELECTROPHYSIOLOGICAL PROPERTIES OF COLON BIOPSIES FROM PATIENTS WITH IRRITABLE BOWEL SYNDROME ARE ALTERED BY EXPOSURE TO E. COLI

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INTRODUCTION: Prior research indicates altered basal bowel permeability in IBS patients and aberrations in the expression of tight junction proteins (TJP). We therefore studied the electrophysiological characteristics of colon biopsies using square wave current analysis *in vitro*.
AIMS & METHODS: Sigmoidal colonic biopsies (unprepared colon) from 35 IBS patients (female = 27, median age 29 years (27-37)), (Rome III; IBS-C = 4, IBS-D = 6, IBS-M = 25) and 20 healthy controls (female = 14, median age 36 years (27-47)) were mounted in miniaturized Ussing chambers and a solution with or without *E. coli* ($1x10^8$ CFU/ml) was added to the luminal side. The electrical properties of the mucosa were assessed by square wave current analysis that enables quantification of epithelial/tight junction resistance, net current generated by the membrane, and membrane capacitance reflecting the process of exocytosis. To induce epithelial chloride secretion and/or release of mucin from goblet cells, carbachol (Cch, 1mM) was added on the serosal side. In addition, TJP, claudin and occludin expression in 114 IBS patients (female = 72, median age 32 years (27-39)) (Rome III; IBS-C = 14, IBS-D = 26, IBS-M = 74) and 37 healthy controls (female = 25, median age 27 years (23-35)) was analysed using qRT-PCR. Immunohistochemistry was used to determine the tight junction protein ZO-1 (TJP1) in 56 IBS patients (female = 38, median age 30 years (24-36)) and 19 healthy controls (female = 12, age median age 33 years (26-48)). Data is shown as median, range 25-75 percentile.
RESULTS: Carbachol addition evoked similar changes in electrophysiological parameters in IBS patients and healthy controls, with no differences seen between IBS subgroups. However, IBS biopsies exposed to *E. coli* had an increased basal membrane resistance (10.4 Ohm *cm^2(9.2-12.5) vs. 8.3 Ohm*cm^2 (7.5-10); p = 0.01) and net membrane current (-203.7 uA/cm^2 (-311.9 – -115.9) vs. -121 uA/cm^2 (-210.3 – -79.7); p = 0.005) compared to unexposed IBS biopsies. *E. coli* exposed IBS biopsies also had an increased response to CCh compared to unexposed IBS biopsies (-321.5 uA/cm^2 (-411.3 – -216.5) vs. -236.8 uA/cm^2 (-335.8 – -102.3); p = 0.01) and a reduced capacitance response (4.3 uF/cm^2 (2.5-8.2) vs. 7.8 uF/cm^2 (6.2-11.7); p = 0.04). qRT-PCR analyses, demonstrated a tendency

towards lower expression of claudin ($p = 0.07$) and TJP1 ($p = 0.06$) in IBS patients compared to healthy controls. Occludin expression was similar in IBS patients and healthy controls, but was higher in IBS-C compared to IBS-M ($p = 0.004$). No significant difference was seen in levels of TJP1 ZO-1 protein expression between IBS patients and healthy controls ($p = 0.4$).
CONCLUSION: Colon mucosa from IBS patients reacts differently to mucosal exposure to E. coli, with increased basal membrane resistance and net membrane current as well as an increased reactivity to the muscarinic agonist CCh. The exact mechanisms behind these phenomena remain unknown but may reflect altered reactivity of epithelial ion channels and/or tight junctions.
Disclosure of Interest: None declared

P0971 MICROANGIOPATHY IS COMMON IN SUBMUCOSAL VESSELS THROUGHOUT THE LARGE INTESTINE

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INTRODUCTION: The pathophysiology behind gastrointestinal dysmotility in diabetes mellitus is unknown. Both esophageal dysmotility and gastroparesis have been shown to be associated with retinopathy, suggesting microangiopathy as important also for dysmotility.
AIMS & METHODS: The aim of the present study was to examine whether patients with diabetes mellitus exhibit microangiopathy in the large intestine, and if present, to correlate this to the clinical picture.
Consecutive patients subjected to surgery of the large intestine at any of the Departments of Surgery in the southernmost districts of Skåne between January 2011 and May 2013 were identified. All medical records were scrutinized, and patients with a history of diabetes mellitus were reconsidered for histopathologic reevaluation, according established criteria (1, 2). Morphometric examination of the vessels was compared with biopsies from non-diabetic patients. Gender, age, type of diabetes, diabetic complications, type of diabetes treatment, and other concomitant diseases were registered from the medical records.
RESULTS: Of 1135 identified patients during the studied time period, 94 patients suffered from diabetes mellitus and were finally examined. Twenty-nine non-diabetic patients served as controls. The mean age was 71.8 ± 10.3 and 70.0 ± 12.1 years in patients and controls, respectively. Microangiopathy was found in 68% of patients and in 17% of controls ($p < 0.001$). The wall-to-lumen relation was 0.31 (0.23–0.46) in patients with diabetes mellitus compared with 0.18 (0.13–0.24) in controls ($p < 0.001$). The records did not include any information about gastrointestinal symptoms. There was no association between microangiopathy and clinical picture available.
CONCLUSION: Microangiopathy in the large intestine is more common in patients with diabetes mellitus than in controls. This may contribute to dysmotility secondary to diabetes mellitus.
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Disclosure of Interest: None declared

P0972 CHARACTERISATION OF NAUSEA IN WELL-CONTROLLED AND LONG-TERM, OPEN-LABEL STUDIES OF LUBIPROSTONE FOR CHRONIC IDIOPATHIC CONSTIPATION, OPIOID-INDUCED CONSTIPATION, AND IRRITABLE BOWEL SYNDROME WITH CONSTIPATION

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INTRODUCTION: Lubiprostone (LBP) has been studied for the treatment of chronic idiopathic constipation (CIC) in adults, opioid-induced constipation (OIC) in adults with chronic non-cancer pain who are taking full-agonist opioids other than diphenylheptanes, and irritable bowel syndrome with constipation (IBS-C). LBP has a favourable overall safety profile, with nausea being the most common adverse event (AE). Here, we provide a detailed characterization of nausea in pivotal studies of LBP across all 3 indications.
AIMS & METHODS: The CIC analysis includes data pooled from 3 short-term (3–4 weeks' duration), randomised, placebo (PBO)-controlled and 3 long-term (one 24-week and two 48-week), open-label studies of LBP. Overall, 316 CIC patients received PBO and 1113 received LBP 24 mcg twice daily (BID). The OIC analysis includes data pooled from three 12-week, randomised, PBO-controlled studies and one 36-week, open-label extension study. OIC patients received PBO ($n = 652$) or LBP 24 mcg ($n = 889$) BID. The IBS-C analysis includes data pooled from three 12-week, randomised, PBO-controlled studies and one 36-week, open-label study. In total, 435 IBS-C patients received PBO and 1011 received LBP 8 mcg BID.
RESULTS: The crude incidence of nausea in patients receiving LBP was 31.1%, 13.9%, and 11.4% in the CIC, OIC, and IBS-C populations, respectively, when exposed to LBP for up to 12 months; corresponding rates in patients treated with PBO over 4- and 12-week periods ranged from 5.1%–6.7%. For the same time-periods, the incidence of severe nausea in patients receiving LBP was 3.5%, 1.0%, and 0.9% in the CIC, OIC, and IBS-C populations, respectively, with corresponding rates in patients treated with PBO ranging from 0%–1.1%. Nausea led to discontinuation in 8.7%, 2.1% and 1.3% of the CIC, OIC, and IBS-C populations receiving LBP, respectively, with corresponding discontinuation rates in patients treated with PBO ranging from 0%–0.7%. Of those CIC, OIC, and IBS-C patients who received LBP and reported nausea at any time during the treatment period, 83.6%, 87.9%, and 88.7%, respectively, reported only 1 event of nausea. Of these patients, 62.1%, 75.2%, and 63.7% did not require a change to their assigned dosing regimen for CIC, OIC, or IBS-C, respectively, with nearly three-quarters of these patients completing the full treatment period with LBP (72.7%, 70.7%, and 73.8%, respectively). Of those CIC, OIC, and IBS-C patients who reported only 1 nausea event, 12.0%, 8.3%, and 17.7%, respectively, either reduced their intake to once daily (QD) dosing or temporarily withheld medication, which allowed for 54.5%, 66.7%, and 100% of these patients, respectively, to complete LBP dosing in the clinical trial. Across the 3 indications, the majority of reported nausea events occurred during the first 5 days after beginning LBP treatment (66.9%).
CONCLUSION: Most patients report only a single event, with a majority of events being mild-to-moderate severity and occurring early in the treatment period. In addition to an emphasis on dosing with meals, dose reduction and/or temporary withholding of doses are strategies that may be employed for management of nausea in patients taking lubiprostone.
Disclosure of Interest: B. Cryer: None declared, L. R. Webster: None declared, T. Losch-Beridon Shareholder of: Sucampo, Other: Sucampo employee

P0973 PUBORECTALIS MUSCLE AND EXTERNAL ANAL SPHINCTER DO NOT, BY DEFINITION, BEHAVE AS ONE FUNCTIONAL UNIT IN PATIENTS WITH FUNCTIONAL DEFECATION DISORDER

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INTRODUCTION: Functional defecation disorder (FDD) is common and underlies about half of the cases of chronic constipation. Rome III-classification distinguishes dyssynergic defecation and inadequate defecatory propulsion, which can be further subdivided according to a classification proposed by Rao et al.[1,2]
Both classifications are based on the unsubstantiated assumption that puborectalis muscle and external anal sphincter behave as one functional unit during attempted defecation. What if it turns out that puborectalis muscle and external anal sphincter do not, by definition, function as one unit and are therefore not, by definition, equally affected in patients suffering from FDD? That could have an impact on both classification, diagnostics and treatment of FDD.
AIMS & METHODS: Anorectal manometry and defecometry test were performed in 124 adult patients suffering from FDD. Pressure changes were recorded at three levels: rectum, puborectalis muscle and external anal sphincter.
RESULTS: Defecometry test revealed that puborectalis muscle and external anal sphincter do not consistently contribute equally to FDD. Three main groups can be identified: congruent FDD (puborectalis muscle and external anal sphincter are more or less equally affected; $n = 105$), anal sphincter-dominated FDD (external anal sphincter is significantly more affected than puborectalis muscle; $n = 10$) and puborectalis-dominated FDD (puborectalis muscle is significantly more affected than external anal sphincter; $n = 9$).
Defecatory propulsive force (increase in rectal pressure that is required for defecation) is stronger correlated to pressure increase at the level of the puborectalis muscle ($\rho = 0.794$) than to pressure increase at the level of the external anal sphincter ($\rho = 0.488$).
Male patients generate a higher defecatory propulsive force than female patients ($p < 0.001$). They also build more pressure on the level of the puborectalis muscle ($p = 0.003$) and suffer relatively more often from puborectalis-dominated FDD.
CONCLUSION: Puborectalis muscle and external anal sphincter do not, by definition, behave as one functional unit in patients suffering from FDD and may thus differ in degree of dyssynergia. This understanding might have some important consequences for classification, diagnostics and treatment of FDD. It questions, for example, the reliability of the single probe electromyographic devices currently used in treatment of FDD.
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Disclosure of Interest: None declared

P0974 CONFIRMATORY FACTOR ANALYSIS OF THE PATIENT ASSESSMENT OF CONSTIPATION-SYMPTOMS (PAC-SYM) IN PATIENTS WITH CHRONIC CONSTIPATION

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INTRODUCTION: PAC-SYM is widely adopted to evaluate constipation severity. However it has been validated in a small sample, few items have been included based on expert opinion and not on empirical grounds and its factor structure has never been replicated. We sought to assess its psychometric

properties, its responsiveness to clinical changes and characterizing its relationship with key outcomes such as quality of life and treatment satisfaction in a large sample of patients with chronic constipation.
AIMS & METHODS: We enrolled 2203 outpatients with chronic constipation in two waves. We used the wave I sample to test psychometric properties and construct validity of the PAC-SYM and wave 2 sample to cross-validate the factor structure with confirmatory factor analysis (CFA), and to assess criterion validity, responsiveness to clinical changes and the minimal clinically important difference.
RESULTS: We observed a large floor effect for rectal tearing (62%). Deletion of such item lead to a 11-item version (M: PAC-SYM). Exploratory Factor Analysis revealed a bifactor model with 2 subscales (stool and abdominal symptoms) and a general severity factor. CFA consucted on the second wave dataset supported this solution. The M:PAC-SYM demonstrated excellent reliability ($\alpha = 0.89$), moderate correlation with SF-12 and treatment satisfaction (r = 0.28-0.45), discrimination across Rome III criteria for functional constipation and abdominal pain (table 1), and responsiveness to clinical change (β -0.49; $\omega^2 = 0.25$). M:PAC-SYM minimal clinically important difference was 0.24.

Clinical Characteristics*	M-PAC-SYM Δ (σ)	M-ABD	M-STO
Rome III			
Lumpy/Hard Stools	**0.32 (0.40)**	0.16 (0.17)	**0.39 (0.42)**
Incomplete Evacuation	**0.44 (0.63)**	**0.29 (0.36)**	**0.52 (0.65)**
Obstruction	**0.57 (0.74)**	**0.29 (0.33)**	**0.68 (0.78)**
Manual Maneuvers	**0.26 (0.33)**	0.04 (0.04)	**0.39 (0.43)**
<3 defecations/wk	0.03 (0.04)	0.13 (0.15)	0.13 (0.14)
Strain	**0.29 (0.37)**	**0.22 (0.25)**	**0.33 (0.36)**
Abdominal Pain	**0.26 (0.32)**	**0.44 (0.48)**	0.16 (0.17)

CONCLUSION: We developed a modified version of the PAC-SYM which might better represent symptom severity of most patients seeking care in gastroenterology referral centers.
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P0975 DIFFERENT INNERVATIONS FOR CONSCIOUS AND AUTONOMIC ANAL SPHINCTER CONTRACTIONS IN ADULT PATIENTS

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INTRODUCTION: Fecal continence is partially maintained by external anal sphincter contraction and the anal-external sphincter continence reflex[1,2]. Whereas the first system is supplied by the pudendal nerve[3], it is unknown if the reflex part of the external anal sphincter is also mediated by the pudendal nerve.
AIMS & METHODS: The present study aims to determine if in patients with pudendal neuropathy both continence systems, concerning the external anal sphincter, are malfunctioning. Retrospectively, we reviewed the medical records of all patients older than seventeen who had undergone an anorectal function test between January 2010 and March 2013 and in which nerve supply to and functional anatomy of the external anal sphincter was not damaged by surgery, trauma, and/or polyneuropathy (N = 70). The study was conducted at University Medical Center Groningen, the Netherlands.
RESULTS: The patients were divided into two groups, one group without signs of pudendal neuropathy (anal electrosensibility ≤ 4 mA at one and two centimeter into the anal canal, PudNP-), and the other group with signs of pudendal neuropathy (anal electrosensibility > 4 mA at one and two centimeter into the anal canal, PudNP+). Of the seventy patients, 76% had pudendal neuropathy. PudNP+ were significantly older than PudNP- ($P = .013$). Maximum anal sphincter contractility, i.e. conscious contraction, was significantly lower in PudNP+ than in PudNP- (median: 165 versus 235 mm Hg, $P = .007$). By contrast, pressure in the anal canal at maximum tolerable or retainable sensation, i.e. autonomic contraction, did not significantly differ between the two groups (median: 135 versus 153 mm Hg). Furthermore, no relation was found between maximum anal sphincter contractility and pressure in the anal canal at maximum tolerable or retainable sensation. Multiple linear regression analyses demonstrated that age and electrosensibility, measured at two centimeters into the anal canal, significantly predicted conscious contraction, but not autonomic contraction.
CONCLUSION: Autonomic reflex contraction of the external anal sphincter is most probably mediated by nerve fibers different from those responsible for conscious contraction (the pudendal nerve). A potential source might be a direct branch from the fourth sacral nerve. This needs to be elucidated in a prospective study set up.
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P0976 LUBIPROSTONE IS WELL TOLERATED FOR TREATMENT OF OPIOID-INDUCED CONSTIPATION IN CHRONIC NON-CANCER PAIN PATIENTS: RESULTS OF THREE PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS

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INTRODUCTION: Chronic opioid use is often associated with the common adverse effect of serious constipation; however, there are limited treatment options for patients with opioid-induced constipation (OIC) in patients with non-cancer pain. The efficacy and safety of lubiprostone (LBP), a selective ClC-2 activator, for treating OIC in subjects taking opioids for chronic, non-cancer pain was evaluated in three multicentre, 12-week, randomised, double-blind, placebo-controlled, Phase 3 trials. An integrated analysis of data from those 3 trials was conducted to determine the overall safety profile of LBP in this population.
AIMS & METHODS: Adults on chronic opioid therapy with documented OIC (i.e., defined as having, on average < 3 spontaneous bowel movements/week), were randomised to receive double-blind LBP 24 mcg or placebo twice daily (BID). Adverse events (AEs) were recorded electronically by the subject or investigator; graded as mild, moderate, or severe; and assessed for seriousness and relationship to study drug.
RESULTS: The combined safety population from the 3 trials (N = 1315; LBP, n = 663; placebo, n = 652; mean age, 50.4 years) comprised mostly female (62.7%) and white (82.6%) subjects. The most common (≥5% in the LBP arm) treatment-emergent AEs (TEAEs) were gastrointestinal (GI) disorders, with nausea, diarrhea, and abdominal pain reported 2.1, 2.5, and 3.3 times more with LBP than with placebo. Incidences of other TEAEs were comparable with LBP and placebo. In both the LBP and placebo arms, most subjects experienced mild (38.3% vs 36.5%) or moderate (31.5% vs 26.7%) TEAEs, with few severe TEAEs (8.9% vs 8.0%); the rest had no TEAEs. The incidence of severe TEAEs was similar with LBP or placebo, except for diarrhea (1.8% vs 0.3%), vomiting (0.3% vs 0.8%), and abdominal distension (0% vs 0.6%). Significantly more subjects in the LBP arm had ≥1 treatment-related AE (TRAE; 30.8% vs 20.2%; P < 0.0001) or ≥1 GI TRAE (24.7% vs 12.9%). The most common (≥5% in the LBP arm) TRAEs were GI disorders, with nausea and diarrhea reported 2.5 and 4.3 times more in the LBP arm. The other TRAEs (≥1% of LBP arm) were, in order of decreasing frequency, abdominal pain, abdominal distension, flatulence, vomiting, headache and oedema peripheral experienced 3.5, 2.2, 1.3, 1.9, 1.4 and 3.7 times more in the LBP-treated patients vs placebo, respectively. Percentages of subjects experiencing ≥1 serious AE (SAE) were similar in the LBP and placebo arms (3.9% vs 3.2%; p = 0.554). The only SAEs reported in >1 subject were migraine and back pain (LBP arm) and upper abdominal pain, fecaloma, and back pain (placebo arm). No SAEs were attributed to LBP; 3 SAEs (pneumonia, hypersensitivity, and fecaloma) were attributed to placebo. One death was reported in the LBP arm (multiple drug toxicity), but was assessed as unrelated to study drug by the investigator. Significantly more subjects treated with LBP (7.2%) compared with placebo (3.1%) withdrew from the studies because of AEs (p = 0.001), most commonly GI AEs (LBP, 4.4% vs placebo, 0.9%; P < 0.001).
CONCLUSION: An integrated safety analysis from 3 randomised, double-blind, placebo-controlled trials demonstrates that LBP, when used in chronic non-cancer pain subjects with OIC, is well tolerated.
Disclosure of Interest: P. Lichtlen Consultancy for: Sucampo, T. Losch-Beridon Shareholder of: Sucampo, Other: Sucampo employee, M. Wang Other: Sucampo employee

P0977 LANREOTIDE AUTOGEL 120 MG FOR CHRONIC REFRACTORY DIARRHEA: A MULTICENTER PROSPECTIVE TRIAL

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INTRODUCTION: Lanreotide has an inhibitory effect on gastrointestinal secretions and motility. We evaluated the efficacy and safety of the prolonged-release somatostatin analogue lanreotide Autogel 120 mg for the treatment of persistent diarrhea in a multicenter, prospective, open label study.
AIMS & METHODS: The study was performed in 10 centers between July 2009 and August 2012. The study protocol was approved by the Ethics Committee of

UZ Leuven, Belgium (V). Male or female adult patients with refractory diarrhea (mean of > 3 stools/24 h) for at least 1 month after workup to rule out inflammatory, infectious causes, and rectum disorders, and insufficient /non-response to standard anti-diarrheal were treated for 8 weeks with lanreotide autogel 120 mg deep s.c. every 4 weeks. Patients' stool frequency and consistency (Bristol Stool Form Scale) were recorded in a daily diary. Quality of life (QOL) was assessed using the SF-36 and IBS-QOL questionnaires. Responders were patients with a ≥50% decrease or a normalization of the mean number of stools. Adverse events (AEs) were recorded during the entire study.
RESULTS: In total, 36 patients (24 women, 12 men) with chronic refractory diarrhea were studied. The mean age was 55.2 ± 16.4 years. Four weeks after the first injection (Day 28), 44.4% of patients were responders, which increased to 54.3% at Day 56. Response rates were higher in male patients (58.3%) compared to females (37.5%). Overall, the mean number of stools decreased significantly from 5.5 ± 2.3 at baseline to 3.6 ± 2.2 at Day 56 (-30.7%) (p = 0.0006). In the responder subgroup at Day 56 this number changed significantly from 5.3 ± 2.4 to 2.2 ± 0.8 (p < 0.0001). The median percentage of days per week with less than 3 stools/day increased from 7.1% at baseline to 57.1% at Day 56. In the responder subgroup at Day 56, the mean stool consistency score dropped significantly from 6.4 ± 0.7 to 5.2 ± 1.2(p = 0.0005). At Day 56, the mean IBS-QOL score increased with 16.3 points. Similarly, the SF36-QOL scores improved at Day 56, especially in the domains of social functioning (+14.0), physical role (+11.8) and mental health (+10.1). The improvement in IBS-QOL was very significant in the responder group with an increase from 48.4 to 76.7 (p = 0.0001), indicating that the improvement in stool consistency and frequency resulted in an improvement of QOL. In total, 93 treatment emergent AEs were reported, of which the majority (79) were mild to moderate and 9 were serious. The most frequently reported AEs were gastrointestinal disorders (abdominal pain, 25% of patients; nausea, 11.1% and steatorrhea, 8.3%), injection site reactions (16.7%) and asthenia/fatigue (11.1%).
CONCLUSION: This study showed improvement of diarrheal symptoms and QOL during therapy with lanreotide autogel 120 mg treatment, which suggest it is effective for the management of persistent refractory diarrhea. Confirmatory studies are needed.
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P0978 SMALL-BOWEL ABNORMALITIES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME - A CAPSULE ENDOSCOPY STUDY

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INTRODUCTION: Irritable bowel syndrome (IBS) is the most common functional digestive disorder globally, affecting 10-20% of the adult population in several western countries. IBS is diagnosed when the symptoms fulfill the Rome III criteria, however, the small bowel was not examined.
AIMS & METHODS: We conducted a case-control study to determine whether capsule endoscopy (CE) detects small-bowel abnormalities in IBS patients. Study subjects were 57 patients who met the Rome III criteria for IBS and were scheduled to undergo CE (PillCam SB or SB2; Given Imaging Ltd., Yoqneam, Israel) for investigation of their symptoms at Hiroshima University Hospital between April 2006 and December 2013 (IBS group) and 57 patients with occult obscure gastrointestinal bleeding (OGIB) were selected as control (OGIB [control] group). Patients in the IBS group were further classified according to the type of IBS: constipation–prevalent IBS (subgroup A, n = 40); diarrhea-prevalent IBS (subgroup B, n = 26); or mixed IBS (subgroup C, n = 9). CE was evaluated in all groups according to the total enteroscopy achievement rate, mean small-bowel transit time, small-bowel lesion detection rate, and the types of small-bowel lesions detected. All statistical analyses were carried out with JMP statistical software version 5.0.1J (SAS Institute Inc., Cary, NC, USA). $P < 0.05$ was considered significant.
RESULTS: Total enteroscopy was achieved by CE in 82% (47/57) of patients in the IBS group and 80% (45/57) of patients in the OGIB group; the difference between the two groups was not significant. For patients in whom total enteroscopy was achieved by CE, mean small-bowel transit time was 270 minutes in the IBS group and 268 minutes in the OGIB group, with no significant between-group difference. In the IBS group, total enteroscopy was achieved per subgroup as follows: subgroup A, 76% (22/29); subgroup B, 89% (17/19); and subgroup C, 89% (8/9). The mean small-bowel transit times were 280 minutes, 254 minutes, and 277 minutes, respectively, with no significant difference among them. The small-bowel lesion detection rates were 29% (20/57) and 28% (16/57) in the IBS group and OGIB group, respectively. Small-bowel lesions detected by CE in the IBS group were non-specific enteritis (n = 16), non-specific ulcer (n = 1), eosinophilic enteritis (n = 1), ischemic enteritis (n = 1), and lesioning due to a parasitic worm (n = 1); otherwise, no abnormality was found (n = 37). Small-bowel lesions detected by CE in the OGIB group were non-specific enteritis (n = 6), non-specific ulcer (n = 6), submucosal tumor (n = 3), and diverticulum (n = 1); otherwise no abnormality was found (n = 41). The prevalence of non-specific enteritis was significantly high in the IBS group versus the OGIB group ($p < 0.05$). Small-bowel lesion detection rates in the IBS subgroups were as follows: subgroup A, 17% (5/29); subgroup B, 68% (13/19); and subgroup C, 22% (2/9). The detection rate in subgroup B (versus subgroup A and subgroup C) was significantly high ($p < 0.05$).
CONCLUSION: CE detected no significant abnormalities that explained the symptoms in the majority of our patients with IBS; thus, the use of CE in IBS patients is not supported by the current data.
Disclosure of Interest: None declared

P0979 A PHASE 1 STUDY TO INVESTIGATE THE ABSORPTION, METABOLISM AND EXCRETION OF 14C PRUCALOPRIDE AFTER A SINGLE ORAL DOSE

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INTRODUCTION: Prucalopride is a 5-hydroxytryptamine receptor agonist that stimulates intestinal motility and is approved in Europe for the treatment of women with chronic constipation in whom laxatives fail to provide adequate relief. The absorption, metabolism and excretion (AME) of prucalopride has been reported previously; however, poor recovery of total radioactivity led to uncertainty regarding the mass balance properties of the drug.
AIMS & METHODS: The aim of this phase 1 study (NCT01807000) was to use microtracer dosing (200 nCi radioactivity) with accelerator mass spectrometry (AMS) to investigate the AME profile of ^{14}C-radiolabelled prucalopride after a single oral dose and to obtain more robust data. Healthy men aged 18–50 years were enrolled in the study. A single oral dose of 2 mg ^{14}C-prucalopride (200 nCi radioactivity) was administered on day 1. Blood samples were collected at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 8 and 12 hours on day 1, and once daily thereafter until day 11. Urine and stool samples were collected and electrocardiogram and vital signs were recorded on every day of the study. Pharmacokinetic parameters were calculated from concentrations of prucalopride measured by liquid chromatography–tandem mass spectrometry (LC–MS/MS). Total radioactivity and metabolites from LC fractions were measured using AMS. Metabolites were identified using authentic standards, when available, and by LC coupled with high resolution MS. Results presented are mean ± standard deviation unless otherwise specified.
RESULTS: Six men were enrolled in the study (mean age: 35.5 ± 10.45 years). Following oral administration, ^{14}C-prucalopride was absorbed rapidly (median time to maximum plasma concentration [t_{max}]: 2.75 h [range: 1.13–4.00 h]) and was eliminated with a half-life ($t_{½}$) of 20.6 ± 5.35 h. For prucalopride, the maximum plasma concentration (C_{max}: 3.79 ± 1.10 ng/mL) and area under the concentration–time curve ($AUC_{0-\infty}$: 96.5 ± 9.64 ngh/mL) accounted for 92% and 95% of the total radioactivity in plasma, respectively. The blood:plasma radioactivity concentration ratios ranged from 1.74 to 2.06 up to 48 hours post-dose. Most of the administered dose of prucalopride (84.2 ± 8.9%) was recovered in urine, and an additional 13.3 ± 1.7% of the dose was recovered in faeces (total recovery: 97.5 ± 8.6%). Approximately 65% of the dose recovered in urine and 5% in faeces was intact prucalopride. Quantitatively important metabolites identified in the urine and faeces were products of O-demethylation, N-dealkylation and oxidation.
CONCLUSION: The AMS with microtracer approach was used successfully in this study, with good total recovery of radioactivity in urine and faeces (97.5 ± 8.6% of the administered radioactive dose). Following oral administration of a 2 mg dose of prucalopride, at least 84% of the drug was absorbed. The observed blood:plasma ratio of radioactivity indicates that there was moderate uptake of prucalopride (and metabolites) into blood cells. Systemic exposure to prucalopride metabolites was low, and both prucalopride and its metabolites were eliminated in urine and, to a lesser extent, faeces. This shows that renal clearance is the primary route of elimination of prucalopride.
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P0980 EFFICACY AND SAFETY OF PRUCALOPRIDE IN MEN WITH CHRONIC CONSTIPATION: A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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INTRODUCTION: Prucalopride (PRU) is a high-affinity serotonin receptor (5-HT_4) agonist approved in Europe for the symptomatic treatment of chronic constipation (CC) in women in whom laxatives fail to provide adequate relief.
AIMS & METHODS: The aim of this phase 3, multicenter, parallel-group, double-blind trial was to evaluate the efficacy and safety of PRU in men (NCT01147926). Men aged ≥18 years with CC who had ≤2 spontaneous complete bowel movements (SCBMs) per week were randomized to receive placebo (PLA) or PRU 2mg (starting dose of 1mg for patients ≥65 years) once daily for 12 weeks. The primary endpoint was the proportion of patients achieving a mean of ≥3 SCBMs per week over 12 weeks. Secondary endpoints included the Patient Assessment of Constipation-Symptoms (PAC-SYM) and -Quality of Life (PAC-QOL) questionnaires. Safety was assessed throughout the study.

RESULTS: In total, 374 patients from 10 European countries were randomized (187 per treatment group). Baseline demographics were similar between treatment groups with an overall mean age of 58.5 (SD: 16.91) years and mean duration of CC of 9.2 (SD: 11.63) years. The primary endpoint was achieved by significantly more patients in the PRU group (37.9%) than in the PLA group (17.7%, $p<0.0001$). More patients on PRU than PLA achieved an improvement of ≥1 SCBM/week (53.7% vs 45.3%; $p=0.0743$) and an improvement of ≥1 SBM/week (65.5% vs 43.1%; $p<0.0001$). At the final on-treatment assessment, there was no significant difference between groups in the proportion of patients with a clinically relevant improvement of ≥1 point in total PAC-SYM score (PRU: 34.9%; PLA: 30.4%; $p=0.3152$), abdominal (39.1% vs 35.1%; $p=0.4874$) or rectal subscale score (34.9% vs 29.2%; $p=0.2759$). However, there was a significant difference in stool symptoms score (53.3% vs 36.3%; $p=0.0005$). The proportion of patients with an improvement of ≥1 in PAC-QOL score was higher with PRU (40.2%) than PLA (32.7%; $p=0.0755$), particularly in the satisfaction (52.7% vs 38.8%; $p=0.0035$) and physical discomfort subscales (50.3% vs 39.2%; $p=0.0249$). The overall safety profile was consistent with previous studies. The most common adverse events (AEs) were abdominal pain (PRU vs PLA: 4.3% vs 5.9%), diarrhoea (6.5% vs 1.6%), nausea (6.0% vs 2.2%), headache (9.2% vs 3.8%) and dizziness (2.2% vs 1.6%). The incidence of serious AEs and ischaemic cardiovascular adverse events was low and comparable between treatment groups.

CONCLUSION: In this first study of efficacy of PRU in an exclusively male patient population, PRU significantly increased the proportion of men achieving an average of ≥3 SCBMs per week compared with PLA. No new safety concerns were identified. These results demonstrate a positive benefit–risk profile for the use of PRU in men with CC.

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P0981 EVALUATION OF A NEW DIAGNOSTIC METHOD FOR ANAL SPHINCTER RUPTURE BY THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY

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INTRODUCTION: Anorectal manometry is the gold standard to explore anorectal disorders. Endoanal ultrasound (EUS) is commonly associated for the diagnosis of anal sphincter rupture. 3-Dimensional High-Resolution Anorectal Manometry (3DHRAM) seems able to provide new topographic information, including an assessment of the integrity of the sphincters.

AIMS & METHODS: The aim of the study was to develop a method for computerized analysis of 3DHRAM results to optimize the diagnosis of anal sphincter defect, compared with the EUS as gold standard.

All patients referred to our center to explore anal incontinence or dyschesia by 3DHRAM and EUS were eligible. 3DHRAM measured anal resting and voluntary contraction pressure which reflected internal anal sphincter and external anal sphincter respectively. A software was created to analyze 3DHRAM records. Significant pressure parameters were calculated to separate patients with anal sphincter rupture and patients without rupture. The combination of these parameters resulted in a 3DHRAM diagnostic score for anal sphincter rupture, compared with the EUS.

RESULTS: A total of 206 patients (91% females) with a mean age of 54.6 ± 14.9 years were included. The EUS diagnosed an anal sphincter defect in 130 (63%) patients, 76 (37%) patients were without rupture. 40 pressure parameters were defined from 3DHRAM records by the software. 5 most significant pressure parameters were selected for the construction of diagnostic scores. Overall, the diagnostic score for the internal anal sphincter defect had a sensitivity of 65% and a specificity of 65%, with a positive predictive value of 75% and a negative predictive value of 53%. For the external anal sphincter defect, the diagnostic score had a sensitivity of 43% and a specificity of 87%, with a positive predictive value of 82% and a negative predictive value of 53%.

CONCLUSION: A computerized diagnostic method of 3DHRAM results was developed for a systematic and comprehensive analysis. However, 3DHRAM has not shown sufficient diagnostic capacity for sphincter defect, compared to EUS. A better distinction between anal sphincter defect and neurological damage, which can also affect the pressure recorded at the 3DHRAM, could improve our diagnostic scores.

Disclosure of Interest: None declared

P0982 PROSPECTIVE EVALUATION OF RECTAL BOTULINUM TOXIN INJECTION IN FECAL INCONTINENCE

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INTRODUCTION: *Botulinum Toxin* (BT) has been widely used to treat urinary incontinence in the context of overactive bladder. It has been previously suggested in 6 patients that injection of BT in the reservoir may relieve faecal incontinence (FI) in patients with either overactive rectum or colonic pouch after protectomy (1). However, the efficacy of rectal BT injection in patients with FI related to anal sphincter incompetence has never been investigated.

AIMS & METHODS: We prospectively investigated the efficacy of rectal BT injection in 21 patients with FI. In 11 patients, FI was related to anal sphincter incompetence, in 4 patients to overactive rectum and in 6 patients to overactive colonic pouch after proctectomy. All patients failed medical therapy, and 7 patients were unresponsive to sacral nerve root stimulation. BT injection consisted in a session of 10 injections of 50 UI of Dysport ® (3-4 injections every 5 cm) in the submucosa of the rectum or of the colonic pouch as previously reported (1). Clinical efficacy and quality of life were assessed at baseline, at 3 and 6 months after BT injection with the Cleveland Clinic and the FIQL scores, respectively. Anorectal manometry was performed before and 3 months after BT injection.

RESULTS: Compared to pre-operative values of the 21 patients, Cleveland Clinic (12.7 ± 1.2) and the FIQL (1.9 ± 0.2) scores improved at 3 months (9.7 ± 1.2 and 2.4 ± 0.2, respectively; $p<0.05$ for both). After a single session of injection ($n=6$), the Cleveland Clinic and the FIQL scores at 6 months returned to pre-operative values. By contrast, in patients with a second session performed 3 months after the first one ($n=8$), the Cleveland Clinic and the FIQL scores remained decreased at 6 months compared to pre-operative values ($p<0.01$ for both). At 3 months, neither anal tone and squeezing pressures, nor rectal volume and compliance were affected by BT injections. Univariate analysis failed to evidence factors associated with a poor clinical response. In particular, similar improvement was noted in patients with anal sphincter incompetence or with an overactive reservoir. No serious adverse events were reported.

CONCLUSION: Our study is the first to demonstrate that injection of BT in the rectum or in the colonic pouch is effective at 3 months to treat FI. A second injection seems to be necessary to achieve improvement at 6 months. Efficacy of BT is not related to FI origin (anal sphincter incompetence vs with an overactive reservoir) and is not explained by modification of rectal volume and/or compliance.

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P0983 TRICYCLIC ANTIDEPRESSANTS FOR SYMPTOMATIC TREATMENT OF INTRACTABLE TENESMUS IN THE SETTING OF RECTAL PROLAPSE

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INTRODUCTION: The spurious feeling of the need to evacuate the bowels, with little or no stool passed (tenesmus) can cause severe distress and a negative impact on quality of life. Management is focused on the primary cause of tenesmus and not on tenesmus itself. Rectal prolapse is occasionally encountered as the main etiology of tenesmus, in those patients surgical consultation is warranted. Tenesmus in this setting is particularly problematic since it leads the patient to a vicious cycle of straining with deterioration of prolapse and subsequent worsening of tenesmus. Tricyclic antidepressants (TCAs) have been shown to reduce ano-rectal hypersensitivity in patients with irritable bowel syndrome (IBS), by centrally mediated mechanisms and are commonly used to treat functional chronic pelvic pain syndromes. We have used the same approach to treat patients referred to our tertiary center suffering from intractable tenesmus that are poor surgical candidates or refuse surgical correction.

AIMS & METHODS: From 2010 we created a registry of patients with rectal prolapse that were poor surgical candidates or refused surgical correction and received treatment with TCA for rectal tenesmus. Only patients with rectal mucosal prolapse or full-thickness rectal prolapse with high internal intussusception or externally visible only with straining were included. Patients with full-thickness rectal prolapse externally visible at all times or with an impending surgical indication were excluded.

RESULTS: Twenty one patients were treated by this approach, 81% were female, the mean age was 74.81+14.39 years, and symptoms were present for a mean of 9±7 months. The feeling of an anal protrusion on straining, anal pain, fecal incontinence and constipation were present in 75, 42.9, 36.8 and 26.3% of patients respectively. Full thickness rectal prolapse was present in 57% of patients, while 43% had internal rectal mucosal intussusceptions. Nortryptiline 25mg, amitriptyline 10mg and desipramine 25mg were used in 43, 38 and 19% of patients respectively. After a mean follow up of 7.18+5.5 months 76% of patients reported significant improvement in symptoms, 14% were lost to follow up and 10% ($n=3$) failed to respond. The response rates were 88% (7/8) for nortryptiline, 100% (4/4) for desipramine and 55% (5/9) for amitriptyline. Noteworthily in 5 patents, symptoms were completely resolved obviating the need for surgery, most probably due to cessation of the vicious cycle of tenesmus, straining and worsening of prolapse. Additionally the treatment was very useful in patients suffering from dementia, who could not be convinced to stop straining.

CONCLUSION: To our knowledge this is the first report to address the symptomatic treatment of tenesmus in patients with rectal prolapse. TCAs may be an acceptable option for poor surgical candidates or patients refusing surgical treatment. Nortryptiline or desiparamine had a trend to better response rates compared to amitryptiline in an uncontrolled setting.

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P0984 NORMAL VALUES FOR 3D ANO-RECTAL HIGH RESOLUTION MANOMETRY: A PRELIMINARY REPORT

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INTRODUCTION: 3D ano-rectal high resolution manometry (3D ARHRM) has been recently developed. Closely spaced pressure sensors allow a precise definition of pressure profile within the anal canal. However normal values are scarce with this device.
AIMS & METHODS: This study aimed to determine normal values for 3D ARHRM and to compare them to those obtained in patients with fecal incontinence. Fifty seven women (29 controls and 28 patients with fecal incontinence (FI)) were included in 3 centers. Vaizey score was used to define fecal incontinence: controls had a score of 0 or 1 and patients a score greater than 6. Anal ultrasound was performed to search for anal sphincter defect in patients with FI. 3D ARHRM was performed using a rigid probe (Given Imaging, Duluth, GA). The protocol consisted of a 2-minute resting period, 2 squeezing periods and 2 bearing down maneuvers. The high-pressure zone (HPZ) corresponding to the anal canal was delineated at the 20-mmHg isobaric contour. The height and mean pressure of the HPZ were measured over a 20-s period at the end of the resting period and after the beginning of each squeezing period. Resting pressure volume and squeezing contractile volume (expressed in mmHg.cm.s) were calculated as the product of HPZ height x HPZ mean pressure x 20 seconds. Data are expressed in median (range) and compared between groups using non-parametric tests.
RESULTS: Controls were younger than FI patients (mean age 45 years (18-70) vs 58 (31-74), $p<0.01$). Fourteen women with FI presented an anal sphincter defect on ultrasound examination. All manometric variables were significantly different between controls and FI women (Table).

	Controls	FI	p
Resting HPZ height (cm)	3 (2-5)	3 (0-5)	0.02
Resting HPZ pressure (mmHg)	51 (29-74)	40 (11-70)	<0.01
Resting pressure volume (mmHg.cm.s)	3217 (1444-6512)	2552 (307-7006)	<0.01
Squeezing HPZ height (cm)	4 (3-5)	4 (1-5)	<0.01
Squeezing HPZ pressure (mmHg)	79 (49-135)	53 (14-124)	<0.01
Squeezing contractile volume (mmHg.cm.s)	7175 (4051-10536)	4195(583-11307)	<0.01

No difference was seen during the bearing down maneuvers between controls and FI women. The 2D map of the 3D sensor plot showed a constant lambda aspect at rest and during squeezing in controls: this aspect may be representative of the posterior pressure applied by the puborectal in the upper part of the anal canal, and the anterior pressure applied by the lower part of the anal sphincter. This typical aspect was much less evident in FI women, especially when a sphincter defect was present.
CONCLUSION: This preliminary study established normal values for 3D ARHRM, and clearly showed differences between controls and patients with FI. 3D data may be interpreted as a typical image pattern rather than as quantified variables.
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P0985 LONG TERM OUTCOMES OF BOTULINUM TOXIN IN THE TREATMENT OF CHRONIC ANAL FISSURE 5 YEAR FOLLOW-UP

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INTRODUCTION: Chronic anal fissure is a frequent and disabling disease, affecting especially young adults. Botulinum toxin (BT) and internal lateral sphincterotomy are therapeutic options for refractory cases. BT is minimally invasive and safer, compared to surgery, which carries a more difficult post-operative state and fecal incontinence risk. The long term effectiveness of BT is not known.
AIMS & METHODS: Evaluate the long term outcomes of BT treatment in chronic anal fissure.
Observational and retrospective study, including the patients treated with BT from 2005 to 2009, each followed over a period of 5 years. Patients were treated with injection of 25U of BT in the intersphincteric groove. The response was registered as complete (CR), partial (PR), refractory (RR) and relapse (RP).
RESULTS: One hundred and twenty-six patients were treated, of which 69.8% (n = 88) were followed over a period of 5 years [48 females (52.3%), mean age 48 years]. The majority presented with a fissure in the anal posterior midline (n = 68, 77.3%). After 3 months, 46.6% (n = 41) had CR, 23.9% (n = 21) had PR and 29.5% (n = 26) had RR. Relapse was observed in 1.2% (n = 1) at 6 months, 11.4% (n = 10) at 1 year, 2.3% (n = 2); no relapse at 5 years. Treatment with BT had a long term efficiency of 64.8%. There was no difference between the groups with CR and RR for gender, age, duration of symptoms, fissure localization and constipation. The treatment was well tolerated by all patients and there were no complications. Patients with no response were assigned to second injection with BT or surgery. The authors highlight the occurrence of two cases of fecal incontinence in the surgery group.
CONCLUSION: BT was an effective and safe alternative to chronic anal fissure long term treatment.
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Disclosure of Interest: None declared

P0986 PATIENT PERSPECTIVES FOR ENDPOINTS IN CLINICAL TRIALS FOR FECAL INCONTINENCE

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INTRODUCTION: Pivotal trials of new treatments for fecal incontinence (FI) often define responders by a 50% reduction in frequency of FI or a report of "adequate relief", but there has been no patient input into these responder definitions.
AIMS & METHODS: Our aim was to survey patient preferences for endpoints in FI treatment trials. In Phase I (focus groups), 30 patients with FI (29 women) were recruited by advertisement to participate in internet chat rooms of 1-5 persons. They were asked open-ended questions on how to define FI treatment success as well as questions about 50% improvement and adequate relief. Based on this input, 3 questions were developed for a national internet survey of individuals with FI (Phase II). This sample, stratified by age, sex, and race/ethnicity, was provided by Cint USA, Inc., a market research company. Descriptive statistics followed by regression analyses were used to identify personal characteristics that influence preferences for endpoints. Subjects also completed the Fecal Incontinence Severity Index (FISI).
RESULTS: In Phase I focus groups, most participants did not believe a 50% reduction in frequency was an adequate definition of success, but neither did they think complete cure was required. When asked how much improvement was needed, the consensus was about 75%. Some did not know what "adequate relief" meant. In the Phase II national survey, 48/234 (20.5%) of responders were excluded because they gave inconsistent responses to two questions that were repeated as a quality control, leaving 186 for analysis: 52% were women, mean age was 48.9 years (range 20-91), and race/ethnicity was 9% Hispanic and 8% African American. Post-bacalaurate education was over-represented (39.2%). Average FISI score was 29.9 on a 0-61 scale. The national survey confirmed focus group findings: only 57.5% thought a 50% reduction is enough to consider a treatment successful (only 26.2% of people over age 65) and 78% considered "adequate relief" a good measure of treatment success. Logistic regression analysis identified several significant predictors of finding a 50% reduction in the frequency of FI an acceptable endpoint in clinical treatment trials: greater severity of FI, younger age, male gender, and higher household income. These would be potential confounders when a 50% reduction is used as the definition of clinical success. For "adequate relief", bivariate analyses confirmed that better educated and wealthier subjects are more likely to accept "adequate relief" as an endpoint. However, in a multivariate logistic regression, only younger age was an independent predictor of endorsing "adequate relief". When asked how much improvement is needed to consider a treatment as successful, the average was a 77% decrease in FI episodes (95% confidence interval 74.5%, 79.5%).
CONCLUSION: Endpoints in clinical trials should be redefined as at least a 75% reduction in the frequency of FI because (a) the 50% decrease criterion is satisfactory to only 57.5% of people with FI (26% of people over age 65), (b) multiple demographic variables predict endorsement of the 50% reduction definition of a responder and are therefore potential confounders, and (c) "adequate relief" appears to be difficult to understand for patients with lower levels of education. [Supported by a grant from Salix Pharmaceuticals]
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TUESDAY, OCTOBER 21, 2014 9:00–17:00
NERVE GUT AND MOTILITY II – POSTER EXHIBITION – HALL XL

P0987 MANOMETRICS CHARACTERISTICS OF OESOPHAGEAL MOTOR ACTIVITY IN TYPE 2 DIABETICS WITH COMPLAINTS OF CONSTIPATION: COMPARISON WITH DIABETICS WITHOUT CONSTIPATION

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INTRODUCTION: Some studies support that there is a significant overlap between the different functional disorders of the digestive tract[1, 2].
AIMS & METHODS: The aim of this study was to compare oesophageal motor characteristics between type 2 diabetics with and without constipation.
Oesophageal manometry was performed in 16 type 2 diabetic individuals with complaints of constipation and 20 without constipation. Glycaemia control was similar. Waves were evaluated in the 3 thirds of the oesophagus (P1 = upper, P2 = middle, and P3 = distal). Results are in mean ± standard error.
RESULTS: In constipated vs. non-constipated diabetics, oesophageal wave distribution was as follows: peristaltic waves, 85.54±3.85% vs. 91.45±2.32%, $p = 0.16$; simultaneous waves, 3.50±%1.19% vs. 0.93±0.28%, $p = 0.015$. The percent of no transmitted waves and of retrograde waves between groups were similar. Wave amplitude did not reveal significant differences between groups. Wave duration (sec.) in constipated vs. non-constipated was as follow: P1-P2, 4.76 ±0.67 vs. 4.15±0.53, $p < 0.47$; P2-P3, 7.24±0.93 vs. 4.90±0.47, $p < 0.017$ and P1-P3, 6.71±1.20 vs. 3.37±0.42 p = 0.013. Wave velocity (cm/s) registered in constipated vs. non-constipated was: P1-P2, 2.93±0.64 vs. 4.03±0.58, $p < 0.21$; P2-P3, 3.42±0.67 vs. 5.07±0.51, $p < 0.05$ and P1-P3, 2.69±0.58 vs. 4.27±0.37, $p < 0.01$.
CONCLUSION: (1) Simultaneous oesophageal waves were significantly more frequent in constipated diabetics. (2) Wave duration was significantly higher within the middle and distal oesophagus of constipated diabetics. (3) Wave velocity was significantly higher within the esophagus of non-constipated individuals. (4) There are some differences in esophageal motility in type 2 diabetic patients with or without constipation
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2-Baran M, et al. *Turk J Gastroenterol* 2012; 23: 634-638.
Disclosure of Interest: None declared

P0988 ANO-RECTAL SENSORIAL AND MOTOR CHARACTERISTICS IN TYPE 2 DIABETICS WITH OR WITHOUT COMPLAINTS OF FAECAL INCONTINENCE: A COMPARATIVE STUDY

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INTRODUCTION: Faecal incontinence is a complaint that some type 2 diabetic patients refer[1]. For some authors, alterations in recto-anal sensory-motor thresholds may be present[2].
AIMS & METHODS: The aim of this study was to compare rectal sensorial and motor characteristics of type 2 diabetics with and without faecal incontinence.
Recto-anal manometry was performed in 35 type 2 diabetics, without signs of autonomic neuropathy, 5 with complaints of faecal incontinence and 30 without this complaint, matched by age and gender. Results are in mean ± standard error.
RESULTS: In diabetics with faecal incontinence vs. without faecal incontinence the values were the follow: rectal resting pressure, 11.5±1.8 vs 12.1±2.3mmHg; p = 0.27 internal anal sphincter resting pressure, 40.0±20. vs 43.6±23.3mmHg, p = 0.24; 39.8±7.02 vs. 47.7±3.30, p = 0.36; minimum rectal sensibility, 56.7±6.7% vs. 80.0±7.6ml, $p = 0.28$; first urge, 80.8±6.1 vs. 132.3±13.5ml, $p = 0.69$; Intense urge,108,3±6.0 vs. 152.8±14.7, $p = 0.80$; maximum tolerable rectal capacity, 169.2±15.6 vs. 225.5 ±20.8ml, $p = 0.95$. The relaxing percent during the recto-anal reflex and the sphincters pressures during the squeeze and squeeze endurance were statistically similar. The anal sphincter fatigue during the squeeze endurance was 0.15±0.70 vs. 0.04±0.32 mmHg/sec, p > 0.05.
CONCLUSION: 1-In type 2 diabetics with faecal incontinence the rectal resting pressure, the resting internal and external sphincter pressures, the volume for minimum rectal sensibility and for maximum tolerable rectal capacity were similar to diabetics without the symptoms. 2-The anal sphincter fatigue was similar between groups. 3-There is no significant differences in recto-anal sensory-motor characteristics in type 2 diabetics with or without faecal incontinence studied.
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Disclosure of Interest: None declared

P0989 RECTO-ANAL SENSORIAL AND MOTOR CHARACTERISTICS IN TYPE 2 DIABETICS WITH OR WITHOUT COMPLAINTS OF CONSTIPATION: A COMPARATIVE STUDY

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INTRODUCTION: Constipation is a very frequent complaint in type 2 diabetic patients[1] and some authors believe that alterations in recto-anal thresholds may be present in individuals with these symptoms[2].
AIMS & METHODS: The aim of this study was to compare rectal sensorial and motor characteristics of type 2 diabetics with and without constipation.
Recto-anal manometry was performed in 35 type 2 diabetics, without signs of autonomic neuropathy, 15 with complaints of constipation and 20 without this symptom, matched by age and gender. Results are in mean ± standard error.
RESULTS: In diabetics with complaints of constipation vs. without constipation, the values registered were the follow: rectal resting pressure, 11.5±1.8 vs. 12.1±2.3mmHg; p = 0.8; internal anal sphincter resting pressure, 40.0±4.7 vs. 43.6±6.1mmHg, p = 0.6; minimum rectal sensibility, 65.5±6.8 vs. 78.6±9.2ml, $p = 0.2$; first urge, 107.5.8±14.1 vs. 119.3±13.1ml, $p = 0.5$; Intense urge, 132.0±14.2 vs. 145.3±15.5ml, $p = 0.5$; maximum tolerable rectal capacity, 197.0±22.6 vs. 208.6 ±19.0ml, $p < 0.7$. The relaxing percent during the recto-anal reflex was 40.9±6.0% vs. 30.5±4.5%, p > 0.05. The sphincter pressure during the squeeze was significantly lower in diabetics with symptoms 67.2±11.2 than without it, 109.7±16.4, p < 0.03; but during the squeeze endurance, 88.0±11.7 vs. 114.9±17.4, was statistically similar. The anal sphincter fatigue during the squeeze endurance, 0.29±0.41 vs. -0.26±0.40 mmHg/sec, was similar. When comparing the recto-anal characteristics according to the severity of constipation, there were no statistic differences between diabetics with slight to moderate or severe to very severe symptoms.
CONCLUSION: 1-In type 2 diabetics with complaints of constipation the resting rectal pressure, the volume for minimum rectal sensibility, first urge, intense urge and maximum tolerable rectal capacity, and the relaxing degree during the recto-anal inhibitory reflex were statistically similar to diabetics without the symptoms. 2-The pressure augment during the squeeze was higher in diabetics without constipation. 3-In general recto-anal sensorial and motor thresholds were similar in type 2 diabetics with or without constipation.
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Disclosure of Interest: None declared

P0990 MANOMETRICS CHARACTERISTICS OF OESOPHAGEAL MOTOR ACTIVITY IN PEOPLE WITH COMPLAINTS OF CONSTIPATION: COMPARISON WITH INDIVIDUALS WITHOUT CONSTIPATION

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INTRODUCTION: Epidemiological and clinical studies in the pediatric[1] and adult[2,3] population support that there is a significant overlap between the different functional disorders of the digestive tract.
AIMS & METHODS: The aim of this study was to compare oesophageal motor characteristics between individuals with complaints of constipation and individuals without this symptom.
Oesophageal manometry was performed in 28 individuals with complaints of constipation and 42 without constipation. Waves were evaluated in the 3 thirds of the oesophagus (P1 = upper, P2 = middle, and P3 = distal). Results are in mean ± standard error.
RESULTS: In constipated vs. controls, oesophageal wave distribution was as follows: peristaltic waves, 85.54±3.85% vs. 91.45±2.32%, $p = 0.16$; simultaneous waves, 3.50±%1.19% vs. 0.93±0.28%, $p = 0.015$. The percent of no transmitted waves and of retrograde waves were similar between groups. Wave amplitude did not reveal significant differences between groups. Wave duration (sec.) in constipated vs. non-constipated was as follow: P1-P2, 4.76 ±0.67 vs. 4.15±0.53, $p < 0.47$; P2-P3, 7.24±0.93 vs. 4.90±0.47, $p < 0.017$ and P1-P3, 6.71±1.20 vs. 3.37±0.42 p = 0.013. Velocity duration (cm/s) registered in constipated vs. non-constipated was: P1-P2, 2.93±0.64 vs. 4.03±0.58, $p < 0.21$; P2-P3, 3.42±0.67 vs. 5.07±0.51, $p < 0.05$ and P1-P3, 2.69±0.58 vs. 4.27±0.37, p < 0.01.
CONCLUSION: (1) Simultaneous oesophageal waves were significantly more frequent in constipated. (2) Wave duration was significantly higher within the middle and distal oesophagus of constipated individuals. (3) Wave velocity was significantly higher within esophagus of non-constipated individuals. (4) Constipated individuals have some differences in esophageal motility when compared with non-constipated individuals.
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Disclosure of Interest: None declared

P0991 INTERACTIONS OF HERBAL CONSTITUENTS INFLUENCES THE EFFECTS OF STW 5 ON INFLAMMATORY PROCESSES AND DISTURBED MOTILITY

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INTRODUCTION: The multi-herbal drug STW 5 (Iberogast®) was effective for treatment of symptoms in patients with functional dyspepsia or irritable bowel syndrome (IBS). Its mode of action is still not fully elucidated. Modulation of gastric motility and an anti-inflammatory action were hypothesized. These findings provide the basis for investigating STW 5 and its components in inflamed small and large intestinal preparations to identify novel anti-inflammatory pathways.
AIMS & METHODS: The aim of this study was to investigate the effect of individual constituents as well as selected combinations on different parameters related to inflammatory processes in the gastrointestinal tract.
For analysis of lactate dehydrogenase (LDH) activity using a commercially available LDH cytotoxicity assay (Roche). TNFa concentration was detected by ELISA in the supernatants. The inflammation was elicited by intraluminal preincubation with TNBS (10 mM). The herbal extracts were applied together with TNBS. For analysing synergism or antagonism the isobologram method was used.
RESULTS: STW 5, STW 5-II (a combination containing only 6 of the 9 extracts) and lemon balm reduced LPS (10 ng/ml)-induced lactate dehydrogenase (LDH) release from CaCo-2 cells by 74-75 %. *Iberis amara*, peppermint, chamomile, angelica and milk thistle inhibited this parameter by 25-37 %. Liquorice, caraway and celandine had no effect. The combinations of *Iberis amara* and peppermint as well as peppermint and milk thistle revealed synergistic or additive effects, whereas the combination of chamomile and angelica evoked additive or antagonistic effects depending on their compositions (i.e. relative ratios of individual extracts).
STW 5, STW 5-II, *Iberis amara*, peppermint, liquorice, caraway, milk thistle and lemon balm inhibited LPS (100 ng/ml)-induced TNFa release from THP-1 cells to 51-67 %. Chamomile and angelica revealed a more potent effect. The combinations of *Iberis amara* and peppermint as well as chamomile and liquorice had additive or antagonistic effects depending on their compositions.
STW 5 and STW 5-II reduced the acetylcholine (ACh)-induced contractions in rat ileum preparations to 81-83 %. The individual components inhibited the contractions to 83-91 % except for lemon balm which had no effect. The combinations of *Iberis amara* and peppermint as well as liquorice and caraway had additive or antagonistic effects depending on their compositions.
CONCLUSION: Our results indicate that synergistic, additive and antagonistic interactions exist between the constituents within STW 5 and STW 5-II. The overall effects depend on their combination and therefore confirm that combined extracts produce an effect different from or greater than the sum of their individual effects. Our results allow greater insight into the interactions between individual herbal constituents of STW 5 and confirm the concept of multi-target actions.
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P0992 NON-GSHR1A MEDIATED EFFECTS OF ULIMORELIN IN ISOLATED RODENT ARTERIES

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INTRODUCTION: Ghrelin receptor agonists cause changes in blood pressure in humans (1) and rodents. The ghrelin receptor agonist ulimorelin (TZP101), recently in clinical trials for the treatment of gastroparesis, has been shown to cause alterations in blood pressure and mesenteric artery tone in rats (2). Here we investigate the role of the canonical ghrelin receptor, GHSR1a, in mediating this effect.
AIMS & METHODS: Saphenous, mesenteric and basilar arteries from Sprague-Dawley rats (male, 8 weeks), and saphenous arteries from mice lacking the GHSR1a receptor or littermates (male, 6-8 weeks) were studied. Arteries were suspended between steel wires in myography chambers containing an oxygenated modified Krebs solution (36.5°C) and given an effective transmural pressure of 100mmHg- mesenteric and basilar arteries were then reduced in diameter by 10%. Phenylephrine (PE) 3-10μM, or 60mM $[K^+]$ in basilar arteries, was used to confirm tissue viability. Ulimorelin was applied non-cumulatively following increases in artery tension induced by application of PE 3-10μM or 60mM $[K^+]$. To investigate direct changes in artery tension, ulimorelin was applied cumulatively. Responses were measured as the % change from the plateau response of the stimulus applied prior to application of agonists. Changes between groups were investigated using 2-way ANOVA and Bonferroni post-tests.
RESULTS: PE 3-10μM contracted saphenous (n = 19 rat, n = 4 mouse) and mesenteric (n = 6) arteries, but had no effect on basilar arteries (n = 4). Ulimorelin (0.03-30μM) caused concentration-dependent inhibition of PE-induced contractions of rat saphenous (IC50 = 697nM; Imax = 66±5% PE response; n = 3-6) and mesenteric arteries (IC50 = 5μM, Imax = 113±16%; n = 3-4), but had no effect on contractions induced by 60mM [K+] in basilar arteries. In rat saphenous and basilar arteries ulimorelin 10-100μM caused an increase in artery tension (EC50 = 9.9μM Emax = 50±7%; and EC50 = 8 μM Emax = 99±16% respectively) but had no effect in mesenteric arteries. These effects were not attenuated by the ghrelin receptor antagonist YIL 781 3μM (e.g. ulimorelin 10μM inhibited the PE response by 62±5% in the absence and 48±8% in the presence of YIL 781 respectively; $P > 0.05$; n = 4) or mimicked by ghrelin 0.001-1μM (n = 3-4), desacyl ghrelin 0.001-1μM (n = 3-4), capromorelin 0.01-10μM (n = 3-4) or AZP-531 0.001-1μM (n = 3-4). In mesenteric arteries pre-incubation of ulimorelin 1-10μM caused a parallel rightward shift in the cumulative response to PE (0.01-1000μM; pA2 = 5.7; n = 3-4). No differences were observed between wild type mice and mice lacking the GHSR1a receptor in the ability of ulimorelin 1-10μM to inhibit PE responses (at 10μM by 61±17 and 51±16 respectively; $P > 0.05$; n = 3, 3) or increase in artery tension (10-100μM; EC50 = 21μM Emax = 15±3%; EC50 = 16μM Emax = 23±6%; n = 3, 3; $P > 0.05$).
CONCLUSION: Ulimorelin inhibited PE induced contractions and, at higher concentrations, increased artery tension. These effects were regionally dependent, and it is likely they were not mediated by GHSR1a as they were not mimicked by other ghrelin receptor agonists, and not attenuated in mice lacking GHSR1a or by the antagonist YIL 781. A possible competitive antagonist action at the α-adrenoceptor is suggested for the inhibition of PE-induced contractions.
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Disclosure of Interest: None declared

P0993 A DECREASE OF ENTERIC PLEXUS AND GANGLION CELLS IN SIGMOID VOLVULUS

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INTRODUCTION: Although sigmoid volvulus (SV) causes acute obstruction, the pathogenesis and pathological mechanism of SV are unknown.
AIMS & METHODS: The aim of our study is to evaluate the clinicopathological characteristics of volvulus and factors contributing to volvulus of the sigmoid colon. Fourteen patients with SV (10 men and 4 women; median age, 78.5 years) were compared with 14 age- and sex-matched control patients with respect to differences in clinical characteristics, focusing on dysmotility (enteric visceral myopathy, neuropathy, and mesenchymopathy).
RESULTS: Of the 14 patients with SV, 7 had recurrent volvulus, 11 had an associated condition, and 5 required emergency surgery. The prevalence of atrophy and fibrosis of the inner muscle in patients with SV was higher than that of the control patients ($P = 0.041$). Median extents (per cm of muscularis propria) of the myenteric plexus (12.5 versus 17.5, $P < 0.001$) and submucous plexus (15.0 versus 25.5, $P < 0.001$) in patients with SV were lower than those of the control patients. Median numbers of myenteric (9.7 versus 30.4, $P < 0.001$) and submucous ganglion cells (10.0 versus 23.2, $P < 0.001$) were also lower than those of the controls. The prevalence of inflammatory neuropathy in patients with SV was higher than that of the control patients ($P = 0.046$). There were no differences in mesenchymopathy ($P = 0.481$).
CONCLUSION: A decrease in the extent of enteric plexus and ganglion cells may play an important role in the diagnosis and recognition of a clear mechanism leading to torsion in SV.
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Disclosure of Interest: None declared

P0994 POSTERIOR TIBIAL NERVE STIMULATION IMPROVES BOTH URGE AND MIXED URGE PLUS PASSIVE FAECAL INCONTINENCE

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INTRODUCTION: Percutaneous Tibial nerve stimulation (PTNS) is a minimally invasive, well tolerated emerging treatment for patients who have not responded to conservative treatment for faecal incontinence (FI). There is limited information about the difference in its efficacy in patients with different FI symptoms. The aim of this retrospective study was to assess the efficacy of PTNS in patients with FI, comparing between patients with different faecal incontinence symptoms.
AIMS & METHODS: Consecutive patients were studied: all had improved following the initial 12 weeks of weekly PTNS treatment and were receiving maintenance. Based on initial presenting FI symptoms the patients were placed into three categories: 1) Urge incontinence 2) Passive 3) Passive + Urge incontinence. The outcome parameters were Wexner FI incontinence score, stool consistency and FI episodes per week (based on diary). Outcomes were compared between

the pre- and post-treatment, and between pre-treatment and latest maintenance (mean 12.4 (SD 7.2 months) scores.
RESULTS: Data is presented on 44 patients (6 male, mean age of 59[25 to 77]) with a mixture of aetiologies. (As there was only 3 patients in the passive incontinence group, no statistical analysis was undertaken.) There was a statistically significant improvement in both other groups when comparing pre-vs post-treatment Wexner Scores (mean and SD in table). In addition, in the pre vs maintenance analysis there was a significant improvement seen in symptoms. There was a statistically significant improvement observed in faecal continence episodes in the pre vs maintenance analysis, but no statistically significant change in stool consistency between any groups in pre vs post and pre vs maintenance analysis.
Table- Wexner Score Comparison table

	Pre-procedure	Post-procedure	Pre vs Post P value	*Maintenance*	Pre vs Maintenance
Urge Incontinence (n = 21)	14.4± 2.7	7.2 ± 2.1	< 0.0001	8.5 ± 3.4	< 0.0001
Passive incontinence (n = 3)	12.0 ± 4.0	6.3 ± 5.3		10.7 ± 8.3	
Urge + passive incontinence (n = 24)	16.1 ± 2.2	9.3 ± 3.5	< 0.0001	9.6 ± 4.4	< 0.0001

CONCLUSION: We have shown that PTNS improves symptoms in patients with urge incontinence and in also in those with a combination of urge and passive symptoms. The symptom improvement was maintained in all our patients. Larger numbers of patients with passive incontinence need to be studied.
Disclosure of Interest: None declared

P0995 THE EFFICACY OF PERCUTANEOUS TIBIAL NERVE STIMULATION IN DIFFERENT ANAL SPHINCTER DEFECTS

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INTRODUCTION: Percutaneous Tibial nerve stimulation (PTNS) is an emerging 'step-up' treatment for patients who have not responded to conservative treatment for faecal incontinence (FI). There is limited information about its efficacy in patients with different sphincteric defects. The aim of this retrospective study was to assess the efficacy of PTNS in patients with FI, comparing between patients with different sphincter pathologies.
AIMS & METHODS: Consecutive patients were studied: all had improved following the initial 12 weeks of weekly PTNS treatment and were receiving maintenance. Based on baseline endoanal ultrasound patients were placed into four categories: 1) Both sphincters intact 2) External anal sphincter (EAS) defect 3) Internal anal sphincter (IAS) defect 4) Both sphincters damaged. The outcome parameters were Wexner FI incontinence score, stool consistency and FI episodes per week (based on bowel diary). Outcomes were compared between the pre- and post-treatment, and between post-treatment and latest maintenance (mean 12.3 (SD 7.2 months) scores.
RESULTS: Data is presented on 46 patients (40 female, mean age of 57[25 to 78]) with a mixture of aetiologies. There was statistically significant improvement in all groups comparing pre- vs post-treatment Wexner Scores (mean and SD in table). In the post vs maintenance analysis there was significant symptom exacerbation only for the intact sphincter groups, whilst persistent improvement was seen in the other three groups. In all groups incontinence episodes were reduced after PTNS, and remained at low levels during maintenance ($p < 0.05$ vs pre-PTNS for both). No such difference in stool consistency was seen however ($p > 0.05$ vs pre-PTNS for both).
Table- Wexner score mean ± SD in the different sphincter states

	Pre-procedure	Post-procedure	*Pre vs Post p value*	Maintenance	*Post vs Maintenance p value*
Intact sphincters (n = 23)	14.4 ± 2.5	7.4 ± 2.3	*< 0.0001*	9.7 ± 4.2	*0.0214*
EAS defecit (n = 8)	15.7 ± 1.9	7.9 ± 1.2	*< 0.0001*	7.6 ± 1.7	*0.3559*
IAS defecit (n = 7)	15 ± 3.7	7.4 ± 3.3	*0.0003*	8.1 ± 2.5	*0.1824*
Both sphincters damaged (n = 8)	16.6 ± 1.7	11 ± 4.5	*0.0063*	11.5 ± 18.3	*0.7627*

CONCLUSION: We have shown that PTNS improves symptoms in patients who have both anal sphincter defects and intact sphincters. The symptom improvement with PTNS was maintained in the sphincter damaged patients but not those with intact sphincters. The effect of PTNS on patients with sphincter disruption suggests a mechanism of action directed at the anorectal unit beyond just the anal sphincter.
Disclosure of Interest: None declared

P0996 THE ROLES OF LENGTH, DURATION OF ESOPHAGEAL HYPERTENSIVE CONTRACTIONS IN DIFFERENT DIAGNOSIS STRATEGIES OF NUTCRACKER ESOPHAGUS

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INTRODUCTION: Some patients with chest pain or dysphasia present esophageal hypertensive contractions (HCs) during esophageal manometry test, but the contraction pattern did not meet any criteria of Chicago classification 2012.
AIMS & METHODS: To evaluate the esophageal segmental or short-time HCs (s-HCs) with Chicago classification criteria and conventional criterion respectively in NCCP or dysphasia patients and preliminarily analyze the roles of HCs location, pressure and duration in diagnosis strategy.
Methods: Patients with NCCP or dysphasia were enrolled. All underwent gastroscopy to exclude organic diseases. Esophageal peristalsis conditions of 10 wet swallows were recorded by HRM with 36 channels of pressure sensors. We defined the area in 180mmHg isobaric contour as hypertensive contraction area (HCA). According to Gothenburg criterion (GC), patients with peristaltic contractions of amplitude > 180mmHg at any level of the esophagus was considered as conventional nutcracker esophagus (c-NE). Patients with mean distal contraction index (DCI) > 5000 mmHgscm, normal integrity relaxation pressure and distal latency were diagnosed as Chicago NE, with DCI > 8000 mmHgscm as Chicago Jackhammer. Patients who met GC but not Chicago criteria were considered as s-HCs.
RESULTS: ①Thirty one patients present HCs and 3 of them were excluded for their EGJ obstructions. The remainder 28 patients (51.8±12.3y, M/F = 10:18) were diagnosed as c-NE (100%, 28/28). Among them, five (17.9%, 5/28) patients were diagnosed as Jackhammer and 2 NE (7.1%, 2/28). The other 21 patients (75%, 21/28) were diagnosed as ''normal'' group by Chicago criteria, which considered as s-HCs in our study. ②seventy swallows in Chicago abnormal group and 210 swallows in s-HCs group were compared. The lengths (3.8(3.3-4.9) vs. 6(5.5-9) cm, $p = 0.023$), durations (3(2.6-3.2) vs. 4.8(4.4-5.1)s, $p < 0.001$)), peak amplitudes (212.8(203.8-233.6) vs. 304.9(221.4-347.7) mmHg, $p = 0.001$) of HCA in s-HCs patients were significantly lower than that of Chicago abnormal group. The mean pressure (132(118-144.1) vs. 188.1(179.6-206.2) mmHg, $p < 0.001$) and duration (3.5(3-3.8) vs. 4.9(4.4-5.2) s, $p < 0.001$) of 3-8cm esophageal segment above LES in s- HCs group were significant lower than that of Chicago abnormal group. There were no differences in IRP 4s, upper margin of HCs, pressure of 8cm and 13cm above LES between the two groups ($p > 0.05$). Further analysis showed negative correlation ($r = -0.435$, $p = 0.021$) between the upper margin of HC area and DCI value, while the length ($r = 0.634$, $p < 0.001$), peak amplitude($r = 0.721$, $p < 0.001$) and contraction duration ($r = 0.819$, $p < 0.001$)of HC area were positively correlated with DCI.
CONCLUSION: A large proportion of c-NE diagnosed by conventional Gothenburg criterion was considered as ''normal'' in Chicago criteria because the hypertensive contractions were segmental or short-time. For patients with typical NCCP or dysphasia, the roles of s-HCs and the relationship between s-HCs and esophageal symptoms need to be clarified.
Disclosure of Interest: None declared

P0997 PATIENTS WITH DYSPEPSIA SYMPTOMS ARE MORE RESPONSIVE THAN HEALTHY SUBJECTS AFTER SPRAYING MENTHOL INTO THE UPPER GASTROINTESTINAL TRACT

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INTRODUCTION: In Japan, the use of antispasmodics such as anticholinergic agents as pretreatment for upper gastrointestinal tract endoscopy has become standard. However, endoscopy without antispasmodics has frequently been performed in recent years; when antral contraction interferes with intragastric observation, 0.8% L-menthol (MINCLEA® 20 mL) is sprayed into the gastrointestinal tract to stop such contractions. However, the mechanism of antral contraction suppression after spraying menthol into the stomach has not been fully elucidated, and differences in gastric and duodenal responsiveness have also not yet been sufficiently studied.
AIMS & METHODS: By focusing on post-spray responsiveness, we separately applied menthol to the antrum and the duodenal bulb using a spray tube and studied associations between changes in antral contractile activity and dyspepsia symptoms. [Subjects] The 18 subjects who underwent endoscopy without antispasmodics consisted of nine patients with dyspepsia symptoms (patient group) and nine healthy subjects without abdominal symptoms (healthy group). [Method] The subjects fasted for a minimum of 12 hours starting the day before the examination and underwent endoscopy without receiving pre-administration of drugs into the stomach or injection of antispasmodics. Prior to detailed intragastric observation, an endoscope was fixed to the site where antral contraction could be evaluated; after spraying 2 mL of menthol solution into the antral region using a spray tube, changes in contraction were observed for two minutes. A tube was then inserted into the duodenal bulb and 2 mL of menthol solution were sprayed in a similar manner, and changes in contraction were observed for two minutes thereafter. In patients in whom antral contractions did not stop, the antral region was again sprayed with another 16 mL of menthol solution. After menthol spraying, we continued normal endoscopy in the subjects and recorded dilatation of the proximal stomach, opening/closing of the pyloric ring, the frequency and intensity of antral contractions, the presence or

absence of hernia, and the presence or absence of bile retention in the stomach and the duodenum.
RESULTS: After menthol spraying we found that the examination time was extended by approximately six minutes on average as compared to normal endoscopy. However, there was no major interference with intragastric observation. In the patient group, antral contraction stopped after spraying menthol into the duodenum in eight of nine patients, while it stopped in only three of nine subjects in the healthy group. No clear difference was identified in responses after menthol spraying between the stomach and duodenum.
CONCLUSION: Although no differences in responses after spraying were identified between the stomach and duodenum, it was revealed that there are differences in responsiveness after menthol spraying which depend on the presence or absence of dyspepsia symptoms. Accordingly, after further improvement and accumulation of patients, this could become a useful examination method for elucidating the pathology of dyspepsia symptoms.
Disclosure of Interest: None declared

P0998 IMPLICATION OF THE ENTERIC GLIAL CELLS IN THE IMMUNOREGULATORY PROCESSES

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INTRODUCTION: The enteric nervous system (ENS), also referred as the second brain, is well-known for its role in the control of intestinal functions such as motility, secretion and absorption. A growing bulk of evidence suggests that cells of the ENS such as the enteric glial cells (EGC) may play an important role in case of inflammatory bowel diseases (IBD). Indeed, astrocytes, their counterparts in the central nervous system, have immunomodulatory properties that might be shared by the EGC.
AIMS & METHODS: To study the immunoregulatory properties of the EGC, glial cells were isolated from the myenteric plexus of the rat digestive tract (rEGC), and their effects were tested in vitro, on activated rat T lymphocytes. Spleen-derived T cells stimulated by anti-CD3 and anti-CD28 antibodies were labeled with CFSE and incubated for three days with increasing ratios of rEGC. The rate of T cell proliferation was analyzed by flow cytometry. Similar approaches were used with human EGC isolated from the myenteric plexus of colonic biopsy. The immunoregulatory properties of human EGC were tested on human peripheral blood mononuclear cells (PBMC) activated with phytohemagglutinin (PHA).
RESULTS: The results show that rEGC inhibit the proliferation of activated T cells. Pretreatment of rEGC with pro-inflammatory stimuli (LPS, interleukine-1/TNFalpha) does not modify these immunomodulatory effects. Preliminary experiments with EGC derived from a human colonic biopsy suggest similar properties as the cells inhibit the proliferation of PHA-activated CD3+ cells in a dose-dependent manner. Investigations are currently performed to determine whether EGC derived from other control patients have the same properties. We also are also analyzing if EGC derived from IBD patients have similar potentialities.
CONCLUSION: The present data show that EGC are able to modulate the proliferation of T cells in vitro. They suggest that neuroimmune interactions between EGC and T cells could occurr in vivo.
Disclosure of Interest: None declared

P0999 USE OF CONSENSUS DEFINITION OF FAILURE OF A TREATMENT TO PROVIDE ADEQUATE RELIEF (F-PAR) FOR CHRONIC FUNCTIONAL CONSTIPATION IN CLINICAL PRACTICE

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INTRODUCTION: Chronic constipation is a common condition characterized by multiple inter-related symptoms. Treatments range from initial self-management by lifestyle modification and laxatives, through to prokinetic drugs, bowel irrigation and complex surgical options. However rates of objective and subjective treatment success are low and the subjective nature of symptoms means that success itself is hard to define. A recent consensus process (funded by Shire) Delphi- has yielded a tool to identify failure of a treatment to provide adequate relief (F-PAR).
AIMS & METHODS: Aims: To establish utility of F-PAR scoring system in identifying treatment failures amongst patients with constipation. Find out specificity of the F-PAR scoring system. Methods: The 5-item self-report F-PAR tool was offered to 236 consecutive patients attending a tertiary care center with Rome III defined functional constipation. Only one patient could not complete it and a total of 281 forms were analysed (196 patients with one form, 32 patients presented twice and 7 presented three times). The form with the tool was filled in by the patient in the waiting room prior to being seen by the clinician, who then consulted ignorant of the responses on the tool, and a clinical decision ('gold standard') about treatment success made. After the consultation an independent researcher reviewed the relationship between results of the tool and clinical assessment.
RESULTS: All 235 patients (212 female, mean age 41) had completed a time-defined prescribed treatment at the time of assessment. The treatments (number, %, of successes as defined by clinic assessment in parentheses) were: 121 (42, 35%) laxatives or enemas, 76 (35, 46%) prokinetics or secretagogues, 64 (36, 56%) biofeedback, 11 (2, 18%) trans-anal irrigation, 9 (1, 11%) sacral nerve stimulation. In total 165 (59%) were deemed not to have responded to treatment. There were 5 'false positives' and 7 'false negatives' generated by the F-PAR. Of 163 F-PAR identified patients, 136 (83%) had 1 item positive, 21 (13%) had 2 items positive, 7 (4%) had ≥3 items positive. This gives specificity 96% (CI 91-98%) and sensitivity 96%(CI 90-99%), a positive predictive value of 97% (CI 93-99%) and negative predictive value 94% (CI 88-98%).
CONCLUSION: The F-PAR is a highly sensitive instrument to identify treatment failure in chronic constipation in
setting.
a tertiary care setting. A single positively reported item out of five in this easy to use tool can identify patients who need a change of treatment. Further validation will come from utilization of the tool in a primary care setting.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
IMMUNOLOGY AND MICROBIOLOGY – POSTER EXHIBITION – HALL XL

P1000 GUT MICROBIOTA ALTERATIONS IN IBS PATIENTS BEFORE AND AFTER 6 WEEKS OF LOW FODMAP DIET VERSUS LACTOBACILLUS RHAMNOSUS GG

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INTRODUCTION: Low fermentable Oligo-Di- and Mono- saccharides and Polyols (FODMAP) diet (LFD) may be effective in patients with irritable bowel syndrome (IBS), and these patients may have altered microbiota (MB). The aim of the study was to investigate the impact of LFD and *lactobacillus rhamnosus* GG (LGG) on fecal MB.
AIMS & METHODS: Fecal samples were collected from IBS patients (Rome III criteria) and randomized to LFD, LGG or normal Western/Danish diet (ND). IBS severity score (IBS-SSS) was registered by patients at week 0 and 6 on an e-health application, www.ibs.constant-care.dk. Bacteria in fecal samples were analyzed by Genetic Analysis AS's GA-map^{TM} Dysbiosis Test, a test utilizing 16SrRNA DNA to recognize the gut bacteria found to best correlate with dysbiosis in IBD/IBS patients. Dysbiosis Index (DI) is calculated by an algorithm based on bacterial abundance and profile in a fecal sample. DI is measured on a scale from 1-10, where values above 2 is considered dysbiotic. Dysbiosis class is defined as either non-dysbiotic or dysbiotic. Change in DI and dysbiosis class between week 0 and 6 were investigated.
RESULTS: In total 58 patients (median age 39, range 20-74 years, 81% females) were included in the study: 17 LFD, 20 LGG and 21 ND. A significant improvement in IBS-SSS total score in LFD and LGG patients was observed at week 6 compared to week 0, 308 [150-460] vs. 189 [25-478], $p<0.001$ and 296 [157-431] vs. 212 [11-471], $p<0.01$. No significant improvement was observed in ND patients, 303 [82-450] vs. 289 [62-428], $p=0.28$. There was no significant improvement in DI at week 6 compared to week 0 in LFD (6 vs 6, $p=0.53$), LGG (5 vs 8, $p=0.88$) or ND (7 vs 6, $p=0.4$). However, a substantial part of the patients (35-43%) changed dysbiosis class (dysbiotic, non-dysbiotic) following the 6 week intervention and alterations in DI were observed in all three groups, both as decreased and increased DI. At week 0, 88% LFD, 65% LGG and 76% ND patients were dysbiotic ($DI>2$), while 76% LFD, 75% LGG and 81% ND patients were dysbiotic at week 6.
There was no correlation between change in IBS-SSS and DI in either LFD or LGG group.
CONCLUSION: Both LFD and LGG groups reported significant reduction in IBS-SSS from week 0 to 6. High proportions (65-88%) were dysbiotic at week 0, and alteration in MB was observed in 35-43% of the patients who changed dysbiosis class following dietary intervention. LFD did not significantly alter the gut MB in this study population, however, the test provides information on alterations in bacterial abundance and profiles that may prove valuable for individual patients.
Disclosure of Interest: None declared

P1001 PROTON PUMP INHIBITORS ALTER GASTRIC MICROBIOTA COMPOSITION IN SUBJECTS WITH UPPER GASTROINTESTINAL SYMPTOMS: PRELIMINARY METAGENOMICS ANALYSIS

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INTRODUCTION: *H. pylori* is known to play a paramount role in the development of both gastric and extragastric diseases.
However, human stomach harbours also a broad variety of microorganisms, often not cultivable with conventional microbiology methods. Metagenomic techniques are improving our understanding of gut microbiota composition, using the 16S rRNA gene as a molecular fingerprint to analyze microbial diversity. Chronic therapy with proton-pump inhibitors is known to increase the risk of gut microbiota-related diseases such as C. difficile infection and spontaneous bacterial peritonitis. Influence of proton-pump inhibitors (PPIs) in modifying gastric microbial ecosystem has not yet been described.
AIMS & METHODS: Our aim is to assess, through metagenomic tools, the composition of gastric microbiota in subjects with upper gastrointestinal symptoms either taking or not PPIs. We analyzed gastric biopsy samples from 10

consecutive patients undergoing upper endoscopy. We enrolled 5 patients taking PPIs (group A) and 5 ones free from gastrointestinal drugs (group B). We collected two biopsy samples for each patient. Roche 454 GS Junior was used for metagenomic analysis. Obtained data were assessed by Qiime suite.
RESULTS: Main indications to upper endoscopy were epigastric pain and/or heartburn and/or dyspepsia. Bacteria amplicons were detected in all samples. *H. pylori* was found in 3 patients from group A and 2 patients from group B, respectively. Overall, prevalent bacteria classes were Epsilonproteobacteria (26.5%), Bacilli (21%), Bacteroidia (19.3%), and Gammaproteobacteria (7.8%). Generally, a higher number of microorganisms was found in group A. Differences in gut microbiota composition were observed between two groups of patients. Respectively, higher abundance of Actinobacteria (9.74% VS 0.98%), Bacilli (27.78% VS 14.22%), Betaproteobacteria (7.68% VS 1.32%) and Gammaproteobacteria (13.86% VS 1.86%) and a lower presence of Epsilonproteobacteria (1.06% VS 51.8%) were found in group A when compared with group B.
CONCLUSION: Until a short time ago the uncultivability of microorganisms did not allow the assessment of gastric microbiota composition. The diffusion of metagenomics tools, not depending on microbial culture, has incredibly enlarged our knowledge on gut microbiota. In this preliminary report, we demonstrated that PPIs modify gastric microbiota composition in subjects with upper gastrointestinal symptoms. Such phenomenon may explain the role of PPIs in the development of many gut-microbiota related diseases. Further investigations are needed to improve our understanding of this cutting-edge topic.
Disclosure of Interest: F. Paroni Sterbini: nothing to declare, G. Cammarota: nothing to declare, F. Bugli: nothing to declare, S. Bibbò: nothing to declare, G. Ianiro: nothing to declare, M. Iacono: nothing to declare, E. D. Capoluongo: nothing to declare, F. Scaldaferri: nothing to declare, A. Gasbarrini: nothing to declare, M. Sanguinetti: nothing to declare, L. Masucci: nothing to declare

P1002 COMPARATIVE ANALYSIS OF GASTROINTESTINAL BACTERIAL MICROBIOTA BETWEEN NORMAL AND CDX2 TRANSGENIC MICE

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INTRODUCTION: Cdx2 is expressed in human intestinal metaplastic mucosa and induces intestinal metaplastic mucosa in Cdx2-transgenic mouse stomach. In humans, atrophic gastritis and intestinal metaplasia due to *Helicobacter pylori* (*H. pylori*) infection commonly lead to gastric achlorhydria. These conditions predispose the stomach to bacterial overgrowth. To date, the few studies have been reported that explored the microbiota of the stomach in negative or positive status for *H. pylori* using molecular methods. However, the studies on characterization of the gastric microbiota in severe atrophic gastritis or intestinal metaplasia have not been published.
AIMS & METHODS: The aim of the present study was to determine the differences in the gut microbiota between normal and Cdx2-transgenic mice using a quantitative RT-PCR method with 16S rRNA-genetargeted species-specific primers.
Twelve normal and twelve Cdx2 transgenic mice (7 weeks age, 6 male and 6 female respectively) were sacrificed, and the gastric, jejunal, ileac, cecal and colonic mucosa, and feces were collected. To analyze bacterial microbiota quantitatively, we used a real time RT-PCR method with 16S rRNA-gene-targeted species-specific primers. Seven primer sets for obligate anaerobes (*Clostoridium coccoides* group, *Clostridium leptum* subgroup, *Bacteroides fragilis* group, *Bifidobacterium*, *Atopobium* cluster, *Prevotella*, *Clostridium perfringens*), 5 sets for facultative anaerobes (*Lactbacillus*, *Enterobacteriaceae*, *Enterococcus*, *Streptococcus*, *Staphylococcus*) and 1 set for a obligate aerobe (*Pseudomonas*) were used.
RESULTS: The total bacterial numbers in the gastric ($\log_{10}(7.7 \pm 0.4)$/g), jejunal ($\log_{10}(6.7 \pm 0.7)$/g), ileac ($\log_{10}(6.3 \pm 0.4)$/g), cecal ($\log_{10}(7.6 \pm 0.3)$/g) and colonic ($\log_{10}(7.7 \pm 0.4)$/g) mucosa of Cdx2-transgenic mice were significantly higher than those ($\log_{10}(5.3 \pm 1.0)$ / g, $\log_{10}(3.4 \pm 1.2)$/g, $\log_{10}(4.9 \pm 0.8)$/g, $\log_{10}(6.6 \pm 0.4)$/g and $\log_{10}(5.4 \pm 1.3)$/g, respectively) of normal mice. *Bacteroides fragilis* group and *Prevotella* were not detected in the stomach of normal mice while they were detected in that of Cdx2-transgenic mice. Moreover, *C. coccoides* group, *C. leptum* subgroup, *Bacteroides fragilis* group and *Prevotella* were not detected in the jejunum and ileum of normal mice while they were detected in that of Cdx2-transgenic mice. In contrast, the fecal microbiota in normal mice was similar to that in Cdx2-transgenic mice.
CONCLUSION: Gastric achlorhydria due to intestinal metaplasia makes an obvious effect on gastrointestinal microbiota.
Disclosure of Interest: None declared

P1003 TOLL-LIKE RECEPTOR 7-DEPENDENT MODULATION OF COLONIC PERMEABILITY DEPENDS UPON THE INTEGRITY OF THE EPITHELIAL BARRIER

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INTRODUCTION: Toll-like receptors (TLRs) are a key component in host-bacterial interactions within the gut. TLRs have been implicated in the regulation of epithelial permeability through the modulation of tight junctions.
AIMS & METHODS: To assess *in vivo* changes in colonic permeability associated to the local stimulation of TLR7 and the implication of tight junctions-related proteins. Adult SD rats were treated intracolonically with the selective TLR7 agonist imiquimod (300 μg/rat) or its vehicle (0.2 ml). In some cases, 4 h after imiquimod administration, the colonic epithelium was challenged with 100% dimetilsulfoxide (DMSO). Colonic epithelial permeability to macromolecules was determined assessing the accumulation of 4 kDa fluorescein isothiocyanate–dextran (FD4; 10 mg/animal, 0.2 ml, intracolonically) in the colonic wall and the passage to blood and urine. Expression of tight-junction-related proteins [occludin, Zona Occludens-1 (ZO-1), claudin-2 and -3, tricellulin and junctional adhesion molecule 1], inflammatory markers (IFNα1 and IL-6) and the barrier modifier factors [Glucagon-Like Peptide 2 (GLP-2) and Myosin Light-Chain Kinase (MLCK)] was assessed by RTqPCR.
RESULTS: Acute stimulation of TLR7 with imiquimod did not alter the colonic passage of FD4. Challenge of the colonic mucosa with DMSO slightly increased colonic permeability (Table). TLR7 stimulation after the challenge with DMSO resulted in an enhancement of FD4 accumulation in colonic tissues and an increased passage to blood and urine (Table). Neither macroscopical nor microscopical nor molecular signs of inflammation were observed, regardless the treatment considered. Intracolonic imiquimod did not modify the expression of the main tight-junction-related proteins or the barrier modifier factors (proglucagon and MLCK).

FD4	Vehicle-Vehicle	IMQ-Vehicle	Vehicle-DMSO	IMQ-DMSO
Serum (μg/ml)	0.49 ± 0.07	0.45 ± 0.07	0.74 ± 0.11	1.12 ± 0.10**
Urine (μg/ml)	0.79 ± 0.27	1.06 ± 0.20	3.14 ± 0.68	6.66 ± 1.21**
Colon (% of FD4 in tissue)	7.93 ± 2.31	4.16 ± 1.78	5.73 ± 3.14	14.25 ± 4.12

CONCLUSION: Local stimulation of TLR7 results in an enhanced colonic permeability only in states of epithelial disruption. The mechanisms mediating these effects seem to be independent of a modulation of the expression of the main tight junction-related proteins or the expression of GLP-2 and MLCK. These observations suggest that microbial factors do not trigger, per se, epithelial alterations, but they can contribute, as enhancing factors, in states of epithelial disruption. Similar mechanisms might operate in functional and inflammatory gastrointestinal disorders. In these conditions, after an initial disturbance of the epithelial barrier, the microbiota would act as an enhancing and/or perpetuating factor.
Disclosure of Interest: None declared

P1004 THE PERSISTENCE OF COLON CANCER-ASSOCIATED ESCHERICHIA COLI WITHIN HUMAN MACROPHAGES INDUCES COX-2 EXPRESSION

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INTRODUCTION: Independent studies have shown that colonic adenomas, carcinomas and the mucosa of patients with colorectal cancer are abnormally colonized by *Escherichia coli* belonging to the B2 phylogroup, with a high prevalence of *E. coli* producing a genotoxin termed colibactin. Macrophages are one of the predominant cellular components of tumor-infiltrating immune cells where they support key processes in tumor progression through the expression of protumoral factors such as the cyclooxygenase-2 (COX-2).
AIMS & METHODS: In the present study, we aimed to analyze the interaction of B2 phylogroup *E. coli* isolated from tumors of patients with human macrophages and the subsequent COX-2 expression.
The ability of B2 *E. coli* isolated from colon cancer to resist macrophages killing was assessed in human THP-1 macrophages using gentamicin assay and microscopy analysis. COX-2 expression and PGE2 secretion were quantified by Western blot and ELISA, respectively. Involvement of MAPK signaling pathways were analyzed by Western blot using specific inhibitors.
RESULTS: Colon cancer associated-*E. coli* were able to survive within human THP-1 macrophages at 24h post-infection indicating that these bacteria are able to resist macrophages killing. Transmission electron microscopy revealed that bacteria are enclosed in two kinds of compartments, some vacuoles containing single bacteria and other ones containing numerous bacteria. In addition, colon cancer-associated *E. coli* induced COX-2 expression and PGE2 secretion to levels significantly higher than those induced by the commensal *E. coli* strain ED1a belonging also to B2 phylogroup. Induced-COX-2 expression by colon cancer-associated *E. coli* was not related to the production of colibactin, since we observed similar COX-2 levels in macrophages infected with wild-type strain

11G5 or a *clbQ* mutant unable to produce colibactin. Interestingly, when macrophages were treated with ofloxacin, a fluoroquinolone antibiotic with intracellular tropism, a decrease in the number of intracellular *E. coli* was observed together with a decrease in COX-2 expression. In addition, in infected macrophages with colon cancer-associated *E. coli*, the p38 MAPK signalling pathway was involved in the control of the number of intracellular bacteria and in COX-2 expression.
CONCLUSION: Colon cancer-associated *E. coli* strains belonging to B2 phylogroup are able to resist macrophages killing and the presence of live intracellular bacteria induces COX-2 expression. We identify the p38 MAPK signalling pathway as a target to control the number of intracellular bacteria within macrophages and to limit the expression of the pro-tumoral factor COX-2.
Disclosure of Interest: None declared

P1005 GUT MICROBIOTA DYNAMICS DURING RADIATION PROCTITIS AND ITS POTENTIAL ROLE IN CONTROLLING DISEASE SEVERITY

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INTRODUCTION: A balanced gut microbiota, is essential for host well-being. Radiation proctitis (RP) may develop following radiation treatment of pelvic malignancies. Microbial changes may occur following radiation and impact radiation-induced tissue damage.
AIMS & METHODS: Aim: To investigate gut microbiota dynamics during different stages of RP in a mouse RP model.
Methods: The microbiome was analysed using fingerprinting and high-throughput approaches, based on fecal samples and colonic biopsies for up to 36 weeks. Biologic effects of microbiota at different stages were investigated using coculture of bacteria with HT-29 cells.
RESULTS: A shift in the gut microbiome during RP was observed (*p-value* Bonferroni-corrected < 0.0001 based on unweighted UniFrac mesure) and each clinical stage was represented by a unique microbial signature. These signatures were correlated with disease progression and immunologic parameters, as analyzed by colonic mRNA expression of several cytokines including TNFα, IL1β, IL6 and TGFβ (*p-value* < 0.05), histopathology (*p-value* < 0.001) and macroscopic symptoms of body weight, diarrhea and rectal bleeding in irradiated mice Vs controls. Using cocultures, RP-induced fecal microbiome obtained from active disease stages was found to induce secretion of TNFα (3.6-fold increase, *p-value* < 0.05) from the intestinal epithelial cells as compared to control flora, while naïve flora caused a decrease in IL1ß secretion (2.3-fold, *p-value* < 0.05). Supernatants and UV inactivated bacteria had no effect on cytokine secretion from the cells.
CONCLUSION: Rectal irradiation alters the local microbiota which have proinflammatory effects and loss of anti-inflammatory activity. Live bacteria are needed in order to mediate these effects. Better understanding of the mucosal-microbiome interaction may aid in future attemps to control disease severity and may potentially allow for manipulation of the microbiota in a clinically beneficial manner.
Disclosure of Interest: S. Gerassy Vainberg: None declared, A. Blatt: None declared, Y. Danin poleg: None declared, A. Dahan: None declared, Y. Kashi: None declared, Y. Chowers Lecture fee(s) from: Abbvie, Takeda, Janssen, Consultancy for: Abbvie, Takeda, Janssen, Pharmacosmos

P1006 PEG-GUT LAVAGE MAY INDUCE CHANGES IN THE FAECAL MICROBIOME OF HEALTHY VOLUNTEERS

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INTRODUCTION: Dysbiosis may play a role in some gastrointestinal conditions such as IBD, IBS and *C diff* diarrhoea. Metagenomic studies indicate that such conditions are associated with reduced bacterial diversity of the gut microbial ecosystem. Using high-throughput 16S rRNA sequencing technique, we explored whether intestinal cleansing with a polyethylene glycol solution (PEG) induces changes in the faecal microbiome of healthy individuals, and whether the eventual changes are reversible over time.
AIMS & METHODS: We analysed the faecal microbiome of 12 healthy volunteers through 7 time points before and after bowel cleansing with PEG. Faecal samples obtained at day -30 (T1) and day -1 (T2) before PEG evaluated stability. A solid sample was obtained during PEG lavage (T3), and further samples on days +1 (T4), +15 (T5), +30 (T6), and +60 (T7) were used to investigate changes induced by PEG and eventual resilience. DNA extracts were analysed by pyrosequencing of the 16S rRNA gene (V4). Raw sequence data collected were analysed with Qiime. We use Chao1 as species richness estimator and Unifrac as Phylogenetic Similarity Index.
RESULTS: Regarding the overall structure of bacterial communities, main enterotype drivers (Bacteroides genus for enterotype 1 and Prevotella genus for enterotype 2) did not change with PEG or during the follow-up. Interestingly, principal component analysis based on the weighted Unifrac distance metric indicated three different outcomes from the intervention. First, six individuals (Group A) showed no change of microbiome structure after PEG. Second, three individuals (group B) showed a clear change in community structure after PEG, since T4 samples did not cluster with T1 and T2. During the follow-up, T7 returned to baseline community structure but in one subject, where the change persisted. In the third group (Group C), there was variability in community structure over time that could not be ascribed to PEG intervention. The table shows species richness according to Chao1 in the three groups.

Chao 1	Timepoint 2 Mean and CI95%	Timepoint 4 Mean and CI95%	Timepoint 7 Mean and CI95%
Group A	744,92 (685,24-804,60)	713,57 (609,94-824,21)	713,99 (685,62-762,35)
Group B	694,12 (481,86-906,32)	520,80 (385,61-656)	610,46 (232,11-988,80)
Group C	878,55 (846,68-910,43)	663,86 (537,86-789,86)	638,91 (138,89-1138,93)

At species level, counts of *Faecalibacterium prausnitzii* (Fprau) markedly increased in T4 samples from group A and C individuals ($p = 0.07$), but decreased in all samples from group B. The increase may be explained by the flushing effect of PEG, since Fprau is usually abundant at ileo-caecum. On the other hand, *Akkermansia muciniphila* was detected at baseline in 6 out of 12 individuals, but only in 3 out of 12 T4 samples and in 4 T7 samples. Mean (±SEM) relative abundance decreased (T2 3.8±2.3; T4 0.13±0.09; T7 and 0.90±0.72).
CONCLUSION: PEG exposure did not modify the overall microbial community structure. In most subjects, detectable changes fell within the expected over time fluctuations. However, changes may persist in a subset of individuals.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS II – POSTER EXHIBITION – HALL XL

P1008 THE CLINICAL CHARACTERISTICS AND MANIFESTATION OF CMV ESOPHAGITIS

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INTRODUCTION: Esophagitis is the second most common gastrointestinal (GI) manifestation of cytomegalovirus (CMV) infection after colitis. CMV esophagitis has been reported in patients who have undergone transplantation, long-term renal dialysis and human immunodeficiency virus (HIV) infection
AIMS & METHODS: This study aimed to investigate the clinical characteristics of CMV esophagitis in patients undergoing diagnostic endoscopy.
A total of 23 patients with histologically proven cytomegalovirus infection from 1539 cases with esophageal ulcers (2003-2013) were identified and analyzed retrospectively. Patients' personal data (age, smoke, alcohol drinking), underlying systemic disease (diabetes mellitus, end stage renal disease, COPD), malignancy, indication of EGD, endoscopic characteristics in viral esophageal ulcer and diagnostic methods (pathological or serological finding) were collected for further analysis.
RESULTS: Among this data base, 23 patients were diagnosed to have cytomegalovirus esophageal ulcers. The age range was 23-84 yr and the male/female ratio 2.3/1. Odynophagia and epigastralgia were common symptoms. Most (15 of 23) of the CMV related ulcers were located at middle to lower third or distal esophagus. 21.7% (5/23) patients were infected with the human immunodeficiency virus. 47.8% (11/23) patients have underlying malignancy, including lung cancer (4), esophageal cancer (4), gastric cancer (1), ampulla vater cancer (1) and lymphoma (1). Eight of 11 patients (73%) had ever received concurrent chemoradiotherapy.
CONCLUSION:
In our study, patients with malignancy who had ever received concurrent chemoradiotherapy are at increased risk for CMV esophagitis, which had not been reported before in the literature review.
Disclosure of Interest: None declared

P1009 UPPER GASTROINTESTINAL ENDOSCOPIC FINDINGS IN HIV-INFECTED ASIAN PATIENTS ACCORDING TO AGE AND CD4 LYMPHOCYTE COUNT

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INTRODUCTION: Upper gastrointestinal (GI) tract diseases are common among patients infected with human immunodeficiency virus (HIV). Upper GI endoscopic evaluation of the GI tract disease remains a cornerstone of diagnosis, especially in a highly prevalent area of gastric cancer and *Helicobacter* infection.
AIMS & METHODS: The study aimed to evaluated the upper GI endoscopic findings by CD4 lymphocyte count and age. We retrospectively studied 191 HIV-infected patients who underwent upper GI endoscopy for any indications from January 1, 2010 to December 31, 2013. The patients were classified in two groups, according to CD4 cells counting ($\geq$200 cells/mm^3 or $<$200 cells/mm^3). The subjects were divided into five groups (those aged 20–29, 30–39, 40–49, 50–59, and 60–69 years old). Parameters studied included age, gender, indications for endoscopic procedure, CD4 cell counts, antiretroviral therapies, upper GI endoscopic finding and histology.

RESULTS: The median age of 191 patients was 43 years (interquartile range [IQR], 35-52 years), and 182 patients were predominantly male (95.3 %). The median CD4+ cell count was 398 cells /mm^3 (IQR, 205- 588 cells/mm^3). GI symptoms including abdominal pain, discomfort, soreness, and dyspepsia were noted in 133 patients (69.6%). The endoscopic diagnosis of upper GI disease is shown in Table. Opportunitic infections were seen exclusively in patient with CD4 < 200 cells/ mm^3 except candidial esophagitis. There was no difference in the prevalence of gastric or duodenal ulcer according to CD4 cell count groups. However, *Helicobacter pylori* related ulcers were seen in only group with CD4 ≥200 cells/mm^3.

	All (n = 191)	CD 4 ≥200 cells/mm (n = 146)	CD4 <200 cells (n = 45)	*p*
Candidal esophagitis	11(5.8)	6(4.1)	5(11.1)	.134
Cytomegalovirus disease	4(2.1)	0(0)	4(8.9)	.003
HIV-related idiopathic ulcer	8(4.2)	3(2.1)	5(11.1)	.019
Malignant lymphoma	1(0.005)	0(0)	1(0.02)	-
Reflux esophagitis, n(%)	48(29.1)	39(26.7)	19	.31
Atrophic gastirits, n(%)	28(14.7)	23(15.8)	5(11.1)	.696
Helicobacter related peptic ulcer, active stage	3(1.5)	3(2.1)	0(0)	-
Gastric adenoma/ adenocarcinoma, n(%)	2(1.0)	1 (adenoma)	1 (early gastric cancer)	-

CONCLUSION: Low CD4 count is considered to be a predictive factor for opportunity GI infection in HIV-infected Asian patients except candidial esophagitis.
Disclosure of Interest: None declared

P1010 MULTICENTRIC EXTERNAL VALIDATION OF PRE-ENDOSCOPIC CLINICAL PREDICTION RULES IN PATIENTS WITH NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

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INTRODUCTION: The risk scoring systems are increasingly used to evaluate patients with Upper Gastrointestinal Bleeding (UGIB). Some of these use clinical and laboratory data, which are collected at the emergency room. Most of them also use the results of procedures such as endoscopy to stratify the results. We are still looking for the optimal scoring system, which is simple, easy to use and remember by the clinicians at the time of the patient́s reception.
AIMS & METHODS: Aims. To validate externally the discriminant ability of the pre-endoscopic clinical prediction rules (CPR) (based on clinical and laboratory data) in patients with Non-Variceal UGIB (NVUGIB) in four tertiary hospitals.
Methods. We carried out an observational retrospective study using the hospital discharges registry *Minimum Basic Data Set* (MBDS) for cases of NVUGIB in Castilla la Mancha, and Valencian Community, Spain which is based on ICD-9 diagnostic codes. We estimated the predictability of ten CPR: pre-endoscopic Rockall score, Blatchford score, modified Blatchford score, AIMS65 score, Zaragoza score, Tammaro score, Rangson score, Cambridge score, Adamopoulos score and UNAL score[1-10]. We estimated the area under the ROC curve (AUC) for each CPR versus every outcome indicator (adverse clinical course, hospital mortality, interventional therapy, unstable bleeding, prolonged hospital stay).
RESULTS: 483 patients from four different hospitals were studied in two different time periods: 2003 to 2006 (Valencian Community centers), those from the oldest cohort and 2009 to 2013 (Castile La Mancha centers), those of the recent cohort. The CPR with better discrimination ability of each analyzed indicator are shown in table 1. In general, the discrimination ability is below 0.70 in almost all analyzed indicators and rules.
Table. Discriminant ability of the Clinical Prediction Rules

Discriminant ability	CPR (Scores)	Area under ROC curve
Adverse clinical course	Adamopoulos[1]	0.58 (0.50 – 0.67)
Unstable bleeding	Rockall[7]	0.62 (0.50 – 0.73)
Interventional therapy	Adamopoulos[1]	0.57 (0.49 – 0.66)
Hospital Mortality	AIMS65[8]	0.86 (0.65 – 1.00)
Prolonged hospital stay	Rockall[7]	0.67 (0.61 – 0.72)

CONCLUSION: The CPŔs discriminant ability for estimating the evolution of a NVUGIB is relatively moderate when they are externally validated in other different centers to which were derived. Rockal, Adamopoulos and AIMS 65 are the rules that best meet the evolution of these diseases and might be the most suitable for assessing their prognosis.
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Disclosure of Interest: None declared

P1011 DABIGATRAN- A RISK FACTOR OF SEVERE BLEEDING IN DISTAL ESOPHAGUS IN ELDERLY WOMEN

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INTRODUCTION: A new generation of oral anticoagulants Dabigatran has been shown to be effective. New studies showed, that the risk of gastrointestinal (GI) bleeding of Dabigatran is increased compared with Warfarin, but the incidence of life-threatening or fatal GI bleeding is lower. The source and localization of the bleeding in patients took Dabigatran are not detailed studied.
AIMS & METHODS: To compare a localization and severity of upper GI bleeding of patients with Dabigatran vs Warfarin.
All anticoagulated patients on Dabigatran or Warfarin with non variceal upper GI bleeding were enrolled in our study from November 2012 to November 2013. The demographic details, laboratory studies, concomitant medication were collected. Urgent endoscopy was performed in 24 hours from admission. A localization of GI bleeding and severity according Rockall score were describe.
All enrolled patients were divided in to two groups. Group A – patients on Dabigatran 2x110 mg. Group B – patients on Warfarin 1 x 5 mg.
RESULTS: A total of 78 patients with non variceal GI bleeding were examinated in our department. Twenty of them (26%) were anticoagulated (14 women and 6 men, medium age 78 range (47-92)).
A total of 12 patients (60%) 9 women medium age 82 and 3 men medium age 75 were on Dabigatran- group A.
8 patients (40%) (5 women, medium age 80, 3 men medium age 78 was on Warfarin- group B.
The source of bleeding had been found in distal esophagus or GE junction in 9 patients (9/12 (75%) 7 women and 2 man) in the group A compared to one patient (man) 1/8 (13%) in the group B, $p < 0.05$).
Rockall score in the group A was medium 8 (range 4-8) in patients with source of bleeding in distal esophagus or GE junction compared with Rockall score 5 (range 3-8) in patients with the source of bleeding in other upper GI locality. Rockall score in the group B was 5 in patients with source of bleeding in distal esophagus compared with Rockall score 5 (range 4-7) in patients with the source of bleeding in other upper GI locality. A total of 2 patients (2/12, 17%) in the group A had a fatal bleeding from source in distal esophagus compared with no patients in the group B.
CONCLUSION: Our study results revealed that Dabigatran is significant frequent cause of severe upper GI bleeding in distal esophagus or GE junction in elderly women compared with warfarin. Dabigatran should be indicated very carefully in this group of the patients.
Disclosure of Interest: None declared

P1012 STANDARD PRE-ENDOSCOPIC AND REDESIGNED POST-ENDOSCOPIC GLASGOW BLATCHFORD SCORE PERFORMED BETTER IN TERMS OF PREDICTING REBLEEDING IN PATIENTS WITH BLEEDING PEPTIC ULCER AS COMPARED TO ROCKALL SCORE - RESULTS OF A PROSPECTIVE DATABASE STUDY

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INTRODUCTION: We present new diagnostic scores that successfully predicted the treatment outcome and the need for early repeated endoscopy in patients with bleeding peptic ulcer.
AIMS & METHODS: The aim of the study was to determine optimal pre-endoscopic and post-endoscopic scores in order to most optimally predict mortality, rebleeding rate, as well as the necessity for surgical intervention, and blood transfusions in patients with bleeding peptic ulcer.
Patients and methods: We prospectively studied 633 patients with bleeding stomach or duodenal ulcer admitted to Department of Internal medicine at the University Hospital Center "Sestre milosrdnice" between January 2009 and December 2012. For every patient we calculated pre-endoscopic (Rockall (RS) and Glasgow Blatchford score (GBS)) as well as post-endoscopic diagnostic scores, according to urgent upper endoscopy findings. In post-endoscopic GBS, the GBS and Forrest classification with redesigned and upgraded formula were integrated.
RESULTS: In the group of patients with bleeding stomach and duodenal ulcer when comparing AUROC for pre-endoscopic GBS and RS we found that latter is superior in predicting mortality (AUROC 0.82 vs 0.67, p 0.002) while GBS was better in predicting the rebleeding rate (AUROC 0.75 vs 0.61, $p < 0.001$). Post-endoscopic RS was also better in predicting mortality (AUROC 0.82 vs 0.66, $p < 0.001$) and post-endoscopic GBS in rebleeding rate (AUROC 0.79 vs 0.70, p 0.002). Pre and post-endoscopic GBSs better predict the need for blood transfusion and surgical intervention when compared to RS in the same group of

patients. Post-endoscopic GBS was better in predicting rebleeding rate (AUROC 0.79 vs 0.75, $p<0.036$) and the need for blood transfusions (AUROC 0.83 vs 0.76, $p<0.001$) compared to pre-endoscopic GBS.
CONCLUSION: In patients with bleeding stomach and duodenal ulcer, pre-endoscopic and newly designed post-endoscopic GBSs are better in predicting the rebleeding rate, surgical intervention and the need for blood transfusion while pre and post-endoscopic RSs are superior in predicting mortality.
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Disclosure of Interest: None declared

P1013 THE PERFORMANCE OF THE GLASGOW BLATCHFORD SCORE (GBS) DEPENDS ON PREDICTING A BLOOD TRANSFUSION

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INTRODUCTION: Among the several scoring systems currently available for calculating the risk of upper-gastrointestinal bleeding (UGIB), the best option at present is the Glasgow Blatchford Score (GBS), which is used widely for assessing the need for admission. [1] The outcome is intervention (blood transfusion, endoscopic treatment, and surgery) or death. However, blood transfusion as an outcome measurement is superfluous in any scoring system since vital signs and hemoglobin level are sufficient to determine the need for a blood transfusion,[2] which in any case does not necessarily indicate either the need for intervention or a high-risk outcome. [3]
AIMS & METHODS: For the reasons stated above, the GBS should be validated based on outcomes that do not include blood transfusion. At Tama Medical Center, Tokyo, Japan, all patients suspected of suffering from UGIB, who were seen between January, 2008 and December, 2012, were enrolled in a validation study of the GBS without blood transfusion in the outcome. The first outcome comprised endoscopic treatment, surgery or death. The second outcome added blood transfusion to this list. We compared the area under the curve (AUC) of both outcomes with the GBS using Delong's test. We then assessed the predictive value of the second outcome with hemoglobin alone against that of the GBS by comparing their respective AUCs.
RESULTS:

	Outcome	AUC	95%CI
GBS	Intervention without blood transfusion or death	0.645	0.606-0.684
GBS	Intervention or death	0.757	0.718-0.796
Hemoglobin alone	Intervention or death	0.738	0.701-0.776

Of the 763 patients, 435(57.0%) received a blood transfusion and 19 patients died (2.5%). With regard to the GBS, the AUC of the first outcome was 0.645 [95%CI(0.606-0.684)] and that of the second outcome, including blood transfusion, was 0.757 [95%CI(0.718-0.796).]It was clear that the performance of the GBS depended largely on predicting the need for blood transfusion. ($p<0001$ by DeLong's method). On the other hand, the AUC of the hemoglobin level alone for the second outcome including blood transfusion was 0.738 [95%CI(0.701.4-0.776)], which was identical to that of the GBS.
CONCLUSION: The hemoglobin level alone was as useful as the GBS when the outcome measurements for the latter included blood transfusion. The results of this study suggest that the performance of risk assessments scores for UGIB should be validated after removing blood transfusion from the outcome measurements.
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Disclosure of Interest: None declared

P1014 ACUTE ESOPHAGEAL MUCOSAL LESIONS MIGHT NOT BE A RARE DISEASE

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INTRODUCTION: Acute esophageal mucosal lesion (AEML) that includes acute necrotizing esophagitis (ANE) and acute erosive esophagitisis relatively rareamong upper gastrointestinal bleedings. Recently, AEML is widely recognized with the development of endoscopic techniques.
AIMS & METHODS: This study aimed to clarify clinical features of AEML. We retrospectively analyse clinical and endoscopic findings of experienced AEMLcases of between January 2008 and March 2014.
RESULTS: We experienced 19cases (16patients)of AEML with 12male patients (75%) and 4 female patients (25%) with an average age of 56 years. Among them, only one patient had repeated 4 times of AEML (once ANE and 3 times of acute erosive esophagitis). During the period, we performed 14746 upper gastrointestinal endoscopies include 807 emergent upper gastrointestinal endoscopies. The rate of AEML accounted for emergency upper gastrointestinal endoscopies was 2.35% and 0.13% for all upper gastrointestinal endoscopies. AEML predominantly affected the lower third of the esophagus, and sliding hernia was the most common (94.7%) coexisting endoscopic finding. AEML was often accompanied by gastro-duodenal mucosal lesion. Two-thirds of ANE cases were accompanied by gastro-duodenal mucosal lesion, however only 7.69% of acute erosive esophagitis cases were accompanied by gastro-duodenal mucosal lesion. All patients had some comorbidity. Thirty three percent of patients with ANE, and fifteen percent of patients with acute erosive esophagitis received non-steroidal anti-inflammatory drugs (NSAIDs). Thirty percent of patients with acute erosive esophagitis had taken PPI or H_2RA,however no ANE patient took gastric secretion inhibitor. Gastric secretion inhibitor is possible to attenuate esophageal damage because the pathology of the 2 diseases is essentially same. Five cases (26.3%) were complicated by esophageal stenosis and eventually 3 cases died. All dead cases were associated with underlying diseases.
CONCLUSION: AEML was considered to be rare disease. However, more cases might be noticed with frequent application of upper gastro-intestinal endoscopy.
Disclosure of Interest: None declared

P1015 THE EFFICACY OF A SECOND-LOOK ENDOSCOPY WITH OR WITHOUT CLIPPING AFTER ENDOSCOPIC RESECTION FOR GASTRIC AND DUODENAL TUMORS: INTERIM RESULTS OF ONGOING PROSPECTIVE RANDOMIZED TRIAL

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INTRODUCTION: The benefit of postoperative EGD in order to control/prevent bleeding after endoscopic resection (ER) of gastric and duodenal tumors is still debatable.
AIMS & METHODS: The aim of this ongoing study is to evaluate whether second-look endoscopy (SLE) and haemostatic endoclipping is essential to prevent delayed gastrointestinal bleeding (GIB) after ER. A total of 35 patients (m-9, f-26, mean age M±s 68.3 ± 8.2 years) who underwent ER for gastric (31) and duodenal (4) tumors: endoscopic mucosal resection (EMR) – 20(57.2%), endoscopic submucosal dissection (ESD) – 9(25.7%), removal of submucosal tumor (RST) – 6(17.1%) from November 2012 to April 2014 were included in this study. All patients were randomly divided into 2 comparable groups. After ER the patients of both groups received antisecretory therapy with proton pump inhibitors (PPI): the first 3 days - pantoprazole 80 mg intravenously, the next 4 weeks - pantoprazole 80 mg per day orally. Each SLE was performed next day after the ER; endoscopic hemoclipping (EHC) was used to prevent GIB. In the group 1 (IPP+EHC) (19 pts.) endoscopic hemostasis (EH) was performed in all cases of visible vessels on the bottom and margins of the mucosal defect. In the group 2 (IPP alone) (16 pts.) EH was performed only in exceptional situations - at active bleeding or extremely high risk of bleeding (major vessels exposed on the mucosal defect). ER was performed under general anesthesia in 26 cases and local - in 9 cases. Coagulating forceps FD-410LR and argon plasma coagulation probe with electrocoagulator VIO 300 were used for hemostasis. Moreover, at the final stage clip fixing device HX-110LR with clips HX-610-135 was applied for the prevention of GIB.
RESULTS: EH at the final step of ER was performed in 52.6% (10/19) patients of Group 1 and 56.3% (9/16) patients of Group 2. The mean size of mucosal defects after ER was 21.2±14.9 mm and 25.3±18.1 mm respectively. All patients underwent SLE at the second day after the ER. In Group 1 EH was performed in 7 patients with stigmata, including 2 patients with vessel's size more than 1.5 mm. In Group 2 only one patient had exposed major vessels on the bottom of the postoperative defect after removal of a large villous duodenal tumor that required prophylactic placement of hemoclips. Only one 60-year-old female patient (5,3% from Group 1) had mild GIB on the second day after ESD for ulcerated tubulovillous adenoma of the stomach. It is remarkable that this complication occured a few hours after preventive endoclipping of all thrombosed vessels during SLE. The patient had a malignant course of hypertonic disease. In our opinion, an uncontrolled sharp increase in blood pressure was the main cause of postoperative bleeding. After succesfully perfomed EH the patient recovered on the background of intensified therapy for hypertention and doubled antisecretory therapy.
CONCLUSION: According to our preliminary data SLE with prophylactic clipping after ER for gastric and duodenal tumors has no significant impact on the frequency of postoperative GIB. SLE is feasible in selected patients with large postoperative mucosal defects after the wide excision of the tumor.
Disclosure of Interest: None declared

P1016 COMPARATIVE ASSESSMENT OF TOLERABILITY, DURATION AND COSTS BETWEEN THE 36-SOLID-STATE AND THE 24-WATER-PERFUSED HIGH RESOLUTION MANOMETRY FOR ESOPHAGEAL MOTILITY TESTING – DATA FROM A PROSPECTIVE, RANDOMIZED, DOUBLE BLIND, CROSSOVER STUDY

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INTRODUCTION: High Resolution Manometry (HRM) is a new technique for intraluminal esophageal pressure measurement, performed with a multitude of closely spaced (<2cm) pressure sensors. Currently, two systems are most widely used in clinical practice: the 36-channel solid-state (SS) HRM and the 24-channel water perfused (WP) HRM. Comparative data regarding their ambulatory use are lacking.
AIMS & METHODS: We aimed to assess and compare the tolerability, procedure duration and costs between the 36-SS and the 24-WP system. These data have been collected conducting a prospective, randomized, double blind, crossover study aimed to measure and compare normal values of conventional and high-resolution manometry metrics as well as to assess the inter-rater and inter-device agreement for the diagnosis of esophageal motility disorders between the 36-SS (Given Imaging, Los Angeles, CA) and the 24-WP system (EB Neuro, Firenze, Italy). Twenty healthy volunteers [HVs; 11M/9F; median age 29 (IQR 26-33)] and 20 patients [11M/9F; 48 (43-55)] with esophageal symptoms (i.e. reflux symptoms, chest-pain or dysphagia) were enrolled. They underwent both procedures blinded and in random order. Tolerability was assessed by using a self-made questionnaire investigating the occurrence of symptoms, presence and location of discomfort and which procedure was better tolerated. System set-up time, procedure duration and analysis time were measured separately. Finally, costs related to their ambulatory use were provided by the Resources Management Office.
RESULTS: Details about tolerability are shown in the Table. Overall, HVs did not found any difference between the two systems, whereas the patients tolerated better the 36-SS HRM procedure [9 (45%) vs. 12 (60%), p = ns]. Significantly longer set-up (454sec vs. 222sec, p < 0.01) and plot analysis (601sec vs. 345sec, p < 0.01) time was required by the 24-WP system compared to the 36-SS system. No difference was observed between the 24-WP and 36-SS system in terms of tracing acquisition time (483sec vs. 552sec, p = 0.6). The single-procedure cost was 58.48 € for the 24-WP HRM and 79.18 € for the 36-SS HRM.

	HVs 24-WP HRM	HVs 36-SS HRM	Patients 24-WP HRM	Patients 36-SS HRM
Symptoms Occurrence, n (%)				
None	4 (20%)	3 (15%)	1 (5%)	14 (70%)
Pain	4 (20%)	3 (15%)	6 (30%)	2 (10%)
Heartburn	4 (20%)	5 (25%)	1 (5%)	0 (0%)
Nausea and Vomiting	1 (5%)	1 (5%)	4 (20%)	3 (15%)
Globus	10 (50%)	9 (45%)	9 (45%)	4 (20%)
Location of Discomfort, n (%)				
Nose/ Throat	16 (80%)	11 (55%)	16 (80%)	7 (35%)
Chest/Stomach	1 (5%)	0 (0%)	1 (5%)	0 (0%)

CONCLUSION: The 36-SS system was better tolerated by patients and required shorter set-up and analysis time. This may be explained by a heightened sensitivity of the patients to intraesophageal stimuli (i.e. water outflow). The procedure cost was substantially higher for the 36-SS system due to the higher price of the 36-SS catheter.
Disclosure of Interest: None declared

P1018 GRADE OF EOSINOPHILIA VS. SYMPTOMS IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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INTRODUCTION: The diagnosis of eosinophilic esophagitis (EoE) is established by symptoms of esophageal dysfunction not caused by GERD and with at least 15 eosinophils/high power field in biopsies from the esophageal mucosa.(1)
AIMS & METHODS: The aim of this study was to assess the correlation between the number of eosinophils and symptoms in untreated EoE-patients both by histopathological staining with haematoxylin-eosin (HE) and by immunohistochemical (IHC) technique against ''Eosinophil Major Basic Protein''. The biopsy slides were encoded, scanned and examined. At the peak value area the eosinophils were separately marked and counted (d = 0.52mm circle at x400). Symptoms and health-related quality of life (HRQL) were recorded using the Watson Dysphagia Scale (WDS), the European Organization for Research and Treatment of Cancer Quality of Life–Oesophageal Module 18 (EORTC QLQ-OES18) and the Short Form–36 (SF-36) questionnaires. Data on the presence of allergies and bolus impaction were reviewed from medical records.
RESULTS: EoE patients (n = 66) were consecutively included from Jan 2007 until May 2012. The mean age was 45 years (19-88) and 74% were males. Allergy occurred in 73% of the patients and 39% were diagnosed in connection with an incident of esophageal bolus impaction. More eosinophils were counted after IHC- than after HE- staining (p < 0.001). Age correlated weakly and negatively with the number of eosinophils in the IHC slides (R = -0.24 peak, R = -0.32 upper part). Bolus impaction was associated with higher numbers of eosinophils in the mucosa from the upper part of the esophagus (IHC p = 0.05 and HE p < 0.05). The response rate for WDS and SF-36 were 92% and for the EORTC QLQ-OES18 100%, however, the number of eosinophils did not correlate with any of the scores from these questionnaires.
CONCLUSION: The significantly higher eosinophil counts obtained after IHC as compared to HE-staining is uncontroversial.(2) So is the non-existing correlation between subjective symptoms and the numbers of eosinophils.(3) Still, higher eosinophil counts were found in biopsies obtained during the course of acute bolus impaction, which might be considered the ultimate grade of dysphagia. The weak negative correlation found between age and numbers of eosinophils should be carefully interpreted but might reflect the ageing immune system.(4) The significantly higher eosinophil numbers in the upper esophagus in patients with concomitant bolus impaction may motivate increased attention to this level regarding histopathology and motility in EoE.
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P1019 IN VIVO HISTOPATHOLOGICAL ASSESSMENT OF THE MUSCULARIS PROPRIA IN ACHALASIA BY USING ENDOCYTOSCOPY

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INTRODUCTION: Histopathology of muscularis propria (MP) is still unknown in patients with achalasia. Endocytoscopy (EC) was developed as ultra-high magnification endoscopy, and through the submucosal tunnel created during per-oral endoscopic myotomy (POEM), not only access but also subsequent consecutive assessment of the MP can be performed endoscopically.
AIMS & METHODS: In 7 achalasia patients (mean [±SD] age; 35±18.1 years, male:female; 4:3) who underwent POEM (myotomy length: 12±2.2 cm), subsequent EC examination was performed from mid esophagus to gastric side. EC images were taken and compared with histopathologic results (two biopsy from mid esophagus and lower esophageal sphincter) which was considered gold standard.
RESULTS: In all the cases, favorable EC images were taken, and spindle-shaped smooth muscle cells were clearly demonstrated. In our series, none of those showed particularly notable features such as atrophy or hypertrophy of smooth muscle cells. And the EC assessment was consistent with the results of biopsy. There were no complications encountered in all the procedures.
CONCLUSION: In clinical setting, real time assessment of the MP is feasible by using EC. It is expected that this technique will play an important role in unraveling the pathology of achalasia and other gastrointestinal functional diseases.
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P1020 AN INVESTIGATION OF GASTROESOPHAGEAL REFLUX DISEASE AFTER PERORAL ENDOSCOPIC MYOTOMY (POEM): CLINICAL RESULTS OF 40 CASES

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INTRODUCTION: POEM is a surgical procedure for esophageal myotomy similar to Heller myotomy, the frequency and the degree of postoperative reflux esophagitis are major outcomes that should be examined in the clinical setting. The purpose of this study was to examine the incidence and degree of reflux esophagitis after performing POEM, and to determine whether POEM causes reflux esophagitis.

AIMS & METHODS: AIMS: POEM has shown promise in overcoming limitations of current treatments for achalasia. This prospective study examined the effectiveness and risk of complications, especially reflux esophagitis, associated with POEM performed on achalasia patients. **METHODS:** Patients with achalasia were recruited from a single center where all POEM procedures were performed. The pre- and postoperative (3 months after POEM) assessments included Eckardt scores, manometry, endoscopy, and pH monitoring (Demeester score).
RESULTS: Forty patients (22 males; mean age, 46.2±16.1 years) underwent POEM between September 2011 and June 2013. A significant reduction was observed postoperatively in the lower esophageal sphincter pressure (from 39.0±16.5 mmHg to 18.6±11.0 mmHg [$P<0.05$]) and Eckardt scores (from 6.3±2.6 to 0.6±0.8 [$P<0.05$]). Four patients developed symptomatic gastroesophageal reflux disease (GERD; 3 patients, grade A; 1 patient, grade B). Twenty-seven patients were diagnosed with erosive esophagitis (19 patients, grade A; 6 patients, grade B; 2 patients, grade C). Both erosive esophagitis and GERD were well controlled with protein pump inhibitors intake without requiring surgery. Univariate logistics regression analysis identified postoperative duration of reflux (odds ratio [OR], 1.15; 95% confidence intervals [CI], 1.01-1.30) and Demeester score (OR, 1.04; 95% CI, 1.00-1.08) as predictors of development of reflux esophagitis (≥grade B). None of the POEM factors were found to be related to reflux esophagitis.
CONCLUSION: POEM is safe and effective in providing symptomatic relief for achalasia patients. Additionally, it is not associated with the development of erosive esophagitis. Periodic postoperative interviews and endoscopic examinations are helpful in evaluating reflux esophagitis.
Disclosure of Interest: None declared

P1021 LIQUID VERSUS VISCOUS SWALLOWS IN HIGH RESOLUTION IMPEDANCE MANOMETRY FOR THE EVALUATION OF PATIENTS WITH DYSPHAGIA

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INTRODUCTION: Oesophageal high resolution impedance manometry (HRiM) is an emerging tool used to assess oesophageal motility and function though it measures the efficiency of oesophageal motility and bolus transit.
AIMS & METHODS: The aim of this study is to assess the changes in HRM parameters and diagnosis as well as the bolus transit depending on the bolus type in patients with dysphagia. 46 patients with dysphagia referred for oesophageal function evaluation. All patients had upper endoscopy to exclude organic disease. Oesophageal HRiM was also performed on all (Manoscan, Given) administering ten liquid and ten viscous swallows in the supine position: The data were analyzed according to 2012 Chicago Classification criteria. Swallows were classified as having complete bolus transit or incomplete bolus transit according to criteria previously reported. Statistical analysis: Chi-Square or Fischer and T-test.
RESULTS: 18 male patients (39.1%), mean age 55.8 [39.9-71.5], mean BMI 25.9 [21.6-30.5]. HRiM parameters and diagnosis are expressed in the table. All patients had dysphagia, also associated with chest pain in 6 patients (13%) and heartburn in 4 (8.7%). 47.8 patients had pervious oesophageal treatment. There were significant differences in DCI between liquid and viscous swallows (2287.9 vs. 2718.1; $p=0.001$), and between complete bolus transit depending on the bolus type (21.7% liquid swallows vs. 13% viscous swallows; $p=0.002$).

HRiM parameters			
	Liquid	Viscous	p
IRP-4s (mmHg)	18.6 [16.2-21.1]	19.9 [16.9-22.8]	0.135
DCI (mmHg.cm.s)	2287.9 [1548.2-3027.6]	2718.1 [1897.5-3538.7]	0.001
VFC (cm/s)	7.0 [4.7-9.3]	9.1[2.8-15.5]	0.401
IBP (mmHg)	16.9 [14.9-19.7]	20.3 [15.3-25.1]	0.062
Complete bolus transit	10 (21.7%)	6 (13%)	0.002
HRiM diagnosis ($p=0.620$)			
Normal	13 (28.3%)	14 (30.4%)	
Oesophageal Motility Disorder	33 (71.7%)	32 (69,6%)	

CONCLUSION: There were some changes in HRiM parameters depending on the type of bolus consistency, but their involvement in final HRiM diagnosis was not relevant, although complete bolus transit was more frequent with liquid swallows. Therefore, viscous swallows are not discriminative enough compared to liquid swallows for the diagnosis of patients with dysphagia.
Disclosure of Interest: None declared

P1022 PERORAL ENDOSCOPIC MYOTOMY: SAFE AND EFFECTIVE. A PROSPECTIVE EVALUATION OF 40 CONSECUTIVE CASES

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INTRODUCTION: Peroral endoscopic myotomy (POEM) is an endoscopic alternative to laparoscopic myotomy. This promising procedure is still considered experimental. Herein, we report single-center mid-term results of POEM in the Czech Republic.
AIMS & METHODS: Since 2012, a total of 41 POEM procedures have been performed in 40 patients (15 women, 25 men, mean age 45). All patients had a diagnosis of achalasia (n = 40) or Jackhammer esophagus (n = 1) based on endoscopic, manometric and radiologic examinations. A 3, 6, and 12 months follow-up was completed in 33, 24 and 12 patients. The primary outcome was treatment success defined as Eckhard score < 3. At three months, high resolution manometry and 24-hour pH metry monitoring were performed.
RESULTS: A. PROCEDURE: POEM was successfully completed in all patients. The median length of procedure was 80 minutes (range 43-145). The median myotomy length was 13 cm (8-15). In 17 patients (42%), capnoperitoneum had to be decompressed and 19 patients (47%) experienced a subcutaneous emphysema which resolved spontaneously. Fever was present on the first postoperative day in 6 patients (15%). We did not experience any serious intraoperative or postoperative complications and all patients were dismissed the 2nd or 3rd postoperative day. We observed the following minor complications: inadvertent mucosotomy 3x (treated with clips), respiratory instability during POEM 2x (decompression of capnoperitoneum was necessary), bleeding at the entry site 1x, difficult entry site closure 2x (necessary to use high resolution clips) and large subcutaneous emphysema 1x.
B. TREATMENT RESULTS: 3, 6 and 12 months after POEM, treatment success (Eckhard score < 3) was achieved in 31, 24 and 12 patients (94%, 100%, 100%), median score pre- vs. post-treatment was 7 vs. 0 at 3 and 6 months, and vs. 1 at 12 months; $p<0.001$. The median percentage of overall symptomatic improvement was 90%. Quality of live significantly improved (median score 107 before POEM vs. 130, 136 and 137 3, 6 and 12 months after POEM, $p<0.001$). Manometric parameters (IRP and LES pressure) normalized in a majority of patients.
Heartburn was present in 7 (21%), 4 (17%) and 2 (17%) patients 3, 6 and 12 months after POEM. Eight patients (20%) have been treated with proton pump inhibitors or antacids on demand. Three months after POEM, a mild reflux esophagitis (LA A) was diagnosed in 10 patients (30%) and a pathological gastro-esophageal reflux (DeMeester score >14) was detected in 16 (48%) patients.
CONCLUSION: POEM is a safe and effective treatment modality in patients with achalasia with excellent mid-term results which seems durable. There is significant (though almost asymptomatic) reflux postoperatively in 48% of patients in 3-months pH metry studies.
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Disclosure of Interest: None declared

P1023 PREVALENCE OF GERD IN PATIENTS WITH DENTAL EROSION: CASE-CONTROL STUDY

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders in Western countries, affecting up to 20% of the general population, with relevant impact on quality of life and health care costs. Apart from the presence of more classic esophageal manifestations, GERD is increasingly associated with extra-esophageal syndromes such as dental erosions (DE). DE is defined as the loss of tooth structure in connection with environmental acidification in the oral cavity, without bacterial activity.
AIMS & METHODS: We aimed to evaluate the prevalence of GERD symptoms in patients with DE. We enrolled 119 patients, who presented at the Dentistry Unit to perform dental hygiene. During the visit, a distinct investigator completed a structured interview to the patients, including a careful medical history and current medications. All patients underwent an accurate evaluation for DE through a validated test: the Basic Erosive Wear Examination (BEWE). Moreover, the presence of behavioral risk factors for DE was evaluated (i.e., consumption of acidic foods and drinks). All patients completed a validated questionnaire (VAS and Likert scale) in order to assess the frequency and intensity of typical reflux symptoms (i.e., heartburn, regurgitation, non-cardiac chest pain -NCCP-) in patients with (cases) and without (controls) DE.
RESULTS: Male/female ratio was 0.54 (44/77). Mean age was 48.2±14.5 yrs. Twenty-three out of 199 patients (17.6%) showed DE clinical signs (BEWE > 1). Eleven out of 119 patients (9.2%) had risk factors for DE, of whom only three had DE. Reflux symptoms were more frequent in patients with DE (18/23; 78.3%) than in patients without DE (41/96; 42.7%) ($p=0.001$). In detail, regurgitation was reported in 14/23 (60.9%) ($p<0.001$), and NCCP in 13/23 (56.5%) ($p<0.001$). Heartburn showed a similar prevalence between patients with DE and controls but was more frequent (Likert scale; $p=0.001$) and more intense (VAS; $p=0.001$) in DE subgroup. Neither patients with DE or patients with positive reflux-symptom questionnaire had ever undertaken PPI therapy. No patients undertaking PPI therapy had DE.
CONCLUSION: Patients with DE showed more frequent and troublesome reflux symptoms than controls without DE. During dental hygiene, patients with DE should be allowed to complete a GERD questionnaire to better identify those with reflux symptoms.
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P1024 THE RELATIONSHIP BETWEEN GASTROESOPHAGEAL REFLUX DISEASE AND ATRIAL FIBRILLATION

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INTRODUCTION: Gastroesophageal reflux disease (GERD) and atrial fibrillation (AF) are common diseases, but the relationship between these two diseases remains controversial. Previous studies suggest a potential association between GERD and AF. We aimed to investigate the association between GERD and AF.
AIMS & METHODS: This was a retrospective study created from chart review for patients who newly diagnosed by GERD or AF between January 1, 2011 and March 31, 2014. Patients were classified by two groups. The patients who diagnosed by newly GERD with presence of AF were classified by Group-1 (n = 129), the patients who diagnosed by newly AF with presence of GERD were classified by Group-2 (n = 134). We analyzed the association and risk factors between two groups.
RESULTS: The average age of two group were 69.3 ± 10.6 years / 73.5 ± 9.5 years (p = 0.001). The duration of diagnosis between GERD and AF were 40.1 ± 37.4 months / 44.5 ± 33.4 months (p = 0.32). In univariate and multivariate analysis, age, alcohol, underlying coronary artery disease, sustained arrhythmia, chronic obstructive pulmonary disease (COPD), hyperthyroidism, use of ACE inhibitor, B-blocker and warfarin were related to incidence of GERD in Group-1 ($p < 0.05$). COPD and proton pump inhibitor (PPI) were related to incidence of newly AF in Group-2 ($p < 0.01$). The presence of AF increased the relative risk (RR) of GERD (RR: 1.37, 95% confidence interval [CI]: 1.33-1.47), and the presence of GERD increased the risk of AF (RR: 1.12, 95% CI: 1.08-1.19).
CONCLUSION: GERD and AF were significantly associated with an increased risk of diagnosis of each other. The presence of AF increased the relative risk (RR) of GERD (RR: 1.37, 95% CI: 1.33-1.47), and the presence of GERD increased the risk of AF (RR: 1.12, 95% CI: 1.08-1.19). A large cohort study to assess the potential relationship between GERD and AF is needed.
Disclosure of Interest: None declared

P1025 QUALITY OF LIFE, PATIENT SATISFACTION, AND DISEASE BURDEN IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE WITH OR WITHOUT LARYNGOPHARYNGEAL REFLUX SYMPTOMS

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INTRODUCTION: Patients with gastroesophageal reflux disease (GERD) have lower health-related quality of life (HRQL) than general population. Increasing frequency and severity of reflux symptom has negative impact on well-being. HRQL in patients with laryngopharyngeal reflux (LPR) is also significantly impaired. However, study comparing HRQL in GERD patients with and without LPR symptoms is rare.
AIMS & METHODS: The aim of the study was to compare HRQL, patient satisfaction, and disease burden in GERD patients with and without LPR symptoms. A national, random-sample, and face-to-face survey of 300 Koreans was conducted. The sampling frame was based on the previous national wide, population-based telephone survey, in terms of distribution of age, gender, occupation, and region of residence by quota sampling. Gastroesophageal reflux symptoms were assessed by the Rome III questionnaire, LPR symptoms by reflux symptom index (RSI), and the quality of life by EuroQol-5 dimension questionnaire (EQ-5D). Structured questionnaire on health service utilization, sickness-related absence, and patient satisfaction were also used.
RESULTS: Face to face interview was conducted from Jan to Mar 2013 in 300 subjects (141 male, 159 female, Mean age 43.5±12.6, GERD without LPR, n = 150, GERD with LPR, n = 150). Median RSI in patients with GERD and LPR was 19.5 (14-36). Mean EQ-5D index was lower in GERD patients with LPR than GERD patients without LPR (0.88 vs. 0.91, p = 0.002). GERD patients with LPR reported more problems in pain/discomfort (58.7% vs. 47.8%, p = 0.049), and anxiety/depression dimensions (39.3% vs. 22.0%, p = 0.001). Severity of LPR was related with HRQL when adjusted for age, gender, marital status, BMI, severity of GERD, household income and comorbidity. GERD patients with LPR have lower overall satisfaction (40.0% vs. 69.1%, p = 0.040). Satisfaction scores were lower in GERD patients with LPR: satisfaction with physician's concern (3.5 vs 3.9, p = 0.002), physician's professional knowledge (3.5 vs 3.9, p = 0.005), physician's explanation (3.5 vs 3.9, p = 0.003), medical cost (3.3 vs 3.7, p = 0.003), and treatment outcomes (3.1 vs 3.5, p = 0.005). There were no significant differences in the patterns of health service utilization between two groups. GERD patients with LPR reported longer sickness related absent hour per week (0.37±1.43 vs. 0.02±0.20, p = 0.016), and poorer work productivity score (3.08±2.28 vs. 2.08±1.72, p = 0.001).
CONCLUSION: GERD patients with LPR have lower HRQL than GERD patients without LPR, and the severity of LPR was related with decreased HRQL. GERD patients with LPR have lower satisfaction with physician, medical cost, and treatment outcomes. The economic burden seems to be higher in GERD patients with LPR in terms of increased loss of work and decreased productivity.
Disclosure of Interest: None declared

P1026 NO INCREASE IN GASTRIC ACID SECRETION IN THE JAPANESE OVER PAST TWO DECADES

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INTRODUCTION: The prevalence of gastro-oesophageal reflux disease (GORD) has been increasing worldwide over recent decades. Although the prevalence was considered to be lower in Asia, GORD has become more prevalent in Asia including Japan [1, 2]. A previous study demonstrated that gastric acid secretion in Japanese individuals increased in the era from the 1970s to 1990s [3]. That increased secretion is thought to be one of the important factors for the increase in rate of GORD. However, it remains to be elucidated whether that increasing trend has continued from the 1990s to the present.
AIMS & METHODS: The aim of this study was to evaluate whether gastric acid secretion has altered over the past 2 decades with and without the influence of *H. pylori* infection in non-elderly and elderly Japanese.
Seventy eight healthy Japanese subjects were enrolled, and divided into those aged between 20 and 25 (young group), around 50 (non-elderly group), and around 75 (elderly group) years old. Gastric acid secretion, concentrations of serum gastrin and pepsinogen I and II, and *H. pylori* infection were determined in each case, and the data were compared among the groups. Furthermore, those findings were compared with data obtained in the 1990s.
RESULTS: Basal acid output (BAO) and maximal acid output (MAO) gradually decreased with age even in *H. pylori*-negative subjects. In addition, those with *H. pylori* infection tended to show decreased gastric acid secretion as compared with those without infection, particularly in the elderly group. Consistently, serum gastrin concentration was significantly higher in the elderly as compared to non-elderly subjects. As for sex difference, MAO decreased gradually with age in males, while it remained unchanged with age in females. Interestingly, gastric acid secretion has not changed over the past 2 decades in Japanese individuals irrespective of the presence of *H. pylori* infection.
CONCLUSION: In contrast to the increased prevalence of GORD, gastric acid secretion has not increased over the past 2 decades in the Japanese as a whole. On the other hand, secretion has decreased with age in males but not in females, which may partly explain the female preponderance of GORD in the Japanese elderly.
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P1027 PREDICTIVE FACTORS OF SILENT REFLUX IN SUBJECTS WITH EROSIVE ESOPHAGITIS

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is a chronic disease which can cause troublesome symptoms. Asymptomatic erosive esophagitis (AEE) is a subgroup of patients with a lack in any symptom. The purpose of the study was to investigate the prevalence of AEE in a large population undergoing health checkups and to identify the predictive factors for the disease.
AIMS & METHODS: From March 2012 to August 2013, 2752 consecutive subjects who underwent upper gastrointestinal endoscopy during health checkup were enrolled. The severity of erosive esophagitis was evaluated according to the Los Angeles classification. A GERD subject was defined as any individual who has a diagnosis of endoscopic LA grade≥A or Barrett's esophagus or having troublesome symptoms as identified by Reflux Disease Questionnaire (RDQ) score. All participants were recorded with demographic characteristics, biochemical data, and evaluated with questionnaires including Pittsburgh Sleep Quality

Index (PSQI) score, Taiwanese Depression Questionnaire (TDQ) score, and State-Trait Anxiety Inventory (STAI) score. The independent predictive factors for asymptomatic erosive esophagitis were analyzed by the logistic regression method.
RESULTS: A total of 676 GERD subjects with erosive esophagitis (EE) were recruited for final analysis, and about 59.2% of subjects with EE had no reflux symptoms. In the univariate analysis, subjects with AEE have more female gender, older age, lower level of education, less alcohol and tea consumption, less depression, less anxiety, lower serum level of triglyceride, and lower prevalence of metabolic syndrome, compared with subjects with symptomatic EE. Multivariate analysis revealed that female sex (OR = 1.645, $p = 0.0146$) was a positive predictive factor for AEE, and higher level of education (OR: 0.564, $p = 0.044$), higher TDQ score (OR: 0.922, $p < 0.001$), and with the metabolic syndrome (OR: 0.625, $p = 0.0379$) were significant negative predictive factors for AEE.
CONCLUSION: Asymptomatic erosive esophagitis is common in subjects undergoing health checkup. Female sex, lower education level, less depression, and lower prevalence of metabolic syndrome are independent predictive factors for developing asymptomatic erosive esophagitis, compared with symptomatic erosive esophagitis.
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Disclosure of Interest: None declared

P1028 IS PH IMPEDANCE MORE USEFUL THAN TRADITIONAL PH MONITORING FOR PATIENTS' MANAGEMENT IN CLINICAL PRACTICE? RESULTS OF A PROSPECTIVE STUDY

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INTRODUCTION: Oesophageal pH tests are deemed to be useful in management of selected gastro-oesophageal reflux (GOR) disease patients. Development of pH impedance (pH-MII) tests has increased the diagnostic yield by documenting the role of weakly acidic refluxes. However to which extent results of pH-MII tests improve patients' management is largely unknown.
AIMS & METHODS: Aim of our study was to prospectively evaluate usefulness of pH MII monitoring in the patients' clinical management compared with traditional pH monitoring. One hundred and eighty four consecutive patients (72 men, median age 52, range 19-82 yrs) were enrolled for traditional pH or pH-MII monitoring. A telephone interview was done 3 and 12 months after the test. A standardized questionnaire was used in the visit before the test and in the telephone interviews, dealing with improvement ($\geq$ 50% reduction of symptom frequency) of the dominant symptom, patient's satisfaction with regards to the dominant symptom (1-10 visual analogue scale, satisfied if VAS $\geq$ 7) and treatment for GOR disease. Nineteen patients were lost at follow up at the 12 month interview. Indications of pH and pH-MII test were evaluated for appropriateness[1]. Mann-Whitney or Krusal-Wallis tests for comparison of quantitative variables and chi-square test for categorical variables were used.
RESULTS: Demographic and endoscopic variables, frequency of previous PPI use were similar in the two arms. Thirty-nine (42.4%) of the pH tests and 34 (37.0%) of the pH-MII tests were positive for GOR disease (pathological GOR and/or positive symptom association probability [SAP]); in the pH-MII arm 10 patients had an increased number of weakly acid refluxes and/or a positive SAP for weakly acid reflux whereas their acid reflux variables were normal/negative. See table for main outcome results. Outcomes were similar for tests with appropriate and those with inappropriate indication (p = NS) in both arms. After the test, as assessed at the 3 months interview, treatment for GOR disease (PPIs except in one pH-MII arm patient who underwent fundoplication) was undertaken in 87.2% of positive, 59.1% of indeterminate (i.e. normal GOR and no symptomatic episodes during the test), and 35.5% of negative tests in the pH arm, and in 97.1% of positive, 47.6% of indeterminate and 54.1% of negative tests in the pH-MII arm (p < 0.001 among groups in both arms).

	positive outcome*		satisfaction#	
	3 months	12 months	3 months	12 months
pH tests	53/92 (57.6%)	52/79 (65.8%)	47/92 (51.1%)	43/79 (54.4%)
pH-MII tests	58/92 (63.0%)	60/86 (69.8%)	45/92 (48.9%)	49/86 (57.0%)
p-value	0.621	0.234	0.768	0.225

CONCLUSION: Patients' outcome and satisfaction were similar in the two arms and independent of the appropriateness of test indication. Although PPI prescription was more frequent after a positive pH or pH MII monitoring, physicians often did not take into account a negative result. Our data cast doubts on the added value of pH MII monitoring for patients management in clinical practice.
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Disclosure of Interest: None declared

P1029 ROLE OF GASTRO-OESOPHAGEAL REFLUX IN SYMPTOMS' GENERATION AND PROTON PUMP INHIBITORS' USE AMONG PATIENTS WITH AUTOIMMUNE ATROPHIC CHRONIC GASTRITIS: A STUDY WITH OESOPHAGEAL PH-IMPEDANCE MONITORING

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INTRODUCTION: Patients affected by autoimmune atrophic chronic gastritis (AACG) often refer digestive symptoms and are prescribed proton pump inhibitors (PPIs). No data are available on the role of gastro-oesophageal reflux (GOR) in clinical presentation and on the appropriateness of anti-secretory drugs' prescription.
AIMS & METHODS: Aims of this prospective observational study were to investigate GOR, psychopathological profile and frequency of use/response to anti-secretory medications (PPIs and H_2 receptor antagonists [H_2RA]) in patients with AACG.
All patients affected by AACG with or without digestive symptoms and in regular follow-up at our hospital who were seen between January 2013 and December 2013 (n = 51) were asked to participate to this study. The study protocol included: (i) 24h intra-oesophageal and intra-gastric pH impedance monitoring (MII-pH) off-PPIs; median intragastric pH, number of acid and weakly acidic (WA) reflux as well as of Symptom Index (SI) and Symptom Association Probability (SAP) were calculated, (ii) a validated questionnaire evaluating psychopathological profile (SCL-90R) and (iii) a standardized clinical questionnaire including items on anti-secretory medications use/response.
RESULTS: Baseline characteristics. Thirty-one of the 51 patients agreed to be investigated, 4 men, median age 60, range 29-78 yrs. Twenty-two of them (71%) were symptomatic: n = 12 symptoms suggestive of GOR (i.e. heartburn, epigastric burning, regurgitation, non cardiac chest pain) and n = 10 dyspeptic symptoms. **MII-pH.** Median intragastric pH was 6.3 (IQR 5.8-6.8). None of the patients had acid reflux. Six patients had an increased number of WA reflux episodes (3 with GOR symptoms, 2 with dyspeptic symptoms and 1 asymptomatic according to our clinical questionnaire) and 4 additional patients had SI and/or SAP positive for WA reflux and GOR symptoms (n = 2) or epigastric pain (n = 2). **SCL-90R questionnaire.** Altered somatisation (defined as t-score $\geq$ 63) was present in 11/22 (50%) symptomatic patients and 3/9 (33%) asymptomatic patients (p = 0.40 by Chi-Square Test). Focusing on symptomatic patients, altered somatisation was similarly present in those with increased WA reflux or positive SI/SAP and in those without, n = 4/9 (44%) and n = 7/13 (54%), respectively. **Anti-secretory drugs** were prescribed in 13/22 (59%) symptomatic patients (PPIs in 12 and H_2RA in 1). A clinical benefit was reported by 8/13 patients, increased WAR being present in 2 of them and altered somatisation in 5.
CONCLUSION: In symptomatic patients with AACG: 1) acid reflux never occurred whereas increased WA reflux was not infrequent, 2) PPIs were often used, however their clinical benefit seemed to be more associated with altered somatizations than with objective variables suggesting GOR as cause of patients' symptoms and 3) MII-pH may be useful to diagnose GOR disease in a minority with severe symptoms who could benefit from anti-reflux surgery.
Disclosure of Interest: None declared

P1030 ESOPHAGOGASTRIC JUNCTION MORPHOLOGY MAY BE USEFUL TO PREDICT A POSITIVE IMPEDANCE-PH MONITORING IN PATIENTS WITH GERD

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INTRODUCTION: High-resolution manometry (HRM) provides a better representation of the esophagogastric junction (EGJ) making it possible to isolate the crural diaphragm (CD) contraction from expiratory lower esophageal sphincter (LES) pressure. According to the Chicago Classification (CC), three different EGJ morphologic subtypes can be detected based on the separation between the LES and the CD. Recently, these EGJ subtypes have been positively correlated with the objective evidence (i.e. endoscopy+ or pH-metry+) of gastro-esophageal reflux disease (GERD). To date, data on the correlation between EGJ subtypes and esophageal acid exposure as well as impedance-detected reflux episodes are lacking.
AIMS & METHODS: We aimed to correlate the different EGJ subtypes with impedance-pH findings in GERD patients. Consecutive patients with heartburn and/or regurgitation and a recent endoscopic assessment were enrolled. All

patients underwent a 36-Solid State HRM with a 5-min baseline recording to assess the EGJ and 10 single water swallows (5 mL) at 30-s intervals to evaluate the esophageal peristalsis and EGJ function. The tracings were analyzed based on the CC for motility disorders and each EGJ was classified as: Type I, no separation between the LES and the CD; Type II, minimal separation (>1 and <2 cm) between the LES and the CD; Type III, >2 cm separation between the LES and the CD. The patients also underwent impedance-pH testing off-therapy. We measured esophageal acid expsosure time (AET), total number of impedance-detected reflux episodes and symptom-reflux association using symptom association probability (SAP+ if $\geq$95%) and symptom index (SI+ if $\geq$50%).
RESULTS: We enrolled 53 [28M/25F; mean age 53 (21-76)] consecutive GERD patients. At upper endoscopy, 12 patients had erosive esophagitis, 2 had Barrett esophagus and 39 had no mucosal breaks. Based on CC, we identified 21 (40%) patients with Type I EGJ, 19 (36%) with Type II EGJ and 13 (24%) with Type III EGJ. Patients with Type III EGJ had an higher median number of reflux episodes [61 (12-305) vs. 38 (4-109) vs. 30 (6-98), respectively; $p<0.01$)], a greater mean AET [20.6 (4.4-43.4) vs. 14.1 (0.2-48.3) vs. 11.9 (0.1-54.3), respectively; $p<0.01$)] and had more frequently a positive symptom-reflux association [9 (69%) vs. 9 (47%) vs. 11 (52%), respectively; $p<0.05$)] compared to patients with Type II and Type I EGJ. Moreover, patients with Type II EGJ tended to have a higher median number of reflux episodes and mean AET compared to patients with Type I EGJ, but statistically significance was not reached ($p=0.06$).
CONCLUSION: With increasing separation between the LES and CD, from Type I to Type III EGJ, patients had a gradual and significant increase of reflux episodes and esophageal acid exposure. Thus, EGJ morphology may be useful to predict an abnormal impedance-pH testing in patients with GERD.
Disclosure of Interest: None declared

P1031 CLINICAL AND ENDOSCOPIC FEATURES OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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INTRODUCTION: According to the literature data, up to 37 % of patients with chronic obstructive pulmonary disease (COPD) suffer from gastroesophageal reflux disease (GERD) [Hom C., et al., 2013], which is higher than in general population (10-20%) [Gadel A. A. et al., 2012]. However, despite the obvious relationship between these pathological conditions, investigators are still looking for risk factors associated with GERD development and progression in COPD patients.
AIMS & METHODS: Aim was to establish clinical, endoscopic and chromoendoscopic features of GERD in COPD patients in association with inhalation corticosteroid treatment. The study involved 75 patients with COPD, 50 of them received inhalation corticosteroid treatment and 25 received no inhalation corticosteroid treatment. The comparison group covered 65 patients without COPD. Esophagogastroduodenoscopy was performed with the endoscope Pentax 290. In esophagoscopy a dye congo red changing its color in acid medium from red into blue-black was injected through a spray-catheter at a maximal air insufflation in the lower third portion of the esophagus. This property of congo red can be used to diagnose acid gastroesophageal reflux. The affected area was calculated with the formula $2\pi rhK$ (r is a radius of esophagus abdominal part equal to 1 cm, h is a length of the affected area from Z-line in cm, K is a coefficient of staining fullness measured as 1, 3/4, 1/2, 1/4).
Statistical analysis was made with the software package Statistica 7.0 (StatSoft, USA) using nonparametric criteria. Statistical significance was considered at p value less than 0.05.
RESULTS: COPD patients complained of heartburn, acid regurgitation and dysphagia rarely in relation to the comparison group (14.7% and 35.4%, $\chi^2=8.13$; $p=0.004$). However, erosive esophagitis (66.7% and 9.2%, $\chi^2=36.6$; $p<0.001$), and well known risk factors for the development of GERD, such as cardioesophageal relaxation (65,6% and 7,8%; $\chi^2=43,43$, $p<0.001$) and hiatal hernia ($p=0.011$) were more frequently observed in patients with COPD. It is worth mentioning that Grade 2 of erosive esophagitis was detected only in patients receiving inhalation corticosteroid treatment (24% and 0%, $p=0.005$). Presence of esophagitis ($r=+0,85$; $p<0.001$) had a direct correlation with the congo red color changing in the main group. The affected area of esophagus in the main group was 6,38 cm^2 [3,14-8,38], in comparison group the size of the area was 2,36 cm^2 [1,57-3,14] ($p<0.001$)] and in COPD patients receiving inhalation corticosteroid treatment it was 6,38 cm^2 [2,36-9,42] (4.71 cm^2 [4,71-6,28] in COPD patients receiving no inhalation corticosteroid treatment, $p=0.041$). Esophagitis grade in COPD patients had a direct correlation with the extension of the affected area ($r=+0,75$, $p<0.001$).
CONCLUSION: In spite of the unmarked clinical picture GERD in a form of erosive esophagitis, induced by the acid gastroesophageal reflux, is more frequently seen in COPD patients. Grade 2 of erosive esophagitis is typical for patients receiving inhalation corticosteroid treatment. Extension of the affected esophageal area is a valid criterion for the quantitative assesment of the pathological acid gastroesophageal reflux in patients with COPD.
Disclosure of Interest: None declared

P1032 OESOPHAGEAL INTRALUMINAL BASELINE IMPEDANCE LEVELS IN PATIENTS WITH NON-EROSIVE REFLUX DISEASE AND IN PATIENTS WITH SYSTEMIC SCLEROSIS

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INTRODUCTION: Oesophageal intraluminal baseline impedance (BI) levels are determined by the conductivity of the oesophageal wall. Patients with non-erosive reflux disease (NERD) showed decreased distal oesophageal BI levels compared to healthy controls and this finding has been correlated to the presence of abnormal distal oesophageal acid exposure time (AET) in them. On the other hand, no differences have been found in the proximal esophagus probably due to the lower amount of acid reflux arriving at the most proximal sites. Systemic sclerosis (SSc) is a clinically heterogeneous and systemic disease characterized by deposition of collagen and other extracellular matrix proteins in the connective tissue of the skin and visceral organs, such as the gastrointestinal tract. This event could potentially affect the conductivity of the oesophageal wall and consequently BI levels, but data in this regard are lacking.
AIMS & METHODS: We aimed to prospectively investigate and compare BI levels between NERD and SSc patients. Consecutive patients with typical reflux symptoms (i.e. heartburn and/or regurgitation) and those with a defined diagnosis SSc underwent upper endoscopy in order to assess the presence of oesophageal mucosal lesions. Then, within 3 days from endoscopy, all endoscopy-negative patients underwent oesophageal manometry and impedance-pH testing off-therapy. During blinded and manual analysis of impedance-pH tracings, we evaluated esophageal AET, reflux episodes (acid/weakly acidic), symptom-reflux association using both symptom association probability (SAP+ if $\geq$95%) and symptom index (SI+ if $\geq$50%) and BI values at 3, 5 and 17cm above the LES, during the overnight rest, for at least 30 minutes after excluding swallows and reflux induced changes. NERD were diagnosed in case of abnormal AET and/or positive symptoms-reflux association.
RESULTS: Thirty patients with NERD and 30 with SSc were enrolled. Among SSc patients, 10/30 (33%) had an abnormal AET and 20/30 (67%) showed a normal. Among NERD patients, 14 (57%) had a pathological AET and 16/30 (53%) showed a normal acid exposure. In patients with SSc, median (25^{th}-75^{th}) BI impedance was 961.3 (734.3-1610.8) Ω at 3cm, 1114.9 (845.4 to 1512.7) Ω at 5 cm, and 2222.4 (1511.6 to 2734.3) Ω at the most proximal impedance recording site. All these BI values were lower than those observed in NERD patients, not only in the distal esophagus [at 3cm 1409.2 (1264.1 to 2118.6) Ω, $p=0.0065$; at 5 cm 1650.1 (1228.4 to 2266.4) Ω, $p=0.0054$], but also in the proximal esophagus [at 17cm 2678.7 (2183.0 to 3309.1) Ω, $p=0.0736$].
CONCLUSION: Despite the lower median AET and percentage of patients with abnormal AET, all BI values in SSc patients were lower than in NERD patients, suggesting that BI levels are related not only to oesophageal AET, but also to oesophageal tissue damage SSc-related. This finding is further corroborated by the differences observed at the proximal oesophagus. Thus, BI levels may be used as indirect markers of alteration of the oesophageal wall and, therefore, of oesophageal involvement in patients with SSc.
Disclosure of Interest: None declared

P1033 EVALUATION OF SLEEP DISRUPTIONS BY MEANS OF IMPEDANCE-PH MONITORING IN PATIENTS WITH NERD

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INTRODUCTION: Gastroesophageal reflux disease (GERD) adversely impacts on sleep, representing a major cause of disrupted sleep mainly due to reflux symptoms. This may lead to an impaired quality of life. Impedance and pH monitoring (MII-pH) is the gold standard technique for GERD diagnosis. During the sleep period, impedance values remain stable unless the occurrence of arousals.
AIMS & METHODS: We aimed to evaluate sleep disruptions in patients with heartburn and negative endoscopy by means of MII-pH. A group (33) of endoscopy negative patients with heartburn underwent MII-pH and were classified accordingly: 18 with non-erosive reflux disease (NERD) (i.e., pathological acid exposure time, AET); 15 with functional heartburn (FH) (i.e., normal AET and reflux number, negative symptom association). MII-pH tracings were reviewed manually using a 5-min window. During recumbent time, we identified sleep disruptions when at least 2 swallows were observed in a 5-min window. This data was evaluated in each group. We also calculated the overnight swallowing breaking sleep (OSBS) index (i.e., number of windows with swallows/total number of 5-min windows during the sleep period). All patients performed a validated questionnaire to assess the quality of sleep.
RESULTS: Male/female ratio was 7/11 in NERD and 3/12 in FH patients. Mean age was 51.3±12.4 in NERD and 49.3±9.7 in FH. The quality of a restful sleep was 64.3±8.3% in NERD and 67.3±7.8% in FH ($p=0.299$). Mean AET was higher in NERD (5.4±0.4) than in FH (0.4±0.4) ($p<0.05$). NERD group recorded higher total reflux number and acid reflux number ($p<0.05$). The total recumbent time was 541.4±64.7 min in NERD and 547.3±59.3 min in FH ($p=0.39$). During the sleep period, NERD patients recorded higher reflux number (9.8±8.7) than FH patients (0.6±0.9) ($p<0.05$). Moreover, the total

number of 5-min windows presenting at least 2 swallows was higher in NERD patients (49.7 ±6.4) compared to those with FH (27 ±5.3; $p<0.01$). The OSBS index was 46.2±4.0 in NERD and 25.3±5.5 in FH ($p=0.023$).

CONCLUSION: The manual analysis of the MII-pH tracings during the recumbent period might be useful to estimate sleep disruptions in patients with NERD, thus helping to identify those patients in whom GERD is perceived more severe and quality of life is much more impaired.

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P1034 BASAL CELL HYPERPLASIA AND DILATION OF INTERCELLULAR SPACES ARE THE MAIN HISTOLOGIC FEATURES ASSOCIATED TO THE ENDOSCOPIC/IMPEDANCE-PH DIAGNOSIS OF GERD AND ITS RELATED MUCOSAL INTEGRITY IMPAIRMENT

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INTRODUCTION: During pathological assessment of esophageal biopsies several histological features characterizing the diagnosis of microscopic esophagitis [basal cell hyperplasia (BCH), papillary enlongation (PE), dilated intercellular spaces (DIS) and epithelial neutrofilic/eosinophilic infiltration (Neu/Eos)] can be assessed. Limited data are available about the single contribution of these histological abnormalities on the diagnosis of GERD and its related mucosal integrity in well-defined patients with reflux disease.

AIMS & METHODS: To determine whether these histological features contribute differently to the diagnosis GERD and to the impairment of mucosal integrity as expressed by baseline impedance (BI) levels. One hundred and four consecutive patients with typical reflux symptoms underwent upper endoscopy and multiple biopsies were taken at Z-line and 2 cm above it, in order to assess the presence and severity of BCH, PE, DIS and Neu/Eos [0 (absent), 1 (mild), and 2 (marked)]. Within 3 days from endoscopy, patients underwent impedance-pH testing off-therapy. During manual analysis of the impedance-pH tracings, we measured the esophageal acid expsosure time (AET) over the 24 hours and the total (acid + non-acid) number of impedance-detected reflux episodes. We evaluated BI values at 3 and 5cm above the LES, during the overnight rest, for at least 30 minutes after excluding swallows and reflux induced changes. Twenty healthy volunteers (HVs; 11F/9M; mean age 44) who underwent the same procedures were also enrolled as controls.

RESULTS: We included 85 patients with an endoscopic/impedance-pH diagnosis of GERD (45F/40M; mean age 46) who had esophageal mucosal breaks at upper endoscopy or an abnormal esophageal acid exposure or a normal esophageal acid exposure but a positive reflux-symptom association at impedance-pH testing. Among these patients, BI values at both 3 and 5 cm above the LES positively correlated with the esophageal AET ($r2=0.2033$, $P<0.001$ and $r2=0.1859$, $P<0.001$, respectively) and the number of impedance-detected reflux episodes ($r2=0.1373$, $P<0.001$ and $r2=0.1526$, $P<0.001$, respectively). Moreover, as shown in the Table, BCH and DIS were the lesions more significantly correlated with the endoscopic/impedance-pH diagnosis of GERD. No significant correlation was observed between BI values and impedance-pH parameters or histological lesions in HVs ($p=$ns).

	BCH	DIS	PE	Neu
BI at 3 cm	$r2=0.2150$; $P<0.001$	$r2=0.1357$; $p=0.001$	$r2=0.0526$; $p=0.035$	$r2=0.0516$; $p=0.036$
BI at 5 cm	$r2=0.2182$; $P<0.001$	$r2=0.1405$; $P<0.001$	$r2=0.0484$; $p=0.043$	$r2=0.0523$; $p=0.035$

CONCLUSION: BCH and DIS contribute more than PE and Eos/Neu to the endoscopic/impedance-pH diagnosis of GERD. Moreover, the same lesions seem to play a greater role than PE and Eos/Neu in determining mucosal integrity impairment as expressed by BI values in GERD patients. Overall, BCH and DIS can be considered the histological markers requiring more careful evaluation during pathologic assessment in order to help the diagnosis of GERD.

Disclosure of Interest: None declared

P1035 PPI RESPONSIVE VS. PPI NON-RESPONSIVE FUNCTIONAL HEARTBURN: THE DIFFERENCE LIES IN THE IMPEDANCE BASELINE

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INTRODUCTION: Recent data indicate that low esophageal basal impedance may reflect impaired mucosal integrity and increased acid sensitivity.

AIMS & METHODS: We compared baseline impedance levels in patients with heartburn and pathophysiological characteristics related to functional heartburn (FH) divided into two groups on the basis of symptom relief after proton pump inhibitors (PPIs). Moreover, we aimed to compare these results with a group of patients affected by hypersensitive esophagus (HE) and with healthy volunteers (HVs).

Patients with heartburn and normal endoscopy underwent MII-pH testing off PPI therapy and those with negative symptom association an 8-week PPI (esomeprazole or pantoprazole 40 mg daily) therapy. Patients with >50% symptom improvement were classified as PPI response FH (FH+PPI) and those with <50% improvements as PPI non-response FH (FH-PPI). In addition we included patients with hypersensitive esophagus (HE) defined as normal endoscopy, normal acid exposure and positive symptom association and a group of healthy volunteers (HV). For each patient and HVs, we evaluated acid exposure time (AET), number of MII-detected reflux episodes, baseline impedance levels at channel 3, during the overnight rest, at three different times and PSPW index.

RESULTS: Data are summarized in the Table. Patients with FH+PPI showed a higher mean AET (1.4%±0.8 *vs* 0.5%±0.6, $p<0.05$), mean reflux number (30.4±8.7 *vs* 24±6.9, $p<0.05$), proximal reflux number (11.1±5.2 *vs* 8.2±3.6, $p<0.05$) and acid reflux number (17.9±6.1 *vs* 10.7±6.9, $p<0.05$) compared to FH-PPI. Patients with HE showed mean AET (1.8%±0.8) and total reflux number (34.4±8.2) similar to those recorded in FH+PPI ($p=$ns). Baseline impedance levels were lower in FH+PPIand in patients with HE then in FH-PPI and in HVs ($p<0.001$). No differences were found for PSPW index between FH+PPIand HE; in those groups PSPW index was lower than in FH-PPI and HV.

	HE (N = 30)	FH+PPI (N = 30)	FH-PPI (N = 30)	HV (N = 20)	P (FH+PPI vs HE)
AET tot (sd)	1.8±0.8#	1.4±0.8*	0.5±0.6	0.7±0.6	n.s
N° refluxes (sd)	34.4±8.2#	30.4±8.7*	24±6.9§	17.9±10.8	n.s
Baseline (sd)	2125.3±450.8#	2169.7±580.4*	3782.2±821.5	3427.8±42.7	n.s.
PSPW (sd)	55.9±4.6#	56.2±8.8*	71.1±6.1	76.1±13	n.s.
PPI Response	100%	100%	0%	N. A.	–

Table legend: (*) $p<0.05$ group FH+PPI versus FH-PPI; (§) $p<0.05$ group FH-PPI versus HV; (#) $p<0.05$ HE vs. FH-PPI vs HV

CONCLUSION: Patients with PPI responsive functional heartburn (FH+PPI) present similar MII-pH features as patients with HE. Esophageal baseline impedance measurements might allow to identify reflux patients who are not confirmed by MII-pH monitoring likely due the day-to-day variability or the limitations of the current reflux-symptom association indexes.

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P1036 DISTAL AND PROXIMAL ESOPHAGEAL IMPEDANCE BASAL VALUES IN PATIENTS WITH NON-EROSIVE REFLUX DISEASE AND FUNCTIONAL HEARTBURN

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INTRODUCTION: Several studies have shown that proximal extent of reflux episodes plays an important role in gastro-esophageal reflux symptom perception. The relative hypersensitivity of the proximal esophagus is most evident in patients with non-erosive reflux disease (NERD). Recent studies demonstrated that low distal basal impedance values may reflect impaired mucosal integrity and increased acid sensitivity.

AIMS & METHODS: The aim was to compare distal and proximal basal impedance values in patients with NERD and functional heartburn (FH).

According to impedance and pH (MII-pH) monitoring off-therapy, we selected patients with NERD (i.e. pathological acid exposure time, AET) and FH (i.e. normal AET and reflux number; negative symptom association). FH patients did not show any symptom relief after acid suppression therapy. For each patient, we evaluated basal impedance values at the distal (3 cm) and proximal (17 cm) channel, during the overnight rest, at three different times: 1, 2, 3 am.

RESULTS: Male/female ratio was 23/23 in NERD and 13/33 in FH patients. Mean age was 52.3±13.2 in NERD and 49.2±11.3 in FH. Mean AET was higher in NERD (6.1%±3.8%) than in FH (0.6%±0.7%) ($p<0.05$). NERD group recorded higher total reflux number (67.8±18.2) than FH group (23.7±9.4) ($p<0.05$).

Basal impedance values were significantly ($p<0.05$) lower in NERD than in FH, both at the distal (1294.3±529.9 Ohm *vs* 3502.1±809.2 Ohm) and proximal (3480.7 ±1322.6 Ohm *vs* 4344.9±976.2 Ohm) channels. Distal basal values were significantly lower than proximal basal values, both in NERD and FH group ($p<0.05$). Moreover, in NERD group, 24/46 patients (52.2%) had an abnormal number of proximal refluxes. These NERD patients with pathological proximal refluxes did not show lower basal impedance values than NERD patients with normal number of proximal refluxes even if distal (1226.7±453 vs 1243.1±497.1; $p=0.5239$) or proximal channels (2670.8±1163.4 vs 2849.2±1434.2; $p=0.5046$) were compared.

CONCLUSION: Patients with NERD showed lower basal impedance values both at the distal and proximal esophagus. Consistently with the concept that low basal impedance may reflect impaired mucosal integrity, our results might be helpful to better investigate the pathophysiological role of proximal refluxes.

Disclosure of Interest: None declared

P1037 ARE WE ANY CLOSER TO A BLOOD-BASED TEST TO MONITOR DISEASE PROGRESSION IN THE BARRETT'S OESOPHAGUS MODEL?

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INTRODUCTION: The increasing incidence of Barrett's Oesophagus (BO) and Oesophageal Adenocarcinoma (OA) has culminated in intensified efforts to better stratify patients at risk of progression. Endoscopic surveillance allows for such monitoring to take place but there still remains a potential for physical and psychological harm to patients undergoing regular surveillance, not to mention increased cost and resource allocation. Given the DNA damage induced by acid and bile reflux to the distal oesophagus as well as to blood cells circulating through this inflamed tissue, the application of novel blood-based toxicological approaches to the monitoring of patients with BO could offer a less invasive approach to current surveillance strategies.

The phosphatidylinositol glycan biosynthesis class A (Pig-A) gene is critical for glycophosphatidyl inositol (GPI) anchor synthesis. GPI-anchors tether specific epitopes to the cell surface membrane and are important in cellular responses to inflammation. Losses of gene function, as a result of a single mutational event within the Pig-A gene form a GPI-anchor negative phenotype, detectable using flow-cytometric methodology. Use of an adapted *ex-vivo* Pig-A gene mutation assay on whole blood, may have the potential to predict patients at a higher risk of progression through the dysplastic process as it is possible that circulating blood cells may acquire mutations whilst passing through the oesophageal mucosa.

AIMS & METHODS: Blood based cell lines were exposed to physiological carcinogens such as bile and the Pig-A mutant frequency measured.

Subsequent *ex-vivo* analysis of blood was undertaken in patients attending endoscopy with symptoms suggestive of GORD. Pig-A analysis of erythrocytes and leucocytes was performed and results correlated with histopathological analysis of oesophageal biopsies as well as a detailed lifestyle questionnaire. Finally, a challenge assay was undertaken whereby physiological doses of bile acids were used to treat enriched lymphocytes of patients with GORD, BO and OA and the change in mutational frequency measured.

RESULTS: *In-vitro* investigations confirmed the carcinogenicity of bile acids to blood based cell lines, with increased mutant frequencies detected through the Pig-A gene mutation assay ($p<0.05$).

Subsequent *ex-vivo* erythrocyte analysis demonstrated higher mutant frequencies in OA patients compared to both normal GORD patients and those with Barrett's ($p<0.01$) but there was no significant difference between BO and normal controls. Patient age, gender and length of Barrett's segment did not appear to have any influence on mutant-frequency, but smoking status suggests some effect.

CONCLUSION: The application of this simple, non-invasive blood-based mutation assay to patients with GORD suggests OA patients have higher mutational events than patients with Barrett's or normal oesophageal mucosa. Whilst it is not clear if Pig-A mutations in these patients are due to exposure to DNA damage inducing chemicals or an increased predisposition to mutation at a bone-marrow level, data from the challenge assay may allow for these questions to be answered. Furthermore, analysis of patients with dysplastic Barrett's will permit for this test to be better validated as a future biomarker for risk of progression.

Disclosure of Interest: None declared

P1038 IMMUNE MICROENVIRONMENT IN ESOPHAGEAL CARCINOGENESIS: CD80 REGULATES EPITHELIAL-CD8 LYMPHOCYTES CROSS TALK AND IT PEAKS IN INTESTINAL METAPLASIA

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INTRODUCTION: Recent studies showed that in patients with Barrett's esophagus (BE) the pooled estimate for annual esophageal adenocarcinoma (EAC) incidence varies between 0.12% and 0.14%. It is unclear whether dysplasia can regress over time but the difficulty in confirming low grade dysplasia presence seems to suggest it. The expression of costimulatory molecules CD80 and CD86 in the esophageal cancer tissue is significantly lower than in the mucosa of healthy patients. In inflammatory colonic carcinogenesis CD80 expression seem to trigger immune surveillance mechanisms in dysplasia. The aim of the study is to investigate the interplay between epithelium and CD8 T cells that characterizes the immune environment of inflammatory esophageal carcinogenesis.

AIMS & METHODS: Fresh esophageal biopsies were obtained from healthy subjects ($n=7$) and from patients with BE ($n=17$) eleven with previous history of dysplasia on BE and six with current dysplasia on BE, Biopsies were analysed by flow cytometry to quantify the expression of CD80 and HLA ABC on esophageal epithelial cells, whereas on CD8 infiltrating lymphocytes the activation marker CD38 and CD28 (CD80 receptor) were determined. Primary human cardia epithelial cells (CEC) were co-cultured with mesenteric nodal lymphocytes in the presence or not of anti-CD80 antibody and assessed by flow cytometry to quantify the frequency of activated cytotoxic lymphocytes. Non parametrical statistics was used.

RESULTS: CD80+ esophageal epithelial cells rate resulted higher in BE during inflammatory esophageal carcinogenesis compared to healthy subjects and to patients with BE and adenocarcinoma ($p=0.08$ and $p=0.03$, respectively). The mean intensity of CD28 was higher in patients with BE and previous history of dysplasia compared to those with BE and adenocarcinoma ($p=0.04$). In vitro, co-culture of mesenteric lymphocytes with CEC significantly increased CD8+CD38+ rate that returned to baseline if antiCD80 antibody was added ($p=0.06$).

CONCLUSION: In inflammation-driven esophageal carcinogenesis, there is evidence of an early active immune surveillance process mediated by CD80 overexpression on metaplastic esophageal epithelial cells. In vitro, CEC activated CD8+ T-cells through a CD80-dependent pathway confirming the role of this molecule in triggering immune surveillance mechanism in esophageal inflammatory carcinogenesis.

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P1039 HOXA13 OVEREXPRESSION IN BARRETT'S ESOPHAGUS IS A POTENTIAL MEDIATOR OF ITS POSTERIOR PHENOTYPE

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INTRODUCTION: Barrett's Esophagus (BE) is a metaplastic and precancerous condition. It is induced by bile and acid reflux and defined by the presence of intestinal-type tissue in the esophagus. The morphology of this tissue resembles a posterior phenotype, as observed in the colon. Identifying the cause of this positional misspecification can lead to a better understanding of BE pathophysiology. The mammalian *Hoxa* cluster encodes master regulators of embryonic anterior to posterior specification, making it a potential effector of positional misspecification. The 3' to 5' sequence of genes in the *Hoxa* cluster, corresponds to the sequence in which they act along the anterior to posterior axes of the body. Acquired deregulation of *HOXA* genes during adulthood can be linked to carcinogenesis and HOXA13 overexpression to poor survival in gastric cancer. However, *HOXA* cluster expression has never been thoroughly investigated in the gastrointestinal (GI) tract, nor in BE. Therefore, the aim of this study was to analyze the expression of *HOXA* genes along the gut, characterize HOXA expression in BE and investigate whether exposure of an esophageal cell line to acid induces *HOXA* gene overexpression.

AIMS & METHODS: Firstly, we collected biopsy specimens from nine places along the GI tract in patients who underwent double balloon enteroscopy for unexplained symptoms. Secondly, we collected biopsy specimens of BE and squamous epithelium from other patients. RT-qPCR was used to quantify the expression of *HOXA1, 2, 3, 4, 5, 6, 7, 9, 10, 11* and *13*. Thirdly, an immunohistochemical staining for HOXA13 was done on BE and squamous epithelium. Additionally, the esophageal cell line HET1A was exposed to an acidic environment, after which *HOXA13* levels were measured.

RESULTS: In this study *HOXA* cluster gene expression differed significantly along the GI tract. Expression of *HOXA* genes in the proximal part of the GI tract, from the esophagus to the proximal ileum, revealed a downward trend. Anterior genes had a higher expression compared to posterior genes. The expression of posterior genes *HOXA11* and *13* was low or absent. From the terminal ileum to the rectum, expression of *HOXA* genes revealed an upward trend. Notably, expression of *HOXA11* and *13* was only found in the colon. *HOXA13* showed the highest expression of all *HOXA* genes in the GI tract. Furthermore, in BE, *HOXA* genes revealed an upward trend of expression with a very high expression of *HOXA13*. Whereas the expression of *HOXA13*

in squamous epithelium was undetectable. These observations were confirmed on protein level for HOXA13. Furthermore, exposure of an esophageal cell line to acid led to overexpression of *HOXA13*.
CONCLUSION: Our data reveal position-dependent *HOXA* coding along the GI tract. This suggests a prominent role of this gene cluster in mediating locational genetic identity. The expression of *HOXA* cluster genes in BE resembles colonic *HOXA* cluster expression. This was confirmed on protein level for HOXA13. Additionally, exposure of an esophageal cell line to acid can induce *HOXA13* overexpression. The high overexpression of *HOXA13* found in BE, is a potential mediator of posterior phenotype in this disease and may play a role in neoplastic progression.
Disclosure of Interest: None declared

P1040 HIGH DOSE ESOMEPRAZOLE INDUCES ROS-DEPENDENT APOPTOSIS IN OESOPHAGEAL ADENOCARCINOMA CELLS

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INTRODUCTION: Proton pump inhibitors (PPIs) are the most potent and widely used drugs for the treatment of Barretís oesophagus (BE) and have been suggested to decrease neoplastic progression. Recently, PPIs have been reported to disrupt tumour pH homeostasis and, in turn, cell viability, by the inhibition of vacuolar ATPase (H^+-VATPase), a proton pump overexpressed in the membrane of some tumour cells. This aspect has not been investigated in Barrett's carcinogenesis yet.
AIMS & METHODS: Aim: To investigate the expression of H^+-VATPase in the human oesophageal adenocarcinoma (EAC) sequence, to evaluate *in vitro* the effects of PPIs on proliferation, apoptosis and invasion of EAC cells and to further elucidate the mechanisms involved in these effects. **Methods:** H^+-VATPase expression was assessed by immunohistochemistry in 22 human biopsy samples of normal oesophagus, BE and EAC. The expression and location of H^+-VATPase was also assessed in cell lines by confocal laser scanning microscopy (Leica TCS SP2) and flow cytometry (ImageStreamX). Two different Barrett's-derived EAC cell lines were used: OE33 (ECACC) and SK-GT-4 (DSMZ); and one metastatic cell line, OACM5.1C (ECACC), obtained from a lymph node metastasis derived from a Barrett's adenocarcinoma. In addition, the effects of PPIs were tested in a non-dysplastic BE cell line, CP-A (ATCC). Esomeprazole (0, 1, 10, 50, 100, 200 μM) was added to the culture medium. Cell proliferation was assessed by ELISA (BrdU, colorimetric assay). Cell invasion was evaluated in a fluorometric assay. Apoptosis was determined by flow cytometry (FACSAria, BD) by staining the cells with Annexin V-FITC and propidium iodide (PI). Intracellular reactive oxygen species (ROS) levels were evaluated at different time points (1-6 hours) in a fluorometric assay using the ROS-sensitive probe DCFDA. Experiments were performed at least in triplicate. Statistical analysis was performed by student-t test.
RESULTS: H^+-VATPase expression was found to be increased in high grade dysplasia and adenocarcinoma samples compared to normal esophagus or non-dysplastic Barrett's samples. In addition, H^+-VATPase was shown both in the cytosol and plasma membrane in EAC cell lines. Treatment with esomeprazole (10-200μM) induced the apoptosis of cancer cells and reduced in a dose-dependent manner cell proliferation (50-200 μM). Conversely, addition of the PPI didn't affect apoptosis of Barrett cells whereas significantly decreased the proliferation rate at the highest dose (100-200 μM). Moreover, the highest dose of esomeprazole significantly diminished cell invasiveness in all three tumour cell lines. ROS seem to be involved in the antineoplastic effect of esomeprazole since the addition of esomeprazole was followed by a significant increase in ROS levels and the proapototic effect of the PPI was abrogated when tumoral cells were preincubated with the ROS scavenger N-acetylcysteine.
CONCLUSION: Esomeprazole exerts *in vitro* antineoplastic effects on esophageal adenocarcinoma cells, suggesting that the use of high doses of PPIs might be effective in the treatment of EAC. These effects seem to be dependent from ROS overproduction. Additional preclinical studies are required to further confirm these results
Disclosure of Interest: None declared

P1041 OESOPHAGEAL CRYOABLATION USING THE NEW CRYOBALLOON FOCAL ABLATION SYSTEM: DEEP TISSUE ABLATION WITH LITTLE OR NO LATE FIBROSIS IN ANIMAL AND HUMAN MODELS

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INTRODUCTION: Eradication of Barrett's oesophagus (BO) can be achieved by either mucosal heating (RFA, APC) or freezing. If the energy penetrates too deeply into the oesophageal wall, heating causes denaturation and destruction of extracellular architecture, resulting in fibrosis and stenosis. In contrast, cryotherapy affecting deeper oesophageal wall layers is believed to cause cell death while preserving the wall architecture, potentially enabling deeper ablation without causing fibrosis, stenosis, or perforation.
AIMS & METHODS: We evaluated the depth of tissue injury after cryotherapy using the newly developed Cryoballoon Focal Ablation System (CbFAS) - consisting of a balloon-based, through-the-scope catheter with a battery-powered handle containing a small disposable canister for delivering cryogenic fluid into the inflated balloon - in various therapeutic as well as supra-therapeutic doses. Ablations of several durations (ranging from 4 to 24 seconds) were performed in pigs (surviving 12 hours, or 2.5, 4 or 28 days) and in normal squamous mucosa of oesophageal cancer patients (directly prior to their scheduled oesophagectomy). All oesophagi were sent for blinded histopathological analysis. For all oesophageal wall layers (mucosa, submucosa, inner and outer muscularis propria, and serosa) histopathological parameters, such as inflammation, necrosis and fibrosis were scored by a injury grading system (scoring for presence/absence of layers, oedema, inflammation, necrosis and fibrosis) with a maximum score of 3 or 4 points per layer (max. total of 17 points). Primary outcomes were the short- and long-term effects of cryoablation on the oesophageal wall.
RESULTS: *Animals:* Forty ablations were performed in 8 pigs, all surviving the pre-determined period without any symptoms or complications. Nine ablations (2x 6 sec, 7x 8 sec) in one pig surviving 12 hours resulted in inflammation, cell necrosis and oedema throughout the entire oesophageal wall (median injury grading system score 11 [IQR 10-11.5]). Depth and severity of these ablation effects was even more severe after 2.5 and 4 days: median scores of 13 (IQR 13-13) in 8 ablations (4x 6 sec, 4x 8 sec) in one pig surviving 2.5 days and 14 (IQR 13-14) in 12 ablations (2x 4 sec, 8x 6 sec, 2x 8 sec) in 3 pigs surviving 4 days. Eleven ablations (3 ablations of 6 and 8 seconds, and 1 ablation of 10, 12, 16, 20, and 24 seconds each) were performed in three pigs surviving 28. Neither necrosis nor fibrosis remained present in these specimens (median score 1 [IQR 1-2]), not even after high ablation doses.
Human: Four cryoablations (6 seconds) on squamous epithelium directly prior to oesophagectomy in three humans showed moderate inflammation mainly limited to the submucosal layer with a median score of 5 (IQR 5-7.3).
CONCLUSION: In both humans and animals, CbFAS cryoablation penetrates deeply through the oesophageal wall resulting in severe early ablation injury. After four weeks, little injury and no fibrosis remain, even after high doses, suggesting that CbFAS cryoablation combines deep ablation with a favorable long-term safety and efficacy profile.
Disclosure of Interest: D. Schölvinck: None declared, B. Weusten Lecture fee(s) from: BEST Academia (Covedien), G. Triadafilopoulos: None declared, T. Valli: None declared, S. Friedland: None declared

P1042 THORACOLAPAROSCOPIC DISSECTION OF ESOPHAGEAL LYMPH NODES: A FEASIBILITY AND PRE-CLINICAL SAFETY STUDY

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INTRODUCTION: Low-risk early esophageal adenocarcinoma (EAC) can safely be managed endoscopically. In case of high-risk early EAC (i.e. submucosal invasion >500 nanometers, poor differentiation and/or presence of lymphovascular invasion), esophagectomy with lymph node dissection is currently advocated given the relatively high rates of lymph node (LN) metastases. However, esophagectomy is associated with substantial morbidity and mortality and a reduced quality of life. Endoscopic *radical* local resection, followed by thoracolaparoscopic dissection of esophageal LNs without concomitant esophagectomy could be an alternative.
AIMS & METHODS: In this study, we aimed to evaluate the feasibility and safety of thoracolaparoscopic dissection of LNs involved in the drainage of the esophagus in human cadavers (1), living swine (2), and two pilot-cases (3).
(1) In human cadavers, thoracolaparoscopic dissection of LNs involved in drainage of the esophagus was performed. Thereafter, esophagectomy was performed and the esophagectomy specimens (ES) were analysed for any retained LNs. Outcome parameters included the number of dissected LNs, the number of retained LNs in the ES and technical success, which was defined as a ratio $\geq$ 0.9 between the number of dissected LNs during lymphadenectomy and the total (resected plus retained) number of LNs. (2) In swine, a thoracolaparoscopic LN dissection was performed. 28 days after the procedure, the swine were sacrificed and esophagectomy was performed. Outcome parameters included the presence of ischemia or stenosis in the ES (safety parameters), and other complications. (3) In the first human pilot-cases, thoracolaparoscopic LN dissection was performed, directly followed by esophagectomy with gastric tube reconstruction (same session). Outcome parameters included the number of dissected LNs during lymphadenectomy, the number of tumor-positive LNs, and the number of retained LNs in the ES.
RESULTS: (1) In 5 human cadavers, a median of 26 LNs (IQR 22-46) was dissected. In 2 ES, 1 retained LN was found. Technical success rate was 100%. (2) None of the 7 porcine ES showed signs of ischemia or stenosis. One swine died because of ventricular fibrillation during surgery; during follow-up no complications were observed in the remaining 7 swine. (3) In 2 patients with early EAC (T1bN0M0), 23 and 43 LNs were dissected, all without evidence of metastasis. In the ES, 2 and 1 retained paraesophageal LNs were found, proximal and distal, respectively.
CONCLUSION: In conclusion, thoracolaparoscopic dissection of LNs involved in the drainage of the esophagus is feasible. The porcine survival study suggests that esophageal vascularity is not severely compromised by this procedure.
Disclosure of Interest: None declared

P1043 ENDOSCOPIC TREATMENT OF EARLY ESOPHAGEAL CARCINOMA: A PROSPECTIVE EVALUATION OF 47 CONSECUTIVE CASES WITH PROMISING RESULTS IN PATIENTS WITH T1B CANCERS

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INTRODUCTION: Endoscopic therapy has become an accepted treatment option for T1a esophageal carcinoma while for T1b cancers, surgery is still considered as a treatment of choice. Endoscopic resection (or dissection) allows precise histopathologic staging which is used to guide therapeutic decisions.
AIMS & METHODS: The aim of this prospective, single center study was to assess the long-term efficacy of endoscopic treatment for early esophageal carcinoma. The main outcome measurement was complete remission defined as an absence of any neoplasia (CR-neoplasia).
RESULTS: The study involved 47 consecutive patients (mean age 65, range 35-85; 41 males and 6 females) undergoing endoscopic treatment (42x endoscopic resection; 5x endoscopic submucosal dissection) for esophageal carcinoma. Forty patients (85%) were diagnosed with early adenocarcinoma (EAC) within Barrett's esophagus, the remaining 7 patients (15%) had early squamous neoplasia (ESC). In 22 patients (47%), ER/ESD was combined with radiofrequency ablation (RFA). The median follow-up was 24 months (range 3-70).
Thirty-one patients (66%) were diagnosed as T1a cancers with mucosal invasion. Among them, four patients were referred for surgery (three patients with multifocal cancer not allowing complete local remission, one patient in which RFA of remaining dysplastic mucosa was not technically feasible). In the remaining 27 patients the endoscopic treatment was considered as curative.
Sixteen patients (34%) were diagnosed as T1b cancers with submucosal invasion (13 patients with sm1 and three patients with sm2-3). Among them, 5 patients were referred for surgery (3 of them achieved a complete local remission after endotherapy, one patient is just waiting for surgery). The remaining 11 patients did not undergo surgical treatment (comorbidity, patient's preference, age etc.) and endoscopic treatment was considered as a definitive treatment.
In all 38 patients who underwent only endotherapy, a 100% local remission rate of neoplasia was achieved and no patients presented with lymph node metastases during the follow up.
CONCLUSION: Endoscopic therapy is effective in the treatment of T1a early esophageal cancer. It appears to be a good alternative to esophagectomy in patients with T1b cancers.
Disclosure of Interest: None declared

P1044 CONTINUOUSLY CESSATION OR REDUCTION OF DRINKING HABIT IMPROVES THE LUGOL VOIDING LESIONS IN PATIENTS OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA AFTER ENDOSCOPIC RESECTION

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INTRODUCTION: Esophageal squamous-cell carcinomas (ESCC) have a high incidence of multiple ESCCs. Lugol-voiding lesions (LVLs) recognized by using iodine chromoendoscopy were reported to be precursors for multiple primary cancers in the esophagus associated with the "field cancerrization phenomenon". LVLs are highly associated with alcohol abuse.
AIMS & METHODS: The aims of this study were to assess the improvement of LVLs according to cessation or reduction of drinking habit after the initial endoscopic treatment of ESCCs. On 331 patients with newly diagnosed ESCC, endoscopic mucosal resection or endoscopic mucosal dissection were performed between September 2005 and May 2010. At initial diagnosis of ESCC, patients were examined by iodine chromoendoscopy and assessed the extent of LVLs according to the number of LVLs per endoscopic view. At study entry, drinking and smoking histories and dietary habits were recorded. All patients were instructed to abstain from smoking and drinking alcohol. After endoscopic treatment, all patients were prospectively followed up by iodine chromoendoscopy every six months with record of LVLs, drinking and smoking habit. Associations between improvement of LVLs and change of drinking habit are analyzed.
RESULTS: Of the 331 patients, 55 patients with no LVLs and 44 patients with no drinking habit at the initial treatment were excluded. Of the remaining 232 patients, 158 patients continuously ceased or reduced the drinking habit (Group A) and 74 patients continued drinking (Group B). Eighteen of 158 patients (11.4%) of Group A had shown improvement of LVLs, whereas two of 74 (2.7%) patients of Group B had shown improvement of LVLs ($p = 0.04$). Patients of Group A are significantly had higher cumulative improvement of LVLs than patients of Group B (log rank $p = 0.023$). Univariate and multivariate analysis including smoking habit and dietary habit show that only continuously cessation or reduction of drinking habit was a significant factor to improve the extent of LVLs (univariate analysis: HR = 4.6, CI 1.3-29.1, $p = 0.013$, multivariate analysis: HR = 8.6, CI 1.7-156.3, $p = 0.004$).
CONCLUSION: By the continuous cessation or reduction of drinking habit, LVLs were significantly improved. To prevent the metachronous multiple occurrences of ESCCs, continuous instruction to abstain from the drinking habit is needed.
Disclosure of Interest: None declared

P1045 LAPAROSCOPIC ESOPHAGECTOMY FOR CANCER: IMPACT ON POSTOPERATIVE INFLAMMATORY AND NUTRITIONAL STATUS

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INTRODUCTION: Recent studies confirmed the feasibility and the safety of minimally invasive esophagectomy for cancer. The purpose of this case-control study was to evaluate the impact of laparoscopic gastric tubulization during esophagectomy for cancer on postoperative inflammatory and nutritional status.
AIMS & METHODS: We retrospectively evaluated all consecutive patients undergoing laparoscopic gastric tubulization (LGT) during esophagectomy for cancer referred to our surgical unit between 2008 and 2013. A group of patients undergoing esophagectomy with open gastric tubulization (OGT) - matched for neoadjuvant therapy, pathological stage, gender and age – were enrolled as controls.
Demographic data, tumor features and post-operative course were compared. In particular, systemic inflammatory and nutritional status were monitored during the postoperative hospital stay. Quality of life was evaluated at one month after surgery using EORTC QLQ-C30 functional scales, EORTC OES-18 Eating scale and EORTC BR23 Body Image scale.
RESULTS: We enrolled 34 patients per group, with similar demographic and tumor characteristics and ASA score. Patients in LGT group had longer procedure ($p = 0.04$). Postoperative course was similar in term of complication rate and severity and of functional result. ICU length of stay was shorter patients in LGT group ($p = 0.002$). In the first postop day LGT patients had lower C-reactive protein (CRP) levels ($p = 0.001$) and white cell blood count ($p = 0.05$), and higher albumin serum level ($p = 0.001$). In this group, albumin remained higher also at third ($p = 0.06$) and seventh ($p = 0.008$) postop day, and CRP resulted lower at third post day ($p = 0.04$). No difference was observed in term of quality of life.
CONCLUSION: LGT during esophagectomy for cancer significantly improved the systemic inflammatory and catabolic response to surgical trauma, contributing to a shorter ICU length of stay. Quality of life and esophageal function were comparable between LGT and OGT patients.
Disclosure of Interest: None declared

P1046 RISK FACTORS OF INTRAOPERATIVE PERFORATION DURING ENDOSCOPIC SUBMUCOSAL DISSECTION OF SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Perforation is the major complication during endoscopic submucosal dissection (ESD) for esophageal squamous cell carcinoma (ESCC), and the frequency is reported to be approximately 5%. However, there are few reports about the risk factors for intraoperative perforations and the subsequent clinical course.
AIMS & METHODS: A total of 147 patients with 157 ESCC lesions were treated by ESD in our hospital from April 2008 to October 2012. We divided the group into intraoperative perforation cases and nonperforation cases, and compared the characteristics and endoscopic findings of the 2 groups. We also retrospectively reviewed the clinical courses after the perforations. A dual knife or an insulation-tipped diathermic knife were used for the ESD procedures. In addition, 0.4% sodium hyaluronate diluted with normal saline solution including epinephrine (1:1) was used as the submucosal injection solution. "Intraoperative perforation" was defined as the detection of a perforation site during ESD, and the presence of mediastinal emphysema seen on computed tomography (CT) or radiograph.
RESULTS: Intraoperative perforation was recorded as having occurred in 9 lesions from 9 patients (5.7%). No significant differences were observed between the perforation group ($n = 9$) and the nonperforation group ($n = 148$) for age, lesion location, depth of invasion, or history of treatment for esophageal cancer. However, in the perforation group the lesion maximum dimension was larger (42.9 mm vs. 30.7 mm, $p = 0.015$) and the rate of 3/4th or larger circumference of mucosal deficiency after ESD was higher (78% vs 31%, $p = 0.007$). Furthermore, the procedure time was longer (183.8 minutes vs 102.5 minutes, $p < 0.001$), and the en bloc resection rate was lower (33.3% vs 93.9%, $p < 0.001$) in ESD for patients who developed perforation during the procedure. The left wall was the predominant site of perforation (67%), and 6 of 9 perforations were successfully closed by clips during the procedures. Two of 9 patients required drainage for

pleural effusions; however, all 9 patients recovered with conservative treatment without surgical intervention. The median fasting duration and hospital stay after the procedure were 6 days (5–22 days) and 12 days (7–41 days), respectively. Three of 9 patients underwent additional treatments including chemoradiotherapy or esophagectomy due to submucosal infiltrations. At the median follow up of 42 months after ESD, no case of local recurrence or metastasis was observed.
CONCLUSION: This study suggests that a larger maximum dimension and mucosal defects after ESD are risk factors for intraoperative perforation during ESD for ESCC.
Disclosure of Interest: None declared

P1047 DIVERGING INCIDENCE OF OESOPHAGEAL ADENOCARCINOMA AND NON-CARDIA GASTRIC CANCER SUGGESTS A COMMON ENVIRONMENTAL FACTOR PREDISPOSING TO ONE AND PROTECTING FROM OTHER

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INTRODUCTION: During the last three decades, the global incidence of oesophageal adenocarcinoma has increased more rapidly than most other cancers in certain populations. A concurrent reduction in the incidence of gastric cancer has been reported from some populations. We aimed to examine the geographical pattern of oesophageal adenocarcinoma versus non-cardia gastric cancer across the world where reliable cancer registry data were available.
AIMS & METHODS: Data were abstracted from "Cancer Incidence in Five Continents" Volume 10. Oesophageal and gastric cancers were selected based on ICD-10 codes C15 and C16, respectively. Oesophageal adenocarcinomas were classified according to histological groups based on ICD-O morphology codes. Out of 424 datasets from 290 cancer registries, 288 were selected as they reported >10 cases for oesophageal adenocarcinoma. We examined the association between the incidence of oesophageal adenocarcinoma and non-cardia gastric cancer. Spearman's test of correlation was used to explore the relationship between Age-Standardised Incidence Rates (ASR) of the two cancers and expressed as correlation coefficients (CC). Furthermore, all cardia cancer cases within a registry were assumed to be either oesophageal or non-cardia based upon the different gender ratios for oesophageal versus non-cardia gastric cancer on individual registries.
RESULTS: A total of 288 datasets covering 62 countries were included in the analyses. There was a statistically significant inverse correlation between oesophageal adenocarcinoma and gastric non-cardia cancer in males (CC = -0.685, p value < 0.001) and females (CC = -0.566, p value < 0.001). After dividing cardia cancer into two subtypes with potentially oesophageal or gastric origin and adding them to original oesophageal adenocarcinoma or gastric non-cardia groups, the correlation remained strong (CC = -0.688, p value < 0.001) in males and (CC = -0.656, p value < 0.001) in females. Oesophageal adenocarcinoma only showed a rise when the incidence of non-cardia gastric cancer fell below 9/100.000 person-years for males and 4.5/100.000 person-years for females.
CONCLUSION: This cross-sectional study is consistent with a common underlying factor predisposing to non-cardia gastric cancer and protecting from oesophageal adenocarcinoma, such as *H.pylori* atrophic gastritis. If this is the case, then the incidence of non-cardia gastric cancer would need to fall to substantially lower levels than currently seen in the Far East populations before any rise in oesophageal adenocarcinoma would be apparent.
Disclosure of Interest: None declared

P1048 RECURRENT ESOPHAGEAL CANCER AFTER RADICAL ESOPHAGECTOMY: PROGNOSTIC FACTORS AND TREATMENT STRATEGIES

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INTRODUCTION: The prognosis of patients with recurrent disease after esophagectomy for esophageal cancer is generally poor.
AIMS & METHODS: The purpose of this study was to examine the prognostic factors in esophageal cancer patients with recurrence after esophagectomy and to determine the appropriate treatment strategy for such patients. **Patients:** Seventy-eight patients (33 %) developed recurrent disease among 237 patients with thoracic esophageal cancer who underwent R0 esophagectomy between 2001 and 2010.
RESULTS: Thirty-three (43%) patients had locoregional recurrence, 26 (33%) patients had recurrence in distant sites, and 19 (24%) had both recurrences. Recurrence occurred within one year in 45 patients (57%), within 2 years in 67 patients (85%), and within 3 years in all these 78 patients (100%). The overall 5-year survival rates after recurrence was 9%. Although there was no significant difference in survival between patients with only locoregional recurrence and those with only distant site recurrence (p = 0.3032), patients with recurrence in both locoregional and distant sites had poorer prognosis compared with only locoregional recurrence (p = 0.0003) or only distant site recurrence (p = 0.0050). Of 78 patients, 23 (30%) patients received chemoradiotherapy, 18 (23%) patients received chemotherapy, 8 (10%) patients received radiotherapy, 15 (19%) patients received surgery, and the remaining 14 (18%) patients received best supportive care alone. Surgery was performed in selected patients only when the lymph node did not invade the neighboring structures, and the distant lesion was detected as a single metastasis in a single organ. The 5-year survival rates after recurrence in patients who received anti-cancer treatment was 11%, and the patients with best supportive care survived less than one year (p = 0.0166). Furthermore, the 5-year survival rates for patients with surgery was 14% compared with 7% for patients without surgery (p = 0.0166). On univariate analysis, tumor location, depth of tumor invasion (pT), recurrent type, time to recurrence and treatment were found to be factors affecting the survival (p < 0.05). In multivariate analysis, the depth of tumor invasion (pT3T4 vs. pT1T2: hazard ratio 1.919; 95 % confidence interval 1.005–3.850; p = 0.0481), recurrent type (both vs. alone: hazard ratio 2.062; 95 % confidence interval 1.126–3.641; p = 0.0199) and treatment (best supportive care vs. anti-cancer treatment: hazard ratio 9.031; 95 % confidence interval 4.130–19.210; P < 0.00001) were independent prognostic factors.
CONCLUSION: The prognosis of patients with both locoregional and distant sites recurrence was poorer than those with each recurrence. The prognosis of patients who received anti-cancer treatment was better than that of the patients who received best supportive care alone. Surgery might be an option for selected patients.
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P1049 ESOPHAGEAL CANCER DEVELOPMENT DURING THE COURSE OF *H. PYLORI*-INFECTED CHRONIC GASTRITIS

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INTRODUCTION: Esophageal squamous cell carcinoma (ESCC) is the most prevalent esophageal cancer worldwide. Although the etiology of ESCC remains unclear, recent studies have revealed that, because they presumably generate an anacidic intraluminar environment that favors bacterial overgrowth in the upper gastrointestinal tract (GI), which leads to an accumulation of carcinogens such as nitrosamines, *H. pylori* (HP) infection and atrophic gastritis are both important risk factors for ESCC. However, studies investigating this association, particularly follow-up studies, are limited, and thus the role of chronic HP infection in ESCC development remains controversial.
AIMS & METHODS: Therefore, we investigated ESCC development during the progression of HP-associated chronic gastritis in a study of 4655 male subjects. Healthy, middle-aged, male subjects (n = 4655; mean age, 49.5 ± 4.6 years) were screened annually for ESCC and gastric cancer (GC) for up to 16 years. Chronic atrophic gastritis (CAG) was diagnosed based on the following prostaglandin (PG)-test positive criteria: PG I ≤70 ng/ml and PG I/II ratio ≤3.0. Highly active gastritis was determined by serum levels of PG II ≥30 ng/ml or HP antibody titer ≥500 U/ml. The stages of HP-associated chronic gastritis were evaluated by serum levels of pepsinogen and HP antibody, and were categorized into 4 groups representing the progression of HP-associated chronic gastritis as follows: Group A (CAG-negative, HP-negative); Group B (CAG-negative, HP-positive); Group C (CAG-positive, HP-positive); and Group D (CAG-positive, HP-negative).
RESULTS: During the study period, 87 GCs developed (annual incidence rate: 0.16%). Cancer development increased in a stepwise manner from Groups A to D, reaching a peak annual incidence rate of 1.1%. In Group B subjects with mild atrophic gastritis (annual incidence rate: 0.14%), highly active gastritis assessed by serum tests showed an annual incidence rate of around 0.25%, which was comparable to that in Group C subjects (0.30%). Eight ESCCs developed during the same period (annual incidence rate: 0.015%). Both smoking and alcohol consumption elevated the risk of ESCC, but only smoking showed a marginal significance ($p = 0.08$). The annual cancer incidence rate in Group A was 0.008%, and neither HP infection nor CAG significantly increased the risk of cancer. Highly active gastritis in a mildly atrophic stomach tended to increase the risk of cancer ($p = 0.04$).
CONCLUSION: Unlike GC, the incidence of which increases with establishment of HP-associated gastritis and the progression of CAG, ESCC development appeared not to be affected by the stages of gastritis. However, the possibility that the activity of gastritis is somehow involved in esophageal carcinogenesis should be further investigated.
Disclosure of Interest: None declared

P1050 LONG TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been widespread treatment for superficial esophageal squamous cell carcinoma (ESCC), since en bloc resection can be performed even in large ESCC lesions of which could not be performed in conventional endoscopic resection. However, there are few reports regarding the long-term outcomes of ESD for ESCC.

AIMS & METHODS: The aim of this retrospective study was to clarify the long-term results of ESCC patients treated by ESD. Between January 2006 and October 2012, a total of 185 patients with 191 lesions underwent ESD in our institution. We analyzed the patients who met the following criteria: 1) histologically confirmed initial ESCC or metachronous ESCC after prior endoscopic resection; 2) depth of lesions suspected as limited to within SM1; 3) absence of lymph node or distant metastasis; 4) a follow up period of 1 year or longer from the ESD procedure; and Cumulative overall, and disease-specific survival rate were calculated by the Kaplan-Meier method along with the log-rank test.
RESULTS: A total of 171 patients with 177 lesions were evaluated in this study. The median age was 67 years ranging from 39 to 85 years, and men were predominant (86%). In addition, 77 of 171 patients (45%) had a history or concomitance of cancer in other organs. Of 177 lesions, 169 (95%) were initial ESCC, and the remaining 8 lesions were metachronous ESCC. In the location, upper, middle, and lower esophagus was in 12, 100, and 65 lesions, respectively, with the median tumor size of 28 mm (range: 7–70). The median operation time during ESD was 100 minutes, and the en bloc resection rate was 89%. While esophageal perforation complicated in 8 patients during the procedure, all recovered with conservative therapy. Esophageal strictures required endoscopic balloon dilation after ESD was found in 55 patients (31%). Additional therapy was recommended in 34 (20%) patients because of the histological diagnosis, such as positive vertical margins, invasion into the submucosal layer, or lymphatic infiltration. Of the 34 patients, 20 received additional chemoradiotherapy, 5 underwent surgery, and the remaining 9 were followed up without additional treatment because of poor physical condition. At the median follow up period of 36 months (range: 12–92 months) after ESD**,** The presence of local recurrence, metastatic recurrence, and metachronus ESCC were 1.1%(2/172), 2.8%(5/177) and 14.7% (26/177) respectively. The overall survival at 3 and 5 years was 95.5% and 93.5%, respectively. During the follow up period, 11 patients died from the following causes: 2 from esophageal cancer, 7 from other cancers, and 2 from benign diseases. Therefore, disease-specific survival at 3 years and 5 years was 99.2% and 97.1%, respectively.
CONCLUSION: The long-term outcomes of ESD for ESCC was excellent. However, during the follow up periods, physicians should pay attention to not only the possibile local and metastatic recurrence or metachronous ESCC, but also the occurrence of other organ cancers
Disclosure of Interest: None declared

P1051 SALVAGE PHOTODYNAMIC THERAPY FOR PATIENTS WITH LOCAL FAILURE AFTER CHEMORADIOTHERAPY FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Local failure is a major problem after chemoradiotherapy (CRT) in patients with esophageal squamous cell carcinoma (ESCC), and salvage surgery for local failures associate with high complication and mortality rate. We have introduced photodynamic therapy (PDT) for local failures to develop a less invasive salvage treatment.
AIMS & METHODS: The aim of this study to clarify the long-term outcome and prognostic factors of salvage PDT. Between 1998 and 2008, 716 patients with ESCC were treated with definitive CRT in our institution. The indication criteria of PDT were as follows: 1) absence of lymph node and distant metastasis, 2) local failures limited within T2, 3) patients who could not tolerate or who refused surgery, 4) provision of written informed consent. PDT involved 2 mg/kg of porfimer sodium followed 48-72 hours later by excimer dye laser with a fluence of 75 J/cm2. We assessed overall survival (OS), progression free survival (PFS), and also prognostic factors. This study was approved by an institutional review board in our institution.
RESULTS: A total of 113 patients with local failure underwent salvage PDT. The characteristics before CRT were as follows; male/ female: 107/ 6, median age: 66 y-o (range: 50-84), T1/ 2/ 3/ 4: 18/ 18/ 60/ 17, N0/ N1: 54/ 59; and those of before PDT were as follows; T1/T2: 72/41; residue after CRT/recurrence after achieving CR with CRT: 64/49. Total 66 patients could achieved CR with PDT (CR rate: 58.4% (95% CI 49.3 – 67.5). Five patients developed esophageal perforation, and two of them died with bleeding due to esophago-aortic fistula after PDT, therefore treatment-related death rate was 1.7%. At the median follow up period of 61 months, the PFS rate and OS rate at 5 years from salvage PDT was 22.1% (95% CI 14.3–30.0) and 35.9% (95% CI: 26.7–45.1), respectively. N0 before CRT and period longer than six months between CRT and PDT were significantly associated with better survival.
CONCLUSION: PDT demonstrated a favorable outcome in an analysis of a large number of patients with local failure after definitive CRT for ESCC.
Disclosure of Interest: None declared

P1052 MULTIMODALITY THERAPY FOR ESOPHAGEAL CANCER WITH DISTANT ORGAN METASTASIS: TREATMENT OUTCOMES AND PROGNOSTIC FACTORS

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INTRODUCTION: Multimodality therapy has been established as an effective treatment for locally advanced esophageal cancer. However, esophageal cancer patients with distant organ metastasis have usually been treated to palliate symptoms without multimodality therapy, and the prognosis of these patients is extremely poor.
AIMS & METHODS: The aim of the study is to evaluate the role of multimodality therapy in esophageal cancer patients with organ metastasis. A prospectively maintained database identified 112 esophageal sqamous cell cancer patients with distant organ metastasis who were treated at our institution between 1989 and 2011.
RESULTS: The metastatic organ was the liver (n = 59), the lung (n = 47), bone (n = 16), and other (n = 10). Twenty patients had metastasis in two and more organs. Multimodality therapy was performed in 78 patients: 62 patients received chemoradiotherapy (CRT), and 17 underwent surgery with chemotherapy (CT) and/or radiation therapy (RT). Twenty patients received single-modality therapy; CT, RT, or surgery alone. The remaining 13 patients received best supportive care (BSC) alone. The median survival (MS) for the whole group was 5.6 months. The MS was 9 months for patients treated with multimodality therapy, 2.8 months for patients with single-modality therapy, and 2 months for patients with BSC alone ($P = 0.0001$, $P < 0.0001$). There was no difference in survival between single-modality therapy and BSC ($P = 0.1505$). By univariate analysis, an improved survival was associated with less advanced N stage (N0-1), the number of metastatic organ site (one organ), and type of therapy (multimodality therapy). Age, gender, performance status, location of tumor, T stage, and organ of metastasis did not affect survival. Multivariate analysis identified multimodality therapy to be the only independent factor for improved survival (hazards ratio, 0.317; 95% confidence interval, 0.207-0.495; $P < 0.0001$).
CONCLUSION: These results suggested that multimodality therapy could improve survival of the esophageal cancer patients with distant organ metastasis. A randomized study is necessary to confirm any definitive role for multimodality therapy in esophageal cancer patients with organ metastasis.
Disclosure of Interest: None declared

P1053 LONG-TERM PROGNOSIS OF SUPERFICIAL ESOPHAGEAL CANCERS AT LEAST 50MM IN DIAMETER TREATED BY ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: The advantage of ESD is high R0 resection rate and low local recurrence rate. However, usefulness of ESD for big ESCC and long term prognosis after ESD for big ECCS is unknown.
AIMS & METHODS: The aim of this study is to clarify the usefulness of ESD for ECCS at least 50mm in diameter, and long term prognosis after ESD. Superficial ECCS at least 50mm in diameter treated by ESD were enrolled to this retrospective study. A total of 138 superficial ECCS at least 50mm in diameter were treated by ESD in 5 territorial hospitals from 2000 to 2013. Patient's characteristics were as follows; Male/Female is 118/20, respectively. Median age was 69 (42 – 88), An additional treatment (AT) such as esophagectomy, chemotherapy (CT), radiation (RT) and chemo radio therapy (CRT) was recommended for the patients who had T1b ESCC.
RESULTS: Result 1. En bloc resection rate was 99 % (137/138), and R0 resection rate was 88% (122/138). Horizontal and vertical margin was positive in 14 (10%) and 2 (1.4%), respectively. There weren't severe complication that needs surgical operation. Invasion depth T1a EP, LPM, MM, and T1bSM1 (200μm or less) and SM2 was 30/51/34/6/17, respectively. Result 2. Local recurrence rate was 1% (1/138). The patient had T1bSM2 ESSC, and refused an additional treatment. A local recurrence was diagnosed 51 months after ESD, and esophagectomy was performed. Result 3. Prognosis of T1a: No recurrence was found in T1aEP and LPM. Eight of 34 MM patients had lymph duct invasion. Four patients were treated by CRT, and two patients were alive without metastasis. Remaing two patients had lymph node metastasis (LNM) and treated by CRT again. One patient who was treated by RT was alive. The remaining 3 patients were followed up without AT, and LNM was found in one patient, and CRT was performed. One patient is alive without recurrence, and the other patient died of other disease. Twenty six patients who didn't have ductal invasion were followed up without AT. Two patients had LNM. One patient was treated by esophagectomy and alive. The other patient was treated by CRT and died of ESCC. Result 4. Prognosis of T1bSM1: One patient of 6 T1bSM1 had LNM, and treated by CRT. The patient is alive without recurrence for 60 months. The remaining 5 patients were followed up without AT, and one patient died of lymph node metastasis, and remaining 5 patients were alive without recurrence. Result 5. Prognosis of T1bSM2: Six of 18 patients had lymph duct or venous invasion. Five of these 6 patients were treated by CRT, and alive without recurrence. The remaining one patient was followed up without AT, and died of other disease 49 months after ESD. Three of 11 patients who didn't have ductal invasion were treated by CRT, and alive without recurrence. Eight patients were followed up without additional therapy. One patient had local recurrence 51 months after ESD, and was treated by esophagectomy. Remaining seven patients were alive without recurrence.
CONCLUSION: ESD is a safe and useful treatment for ECCS at least 50mm. The prognosis of T1aEP and LPM is excellent. And, prognosis of T1aMM, T1bSM1 or SM2 with an adequate AT was also excellent.
Disclosure of Interest: None declared

P1054 DISTRIBUTION OF LYMPH NODE METASTASES IN ESOPHAGEAL CARCINOMA: A SYSTEMATIC REVIEW

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INTRODUCTION: Lymph node status is an important prognostic parameter in esophageal carcinoma and an independent predictor of survival. Distribution of metastatic lymph nodes may vary with tumor location, tumor histology, tumor invasion depth and neoadjuvant therapy. Surgical strategy depends on the distribution pattern of nodal metastases but consensus on the extent of lymphadenectomy differs worldwide. Aim of the present study was to evaluate the distribution of lymph node metastases in esophageal carcinoma specimens following transthoracic esophagectomy.
AIMS & METHODS: The Cochrane database of systematic reviews, the Cochrane central register of controlled trials, Embase and Medline databases were searched by two independent researchers using a combination of keywords relating to esophageal cancer, surgery, lymphadenectomy and lymph nodes. Studies were included if published from 1990 until July 1st 2013. Excluded were studies with 1-field lymphadenectomy, studies with neo-adjuvant therapy, studies describing only the sentinel node, animal studies and case reports. The primary end point was the distribution of lymph node metastases.
RESULTS: Out of 2406 articles, 8 studies, reporting on 5038 patients, fulfilled the eligibility criteria and were included. Seven studies described the distribution of nodal metastases in squamous cell carcinoma (4869 patients) and 2 studies in adenocarcinoma (169 patients; 1 study described both squamous cell and adenocarcinoma). All studies were retrospective analyses except for 1 prospective cohort trial on squamous cell carcinoma (1893 patients). The studies on squamous cell carcinoma discriminated between tumor location in the upper, middle and lower esophagus. All selected studies used a different classification system for lymph node stations and were therefore not comparable in a meta-analysis. For adenocarcinoma both studies found mediastinal and abdominal lymph node metastases, but in only 1 of 2 studies cervical metastatic lymph nodes were reported (10/32 patients; 27%). For squamous cell carcinoma all studies described cervical, mediastinal and abdominal lymph node metastases, independent of the location of the tumor, except for 1 trial with 9 patients, in which there were no abdominal lymph node metastases in upper esophageal squamous cell carcinoma and 1 trial with 41 patients in which there were no cervical lymph node metastases in lower esophageal squamous cell carcinoma.
CONCLUSION: Esophageal cancer frequently metastasizes to the neck, mediastinum and abdomen. However, few studies describe the distribution of lymph node metastases for esophageal adenocarcinoma. Additionally, there is no homogeneity concerning classification of lymph node stations, which makes interpretation of studies difficult and data hard to compare. This makes the choice for surgical strategy demanding, especially when considering the significant morbidity involved in esophageal surgery. A multicenter prospective study is needed to determine distribution of lymph node metastases in order to establish optimal surgical treatment for esophageal cancer patients.
Disclosure of Interest: None declared

P1055 LOCOREGIONAL STEROID INJECTION TO PREVENT STRICTURE FORMATION AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL CANCER USING A PROPENSITY SCORE MATCHING ANALYSIS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) to treat superficial esophageal cancer has become accepted owing to its high quality control for the disease. However, incidence of strictures caused by ESD for widespread lesions is high and sometimes leads to a low quality of life. Locoregional steroid injection was reported to be useful for prevention of such strictures formation (1). However, no prospective randomized comparative study about steroid has been observed.
AIMS & METHODS: We evaluated the prophylactic efficacy of locoregional steroid injection for stricture formation after ESD for superficial esophageal cancer using a propensity score matching analysis.
This is a retrospective study in single referral center. Between April 2006 and July 2013, a total of 357 patients with superficial esophageal cancer underwent ESD in our hospital. Four patients treated with metallic stent and 4 patients with lacking data were excluded. Consequently, 349 patients were enrolled in this study. We have used two fashions of locoregional steroid injection: one is an injection of 80 mg triamcinolone once just after ESD; second is an injection of 6.6 mg dexamethasone just after ESD and twice a week (1-6 times). Endoscopic evaluation of the stricture was performed after 4 and 8 weeks after the treatment. A propensity score matching analysis was performed to reduce the effects of selection bias of steroid injection and potential confounding factors. We compared the incidence of stricture formation by univariate analysis between patients with and without locoregional steroid injection before and after matching. In addition, multivariate analysis was used.
RESULTS: Of 349 patients, 42 patients underwent locoregional steroid injection (dexamethasone/triamcinolone, 23/19) after ESD and esophageal stricture formation occurred in 36 patients. Twenty-eight patients with or without steroid injection were matched after a propensity score matching. In univariate analysis, the incidence of stricture formation with steroid injection decreased to 10.7% (3/28) from 35.7% (10/28) as without steroid ($p = 0.035$). Multivariate analyses indicated that lcoregional steroid injection decreased the incidence of stricture formation (OR, 0.15; 95% CI, 0.03–0.73; $p = 0.02$). No serious adverse events such as delayed bleeding and perforation were encountered.
CONCLUSION: Locoregional steroid injection was efficient for preventing stricture formation after ESD for superficial esophageal cancer.
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P1056 ROLE OF ENDOGENOUS AND EXOGENOUS HYDROGEN SULFIDE (H2S) IN GASTRIC PROTECTION AGAINST EXPERIMENTAL GASTRIC LESIONS

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INTRODUCTION: Hydrogen sulfide (H_2S) plays an important role in a number of physiological actions including vasodilatation, inhibition of oxidant stress, the anti-inflammatory activity and the inhibition of apoptosis. Three enzymes cystathionine γ-lyase (CSE), cystathionine β-synthetase (CBS) and 3-mercaptopyruvate sulfurtransferase (3-MST) are essentioal in the biosynthesis of H_2S by gastric epithelium. However, whether this gaseous molecule could be effective in protection against acid-dependent stress-induced lesions and whether the expression of CSE and CBS and the gastric mucosal biosynthesis of H_2S could affect the mucosal damage induced by stress in the presence or absence of exogenous H_2S, have been little elucidated.
AIMS & METHODS: We studied the effect of NaHS, a H_2S-donor and L-cysteine, a H_2S precursor against 3.5 h of water immersion restraint stress (WRS)-induced gastric lesions in rats with intact and capsaicin-denervated sensory nerves (large dose 125 mg/kg s.c for 3 days). Animals were pretreated i.g. 30 min before the oneset of WRS with A) NaHS (5 mg/kg); B) L-cysteine (10 mg/kg) with or without the combination with inhibitors of CSE activity, D,L-propargylglycine (PAG 15 - 80 mg/kg) and beta-cyano-L-alanine (BCA, 50 mg/kg). The number of gastric lesions was measured by planimetry, the gastric blood flow (GBF) by H_2-gas clearance technique and the gastric H_2S production resulting from CSE/CBS and 3-MST activity pathways and the gastric H_2S content were determined by modified methylene blue method and ELISA, respectively. In addition, the mucosal mRNAs expression of CSE, CBS, 3-MST, HIF1α and antioxidizing enzymes SOD and GPx were evaluated by RT-PCR.
RESULTS: Exposure to WRS caused mucosal hemorrhagic lesions accompanied by the fall in GBF, gastric H_2S content and an increase in H_2S production *via* CSE/CBS and 3-MST pathways and mRNA expression of CSE and CBS. NaHS (1-20 mg/kg) and L-cysteine (5-40 mg/kg) dose-dependently reduced WRS-induced gastric damage and significantly raised GBF and mucosal content of H_2S and these effects were completely lost in animals with capsaicin denervation. BCA and PAG which dose-dependently augmented the number of WRS lesions and decreased H_2S production and its tissue content, reversed the NaHS and L-cysteine-induced decrease in the WRS lesions and the accompanying increase in the GBF. Upregulation of mRNAs expression for HIF-1α mRNA, CSE and CBS in the gastric mucosa exposed to WRS was diminished by NaHS (5 mg/kg i.g.) and L-cysteine (10 mg/kg i.g.) and these effects were further enhanced in capsaicin-denervated rats treated with NaHS and L-cysteine. The increased expression of SOD and GPx mRNA was observed in NaHS- and L-cysteine-pretreated rats but not in those with capsaicin-denervation.
CONCLUSION: We conclude that: 1) an increase in H_2S production and the expression of CSE and CBS, two key enzymes in H_2S biosynthesis, could compensate for the stress-induced impairment of gastric mucosal defense; 2) an increase in endogenous production of H_2S in gastric mucosa contributes to the NaHS-induced protection against stress lesions, and 3) H_2S-induced gastroprotection and hyperemia against WRS-induced ulcerogenesis is mediated by vasoactive sensory neuropeptides such as CGRP and the activity of antioxidizing enzymes SOD and GPx.
Disclosure of Interest: None declared

P1057 CARBON MONOXIDE (CO) RELEASED FROM CORM-2 RELEASING CO ATTENUATES ASPIRIN-INDUCED GASTRIC LESIONS. INVOLVEMENT OF GASTRIC SECRETION, HEME OXYGENASE (HO-1) AND NITRIC OXIDE

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INTRODUCTION: Previuos studies revealed that enzyme heme oxygenase (HO)-1 exerts an important protective action in acute and chronic inflammation of the gastrointestinal mucosa. Carbon monoxide (CO) synthesized due to activity of HO-1 has been shown to exert important physiological functions in the regulation of blood flow and motility but the contribution of this gaseous molecule to the mechanism of protection against nonsteroidal anti-inflammatory drugs (NSAID)-induced gastric mucosal damage has been little studied.

AIMS & METHODS: We determined the effect of tricarbonyl dichloro ruthenium(II) dimer (CORM-2), a CO releasing molecule, on gastric acid secretion in rats equipped with chronic gastric fistulas (GF) (series A) and gastric lesions induced by acidified aspirin (ASA) (series B). Rats were treated with CORM-2 (0.1-50 mg/kg i.g.) and received 30 min later ASA (125 mg/kg i.g.) without or with: 1) NO-synthase inhibitor L-NNA (20 mg/kg i.p.) without or with L-arginine (200 mg/kg i.g.), a substrate for NO-synthase activity, 2) ODQ (10 mg/kg i.g.), a guanylyl cyclase inhibitor, and 3) zinc protoporphyrin IX (ZnPPIX), an inhibitor of HO-1 activity. In addition, the effect of hemin, a HO-1 inducer which provides endogenous CO, and biliverdin, the product of heme catalysis, on ASA damage and the alterations in the GBF were also studied. The area of gastric lesions was measured by planimetry, the gastric blood flow (GBF) determined by H_2-gas clearance technique, plasma proinflammatory cytokines (IL-1β and TNF-α) were determined by ELISA and the mRNA and proteins for HO-1-, HO-2- and COX-1- and proinflammatry markers COX-2-, IL-1β-, and TNF-α were assessed by RT-PCR.

RESULTS: CORM-2 inhibited basal and histamine stimulated gastric acid secretion in rats with GF (series A) and dose-dependently attenuated ASA damage while increasing GBF; the dose inhibiting ASA damage by 50% (ED_{50}) being 5 mg/kg (series B). These protective and hyperemic effects of CORM-2 were significantly attenuated by L-NNA and restored when L-arginine but not D-arginine was co-administered with CORM-2. ODQ also significantly attenuated the gastroprotective and hyperemic effects of CORM-2. Pretreatment with hemin (5 mg/kg i.g.) significantly reduced ASA-induced gastric damage and significantly increased the GBF similarly as in case of CORM-2 while biliverdin was less effective. ZnPPIX which exacerbated ASA damage significantly atternuated the protection and the rise in GBF induced by CORM-2 (5 mg/kg i.g.). The increased mucosal expression of mRNA for HO-1, COX-2 mRNA, IL-1β and TNF-α and plasma levels of these cytokines were detected in rats exposed to ASA and these effects were significantly ameliorated by pretreatment with CORM-2.

CONCLUSION: We conclude that 1) CO released from CORM-2 exhibits gastroprotective activity against ASA-induced gastric lesions *via* mechanism involving an increase in the gastric microcirculation mediated by activation of HO-1/CO, NO-NOS and PG-COX systems and the inhibition of the expression and activity of proinflammatory markers COX-2, IL-1β and TNF-α, and 2) antisecretory activity of CORM-2 releasing CO can contribute to CO-induced protection against acid-dependent mucosal damage evoked by ASA.

Disclosure of Interest: None declared

P1058 THE PECULIARITIES OF COLONIC MICROBIOTA IN HELICOBACTER PYLORI-NEGATIVE PATIENTS WITH NSAIDS-GASTROPATHY

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INTRODUCTION: Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed for a variety of inflammatory conditions. Among the most common side effects are NSAID-enteropathy/-gastropathy. It is known that in animal models NSAID-enteropathy is accompanied by shifts in numbers and types of intestinal bacteria. That's why probiotics (P) are thought as potential drugs for treatment and prevention of NSAID-enteropathy. The peculiarities of colonic microbiota and its correlation with the severity of gastric lesions in patients who used NSAIDs for more than 3 months haven't been studied before.

AIMS & METHODS: to study the peculiarities of colonic microbiota in *H. pylori*-negative patients who used NSAIDs more than 3 months with and without NSAIDs-gastropathy; to determine a correlation between the intensity of dysbiosis and age, severity of gastric mucous lesions (GML); and to optimize the treatment of NSAIDs-associated GML with the help of P. We observed 45 patients who were *H. pylori*-negative and used NSAIDs more than 3 months. The mean age was 64.1±6.1. For all of them gastroscopy, laboratory examination were performed. The fecal microflora has been analyzed by bacteriological culture methods. Patients with GML were divided into 2 equal groups. The first group (control) was treated with pantoprazole (20 mg 2 times daily) for 28 days. The second group (main) received combined therapy: pantoprazole (20 mg 2 times daily) for 4 weeks and P ''Symbiter acidophilic'' concentrated in dose 10 ml per day for 20 days. Over 1 month after the beginning of treatment we repeated all examinations which were done before. Normal distribution of studied parameter for each sampling was checked using Shapiro-Wilka's criteria. Average value (M) error and standard deviation (SD) were calculated to discover significant changes of investigated indices. Sampling comparison was performed using the paired Student's t-test.

RESULTS: Among 45 patients, who were examined, in 30 patients GML were observed, in 15 patients visible changes of GM were absent. Changes in colonic microbiota were observed in all patients who used NSAIDs for more than 3 monts. In 33.3% of them the level of Lactobacillus was less than 10^6. It was detected correlative conjunction between the severity of injuries and intensity of dysbiosis ($r = 0.67$, $p < 0.001$). The correlation between the intensity of dysbiosis and age of the patients is also observed ($r = 0.43$, $p < 0.003$). Over 1 month in the control group erosive lesions of GM were observed in 26.7%, in the main group erosive lesions after the treatment were absent ($p < 0.05$). In the main group the elevation of the level of haemoglobin, red blood cells were significantly more expressed. In the control group the intensity of dysbiosis was enhanced, in the main group dysbiosis was not registered.

CONCLUSION: The changes in the colonic microbial community structure correlate with the intensity of the GML and age of patients with NSAIDs-gastropathy. The inclusion of P in the general scheme of treatment of NSAIDs-gastropathy eliminates the detected dysbiosis and improves the indicators of complete blood count and what is important - it leads to the total healing of gastric mucous over 4 weeks from the beginning of treatment that allows us to recommend the inclusion of P in the general scheme of the treatment of NSAIDs-gastropathy.

Disclosure of Interest: None declared

P1059 THE ROLE OF SINGLE NUCLEOTIDE POLYMORPHISMS LINKED TO VITAMIN B12 MALABSORPTION IN ATROPHIC GASTRITIS AND PERNICIOUS ANEMIA

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INTRODUCTION: Atrophic body gastritis (AG) is characterized by oxyntic glands and parietal cells destruction with loss of hydrochloric acid and intrinsic factor production. Vitamin B12 (vitB12) malabsorption may occur and lead to pernicious anemia (PA), the global burden of which is still unknown. AG and PA pathogenesis are linked to autoimmune mechanisms and to *Helicobacter pylori* (Hp) infection[1]. The role of single nucleotide polymorphisms (SNPs) in vitB12 malabsorption and PA is unknown.

AIMS & METHODS: To determine the frequency of SNPs potentially related to vitB12 absorption pathway in AG patients, with or without PA, compared to healthy controls.

83 AG caucasian patients were enrolled: 43 with PA (51% F, median age 59 years) and 40 without (85% F, median age 51 years). Controls included 173 caucasian subjects (73% F, median age 51 years). Genomic DNA from peripheral blood leukocytes was extracted. Fourteen SNPs potentially related to vitB12 absorption were analyzed by genotyping: TCN1 rs526934, TCN2 rs9606756, CUBN rs1801222, rs11254363, FUT2 rs492602, rs601338, rs602662, FUT6 rs3760776, GIF rs35211634, rs121434322, MUT rs9473555, rs1141321, MTHFR rs1801133, CLYBL rs41281112 [2,3]. Results are expressed as allele and genotype frequencies.

RESULTS: TCN2 (rs9606756) C/C genotype was significantly more frequent in all cases compared to controls: 3.6% vs 0%, χ^2 0.02. MUT (rs9473555) G allele was significantly less frequent in all cases compared to controls: 27% vs 72%, $\chi^2 < 0.0001$. The genotype and allele frequencies of remaining SNPs were similar in the two groups.

TCN2 (rs9606756) C/C and FUT6 (rs3760776) T/T genotypes were more prevalent in PA cases compared to controls: respectively, 4.6% vs 0%, χ^2 0.02; 9.3% vs 1.7%, χ^2 0.01. No difference was found in terms of allele frequency. GIF gene (rs121434322) T allele was not expressed in the examined population.

CONCLUSION: Compared to controls, AG patients, with and without PA, have a higher prevalence of TCN2 C/C genotype, which may be associated with altered plasma transcobalamin and thus with altered cellular vitB12 uptake. Among PA cases, FUT6 T/T genotype is more prevalent; this may alter FUT6 activity and individual susceptibility to Hp infection, a trigger of gastric autoimmunity. MUT G allele is more prevalent in controls and it has been linked to higher vitB12 levels, as it is expected in an healthy gastric body mucosa. This study shows that genetic polymorphisms related to vitB12 absorption pathway are associated to AG and PA; this suggests that specific SNPs in AG may lead to vitB12 malabsorption.

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P1060 THE IL-1B GENETIC POLYMORPHISM IS ASSOCIATED WITH LOW-DOSE ASPIRIN-INDUCED PEPTIC ULCER IN KOREANS

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INTRODUCTION: Single nucleotide polymorphisms (SNPs) are associated with aspirin-induced peptic ulcer, but they are discrepant among races. There are few data on Koreans.

AIMS & METHODS: This study investigated the relationship of SNPs of COX-1, IL1B, TNF and IL-1RN genes on aspirin-induced peptic ulcer in Korean adults.

The subjects taking a low-dose aspirin of 100 mg for at least 4 weeks were enrolled in the study, and they underwent an upper GI endoscopy at Myongji Hospital. The subjects were divided into two groups: the control group that had no peptic ulcer in upper GI endoscopy, and the peptic ulcer group that had gastric or duodenal ulcer in upper GI endoscopy. The DNA was extracted from the subjects' whole blood, polymerase chain reaction was performed to detect SNP, and mutation analysis was performed.

RESULTS: A total of 48 patients consisting of 23 patients with peptic ulcer and 25 healthy controls were enrolled. In IL-1β -581C/T (rs1143627), the prevalence of CC, CT and TT alleles were 21.74%, 65.22%, and 13.04% in the peptic ulcer group, whereas 16%, 40%, and 44% in the control group, respectively. In IL1B-1061C/T (rs16944), the CC, CT and TT alleles were 13.04%, 65.22%, and 21.74% in peptic ulcer group, whereas 44%, 40%, and 16% in the control group, respectively. After adjustment for age and gender, the CT and CC allele of IL-1β -581C/T had an odds ratio of 4.625 (95% confidence interval: 1.054-20.303) for peptic ulcer. In IL-1β -1061C/T, the CT and TT allele had an odds ratio of 4.625 (95% confidence interval: 1.054-20.303) for peptic ulcer.
CONCLUSION: The C allele of IL-1β -581C/T and T allele of IL-1β -1061C/T had an increased risk of low-dose aspirin-induced peptic ulcer in Korean adults. It would be reasonable to screen patients for these SNPs before low-dose aspirin is prescribed, and to prevent peptic ulcer induced by low-dose aspirin.
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P1061 LOCAL IMPLANTATION OF ADIPOSE-DERIVED MESENCHYMAL STEM CELLS (ADMSCS) ENHANCED HEALING OF GASTRIC ULCER VIA ACTIVATION OF ERK1/2-MAPK PATHWAY

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INTRODUCTION: Numerous studies confirmed the efficacy of ADMSCs in enhancing healing in injury to various organs including heart, liver, colon, brain and kidney. The aim of our study was to investigate the effect of ADMSCs in enhancing the healing of gastric ulcer and to explore the potential mechanisms for this effect.
AIMS & METHODS: Gastric ulcer model was successfully created in rats using 70% acetic acid. These ulcers were divided into three groups and received one of the following treatments: 1. Single dose of 1×10^7 ADMSCs directly transplanted to around ulcer by injection; 2. intragastric administration of pantoprazole; 3. Phosphate buffered saline alone (PBS). The healing of ulcer was assessed by the area measured at different time points after sacrifice of rat. Molecular mechanisms and potential signal pathway activated by ADMSCs were assessed using PCR-array. In addition, the therapeutic potentials of ADMSCs were also assessed when NSAIDs was simultaneously used.
RESULTS: The results showed that ADMSCs accelerated healing of peptic ulcer as evidence by the significant reduction in ulcer area at day 10 and 15 for ADMSC group compared to other two groups (ADMSCs vs. PBS group: $P<0.01$ for day 10 and $P<0.05$ for day 15). Histological assessment indicated that ADMSCs significantly increased re-epithelialization, angiogenesis and collagen deposition, meanwhile suppressing inflammatory reaction. ADMSCs group had more cell proliferation and angiogenesis compared with PBS group. Transplanted ADMSCs homed into the gastric ulcer and differentiated into endothelial and smooth muscle cells. The results of PCR-array indicated that genes for anti-inflammation, chemokines, growth factors and remodeling enzymes were significantly up-regulated in ADMSCs group. In addition, ADMSCs activated Erk1/2-MAPK signal pathway, which has been suggested as the most important pathway for the healing of peptic ulcer. Simultaneous use of indomethacin (a commonly used NSAIDs) greatly attenuated the therapeutic effect of ADMSCs as shown by reduced cell proliferation and angiogenesis, increased apoptosis and delayed ulcer healing at day 10.
CONCLUSION: Local injection of ADMSCs enhanced healing of gastric ulcer through activation of Erk1/2-MAPK signal pathway.
Disclosure of Interest: None declared

P1062 FEASIBILITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY GASTRIC CANCER IN ELDERLY PATIENTS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for early gastric cancer can achieve a higher rate of en bloc resection which allows more accurate pathological diagnosis, even for large lesions. If the correct indications are used, ESD can be a radical treatment with results comparable to open surgery. Therefore, ESD is thought to greatly improve the patient's quality of life (QOL). In Japan, life expectancy is approximately 80 years, and Japan has the longest life expectancy in the world for both men and women. In its increasingly aged society, a growing number of endoscopic treatments are performed on the elderly with age-associated comorbidities such as cardiovascular diseases. The proportion of people who regularly attend hospital for at least one chronic disease is nearly 70% among people who are 75–84 years of age, which is the highest rate compared to other age groups. Therefore, even esophagogastroduodenoscopy (EGD) itself can have risks for elderly patients, and further caution is particularly needed for those with comorbidities of heart or lung diseases. Elderly patients often have surgically operative risks due to complicated diseases, and the feasibility of ESD for such patients will improve the QOL. In the present study, we aimed to evaluate the efficacy and safety of ESD for early gastric cancers in elderly patients aged 75 years or older. The technical feasibility, the en bloc resection rate, and the complications of ESD in the treatment of early gastric cancers were compared with those of younger patients.
AIMS & METHODS: The subjects were selected from 213 consecutive patients with early gastric cancers for which ESD was performed between January 2006 and December 2013. They were divided into two group; 74 patients who were 75 years of age or older (elderly group) and 139 patients under 75 years old (non-elderly group). The following were used for analysis between the groups: pre- and postoperative performance status (PS) of subjects, prevalence rates of pre-existing comorbidities, characteristics of lesions, treatment outcomes, durations of hospitalization, operating times and incidence rates of complications.
RESULTS: In the elderly, there was one patient (1.4%) with PS of 3 before ESD. None of the non-elderly had a PS of 3 before or after the procedure. The PS increased in only one elderly patient (1.4%) after the ESD procedure. However, none of the non-elderly had the PS increase after the ESD procedure. There was no significant difference related with PS increase between the two groups. The ratio of patients with a pre-existing comorbidity was higher in the elderly than in the non-elderly. There were no differences between the two groups in the characteristics of the lesions, operating times, duration of hospitalization, or the incidence rates of complications such as perforation and post-ESD bleeding. The percentage of the patients taking anticoagulant drugs was significantly higher in the elderly. Of the patients on anticoagulant therapy, the duration of hospitalization tended to be longer in the elderly but no significant difference was found.
CONCLUSION: The present study shows feasibility of ESD for early gastric cancers in elderly patients. We conclude that ESD is useful in elderly patients because there is a similar risk as for the non-elderly regardless of PS or pre-existing comorbidity.
Disclosure of Interest: None declared

P1063 SUCCESSFUL TREATMENT OF MÉNÉTRIER'S DISEASE USING THE EGF-RECEPTOR-ANTIBODY CETUXIMAB

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INTRODUCTION: Ménétrier's disease (hypertrophic gastropathy) named after French physician Pierre E. Ménétrier; (1859–1935) is a rare, acquired, premalignant disease of the stomach characterized by enlarged gastric folds, excessive mucous production with resultant protein loss. The histology is characterized by massive foveolar hyperplasia. The glands are elongated with a corkscrew-like appearance and cystic dilation is common. There is no standard therapy as of yet. A few case series describe a dramatic response to the inhibition of the EGF-Receptor pathway (NEJM 2000; 343: 1697-1701).
AIMS & METHODS: We report the case of a 48-year old Caucasian male with a three year history of dyspepsia associated with lower extremity edema caused by hypoalbuminemia. Helicobacter serology was negative. The epigastric pain was only minimally responsive to PPI-treatment. An EGD was performed and showed large, tortuous gastric folds in the fundus and body of the stomach, with sparing of the antrum. Radial EUS at 10 mHz showed significant thickening of the gastric wall up to 9 mm caused by effacement of the first three wall layers. Five large biopsies using a hot snare were obtained. The histology did reveal the characteristic findings of Ménétrier's disease with extensive foveolar hyperplasia.
RESULTS: Given the persistent epigastric complaints and significant enteral protein loss leading to edema, we did recommend the off-label use of cetuximab, a monoclonal antibody against the EGF-receptor, according to the Vanderbilt University/Nashville/TN- study protocol. After informed consent and approval by the internal review board, four weekly infusions of cetuximab were administered ($400mg/m^2$ loading dose, followed by $250mg/m^2$). Prophylactic Pliazon® (Merck Serono) cream was applied in order to prevent drug-induced skin rash, which is a common side effect of anti-EGFR therapy. The patient only developed a mild erythematous rash without pruritus after the second infusion. The epigastric discomfort was relieved completely and the serum albumin level normalized after 6 weeks leading to resolution of the peripheral edema. EGD 8 weeks after completion of the anti-EGFR therapy showed normal gastric folds with only mild chronic gastritis on histology. The patient is currently without and GI symptoms 6 months after completion of therapy and will undergo annual EGDs for surveillance.
CONCLUSION: Anti-EGFR antibody therapy using cetuximab seems to be an effective treatment of symptomatic Ménétrier's disease and should be considered before more aggressive treatment options like gastrectomy are entertained.
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Disclosure of Interest: None declared

P1064 CAN THE FICE ENDOSCOPY IDENTIFY INDIVIDUALS WITH ADVANCE STAGES OF GASTRIC ATROPHY AND/OR INTESTINAL METAPLASIA?

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INTRODUCTION: Patients with chronic atrophic gastritis (AG) or intestinal metaplasia (IM) should be considered to be at higher risk for gastric adenocarcinoma [1]. This study aimed to evaluate if the flexible spectral imaging color enhancement (FICE) endoscopic assessment of gastric mucosa could replace random biopsies to identify individuals with advance stages of gastric atrophy and/or intestinal metaplasia.

AIMS & METHODS: We included 191 consecutive patients (male 28%, average 62, range 50-87) from January 2013 to April 2014 aged over 50 undergoing FICE (gastroscope EG-590WR) endoscopy at Digestive diseases centre GASTRO. Targeted biopsies were obtained at the locations of visually suspected lesions. If no changes were determined by FICE, random biopsies were performed in antrum, incisura and corpus according to Sydney-Houston protocol. Histology assessment was performed according to the updated Sydney System. Both OLGA and OLGIM were used and individuals classified accordingly.
RESULTS: Table 1. FICE diagnostic accuracy for AG and IM.

	Sensitivity	Specificity	LR+	LR-
Atrophy (OLGA III/IV)	82.35	78.57	3.84	0.22
IM (OLGIM III/IV)	78.57	86.17	5.68	0.25
Atrophy (OLGA I/II)	46.88	78.57	2.19	0.68
IM (OLGIM I/II)	61.45	86.17	4.44	0.45

The overall prevalence of endoscopically and histologically diagnosed AG and IM cases were 48% and 93% (68% OLGA I), 39% and 50% (45% OLGIM I), respectively.
CONCLUSION: FICE endoscopy yielded favourable results in the endoscopic diagnosis of advance stages of gastric atrophy and/or intestinal metaplasia (OLGA/OLGIM III/IV) and this is very practical and easy way to use in a daily clinical practice for unselected patients.
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Disclosure of Interest: None declared

P1065 RISK STRATIFICATION AND MANAGEMENT OF NON-CURATIVE RESECTION AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Non-curative resection after endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) can contribute to local recurrence or lymphatic and distant metastasis of the tumor. We stratified the risk of local recurrence in non-curative resection after ESD for EGC.
AIMS & METHODS: There were 892 EGC cases treated with ESD from 2001–2012; histology determined that 152 (17.0%) cases resulted in non-curative resection after ESD. These cases included positive cancer cells in the margin, lymphovascular invasion, or were beyond the expanded criteria of ESD from ESD specimens. The clinical outcomes and risk factors associated with local recurrence were analyzed retrospectively in non-curative resections after ESD.
RESULTS: Among 152 non-curative resections, 46 (30.3%) were interpreted as incomplete resection based on the margin and criteria fulfillment, 31 (20.4%) as complete resection based on margin and beyond the criteria, 41 (27.0%) as incomplete resection based on margin and beyond the criteria, and 34 (22.4%) as lymphovascular invasion regardless of complete resection. The patients with factors related to incomplete margin resection beyond the criteria (odds ratio [OR], 3.991; $P = 0.015$) or lymphovascular invasion (OR, 4.487; $P = 0.014$) showed a higher rate of local recurrence in non-curative resection. In those high-risk groups, endoscopic surveillance without additional treatment allowed significantly more local recurrence than those received additional treatment ($P = 0.029$).
CONCLUSION: Risk stratification for non-curative resection is important for EGC prognosis after ESD. Moreover, additional treatment for non-curative resection influences long-term outcomes, in a high-risk group that have incomplete resection of margin beyond the ESD criteria or lymphovascular invasion.
Disclosure of Interest: None declared

P1067 STUDY FOR CASES OF RECURRENCE AFTER ENDOSCOPIC RESECTION IN EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic resection (ER) is widely accepted treatment for early gastric cancer (EGC), but little is known about recurrence after ER.
AIMS & METHODS: The aim of this study is to investigate cases of recurrence after ER for EGC.
We performed a retrospective review of medical records of 126 patients with EGC underwent ER.
RESULTS: The median follow up period was 26.7 months. During a follow up, a total of 10 patients (7.94%) developed recurrence in enrolled patients. According to univariate logistic regression analysis, piecemeal resection (odds ratio [OR] 7.067, 95% confidence interval [CI] 1.706-29.285, $P = 0.007$) and tumor-positive resection margin (OR 33.292, 95% CI 7.064-159.904, $P < 0.0001$) were significant risk factors for cancer recurrence after ER. However, there was no significant factor for recurrence in multivariate logistic regression analysis.
CONCLUSION: This study showed that piecemeal resection and tumor-positive resection margin were probable risk factors for recurrence after ER for EGC. Therefore, a study in a large number of patients and a longer period might show that piecemeal resection and tumor-positive resection margin are risk factors for recurrence.
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Disclosure of Interest: None declared

P1068 VESSEL PLUS SURFACE CLASSIFICATION SYSTEM OF MAGNIFYING-NARROW BAND IMAGING FOR PREDICTING PRESENCE CANCEROUS LESION AND OTHER PROGNOSTIC HISTOLOGIC FACTORS IN GASTRIC EPITHELIAL NEOPLASMS: A RETROSPECTIVE SINGLE CENTER STUDY

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INTRODUCTION: Although studies have addressed the predictive role of magnifying-narrow band imaging (MNBI) for gastric epithelial neoplasms, little is known of the relationship between MNBI indicators and histologic prognostic factors other than the presence of cancer.
AIMS & METHODS: We conducted this study to validate MNBI indicators for differential diagnosis of gastric neoplasms and as predictors for other prognostic histologic factors, using vessel plus surface classification system. The medical records of 171 consecutive gastric epithelial neoplasms which received MNBI before undergoing curative surgery or endoscopic treatment were retrospectively reviewed.
RESULTS: Irregular and absent microvascular pattern (MVP) ($p = 0.008$), absent microsurface pattern (MSP) ($p = 0.028$), presence of demarcation line (DL) ($p = 0.03$) and presence of irregular type white opaque substance (WOS) ($p = 0.015$), along with flat or depressed macroscopic morphology ($p < 0.001$), were significantly and independently correlated with presence of cancerous lesion. There was no significant difference in the AUC value prediction of cancer between MSP and MVP, while the AUC value of DL and WOS was lower than that of the MVP and MSP. Significant correlations were also evident between irregular or absent MVP, irregular WOS and submucosal cancer invasion. Absent MSP was independently correlated with presence of undifferentiated cancer and microscopic ulcer. Presence of irregular WOS was also significantly related with presence of LVI.
CONCLUSION: MNBI findings are valuable for predicting the presence of cancerous lesions, cancer differentiation, depth of cancer invasion, presence of microscopic ulcer and LVI.
Disclosure of Interest: None declared

P1069 RETROGRADE ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC NEOPLASM INVOLVING THE PYLORIC CHANNEL

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INTRODUCTION: Recently, successful resection of the pyloric tumors by endoscopic submucosal dissection (ESD) using retroflexion in the duodenum has been reported. However, the detailed dissection method of the procedure was not well defined yet. We also had done the retroflexion ESD of dissecting retrogradely from the duodenum to the pyloric channel of duodenal part, after then antegradely from the antrum to the pyloric channel. But, we introduced a new retroflexion method of retrogradely dissecting mucosa from duodenum to transpyloric antrum as extensively as possible since February 2012. We studied the feasibility and effectiveness of the new retrograde prepyloric antral dissection using retroflexion ESD.
AIMS & METHODS: 61 patients with gastric neoplasm involving the pyloric channel underwent ESD from January 2007 to March 2013. In 27 patients, the conventional anterograde ESD were performed without using the endoscope retroflexed in the duodenum. The other 34 patients were procedured by the retroflexion method. Among that 34, the latest 16 patients underwent the new retrograde trans-pyloric antral dissection method. We retrospectively analyzed the procedure times, en bloc rates, complete resection rates and complications associated with each different techniques.
RESULTS: In retroflexion ESD group ($N = 34$), the rate of en bloc resection was 97%, and the rate of complete resection was 96%. The conventional group ($N = 27$) shows relatively 89% and 88%. There were statically significant differences between the 2 procedure methods ($p = 0.01$, $p = 0.02$). But, procedure times had no statically significant (45min vs 33 min, $p = 0.10$). In newly attempted retrograde trans-pyloric antral dissection method group, en bloc resection rate was 100%, and the rate of complete resection was 94%. The average time of procedure was 42min. Compared with the previously procedured retroflexion

ESD, the new technique had an advantages of saving procedure time (42min vs 48min, p = 0.035). but there was no statically significant differences at En-block resection and complete resection (100% vs 94%, p = 0.054 / 94% vs 83%, p = 0.059). Major procedure-related complications consisting of perforation and major bleeding were not encountered in all cases.
CONCLUSION: This new retrograde trans-pyloric antral dissection method for resecting tumors involving the pyloric channel tumor is feasible and effective therapeutic ESD method. So it could be the standard treatment method in such cases, based on the favorable outcomes.
Disclosure of Interest: None declared

P1070 PERIOPERATIVE CHEMOTHERAPY IN ELDERLY PATIENTS WITH GASTRIC CARCINOMA: YES OR NO?

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INTRODUCTION: Perioperative chemotherapy (POC) is recommended for patients with advanced resectable gastric (GC) or esophagogastric junction (EGJ) carcinoma. However, its application in elderly patients could be limited due to comorbidities.
AIMS & METHODS: We intend to assess compliance, toxicity and survival in patients proposed to POC who are >70 years old. Among 418 patients with GC or EGJ carcinoma (February 2009 – June 2013), 148 were eligible for POC, of whom 54 were >70 years old (group 1) and 94 <70 years old (group 2). We evaluated clinical characteristics, Charlson comorbidity index (CCI), compliance and toxicity, resectability and survival. In our institution, patients who are >80 years old are excluded from POC. Statistics: chi2, t-Student, Kaplan Meier, Logrank (Stata 10).
RESULTS: Group 1: 54 patients (34 males, mean age 74 years, intestinal type adenocarcinoma 75.9%, diffuse carcinoma 24.1%. Mean CCI 7 (44 patients had >3 comorbidities). Out of 54 patients, 50 started pre-operative chemotherapy but 9 did not complete it (6 – treatment complications; 1 – disease progression; 1 – refusal; 1 – death). 45/50 (90%) patients were submitted to surgery (R0 – 35; R1 – 2; R2 – 1; unresectable disease – 1). Among 23 patients proposed to post-operative chemotherapy, 21 completed 3 cycles. Comparing both groups, 21/54 patients (39%) in group 1 completed POC vs 51/94 (54%) in group 2 (p = 0.1). In group 1, patients experienced more complications during pre-operative chemotherapy (major complications: 15/54 vs 11/94; p = 0.006), fewer patients were submitted to surgery (45/54 vs 94/94; p = 0.002) and started post-operative chemotherapy (22/54 vs 24/94; p = 0.036). However, recurrence and survival were not influenced by age (p = 0.8).
CONCLUSION: In patients with >70 years old, POC is associated with more risks. However, overall and disease free survival in this group is similar to the one observed in younger patients. Therefore, elderly patients should not be excluded from POC considering only their age.
Disclosure of Interest: None declared

P1071 SHOULD WE PERFORM PERIOPERATIVE CHEMOTHERAPY TO ALL PATIENTS WITH LOCALLY ADVANCED GASTRIC CANCER?

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INTRODUCTION: Perioperative chemotherapy (POC) is currently the gold-standard treatment of locally advanced gastric cancer, increasing in 10% the overall survival. Histopatological tumor regression (HTR) is an important objective parameter of response, being associated with a better outcome. However, in patients with limited response, surgery delay may compromise a curative treatment.
AIMS & METHODS: To evaluate in patients proposed to POC: 1) disease progression during POC; 2) HTR and its correlation with clinicopathological variables. 148 patients were proposed for POC and 2 for POC plus intraperitoneal chemotherapy. All surgical specimens were reviewed by two pathologists. HTR was defined by Becker's classification (Ia – no residual tumor; Ib – residual tumor: <10%; II – residual tumor: 10-50%); III – residual tumor: >50%) and correlated with clinicopathological variables and survival. Statistics: chi2, Kaplan-Meier, Logrank (Stata 10).
RESULTS: Among 150 patients, 143 were treated with POC (5 excluded due to disease progression). 135 of whom were submitted to surgery (no surgery: 1 – treatment complications; 4 – death due to chemotherapy; 2 – refusal; 1 – disease progression). Type of resection: R0 – 102; R1 – 5; R2 – 11; unresectable disease – 17. Therefore, disease progression was observed in 34 patients and complications / death in 5. HTR was evaluated in all patients submitted to resection: Ia = 11 (9.3%), Ib = 9 (7.6%), II = 30 (25.4%), III = 68 (57.6%). Besides early tumor staging (T = 1/2) (p = 0.008) no other variables (age, sex, differentiation degree, histologic subtype, tumor location) predicted HRT. All patients with palliative resections had partial (II) or minimal (III) HRT. Patients with Ia/Ib HTR showed less relapse rate (1/20 vs 26/87, p = 0.037) and better overall survival (88 vs 54%, p = 0.041).
CONCLUSION: We didńt find predictive variables of HRT and 39 patients (26%) could have been harmed due to delayed surgery. We admit that the benefit from POC is observed in a small group of patients. It is necessary to identify new markers of HTR which could help in the selection of patients who can really benefit from POC.
Disclosure of Interest: None declared

P1072 CLINICOPATHOLOGIC FEATURES OF TYPE 3 GASTRIC NEUROENDOCRINE TUMOR

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INTRODUCTION: Type 3 gastric neuroendocrine tumor (NET) is different from type 1 and type 2 gastric NET in view of management approach. The standard treatment of type 3 gastric NET is suggested as radical gastrectomy. Clinically endoscopic treatment has been tried. The aim of this study was to investigate clinicopathologic features of type 3 gastric NET according to the treatment modalities.
AIMS & METHODS: The Korean Society of Gastrointestinal Cancer has been conducting the Korean Gastroenteropancreatic Neuroendocrine Tumor Registry from 2012. This is a retrospective registry database of gastroenteropancreatic neuroendocrine tumor collected from 16 hospitals between 2002 and 2012. From the Registry, gastric NET patients with normal serum gastrin level (<100 pg/mL) were selected for analysis.
RESULTS: A total of 20 patients from 327 patients with gastric NET were classified as type 3 Gastric NET. The mean age was 55.5 ± 11.52 years. The mean tumor size was 1.08 ± 1.10 cm. According to the WHO 2010 classification, 14 (70%) patients had grade 1, and 5 (25%) patients had grade 2. Endoscopic treatment was performed in 13 (65%) patients, and surgery was performed in 6 (30%) patients. Endoscopic treatment group was younger than surgery group. T1 stage was more prevalent in endoscopic treatment group than in surgery group. After treatment, the median follow-up time was 10 months, during when there was no death related to NET, but there was one disease-progression in surgery group.
CONCLUSION: Clinically, Type 3 gastric NET has been frequently managed by endoscopy. However, proper evidence for endoscopic management should be further evaluated.
Disclosure of Interest: None declared

P1073 ASSESSMENT OF THE SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN VERY ELDERLY PATIENTS

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INTRODUCTION: Since endoscopic submucosal dissection (ESD) has been developed for en bloc resection of large superficial tumors, it is widely accepted as a reliable therapeutic procedure. This recent innovation allows safe treatment in elderly patients; however, there are only few reports of ESD in very elderly patients, aged 85 years old or above. This study aimed to assess the safety and feasibility of ESD in very elderly patients.
AIMS & METHODS: Between 2013 and 2014, patients with superficial gastrointestinal lesions at our institution were treated with ESD. A standard gastroscope (GIF-Q 260Z, Olympus) and a Dual knife (KD-650Q, Olympus) were used for ESD. All patients were treated under conscious sedation with midazolam (1-10mg). Patients were divided to an elderly group (60-84 years of age) and a very elderly group (85-92 years of age). For both groups, lesion sizes, procedure times, total amounts of midazolam, and ESD-related complications (hypotension, hypertension, hypoxia, arrhythmia, and bleeding) were analyzed.
RESULTS: From the database, we collected data on a total of 67 patients who underwent ESD for esophageal (5 cases), gastric (44 cases), and colorectal lesions (18 cases). In the elderly group, 49 patients were treated (35 males/ 14 females, 60- 84 years of age, mean age 78) and in the very elderly group, 19 patients were treated (4 males / 14 females, 85-92 years of age, mean age 87.9). All patients were successfully treated with ESD in both groups. The mean resected specimen size was 29.8 mm in the elderly group and 28.37 mm in the very elderly group (p = 0.8). ESD time was 79.5 minutes in the elderly group and 64.5 minutes in the very elderly group (p = 0.4). Midazolam doses of 6.7mg and 3.9 mg were administered (p < 0.01), and the complication rate was 12.0% and 57.9% (p < 0.01), in the same groups, respectively. Complications were 1 event of hypotension, 1 of hypertension, 4 of hypoxia, and 3 of bleeding in the elderly group, and 4 of hypotension, 1 of hypertension, 6 of hypoxia, and 0 of bleeding in the very elderly group. Based on the final pathological results, there were 2 cases on whom additional gastrectomy was performed, and 1 case of radiation in the

elderly group; and no additional therapy was performed in the very elderly group.
CONCLUSION: Our data suggests that ESD is safe and feasible in very elderly patients; however, such patients tended to be more sensitive to sedation. Our data also suggests that general anesthesia might not necessary for elderly and very elderly patients undergoing ESD, as long as there is intraoperative management. Further investigations to evaluate various other factors including past medical history, performance status, and anticoagulant medicine are necessary.
Disclosure of Interest: None declared

P1074 PREVALENCE OF GASTRIC PRECANCEROUS LESIONS AMONG CHRONIC DYSPEPTIC PATIENTS AND RELATED COMMON RISK FACTORS

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INTRODUCTION: Gastric cancer is one of the leading causes of cancer-related deaths worldwide. Progression of gastric cancer follows a several steps from gastritis to atrophy, intestinal metaplasia, dysplasia, and finally cancer.
AIMS & METHODS: To determine the prevalance of precancerous gastric cancer lesions and related common risk factors in our area.
A total of 688 Iranian chronic dyspeptic patients over the age of 40 years were enrolled. The exclusion criteria were pregnancy, history of gastric cancer and gastric surgery. A questionnaire including demographic and clinical data, smoking habits, alcohol use, NSAIDs and regular aspirin use was completed for all subjects. Upper endoscopy was done for all of participants and biopsies were taken according to biopsy protocol. The specimens were studied by two expert GI pathologists blindly.
RESULTS: The prevalence of intestinal methaplasia, gastric atrophy, and dysplasia were 19.8%, 12.8%, and 3.2%, respectively. The mean age of participants was 57.87±9.10. Positive *H.pylori* infection was 64.5%. Age and *H.pylori* infection had a significant association with pathological findings with OR = 3.10, P < 0.01, 95%CI: 1.91-4.72 and OR = 1.03, P < 0.01, 95%CI: 1.03-1.07 respectively. Male gender also had an association with gastric atrophy (OR = 1.57, 95% CI = 1.00-2.46).
CONCLUSION: According to high prevalence of precancerous lesions in patients with chronic dyspepsia over 40 years old, upper endoscopy and gastric mapping sampling for detection of these lesions is recommended in intermediate to high risk areas.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
H. PYLORI II – POSTER EXHIBITION – HALL XL

P1075 CAGA+, VACAS1M2 +, AND HPAA+ *H. PYLORI* STRAINS PROMOTES TH-17 DRIVEN INTESTINAL METAPLASIA IN *H. PYLORI*-INFECTED PATIENTS

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INTRODUCTION: Helicobacter pylori (*H.pylori*) is a gram-negative bacterium that colonizes the stomach of more than half of the world's population during their life span. *H.pylori* infection can cause peptic ulcer, chronic gastritis, mucosa-associated lymphoid tissue (MALT) lymphomas in 20 % of infected individuals. *H.pylori*-induced diseases can be associated with virulence factors of bacteria, host genetic factors and immune response. Virulence factors with potential value for specific pathologies are the cytotoxin associated gene A (cag A), vacuolating cytotoxin A (vacA), outer inflammatory protein A (oipA), the blood group antigen binding adhesin gene A (babA), and the putative neuraminyllactose-binding hemagglutinin homolog (hpaA). *H.pylori* infection induces T helper 1 (Th1) & T helper 17 (Th17) driven immune response in patients.
AIMS & METHODS: The aim of this study was to investigate the correlation of *H.pylori*- induced gastric pathologies with various H.pylor virulence factors and T cell response. Eighty consecutive *H.pylorii* positive endoscopy patients were included in the study. Mucosal biopsy samples were obtained from corpus and antrum parts of the stomach during endoscopy. All samples were tested for various *H.pylori* virulence factors using multiplex polymerase chain reaction (Multiplex-PCR) including cagA, vacA (s1,s2;m1,m2), hpaA, oipA, babA. Also, IFN-g (Th1) and IL-17 (Th17) mRNA expression levels of patients were measured using Quantitative RT-PCR.
RESULTS: Our study group consisted of 43 women and 37 men, mean age was 35 years (range 16-65 y). Twenty-three out of 80 *H.pylori* positive patients also had peptic ulcer. The majority of *H.pylori* strains are positive for hpaA (82% of ulcer, 75% of nonulcer patients) and vacA s1, m2 (52% of ulcer, 73% of nonulcer patients) but negative for oipA and babA. Also, the vast majority of the *H.pylori* strains isolated from nonulcer patients were cagA positive (61%). However, 56% of peptic ulcer patients carry cag A negative *H.pylori* strains. Eleven out of the 80 patients had intestinal metaplasia also (4 of 11 were peptic ulcer patients). All *H.pylori* strains isolated from ulcer and non-ulcer patients with intestinal metaplasia are positive for vacA s1/m2 genotype. All patients with the peptic ulcer and 71% of the nonulcer with intestinal metaplasia patients positive for hpa A. Also the *H.pylori* hpaA positive strains are negative for babA. Additionally, *H.pylori* infected patients are showing mainly a Th17 response (for ulcer 75%, for nonulcer 60 %) instead of Th1 response (for ulcer 25%, for nonulcer 40 %).
CONCLUSION: Overall our data suggests that patients infected with *H.pylori* strains positive for cagA, vacAs1m2, and HpaA are at higher risk for developing Th17- driven intestinal metaplasia.
Disclosure of Interest: None declared

P1076 THE RELATIONSHIP BETWEEN THE DENSITY OF HELICOBACTER PYLORI COLONIZATION AND THE DEGREE OF GASTRITIS SEVERITY

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INTRODUCTION: Helicobacter pylori (*H. pylori*) is a major factor in determining the risk for development of gastric adenocarcinoma through the intermediate steps of atrophic gastritis and intestinal metaplasia. Because *H. pylori* infection is highly prevalent in asymptomatic populations and only a few people develop cancer, additional factors may influence the risk for development of cancer and preneoplastic lesions, once infection is established.
AIMS & METHODS: The aim of this study is to examine the relationship between the density of *H. pylori* colonization in gastric mucosa and the degree of severity of certain histologic parameters of gastritis, such as inflammation activity, atrophy and intestinal mataplasia.
Upper gastrointestinal endoscopy was performed in 410 *H. pylori* positive patients. Status and semiquantitative assessment of *H. pylori* was determined by histology. Gastric biopsies were examined under hematoxylin and eosin and Giemsa stains. Density of *H. pylori* colonization, activity of gastritis, gastric atrophy and intestinal metaplasia at different parts of stomach were graded according to Updated Sydney system.
RESULTS: There were 410 *H. pylori* positive patients (214 males and 196 females), whose age ranged from 18 to 90 years (mean age = 46 years).
The density of *H. pylori* was mild in 30.2%, moderate in 51.5%, and marked in 18.3% of cases.
The results of the study showed that along with the increase of density of *H. pylori* colonization there was a tendency of increasing the gastritis severity:

	Mild density of *H. pylori*	Moderate density of *H. pylori*	Marked density of *H. pylori*	p
Active gastritis	58.1%	70.1%	88%	**$p < 0.01$**
Gastric atrophy	26.6%	33.2%	42.7%	**$p < 0.01$**
Intestinal metaplasia	7.3%	10%	14.7%	$p < 0.1$

CONCLUSION: It can be concluded that a marked density of *H. pylori* colonization significantly increases the gastritis severity.
Disclosure of Interest: None declared

P1077 PREVENTION OF LARGE INTESTINE DYSBIOSIS IN THE PATIENTS WITH DUODENAL ULCER ASSOCIATED WITH HELICOBACTER PYLORI

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INTRODUCTION: To study efficacy of eradication therapy and inclusion of Enterojermin as prevention of intestine dysbiosis in the patients with gastroduodenal ulcer disease in association with the Helicobacter pylori.
AIMS & METHODS: In the investigation there were participated 64 patients with ulcer disease of duodenum associated with *H.pylori*. The patients were randomly divided into 2 groups by 32 patients in each group. Group 1 received three-component therapy in the complex with Enterojermin 1 bottle 3 times a day for 14 days. Diagnosis was verified by endoscopy findings. In order to study the state of microbiocenosis of the large intestine the microbiological examination of the feces was performed in the patients before and after treatment.
Group 2 received only three-component therapy with inclusion of IPP pantoprasol (Kontrolok) and 2 antibiotics during 14 days.
RESULTS: The standard three-component scheme of eradication on the basis of kontrolok and two antibiotics seem to be effective in relation to the scarring of the ulcer defect (96.6%), however, exactly in this group of patients to the end of treatment, by data of bacteriological feces cultivation there was noted dysbiosis of stage 3, while by the results of the same data in patients from group 2 who additionally received enterojermin the ulcer scarring was achieved in 97.2% of patients without changes of the state of microbiocenosis of the large intestine.
CONCLUSION: The results of investigations performed showed, that inclusion of the Enterojermin into the complex of eradication therapy of the duodenal ulcer associated with *H.pylori* resulted in attenuation of the undesirable actions of the used antibiotics which effected on the obligatory flora of the large intestine.
Disclosure of Interest: None declared

P1078 A RAPID AND ACCURATE METHOD TO EVALUATE HELICOBACTER PYLORI INFECTION, CLARITHROMYCIN RESISTANCE AND CYP2C19 GENOTYPES SIMULTANEOUSLY FROM GASTRIC JUICE

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INTRODUCTION: Because *Helicobacter pylori* (*H.pylori)* can cause carcinogenesis of the stomach, we need sufficient information for deciding on an appropriate strategy of eradication. Many factors affect the efficacy of eradication including antimicrobial resistance (especially clarithromycin resistance) and *CYP2C19* polymorphism. This study was to survey the efficiency of gastric juice for detecting the clarithromycin resistance and CYP2C19 polymorphism.
AIMS & METHODS: The specimens of gastric juice were collected from all patients while receive gastroendoscopy. DNA was extracted from gastric juice and then *urease A* and *cag A* were amplified by polymerase chain reaction (PCR) for detecting the existence of *H.pylori*. By PCR-RFLP, the *23S rRNA* of *H.pylori* and *CYP2C19* genotypes of host were examined, respectively. During endoscopy examination, biopsy-based specimens were also collected for rapid urease test, culture and histology. The blood samples were also collected for analysis of *CYP2C19* genotypes. We compared the results of gastric juice tests with the results of traditional clinical tests.
RESULTS: Our results showed that the sensitivity(SEN), specificity(SPE), positive predictive value(PPV), negative predictive value(NPV) and accuracy(ACC) of gastric juice test to detect *H.pylori* infection were 92.1%(105/114), 92.9%(143/154), 90.5%(105/116), 94.1%(143/152) and 92.5%(248/268) respectively. The SEN, SPE, PPV and NPV to detect clarithromycin resistance were 97.3% (36/37), 91.5% (43/47), 90.0%(36/40) and 97.7%(43/44) respectively. By using PCR-RFLP, the consistency of human *CYP2C19* gene polymorphism from blood samples and gastric juice was as high as 94.9%(149/157).
CONCLUSION: The manipulated gastric juice is actually an effective diagnostic sample for evaluation of *H.pylori* existence, clarithromycin resistance, and host *CYP2C19* polymorphism.
Disclosure of Interest: None declared

P1079 HIGH RESOLUTION MELT CURVE ASSAY FOR THE DETECTION OF POINT MUTATIONS ASSOCIATED WITH CLARITHROMYCIN RESISTANCE IN HELICOBACTER PYLORI

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INTRODUCTION: Clarithromycin is used in the first line treatment of *Helicobacter pylori* (HP) infection and therefore, the prevalence of HP resistance to clarithromycin is increasing continuously. Clarithromycin resistance, the major cause of HP treatment failure, is attributed to three point mutations (PM): A2142C, A2142G and A2143G within the peptidyl-transferase region of the 23S rRNA gene.
AIMS & METHODS: To develop a fast and accurate method for the detection of the three mutations mentioned previously, from HP isolates. A total of 85 HP isolates, previously obtained from patients with general gastric discomfort, were analyzed using a high resolution melt (HRM) curve analysis. The isolates were compared to 4 reference plasmids that incorporate the three mutations and the wild type (WT) sequences.
RESULTS: There was a perfect correlation between the HRM results and the 85 positive isolates – all were positive using the HRM analysis. Of the 85 isolates, 18 had a WT sequence (21.2%), and 67 (78.8%) contained a 23S rRNA PM. Of the 67 isolates that include 23S rRNA PM, 18 had an A2142G PM sequence (26.8%), 22 had an A2142C PM sequence (32.8%) and 27 had an A2143G PM sequence (40.4%).
CONCLUSION: Our developed HRM assay has a perfect correspondence in its accuracy to other detection methods, including HP isolation. It serves as an option for detecting Clarithromycin resistance prior to administration of HP eradication therapy.
Disclosure of Interest: None declared

P1080 STABILITY OF 13CO2 BREATH TESTS SAMPLES OVER TIME IN THE DIAGNOSIS OF HELICOBACTER PYLORI

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INTRODUCTION: The accuracy and repeatability of breath test in the diagnosis of *Helicobacter pylori* (HP) infection is debatable. Although it has been shown that storage for long periods does not affect the analysis results, no data are available, on the effect of repetitive testing.
AIMS & METHODS: To evaluate the repeatability of the analysis of the breath samples. A total of 202 breath samples were collected in duplicates, before and after administration of 75 mg urea-^{13}C dissolved in 50 ml of orange juice and the results were expressed as delta $^{13}CO_2$ ($d^{13}CO_2$). The cut-off value was 3.5 parts per thousand. Each sample was analyzed in a mass spectrometer 7 days after collection and in intervals of 7 days for the duration of additional 3 weeks. The precision calculation was based on the comparison of the $d^{13}CO_2$ obtained in the three consecutive weeks following the first run to the $d^{13}CO_2$ obtained in the first run. The samples were stored at room temperature.
RESULTS: In the second run, 200 out of the 202 (99%) samples were tested positive for HP and the precision of the $d^{13}CO_2$ was 98.6%. In the third run, 197 out of the 202 (97.52%) samples tested positive and the precision was 99.2%. In the fourth and final run 196 out of the 202 (97%) samples tested positive and the precision was 96.7%.
CONCLUSION: We conclude that short term storage of 1 month, does not affect sample stability and the results of HP diagnosis for up to three consecutive repeats.
Disclosure of Interest: None declared

P1081 HIGH PREVALENCE OF MULTI-DRUG RESISTANCE IN *H. PYLORI* ISOLATES IN 1001 TREATED NAÏVE PATIENTS

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INTRODUCTION: Antibiotic resistant strains of H pylori have been increasing worldwide, and it has been speculated that this may account for progressive decrease in eradication rates reported in the literature.
AIMS & METHODS: To assess the prevalence of resistant strains to metronidazole, clarithromycin, and levofloxacin in a cohort of treatment naïve patients undergoing EGDS for dyspeptic symptoms in Italy. 1065 *H.pylori* infected patients who had never been treated for H pylori (median age: 51 years; IQR: 39 and 62 years) underwent upper endoscopy and a biopsy sample was also obtained to perform culture and an *in vitro* antimicrobial susceptibility testing. According to EUCAST 2012 guidelines, susceptibility testing was performed by epsilometer test (Etest) and the following MIC breakpoints were used: resistance to clarithromycin (>0.5 microgram/ml); resistance to metronidazole (>8 microgram/ml), and resistance to levofloxacin (>1 microgram/ml).
RESULTS: Data on resistance were available for 1001 out of 1065 (93.9%) patients. Resistance to metronidazole was found in 38.3%; to clarithromycin in 32.7%; and to levofloxacin in 23.7% of the strains. Double resistance to clarithromycin + metronidazole was found in 10.4%; to clarithromycin + levofloxacin in 2.8%; and to metronidazole + levofloxacin in 5.6% whilst 10.4% of the strains were resistant to metronidazole + clarithromycin + levofloxacin. Female sex was found to be an independent factor of both metronidazole resistance (OR: 2.5, 95% CI = 1.9-3.3; p = 0.0001) and double resistance to metronidazole and clarithromycin (OR: 2.5, 95% CI = 1.5−4.0; p = 0.0001). Similarly, an association with single metronidazole and clarithromycin resistance was found among non-Italian patients (OR: 2.0, 95% CI = 1.4−3.0; p = 0.0001 and OR: 1.8, 95% CI = 1.2- 2.6, p = 0.003 respectively). Smoking, alcohol consumption, and BMI were not significant risk factors.

Resistance	%
ClaR (overall)	32.7
MetroR (overall)	38.3
LevoR (overall)	23.7
ClaR + MetroR	10.4
ClaR + LevoR	2.8
MetroR + LevoR	5.6
ClaR + MetroR + LevoR	10.4

CONCLUSION: 1. Single and multiple-drug resistant strains are widely prevalent in patients who have never been treated for H pylori. 2. First line therapies for H pylori need to account for these changes because failure rates for clarithromycin based therapy will increase further 3. Levofloxacin based triple therapies are unlikely to represent an alternative front-line therapy as the resistance rates are already quite high.
Disclosure of Interest: V. Castelli: None declared, J. M. Bland: None declared, G. Fiorini: None declared, N. Vakil Consultancy for: Astra Zeneca, Takeda, Shareholder of: Meridian Diagnostic, Orexo, I. M. Saracino: None declared, C. Zaccaro: None declared, C. Ricci: None declared, A. Zullo: None declared, L. Gatta: None declared, D. Vaira: None declared

P1082 THE MEANING OF THE BORDERLINE RANGE OF THE 13C-UBT VALUE AFTER HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: The ^{13}C-urea breath test (^{13}C-UBT) (UBiTkit; Otsuka Pharmaceutical, Tokyo, Japan) is a reliable non-invasive method for diagnosing *Helicobacter pylori* (*H. pylori*) infection. However, in some range of ^{13}C-UBT value, the accuracy is doubtful after eradication of *H. pylori* infection.
AIMS & METHODS: In this study, we evaluated the diagnostic accuracy of the ^{13}C-UBT value ranging from 2.0‰ to 3.0‰ and affecting factors were evaluated. Among 820 patients who showed the result of the ^{13}C-UBT value from 2.0‰ to 3.0‰, one hundred seventy one patients were compared with the results of endoscopic biopsy-based methods (modified Giemsa study, CLOtest, and culture) from antrum as well as body for two years or more endoscopic surveillance. In addition, the possible affecting factors such as age, gender, underlying disease, history of gastrectomy, number of eradications, and histological atrophy and intestinal metaplasia were analyzed.
RESULTS: Of 91 and 80 patients who showed ^{13}C-UBT positive and negative results after *H. pylori* eradication, 38 patients (41.8%) and 2 patients (2.5%) were proved false positive and false negative results by biopsy-based methods evaluation, respectively. The sensitivity, specificity, false positive rate, and false negative rate of ^{13}C-UBT were 96.4%, 67.2%, 33.8%, and 3.6%. The positive predictive value and negative predictive value were 58.2% and 97.5%. The positive likelihood ratio and negative likelihood ratio is 2.85 and 0.05. In multivariate analysis (Table 1), moderate to severe intestinal metaplasia (OR = 1.953, 95%CI = 1.208-3.159, p = 0.006) and two or more trial of treatment for *H. pylori* (OR = 2.482, 95%CI = 1.109-5.555, p = 0.027) were significantly related false positive result of ^{13}C-UBT value after *H. pylori* eradication.
Table 1. The risk factors of false positive results for ^{13}C-Urea breath test

	Final UBT result		Univariate p-value	Multivariate p-value
	Positive	False positive		
Gender (Male:Female)	30(56.6%)/ 23(43.4%)	24(63.2%)/ 14(36.8%)	NS	
Age (≥ 60 years old)	23 (43.4%)	18 (47.4%)	NS	
Diabetes mellitus	6 (11.38%)	3 (7.9%)	NS	
Hypertension	11 (20.8%)	7 (18.4%)	NS	
History of gastrectomy	12 (22.6%)	8 (21.1%)	NS	
The number of eradication for *Helicobacter pylori* (Once / Two or more)	40(75.5%)/ 13(24.5%)	19(50.0%)/ 19(50%)	0.034	0.027
The degree of gastric mucosal atrophy (None to mild/moderate to severe)	49(92.4%)/ 4(7.5%)	31(81.6%)/ 7(18.4%)	NS	
The degree of gastric intestinal metaplasia (None to mild/moderate to severe)	44 (83.0%)/ 9(17.0%)	21(55.3%)/ 17(44.7%)	0.015	0.006

CONCLUSION: In the range of ^{13}C-UBT value from 2.5‰ to 3.0‰, false positive was found to be increased in this study. In this case endoscopic surveillance with biopsy based evaluation would be helpful to avoid unnecessary additional treatment for *H. pylori* infection.
Disclosure of Interest: None declared

P1083 THE EFFECTS OF N-ACETYLCYSTEINE ON FIRST-LINE 10-DAY SEQUENTIAL THERAPY FOR HELICOBACTER PYLORI INFECTION: A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: There have been a few reports suggesting that N-acetylcysteine (NAC) which is mucolytic and antioxidant could destroy biofilm formed by *Helicobacter pylori* (*H. pylori*). The aim of this study was to identify whether the addition of NAC on first-line sequential therapy for *H. pylori* infection could improve the eradication rate.
AIMS & METHODS: Ninety nine patients with *H. pylori* infection were randomly assigned to receive either sequential therapy with (study group, n = 49) or without (control group, n = 50) NAC. Sequential therapy consisted of rabeprazole 20mg and amoxicillin 1g for the first 5 days, followed by rabeprazole 20mg, clarithromycin 500mg and metronidazole 500mg for the remaining 5 days; all drugs are given twice daily. For study group, NAC 400mg b.i.d. was added for the first 5 days of sequential therapy. Four weeks after completing therapy, *H. pylori* eradication was evaluated by the ^{13}C-urea breath test, histology, or the rapid urease test. The eradication rate, drug compliance, and adverse event rates were compared between the two groups.
RESULTS: The eradication rates by intention-to-treat analysis were 58.0% (29/50) and 67.3% (33/49) in the control group and the study group, respectively ($P = 0.336$). The eradication rates by per-protocol analysis after excluding16.2% of patients who were lost to follow-up were 70.0% (28/40) and 80.5% (33/41) in the control group and the study group, respectively ($P = 0.274$). Compliance was very good in the both groups (control/study group: 95.2%/100%). The adverse event rates were 26.2% (11/42) and 26.8% (11/41) in the control group and the study group, respectively ($P = 0.947$).
CONCLUSION: The addition of NAC to first-line sequential therapy for *H. pylori* infection resulted in an approximately 10% increase in eradication rate. However, this feature did not reach statistical significance, indicating that larger trials are needed.
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Disclosure of Interest: None declared

P1084 THE EFFECT OF MOXIFLOXACIN CONTAINING TRIPLE THERAPY AS SECOND-LINE TREATMENT FOR HELICOBACTER PYLORI ERADICATION INFECTION

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INTRODUCTION: The aim of this study was to evaluate the efficacy of a moxifloxacin-containing triple therapy as second-line treatment for *Helicobacter pylori* infection. We investigated the value of triple therapy with rabeprazole, moxifloxacin, and amoxicillin in second-line treatment and the impact of treatment of treatment duration on eradication success.
AIMS & METHODS: Between 2011 and 2013, one hundred and thirty-three patients who had failed first-line proton pump inhibitor-based triple therapy were randomized to oral rabeprazole (20 mg b.i.d.), axoxicillin (1000 mg b.i.d.), and moxifloxacin (400 mg q.d.) for either 7 (RAM-7 group, n = 52) or 14 days (RAM-14 group, n = 81). The eradication was compared by confirming of eradication rate. *H. pylori* status was evaluated by histologic finding, Campylobacter-like organism test and ^{13}C urea breath test. Antibiotic susceptibility test for *H. pylori* was not done in all cases.
RESULTS: The eradication rates by intention-to-treat analysis were 69.2% (36/52) and 81.4% (66/81) in the RAM-7 group and the RAM-14 group, respectively (p = 0.031). The eradication rates by per-protocol analysis after excluding 8.4% of patients who were lost to follow-up were 73.5% (36/49) and 90.4% (66/73) in the RAM-7 group and the RAM-14 group, respectively (p = 0.013). Compliance was very good in the both groups (RAM-7/RAM-14 group: 100%/100%). The adverse event rates were 26.5% (13/49) and 20.5% (15/73) in the RAM-7 group and the RAM-14 group, respectively (p = 0.441). There was no significant difference in the 1st-line treatment, previous ulcer history, smoking, alcohol, and endoscopic finding between RAM-7 and RAM-14 group.
CONCLUSION: Second-line *H.pylori* eradication therapy with rabeprazole, amoxicillin, and moxifloxacin is very effective and well tolerated. Fourteen days of treatment significantly showed lower adverse event rates (20.5% vs 26.5%) and higher eradication rates (90.4% vs 73.5%, p = 0.013) than seven days of treatment. Compliance was very good in both groups (100%).
Disclosure of Interest: None declared

P1085 OPTIMIZED TRIPLE AND CONCOMITANT THERAPY FOR *H. PYLORI* INFECTION: THE OPTRICON STUDY

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INTRODUCTION: Triple therapy for *H. pylori* infection is discouraged when clarithromycin resistance rate is > 15-20%. Despite increasing antimicrobial resistance, triple therapy keeps on being the most prescribed eradication therapy, almost always on an empirical basis (this is, with unknown resistance rates). In this context, it remains unknown whether a non-bismuth quadruple concomitant therapy may be a preferable choice as empiric first-line eradication therapy.
AIMS & METHODS: To compare the effectiveness and safety of two optimized triple and concomitant quadruple therapies for *H. pylori* empiric treatment. Prospective multicenter study in 16 Spanish hospitals in which triple therapy was the first-line eradication regimen in clinical practice. In a first 3-month phase, patients received an optimized triple therapy, defined by esomeprazole (40 mg/12h), amoxicillin (1 g/12h) and clarithromycin (500 mg/12h) for 14 days. Over the second 3-month phase, patients received an optimized concomitant treatment, which consisted of an optimized triple therapy plus metronidazole (500 mg/12h) for 14 days.
RESULTS: 658 consecutive patients have been included so far (360 triple, 298 concomitant). Mean age 50 years, 58% females, 21% smokers, and 26% peptic ulcer. Intention-to-treat eradication rates were 82.6% (95%CI = 79-87%) and 91.2% (88-96%) for triple and concomitant therapy (p = 0.008). Respective per-protocol rates were 83% (79-88%) and 93.7% (89-96%) (p = 0.003). Compliance was 92% for both therapies. Adverse events (AEs) were reported in 54% of patients (triple 42% vs. concomitant 61%, p < 0.001). The most common AEs were metallic taste (46%), diarrhea (18%) and nausea (11%), with significant differences (p < 0.05) between therapies. Concomitant therapy achieved good eradication rates (> 90%) in a higher proportion of centers (64% vs. 35%) and triple therapy led to unacceptable cure rates (<80%) in a higher proportion of centers (41% vs. 14%).
CONCLUSION: On an empiric basis, an optimized non-bismuth quadruple therapy achieved significantly higher cure rates (>90%) when compared to an optimized triple therapy. Addition of metronidazole to an optimized triple therapy increased eradication rates by 10%, resulting in a higher rate of adverse events but withouth impairing compliance. An optimized triple therapy achieved unacceptable cure rates in 41% of participating centers, so concomitant therapy should be the choice for empiric eradication in clinical practice.
Disclosure of Interest: None declared

P1086 SECOND-LINE RESCUE THERAPY WITH LEVOFLOXACIN AFTER FAILURE OF TREATMENT TO ERADICATE HELICOBACTER PYLORI INFECTION: TIME TRENDS IN A SPANISH MULTICENTER STUDY OF 1,400 PATIENTS

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INTRODUCTION: Second-line bismuth-containing quadruple therapy is complex and frequently induces adverse effects. A triple rescue regimen containing levofloxacin is a potential alternative; however, resistance to quinolones is rapidly increasing.
AIMS & METHODS: AIM: To evaluate the efficacy and tolerability of a second-line triple regimen containing levofloxacin in patients whose *Helicobacter pylori* eradication treatment failed and to assess whether the efficacy of the regimen decreases with time.
METHODS: *Design:* Prospective multicenter study. *Patients*: Patients in whom treatment with a regimen comprising a proton pump inhibitor (PPI), clarithromycin, and amoxicillin had failed. *Intervention:* Levofloxacin (500 mg b.i.d.), amoxicillin (1 g b.i.d.), and PPI (standard dose b.i.d.) for 10 days. *Outcome*: Eradication was confirmed using the ^{13}C-urea-breath test 4-8 weeks after therapy. *Compliance/tolerance:* Compliance was determined through questioning and recovery of empty medication envelopes. Incidence of adverse effects was evaluated by means of a questionnaire.
RESULTS: The study sample comprised 1,400 consecutive patients (mean age 49 years, 49% males, 28% peptic ulcer and 72% with functional or non-investigated dyspepsia), of whom 96% took all medications correctly. Per-protocol and intention-to-treat eradication rates were 74.6% (95% CI, 72-77%) and 73.4% (71-76%). Efficacy (intention-to-treat) was 76% in the year 2006, 68% in 2007, 70% in 2008, 76% in 2009, 73% in 2010, 71% in 2011, 75% in 2012, and 76% in 2013. In the multivariate analysis, none of the studied variables (including diagnosis and year of treatment) were associated with success of eradication. Adverse effects were reported in 19% of patients, most commonly nausea, metallic taste, myalgia, abdominal pain, diarrhea and aphthous stomatitis. In 9 cases, the adverse effects were classified as "intense" (nausea, metallic taste and myalgia), but none of them was severe.
CONCLUSION: Ten-day levofloxacin-containing therapy is an encouraging second-line strategy, providing a safe and simple alternative to quadruple therapy in patients whose previous standard triple therapy has failed. The efficacy of this regimen remains stable with time.
Disclosure of Interest: None declared

P1088 THE ULTIMATE ERADICATION RATE OF *H. PYLORI* AFTER 1ST, 2ND OR 3RD LINE THERAPY IN KOREA

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INTRODUCTION: The resistance rates of *H. pylori* to clarithromycin, metronidazole and quinolone are known to be over 20% at the tertiary hospital in S. Korea.
AIMS & METHODS: The aim of this study was to evaluate the ultimate eradication rate of *H. pylori* after 1st, 2nd or 3rd line therapy and to compare the efficacy of each treatment regimen at the tertiary institute in Korea. 2,444 patients infected with *H. pylori* were prospectively treated with proton pump inhibitor (PPI)-based triple therapy for 7 days. In case of treatment failure or recurrence, moxifloxacin-based triple therapy (MNA) or bismuth-based quadruple therapy (QUAD) was randomly given. When the 2nd-line treatment failed or *H. pylori* recurred, the unused MNA or QUAD was used as a third-line treatment.
RESULTS: The intention-to-treat (ITT) and per-protocol (PP) rates of 'final' eradication up to 3rd line treatment were 69.1% and 92.1%, respectively. In detail, six-hundred eleven patients (25% of total population) were lost to follow up or refused further treatment at certain time during specific treatment plan. For the patients with 1st-line treatment failure (n = 415), the eradication rates (ITT/PP) with 2nd-line treatment were 49.9%/74.4%. There was no significant difference in the efficacy between MNA and QUAD as 2nd line treatment (p = 0.862/0.480, as ITT/PP, respectively). The 'final' eradication rates (ITT/PP) of recurred patients after the 1st line treatment (n = 63, mean interval from 1st line to recurrence: 26.9±19 mos) were 84.1%/94.1%.
CONCLUSION: The final PP eradication rate was relatively high, 92.1% at the tertiary hospital in Korea in spite of high antibiotic resistance rates. However, high rate of refusal of further treatment and follow-up loss made ITT eradication rate low. There should be strategy to raise the treatment adherence.
Disclosure of Interest: None declared

P1089 PREVALENCE OF ACTIVE *H. PYLORI* INFECTION AND CLARITHROMYCIN-CONTAINING TRIPLE THERAPY EFFICACY IN PATIENTS WITH DYSPEPSIA - EXPERIENCE OF A TERTIARY CENTRE IN NORTH OF ITALY

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INTRODUCTION: *H. pylori* (Hp) infection affects almost 50% of the world population, and it is recognized as first grade risk factor for gastric cancer. Moreover, it is commonly considered a potential cause of dyspepsia and peptic ulcer. In European populations, without alarm signs, the test-and-treat strategy is usually preferred rather than other invasive investigations. Clarithromycin-containing triple therapy is considered the first line treatment. However, several warnings about the reduction of its efficacy has been published in the last years.
AIMS & METHODS: To assess the prevalence of active Hp infection in patients with dyspepsia and the eradication rate of the clarithromycin-based triple therapy.
We retrospectively evaluated the presence of active Hp infection in consecutive patients undergoing urea breath test (UBT) because of dyspepsia (i.e. epigastric pain, bloating, nausea, early satiety, post-prandial fullness, belching) without alarm signs and family history of gastric cancer. Patients were asked to stop proton pump inhibitors or antibiotics at least 15 days prior to testing. All the tests were performed directly at our Department, by specialized nurses, after an overnight fast, with the same kit (Sofar, Milano, Italy). Two basal breath samples and two breath samples 30 min after the ingestion of labelled urea diluted in acidic solution, were collected from every patients.
RESULTS: From July 2010 to July 2012, 3000 patients referred to our ambulatory (1881F/1119M; mean age 54, 6-92) because of dyspeptic symptoms. Prevalence of active H pylori infection was 32.1% (963). The prevalence per age-related decades was: 26%(<20yy), 33%(21-30), 34%(31-40; 41-50; 51-60), 33% (61-70), 32%(71-80; >80yy) [p = n.s.]. Prevalence was higher in women 33.7% (n = 634) than in men 29.4% (n = 329), but this tendency failed to reach statistical significance [p = 0.07]. No differences in terms of age were found between male and female Hp-positive patients (n.s). One hundred and forty-five patients (10.9%) were originally from South-America (111F/703M; mean age 41, 10-76) and younger than Italian patients [p < 0.001]. Higher UBT values were positively related with female sex (r2:0.01; p < 0.01). Only 789 (82%) positive patients returned after the first treatment attempt and 31%

(n = 244) had a second positive test, but no differences in terms of age, sex and ethnic group were found.
CONCLUSION: In our population, the prevalence of active *H. pylori* infection in patients with dyspepsia was similar to that reported by previous analysis in the general Italian population. Nevertheless, we found a dramatic low eradication rate achieved by using clarithromycin-containing triple therapy, thus confirming the worrisome reports of recent studies.
Disclosure of Interest: None declared

P1090 DIFFERENT ANTIBIOTIC SUSCEPTIBILITY BETWEEN ANTRUM AND CORPUS OF THE STOMACH, A POSSIBLE REASON FOR TREATMENT FAILURE OF HELICOBACTER PYLORI INFECTION

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INTRODUCTION: *H. pylori* eradication rates with standard triple therapy show a constant decrease, mainly due to increasing antibiotic resistance. Antibiotic susceptibility guided therapy is recommended in patients receiving rescue therapy. So far, there are no reports whether only one biopsy from one anatomic site of the stomach is sufficient to detect antibiotic resistant *H. pylori* strains.
AIMS & METHODS: Aim: We assessed whether antibiotic resistance varies between the antrum and corpus of the stomach of patients that are either *H. pylori* therapy-naive or pre-treated.
Methods: *H. pylori* strains were isolated from antrum and corpus biopsies from 66 patients that underwent gastroscopy for different clinical indications. Susceptibility to commonly used antibiotics for *H. pylori* treatment was determined by Etest.
RESULTS: Primary, secondary and tertiary resistance to clarithromycin was 6.9%, 53.8% and 83.3%, retrospectively. Metronidazole and levofloxacin resistance also increased according to the number of previous treatments (17.2%, 69.2%, 83.3%; 13.8%, 23.1%, 33.3%). Tertiary resistance to rifabutin was detected in 12.5% of patients. Discordant antibiotic susceptibility between antrum and corpus isolates for different antibiotics was seen in 15.2% of the patients. DNA fingerprinting analysis revealed no substantial differences among DNA patterns between antrum and corpus isolates in the majority of patients suggesting an infection with a single *H. pylori* strain.
CONCLUSION: Different antibiotic susceptibility between antrum and corpus biopsies is a common phenomenon and a possible explanation for treatment failure. Resistant *H. pylori* strains may be missed if just one biopsy from one anatomic site of the stomach is taken for *H. pylori* susceptibility testing.
Disclosure of Interest: None declared

P1091 THE RESULTS OF USING SEQUENTIAL THERAPY IN *H. PYLORI* ERADICATION

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INTRODUCTION: To evaluate efficiency of using sequential *H. pylori* eradication therapy in patients with gastric and duodenal ulcer disease of Yekaterinburg.
AIMS & METHODS: 95 patients (55 male, 40 female, average age – 43 (16-74) years) with exacerbated gastric and duodenal peptic ulcer with severe and complicated clinical course: giant and multiple ulcers (42 patients), gastroenterorrhagia in near-term (2-3 weeks) anamnesis (48 patients), perforations (5 patients) are examined. Biopsy material of gastric and duodenal mucous tunic from standard and periulcerous areas is researched with electronic and light microscopy methods on machine «Morgagni 268». *H. pylori* diagnostic methods are histological, immunological methods, such as identification the quantity of anti - *H. pylori* IgG in blood serum, evaluation of *H. pylori* antigen in stool, detection DNA and pathogenic factors of *H.pylori* (CagA, VacA s1/s2) by PCR with fluorescent detection in real time. Intensity of gastritis is estimated by visual-analogy scale and system OLGA. Sequential therapy (pantoprazole, amoxycillin, clarithromycin, metronidazole) used in 75 patients (1 group), standard triple therapy (pantoprazole, amoxycillin, clarithromycin) – in 20 patients (2 group). All patients did not previously receive an eradication therapy. Control carried out in 2, 4, 8 weeks.
RESULTS: Ulcer cicatrization is attained in 70 (93%) of 1 group patients and 15 (75%) of 2nd group patients in 2 weeks. 100% ulcer cicatrization is attained in both groups in 4 weeks. Intensity of gastritis and efficiency of *H. pylori* eradication are estimated after 8 weeks. Before treatment the I grade of inflammation is discovered in 7 (9%) of 1 group patients, 1 (5%) of 2nd group patients, the II grade of inflammation – in 10 (13%) of 1 group, 3 (15%) of 2 group, III – 52 (69%) of 1 group, 13 (65%) of 2 group, IV – 6 (8%) of 1 group, 3 (15%) of 2 group. After treatment the I grade of inflammation is discovered in 45 (60%) of 1 group, 10 (50%) of 2 group, II – 29 (39%) of 1 group, 7 (35%) of 2 group, III – 1 (1%) of 1 group, 3 (15%) of 2 group, IV grade of inflammation aren't discovered at all ($p < 0,05$). Efficiency of *H. pylori* eradication in using sequential therapy is 96%, standard triple therapy – 87%.
CONCLUSION: Using sequential regimen of eradication of *H.pylori* infection in Russian patients with severe peptic ulcer disease demonstrated higher efficacy compared with standard triple therapy.
Disclosure of Interest: None declared

P1092 MARKERS OF INTESTINAL INFLAMMATION ARE COMMONLY ELEVATED IN LUNG-TRANSPLANTED PATIENTS WITH CYSTIC FIBROSIS

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INTRODUCTION: With increased survival in cystic fibrosis (CF), gastrointestinal complications are becoming more prevalent. Small intestinal bacterial overgrowth (SIBO) has been discussed as a determinant of intestinal inflammation in CF patients before lung transplantation (LuTx). Data on intestinal inflammation in CF patients in the post-transplant setting are scarce.
AIMS & METHODS: Aim of this ongoing prospective study is to evaluate intestinal inflammation and its underlying mechanisms in CF patients after LuTx. So far, 23 adult CF patients after LuTx (all with pancreatic insufficiency, median age 34y, range 24-58y; 42% male) attending our outpatient clinic were evaluated for presence of intestinal symptoms. Intestinal inflammation was assessed by stool calprotectin (Bühlmann Co, Switzerland) and serum antisaccharomices cerevisiae antibodies (ASCA IgG, IgA, INOVA Co, San Diego,USA) measurement. Intestinal infection was excluded by stool cultures, celiac disease by negative EMA/TTG antibodies. Glucose-H2 breath test was performed to diagnose SIBO. 5 non-CF patients with solid organ transplantation were recruited as controls.
RESULTS: 10 of 23 (43%) patients presented with intestinal symptoms. Calprotectin was increased (cut off 100 μg/g stool) in 65% of patients (mean 186±82 μg/g). 83% of patients were positive for either serum IgG (65%, mean 49±23 U/ml) or IgA (61%, mean 35±17 U/ml) ASCA. In 53% of patients SIBO was diagnosed. Patients with SIBO had markedly increased fecal calprotectin levels (median 177±94 μg/g) compared with patients without SIBO (median 98±63 μg/g) ($p < 0,05$). Patients with intestinal symptoms had significant increase in IgG and IgA ASCA, but no difference in calprotectin was found in comparison to asymptomatic CF patients. No differences in serum IgG, IgA ASCA or stool calprotectin levels were observed between transplanted patients with or without CF.
CONCLUSION: Gastrointestinal symptoms and elevated markers of intestinal inflammation are common in CF patients after LuTx. SIBO may be a causative factor for increased calprotectin in these patients. Our data suggest that not only CF, but also other factors, such as immunosuppression, may contribute to the intestinal inflammation in transplant setting.
Disclosure of Interest: None declared

P1093 FEMALES ARE BETTER PROTECTED FROM GUT INJURY DURING ISCHEMIA-REPERFUSION THAN MALES: SEX MATTERS

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INTRODUCTION: Gender differences in the pathophysiological response to ischemia-reperfusion (IR) have particularly been recognized in cardiovascular and cerebral systems. However, it is unknown if sexual dimorphism exists in human intestinal IR, a frequent occurring and highly lethal disease. Recognition of such differences and elucidation of the underlying pathophysiological mechanisms could lead to more evidence-based medicine for females, and the development of novel therapeutic strategies to reduce IR-associated morbidity and mortality. Therefore, we aimed to investigate sex differences in human intestinal mucosal responses to IR.
AIMS & METHODS: Intestinal IR was studied using a human experimental model. In 16 patients (M8:F8) undergoing pancreaticoduodenectomy, an isolated part of jejunum was subjected to 45 minutes of ischemia (45I) followed by 30 (30R) or 120 minutes of reperfusion (120R). Intestinal tissue was collected at all time points to assess morphology (hematoxylin/eosin (HE)), neutrophil influx (myeloperoxidase (MPO)) and Paneth cell apoptosis (Lysozyme/M30 double staining). Endoplasmic reticulum (ER) stress was analyzed using an X-box binding protein-1 (XBP1) splicing assay and XBP1-spliced/XBP1-unspliced (XBP1s/XBP1u) ratios were calculated. QPCR techniques were used to determine inflammatory cytokine expression. Arteriovenous (V-A) concentration differences of intestinal fatty acid binding protein (I-FABP) were measured using an enzyme-linked immunosorbent assay (ELISA) to assess the level of enterocyte damage. Results were analyzed using Mann-Whitney U tests. Data are presented as mean±SEM. A P-value < 0.05 is considered statistically significant.
RESULTS: HE staining revealed more extensive small intestinal epithelial damage in male subjects compared to females. In line, I-FABP V-A concentrations differences were higher in males compared to females, both at 45I (233.9±73.3 ng/ml vs 55.5±18.3 ng/ml, $P < .05$) and at 45I30R (79.2±19.4 ng/ml vs 24.4±6.6 ng/ml, $P < .05$). Furthermore, male small intestine showed higher XBP1s/XBP1u ratios at 45I30R than female small intestine (4.3±0.8 vs 2.2±0.4, $P < .05$), indicating enhanced ER stress in males. As expected, this was associated with a higher number of apoptotic Paneth cells per crypt in male subjects compared to females at 45I (5.8±1.2 vs 1.7±0.4, $P < .05$) and 45I30R (18.3±2.9 vs 7.6±1.9, $P < .05$). Furthermore, males had a more pronounced influx of neutrophils per villus at 45I30R (6.9±1.2 vs 3.6±0.6, $P < .05$) and a higher relative

mRNA expression of inflammatory cytokines TNF-a and IL-10 after 45I120R, compared to females (2.6 fold and 6.4 fold respectively, P < .05).
CONCLUSION: The human female small intestine is better protected from IR-induced epithelial damage than the male small intestine, and correspondingly displayed notably less inflammatory responses. Unravelling the molecular mechanisms underlying this effect could lead to new therapeutic strategies for intestinal IR.
Disclosure of Interest: None declared

P1094 ENVIRONMENTAL ENTEROPATHY: IMAGING THE CELLULAR BASIS OF DISRUPTED BARRIER FUNCTION

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INTRODUCTION: Environmental enteropathy (EE), originally termed tropical enteropathy, is very common in overcrowded living conditions in developing countries. It predisposes to growth failure in the young, and probably to poor performance of oral vaccines. By permitting microbial translocation it probably contributes to insidious systemic immune activation. In order to understand the impairment of barrier function in EE, we performed confocal laser endomicroscopy (CLE) in 57 healthy volunteers from a poor community in Lusaka, Zambia.
AIMS & METHODS: These asymptomatic volunteers were drawn from a community in which we have been conducting studies for 15 years. On day 1 a 3 hour lactulose: mannitol permeability and zinc absorption test was performed. On day 2 CLE of the duodenal mucosa was performed with diazepam/pethidine sedation and 5-10ml 2% intravenous fluorescein, and images collected for 10 minutes exactly (mean number of images analysed 135, SD57). Biopsies were subsequently taken to analyse villous morphology and markers of bacterial translocation and inflammation.
RESULTS: In the first 57 volunteers (40 female, 17 male) studied, a wide range of villous architectural patterns was observed from leaf-like to convolutions. Similarly, a wide range of barrier abnormalities was observed, with some volunteers showing severe fluorescein leakage within one minute of fluorescein injection. Epithelial breaks, particularly multicellular breaks (microerosions), were strongly correlated with the rate of fluorescein efflux (Spearman's rho 0.92; P < 0.0001). The number of plumes was almost as strongly correlated (rho = 0.69; p = 0.0004). Fluorescein leakage and epithelial barrier defects were not correlated with villous architectural change (rho = 0.01: p = 0.96), suggesting that villous remodelling and barrier defects are differentially determined. Fluorescein plumes were correlated with serum CD163, a marker of Kupffer cell activation, but only in HIV seropositive individuals (rho = 0.76; P,0.05).
CONCLUSION: CLE permits imaging of small intestinal epithelial barrier defects and suggests that cellular breaches are major routes of intestinal permeability but independent of villous architecture.
Disclosure of Interest: None declared

P1095 CELECOXIB MONOTHERAPY DEVELOPED FEWER SMALL INTESTINAL MUCOSAL BREAKS COMPARED TO LOXOPROFEN AND LANSOPRAZOLE CONCOMITANT TREATMENT: A DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL

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INTRODUCTION: Two American studies report that COX-2 selective inhibitor celecoxib develops fewer small intestinal injuries than non-selective NSAIDs (1,2). Loxoprofen, which is a pro-drug for gastroprotection of non-selective NSAIDs, is the most frequently used in Japan for pain relief.
AIMS & METHODS: The purpose of the study was to compare celecoxib with loxoprofen for small intestinal protection, and to confirm celecoxib suppression of small intestinal mucosal injury compared with non-selective NSAIDs in Japanese people. 150 healthy volunteers between 40 to 70 years of age were enrolled. After medical check-up including physical, bloody, urinary examination, and fecal occult blood test, subjects were randomly assigned to either the CEL-group to receive celecoxib (200 mg daily) or the LOX-group to receive loxoprofen (180 mg daily) in addition to lansoprazole (15 mg daily). All drugs were pulverized to fill capsules and were prepared in the same manner as placebo capsules. After randomization, all subjects were first examined by baseline capsule endoscopy (baseline CE). After 14 days, subjects underwent post-treatment CE. Baseline and post-treatment CE were evaluated for small intestinal mucosal breaks, and the findings compared between the two groups. All capsule endoscopy data including baseline and post-treatment CE were evaluated blindly by 3 reviewers. Final evaluation of small intestinal mucosal breaks was made based upon the agreement of reviewers agreement before opening the key. This study was approved by the Ethics Committee at Nippon Medical School and Kyushu clinical pharmacology research clinic institutional review board, and all subjects provided written informed consent for enrollment (UMIN: 000007936). The study was funded by Pfizer Japan Inc.
RESULTS: Among 74 subjects (49±6 years of age, F/M: 36/38)in the CEL-group, five were excluded from analysis due to four incomplete CE examinations and one withdrawal from the study due to influenza. Among 76 subjects (49±7 years of age, F/M: 39/37)in the LOX-group, four were excluded from analysis due to three incomplete CE examinations and one withdrawal due to non-compliance for study protocol. Thus, 69 subjects in the CEL-group and 72 subjects in the LOX-group were compared. Small intestinal mucosal breaks were detected 0.2±1.1 at baseline and 0.3±1.0 at post-treatment in the CEL-group, and 0.4±1.8 at baseline and 6.8±21.5 at post-treatment in the LOX-group. Small intestinal mucosal breaks were much fewer in the CEL-group than in LOX-group (P < 0.0001). The percentage of subjects with at least one mucosal break at post-treatment was also lower in the CEL-group (10%) than in the LOX-group (49%) (P < 0.0001).
CONCLUSION: Celecoxib monotherapy developed fewer small intestinal mucosal breaks than loxoprofen and lansoprazole concomitant treatment in the Japanese population.
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P1096 DIETARY WHEAT ALPHA-AMYLASE/TRYPSIN INHIBITORS (ATIS) EXACERBATE ALLERGIC AIRWAY INFLAMMATION

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INTRODUCTION: Wheat alpha-amylase/trypsin inhibitors (ATIs) are potent activators of innate immunity by engaging the toll like receptor 4 (TLR4)-MD2-CD14 complex in monocytes, macrophages and dendritic cells (Junker Y et al, J Exp Med 2012). ATIs, non-gluten proteins, that occur as contaminants even in "pure" gluten preparations are implicated in the pathogenesis of celiac disease (CD) and other autoimmune / inflammatory diseases.
AIMS & METHODS: We would like to investigate the effects of dietary ATIs on allergic airway inflammation. Therefore, female C57BL/6 mice on a gluten-free diet (GFD) were sensitised and challenge with ovalbulmine (OVA). Animals were divided in 5 groups: 1 continued with the GFD and mock-sensitised with PBS, 2: continued with the GFD and sensitised with OVA, 3: changed to a diet containing 25% gluten (containing amounts of ATIs equivalent to the human wheat based diet), 4: changed to a diet containing purified ATIs, and 5: changed to a diet containing 25% gluten de-enriched of ATIs. Furthermore, we evaluated the effect of ATIs, OVA or both during sensitisation and challenge.
We measured invasive lung function, bronchoalveolar lavage (BAL), IgG1 levels and proliferation of splenocytes and cytokine secretion after OVA stimulation. In addition, histological sections of lung were stained with Hematoxylin and Eosin (HE) *and* Periodic acid–Schiff (PAS) and scored according to the degree of cell infiltration and goblet cell hyperplasia.
RESULTS: Mice on a GFD sensitized with PBS did not develop airway hyperreactivity (AHR) after local provocation with OVA. Interestingly, mice on a GFD or on a diet containing 25% gluten de-enriched of ATIs and sensitized with OVA developed a reduced AHR compared to mice fed the pure ATIs rich diet or 25% gluten diet. Similar results were observed for IgG1 production, eosinophilic infiltration in BAL (HE) and mucus production (PAS) in the lung. We also observed that animals sensitised with OVA/ATIs and challenged with OVA, showed higher AHR compared to animals sensitised with OVA or ATIs alone.
CONCLUSION: We demonstrate that 1) dietary ATIs enhance allergic airway inflammation in OVA-challenged mice 2) sensitization with ATIs/OVA enhances further AHR in OVA-challenged mice 3) a gluten-free (ATI-free) diet appears to have a protective effect on allergic airway inflammation 4) Gluten depleted of ATIs has a reduced stimulatory effect compared with gluten containing ATIs or ATIs alone. Therefore, ATIs appear to be major and clinically relevant nutritional triggers of innate immunity in allergic airway inflammation and other autoimmune diseases.
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P1097 MILD HISTOLOGICAL ABNORMALITIES IN NON-COELIAC GLUTEN SENSITIVITY DO NOT REPRESENT EARLY COELIAC DISEASE

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INTRODUCTION: Coeliac disease (CD) is defined by positive serology plus Marsh (M) grade 1-3 on duodenal biopsies; CD-M1 to CD-M3. In contrast, non-coeliac gluten sensitivity (NCGS) is defined by negative serology and duodenal biopsies that are normal, or show mild histological abnormalities, whilst on a gluten containing diet; NCGS-M0 to NCGS-M1.
AIMS & METHODS: As coeliac serology can be negative in those with mild histological abnormalities we aimed to determine whether NCGS-M1 actually represents early CD.

Baseline clinical characteristic, biochemical parameters and human leukocyte antigen (HLA) DQ2-DQ8 typing was compared between 100 NCGS-M0, 50 NCGS-M1 and 30 CD-M1 patients. Finally, serological and histological response to a repeat gluten challenge was assessed between HLA-DQ positive NCGS-M1 and CD-M1.
RESULTS: There was no statistical difference in age, sex, autoimmunity, family history of CD or baseline body mass index between the three groups. However, anaemia was significantly more prevalent in CD-M1 (20%) compared to NCGS-M1 (6.4%, p 0.05, OR 4.7, C. I 1.0-21.6) and NCGS-M0 (3%, p 0.009, OR 7.58, C. I 1.67-34.4).
Furthermore, HLA-DQ positivity was seen in 100% (n 30) of CD-M1 patients, in contrast to 70% NCGS-M1 (n 35, p 0.001) and 55% NCGS-M0 ($p < 0.001$).
26/30 CD-M1 patients and 30/35 HLA-DQ positive NCGS-M1 individuals agreed to undergo repeat gluten challenge. In CD-M1 there was a significant rise in coeliac serology (mean TTG value 124 U/ml before: 164 U/ml after, p 0.04) and histological deterioration on duodenal biopsies (35% M1, 15% M2, 50% M3, $p < 0.0001$). In contrast, all individuals with HLA-DQ positive NCGS-M1 maintained negative coeliac serology (mean TTG value 7 U/ml before; 8 U/ml after, p 0.12) and the majority improved their duodenal biopsies from M1 to M0 (23/30, 77%, $p < 0.0001$), with 7 cases persisting as NCGS-M1
CONCLUSION: NCGS-M1 individuals do not represent CD as demonstrated by i) negative HLA-DQ typing in 30% of cases or a ii) a lack of immune deterioration following repeat gluten challenge in those with HLA-DQ positivity. In cases with persisting NCGS-M1 duodenal immunohistochemical analysis may shed further light on the eventual diagnosis.
Disclosure of Interest: None declared

P1098 PREDICTORS FOR COELIAC DISEASE IN CASES OF LYMPHOCYTIC DUODENOSIS

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INTRODUCTION: Lymphocytic duodenosis (LD) is an early marker for coeliac disease (CD). However, the majority of cases are due to non-CD related conditions.
AIMS & METHODS: We aimed to identify the predictors of CD when presented with LD.
215 LD patients had undergone prospective and systematic evaluation for CD and other recognized associations.
The gold-standard diagnosis of CD was based upon the presence of HLA-DQ2 and/or DQ8, persistence or progression of LD following a gluten challenge, followed by a symptomatic improvement on a gluten-free diet.
Binary logistic regression models, adjusting for age and gender, were subsequently performed to compare presenting variables between CD and non-CD cases, and to determine their sensitivity, specificity, positive and negative predictive values (PPV and NPV).
RESULTS: CD was diagnosed in 48 cases (22%) and non-CD in 167 cases (78%). There was no statistical difference in demographics, clinical symptoms (i.e. diarrhea, weight loss, abdominal pain), anemia or hematinics between the CD and non-CD group.
Patients with CD, in comparison to non-CD, were significantly more likely to have a positive family history of CD (21% vs. 3.6%, OR 6.73; PPV 62.5%, NPV 81%, specificity 96.4%), positive HLA-DQ status (100% vs. 49.1%; PPV 36.4%, NPV 100%, specificity 50.9%), and presence of endomysial antibody [EMA] (48% vs. 0%; PPV 100%, NPV 87%, specificity 100%); all $p \leq 0.001$
A normal tissue transglutaminase antibody (TTG) level was seen in 29.2% CD and 83.2% non-CD cases (OR 0.084, $p < 0.001$; PPV 9.2%). There was no difference in the prevalence of TTG levels 1-2 x upper limit of normal (ULN) between the groups (29.2% CD vs. 14.4% non-CD; PPV 33-38%). However, TTG levels between 3-20 x ULN were significantly more prevalent in the CD group (33.3% vs. 2.4%; PPV 66.6%>89%), whilst a TTG > 20 x ULN was exclusive to CD (8.3%, $p < 0.001$, PPV 100%).
CONCLUSION: In the setting of LD, only the presence of a positive EMA or TTG > 20 x ULN at the outset can be used to make an immediate diagnosis of CD. Gastrointestinal symptoms, family history, anemia, or other celiac serology results do not reliably distinguish CD from non-CD without further investigations.
Disclosure of Interest: None declared

P1099 CHANGE IN AWARENESS OF GLUTEN-RELATED DISORDERS AMONGST CHEFS AND THE GENERAL PUBLIC IN THE UNITED KINGDOM: A 10 YEAR FOLLOW-ON STUDY

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INTRODUCTION: For individuals with gluten-related disorders (GRD) eating out has traditionally been difficult, and socially impacting, due to concern over the lack of public awareness regarding GRD and a gluten-free diet (GFD). However, the recent rise in media coverage highlighting these conditions may have altered knowledge amongst the general public and chefs.
AIMS & METHODS: We assessed whether knowledge of GRD has altered amongst the general public and chefs.
A face-to-face questionnaire about coeliac disease (CD) and gluten sensitivity (GS) was performed on the general public and chefs based in Sheffield, United Kingdom. The assessment was first conducted in 2003 and repeated in 2013.
RESULTS: 513 public members in year 2003 (mean-age 49.2, 62% female) were compared to 575 public members in year 2013 (mean-age 37.8, 57% female). There was a significant rise in the awareness of GRD from the years 2003 to 2013; CD (44.2% to 74.4%, AOR 3.9 [C. I 3-5.19]) and GS (58.3% to 89%, AOR 7.1 [C. I 5-9.98]), p-value < 0.001.
322 chefs in year 2003 (mean age 37.6, 15% female) were compared to 265 chefs in year 2013 (mean age 27.1, 38% female). There was a significant rise in the awareness of GRD from the years 2003 to 2013; CD (17.1% to 78.1%, AOR 12.5 [C. I 7.9-19.6]) and GS (9.3% to 87.5%, AOR 65.7, C. I [35.4-122]), $p < 0.001$. Whereas in 2003 the public were significantly more aware of GRD than chefs, by 2013 this had reached similar prevalence in both groups. In addition, the correct recognition of the gluten-free symbol was 44% for the public and 40% for chefs (p 0.28). 41% of restaurants and 27% of takeaways sold gluten-free products (p 0.07).
CONCLUSION: There has been a dramatic rise in both the public and chefs awareness of GRD. This may ease the social phobia that individuals with GRD have traditionally been accustomed to.
Disclosure of Interest: None declared

P1100 UNSUSPECTED PREVALENCE OF CONDITIONS PREDISPOSING TO CELIAC DISEASE IN THE AMERINDIAN TOBA COMMUNITY OF ARGENTINA: A STUDY ON GLUTEN CONSUMPTION, GENETIC PREDISPOSITION AND AUTOIMMUNITY MARKERS

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INTRODUCTION: The Toba indigenous ethnic community comprises more than 60,000 individuals living in very poor conditions in northeastern Argentina. The lower than average life expectancy in this population has been attributed, in part, to primary malnutrition, and very low socio-economic, sanitary and educational conditions. In recent years, they have experienced a change in dietary habits with wheat and wheat-products replacing ancestral alimentary practices mainly due to the governmental support. No studies have explored conditions predisposing to celiac disease (CD) in Amerindians.
AIMS & METHODS: Aims: 1- To estimate the consumption of gluten; 2- To explore the genetic background (HLA DQ2/ DQ8 haplotype); and 3- To determine the prevalence of CD autoimmunity in a population of members of the Toba community requesting medical attention by a multidisciplinary sanitary mission.
Methods: After written consent, individuals attending the mission underwent a detailed questionnaire by an expert nutritionist recalling the last 48-hs dietary intake. Gluten consumption was estimated by conventional formula. Clinical, biochemical and anthropometric parameters were collected. CD specific gene typing for the detection of HLA class II alleles was performed on DNA extracted from peripheral blood (DQ-CD Typing Plus. BioDiagene S. R. L.; Palermo; Italy). Serum samples were tested for IgA antibodies to tissue transglutamise (IgA tTG) and the deamidated gliadin peptides (DGP)/tTG Screen test. Those with positive results were tested for IgA endomysial (EmA) antibodies (INOVA Diagnostics Inc. San Diego, Ca).
RESULTS: One hundred and forty-three subjects (63% females) were enrolled. The median age of the study population was 30 yr (range: 3 to 72), and the mean body mass index was 27.1 kg/m^2 (SD: 6.7). The estimated mean gluten consumption was 47 g/day (range: 4 to 185), which resulted higher than that recommended by National Nutritional Guideline (18 g/day). Sixty out of 116 subjects (51.7%) had alleles associated with CD. Fifty-six cases (95%) had alleles codifying for HLA DQ8 and three for DQ2. Three and four subjects had serum concentrations above the cut-off of risk established by our group (>3 times the upper limit of normal) for tTG and DGP/tTG Screen antibodies, respectively. Three of these patients had concurrent positivity for both assays and EmA was positive in two of these patients who also presented the haplotype HLA DQ2 and DQ8.
CONCLUSION: Our study explores for the first time an Amerindian population previously unsuspected of having conditions predisposing to CD. The dietary analysis estimated a very high consumption of gluten due to the alimentary governmental support. The genetic background was dominated by alleles codifying for DQ8 antigen. We detected evidence of CD autoimmunity and, at least, two subject fulfilled serologic criteria of CD.
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P1101 ADHERENCE TO DUODENAL BIOPSY GUIDELINES INCREASES THE DETECTION OF COELIAC DISEASE: A MULTICENTRE UK STUDY

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INTRODUCTION: Coeliac disease (CD) is a common autoimmune condition affecting 1% of the adult population. However large numbers of patients remain undiagnosed which may have significant health consequences and so methods to increase detection should be sought. Guidelines suggest that at least 4 duodenal biopsies should be taken to rule out CD. A previous US study showed that biopsy guidelines were only followed in 35% of cases. The aim of the present study was to see whether guidelines were being followed in the UK and if adherence to the guidelines improved detection of CD.
AIMS & METHODS: Endoscopy and histology reports were retrospectively reviewed for all patients who had a duodenal biopsy in a 3 month period between November 2012 and January 2013 from 4 UK hospitals. Indications for biopsy, role of the endoscopist (physician, surgeon, nurse endoscopist), number of duodenal biopsies received by histopathology and the final diagnosis were recorded. The presence of villous atrophy was required for CD diagnosis. Patients were excluded if they had known CD.
The difference between a double and single bite biopsy technique was also assessed.
RESULTS: 1423 patients underwent duodenal biopsy for possible CD across the 4 sites in the study period. 97 (6.8%) of these were diagnosed with CD. Guidelines to take at least 4 biopsies were met in 40% of patients and the median number of duodenal biopsies taken for all patients was 3. CD was more likely to be diagnosed if guidelines were followed (10.1% vs 4.6%, $P<0.0001$). The median number of biopsies was greater in patients diagnosed with CD (4 vs 3) $P<0.0001$. Gastroenterologists and nurse endoscopists were more likely than surgeons to follow guidelines (41.8% vs 51.2% vs 18.2%, $P<0.0001$) and took a higher median number of biopsies (3 vs 4 vs 2, $P<0.0001$). As a result gastroenterologists and nurse endoscopists made a diagnosis of CD in more cases than surgeons (7.1% vs 6.7% vs 3.0%, P 0.1). All presenting characteristics (other than positive serology in which guidelines were followed in 65%) were associated with poor adherence to guidelines. 12.4% of newly diagnosed CD patients had at least 1 non-diagnostic gastroscopy in the 5 years prior to diagnosis. Changing biopsy technique to single bites resulted in improvement of median D2 biopsies from 3 to 4. (P 0.02).
CONCLUSION: We have shown that 12.4% of patients with CD had a previous gastroscopy 5 years prior to their diagnosis. Taking 4 duodenal biopsies results in increased detection of CD. We are the first investigators to demonstrate that there is variation in biopsy rates based on the speciality of the endoscopist and biopsy technique (single or double bite). Furthermore this variability has a direct relationship with the detection rate of CD. Education of all groups of clinicians in duodenal biopsy techniques may result in more patients receiving a prompt diagnosis of CD.
Disclosure of Interest: None declared

P1102 POINT OF CARE TESTING FOR ADULT COELIAC DISEASE: A POTENTIAL ROLE IN ENDOSCOPY

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INTRODUCTION: Endoscopic markers of coeliac disease (CD) lack sensitivity; therefore many centers take routine duodenal biopsies or have a low threshold for biopsy, ensuring high detection rates. Newly available, point of care tests (POCT) provide rapid findings unlike conventional serological markers, potentially reducing the need for duodenal biopsies. This study evaluates a new POCT (Simtomax) which detects IgA and IgG deamidated gliadin peptide (DGP) with comparisons made to conventional serological markers and duodenal biopsies.
AIMS & METHODS: Patients referred from primary and secondary care for a gastroscopy to a specialist CD list were prospectively recruited between March 2013 to November 2013. Patients were excluded if they were on a gluten free diet at the time of the test or if they had previously been diagnosed with seronegative villous atrophy or coeliac disease. All patients had a duodenal biopsy as the gold standard for detecting coeliac disease. Concurrently serological testing for IgA tissue transglutaminase (TTG), endomysial antibody (EMA), total IgA immunoglobulin level and the DGP based rapid test was performed. Sensitivity, specificity, positive predictive and negative predictive values were calculated.
RESULTS: 354 patients met the inclusion criteria (45.8% male mean age 53.3 ±18.5). Of these, 52 (14.7% 11.2 – 18.9) had newly diagnosed CD and 302 were controls with a normal duodenal biopsy. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the POCT were 94%, 83%, 49% and 99% respectively. This compares with results for TTG of 92%, 88%, 57%, 99% and EMA of 88%, 97%, 85%, and 98% respectively.
CONCLUSION: This is the first study to prospectively demonstrate the value of a novel POCT for adult CD in endoscopy compared to the gold standard of histology. The sensitivity and specificity of the POCT is comparable to conventional serology. Simtomax could be used to appropriately identify patients requiring a duodenal biopsy within the endoscopic setting. This strategy may be cost effective by reducing the number of routine duodenal biopsies taken.
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P1103 COMPARISON OF THREE COMMERCIALLY AVAILABLE POINT OF CARE TESTS FOR COELIAC DISEASE

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INTRODUCTION: Coeliac disease (CD) remains an underdiagnosed condition. A rapid finger prick based point of care test may increase uptake of serological testing in appropriate patient groups. There are 4 commercially available point of care tests (POCT) on the market in the UK: Biocard an IgA tissue tranglutaminase (tTG) test (BHR pharmaceuticals); Coeliac Quick Test (Biohit healthcare) which detects IgA, IgG and IgM tTG; Xeliac Test Pro (Personal Diagnostics) which detects IgA and IgG tTG; and Simtomax (Tillott's Pharma) which detects IgA and IgG de-amidated gliadin peptides (DGP). However there is a limited evidence base for these tests (Biocard 10 studies; Simtomax 2 studies; Coeliac Quick Test and Xeliac Test Pro have no published data) and frequently patients only have a duodenal biopsy if the POCT is positive leading to ascertainment bias. In our recent cohort the sensitivity of Biocard was disappointing at 70.1% when results were compared to histology in all patients [1]. For this reason we decided to compare 3 commercially available tests in an endoscopic setting.
AIMS & METHODS: Patients referred with a positive endomysial antibody (EMA) for duodenal biopsy to confirm CD were invited to take part. All patients had whole blood taken for repeat serum EMA, tTG and immunoglobulins. All patients were tested simultaneously with the 3 POCTs as per the manufacturers' instructions. All patients had quadrantic duodenal biopsies from the second part of the duodenum as well as a duodenal bulb biopsy. Demonstration of villous atrophy on duodenal biopsy was required to diagnose CD.
RESULTS: 47 patients (27 female, mean age 39.1) have been recruited. In 9 patients the EMA had normalised on repeat testing. None of these patients had villous atrophy on duodenal biopsy. 7 of these patients were referred with a weak EMA and had a negative tTG. Of the other 2, 1 patient referred with a positive EMA, had a tTG of 155 and subsequent gluten challenge revealed a positive EMA and villous atrophy.
Of the remaining 38 patients 30 new cases of coeliac disease were confirmed with the presence of villous atrophy, of the remaining 8 EMA positive patients 6 had Marsh 1 or 2 changes present with the remaining 2 patients having normal histology. Full sensitivity, specificity PPV and NPV for all of the tests compared to villous atrophy on duodenal biopsy are shown in the table below.

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Serum tTG	97 (81-99)	41 (19-67)	74 (58-86)	88 (47-99)
Biocard	63 (44-79)	76 (50-92)	83 (60-94)	54 (33-74)
Coeliac Quick Test	80 (61-92)	59 (33-81)	77 (58-90)	63 (36-84)
Simtomax	93 (76 -99)	35 (15-61)	72 (55-84)	75 (36-96)

CONCLUSION: In this pilot data set Simtomax appears to be the most sensitive of the POCTs when compared to histology with similar results to serum tTG as screening test. Further work is required in larger cohorts and lower prevalence populations to confirm the utility of these tests in adult coeliac disease.
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P1104 ASSESSING ADHERENCE TO GLUTEN FREE DIET IN COELIAC DISEASE: CAN WE AVOID DUODENAL BIOPSY?

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INTRODUCTION: Up to 30% of patients with coeliac disease will have persistent symptoms despite the introduction of a gluten free diet. Assessment of adherence in coeliac disease can involve any combination of patient self-reporting adherence, dietetic assessment, serology and biopsy with histology. Histology is considered to be the 'gold standard' but this requires a repeat endoscopic examination with its associated risks and problems with tolerance. As a result surrogate markers of persistent gluten exposure and histological changes such as serology are frequently used but the relationship between serology and persistent histological changes is not linear. A structured interview with a dietician has been shown to be the most accurate method of assessing gluten exposure however this is time consuming and requires extra clinic visits. The aim of this study was to assess the usefulness of two novel options. Firstly a previously internally validated scoring system for assessing dietary adherence[1] (which has never been externally validated) and secondly a rapid de-amidated gliadin peptide based point of care test (POCT, Simtomax) for the prediction of persistent VA.
AIMS & METHODS: All patients with known coeliac disease and persistent symptoms coming to a specialist coeliac endoscopy list for the re-assessment of histology were invited to take part. All patients were tested for Endomysial

Antibody (EMA), tissue transglutaminase (tTG), immunoglobulins and the POCT. They were also asked to complete a questionnaire to calculate a 5 point score (0 – 4) with a high score representative of improved adherence to a gluten free diet. All patients underwent gastroscopy with at least 4 biopsies from the second part of the duodenum and 1 to 2 biopsies from the bulb.
RESULTS: 60 patients (78% female, mean age 51.4 range 16-79) were recruited between April 2013 and April 2014. 22 (36.7%) of these patients had persistent VA on duodenal biopsy. The POCT was the most sensitive marker with 73% of patients with VA having a positive test. EMA was the most specific surrogate marker at 84% although it was highly insensitive with only 36% of patients with VA having a positive EMA. No patients with completely normalised histology had a positive EMA. The adherence score could not be reliably used to predict villous atrophy with a sensitivity of only 32%.

Measure	Sensitivity	Specificity	PPV	NPV
Adherence Score	32%	82%	50%	67%
tTG	55%	76%	57%	74%
EMA	36%	84%	57%	70%
POCT	73%	66%	55%	81%

CONCLUSION: An accurate surrogate marker for villous atrophy could reduce the number of endoscopies required. In this cohort the POCT had the best sensitivity, detecting 16/22 (73%) cases of villous atrophy, however this is pilot data and further work is required. It maybe that additive methods for assessing adherence could achieve 100% sensitivity
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Disclosure of Interest: P. Mooney: None declared, M. Kurien: None declared, S. Wong: None declared, D. Sanders Financial support for research from: Tillotts Pharma

TUESDAY, OCTOBER 21, 2014 9:00–17:00
NUTRITION II – POSTER EXHIBITION – HALL XL

P1105 METABOLIC ADAPTATION OF COLONIC MICROBIOTA TO DIET

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INTRODUCTION: We recently showed that a diet rich in non-absorbable, fermentable residues in the short term increases intestinal gas production and induces digestive symptoms such as flatulence, bloating and abdominal distention. On the contrary, it has been shown that some prebiotics, which are also fermented by colonic bacteria, improve this type of symptoms. Hence, it is not clear whether fermentable residues from the diet have a beneficial or deletereous effect on digestive symptoms.
AIMS & METHODS: To demonstrate changes in metabolic activity of gut microbiota and colonic biomass induced by prebiotics. Healthy subjects (n = 20) were administered a prebiotic (Bimuno prebiotic powder, Clasado, London, UK; 2.8 mg/d) for three weeks; they also received a standardized diet during three days immediately before, at the beginning and at the end of the treatment. During these periods the following outcomes were measured: a) number of gas evacuations during daytime, by means of an event marker; b) volume of gas evacuated per anus during four hours after a test meal, by means of a rectal tube connected to a barostat that maintains a minimal resistance to flow across the collection line; and c) the volume of content in the undisturbed colon in the 24-h period after a bowel movement (n = 5), by means of magnetic resonance imaging of the abdomen using an original, previously validated analysis program.
RESULTS: Before treatment healthy subjects evacuated gas per anus 12.6 ± 0.9 times during daytime and evacuated 151 ± 15 mL of gas during four hours after the test meal. At the beginning of treatment, prebiotic administration significantly increased the number of anal gas evacuations (18.6 ± 1.8 times daily; $p < 0.001$) and the volume of gas evacuated after the test meal (235 ± 24.6mL; $p < 0.001$). Interestingly, by three weeks treatment, both the daily number of gas evacuations (11.2 ± 1.3), as well as the volume of gas evacuated after the test meal (161 ± 24) decreased and returned to pre-treatment levels. Prebiotic intake significantly increased the volume of content in the undisturbed colon (740 ± 73 vs 628 ± 62 pre-treatment; $p < 0.05$), and this increase in colonic biomass was maintained during the treatment period (792 ± 64 by three weeks; $p < 0.05$ vs pre-treatment).
CONCLUSION: Availability of substrates induces an adaptation of colonic microbiota ativity towards more efficient metabolic pathways.
Disclosure of Interest: F. Azpiroz Financial support for research from: Danone, Given, Beneo, Shire, Consultancy for: Danone, E. Barba: None declared, M. Mego: None declared, A. Bendezu: None declared, M. Mego: None declared, A. Accarino: None declared, X. Merino: None declared, S. Mendez: None declared, J. Malagelada: None declared, A. Accarino: None declared, E. Monclus: None declared, M. Izquierdo: None declared, I. Navazo: None declared

P1106 FODMAP-RESTRICTED DIET AND EFFECTS ON FUNCTIONAL DYSPEPSIA

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INTRODUCTION: FODMAPs (fermentable oligo-, di-, monosaccharides and polyols) is a group of carbohydrates poorly absorbed in the small intestine – some will therefore serve as substrate for colonic fermentation. Studies show effect of FODMAP-restricted diet on symptoms of irritable bowel syndrome (IBS) – none have been conducted on patients with functional dyspepsia (FD). We aimed to see whether a 6-week diet low in FODMAPs would have an effect on symptoms (epigastric pain, postprandial fullness and nausea), quality of life (QoL) and gas produced during lactulose breath-test.
AIMS & METHODS: 11 FD patients according to the ROME III-criteria were included in the study (8F/3M, 32.4±12.2), instructed and followed up closely by a dietician during a 6-week diet. FD-symptoms (VAS 0-100) and QoL (SF-36) were collected at baseline, 3 and 6 weeks. FODMAP-intake (grams) was calculated at baseline and 6w using 4-day food records. Lactulose breath testing (n = 10) was performed at baseline and 6w to observe changes in gas production. Results were compared using t-tests, one-way ANOVA and correlation.
RESULTS: There was a significant reduction in FODMAP-intake (mean from 53.2g to 3.3g, $p < 0.001$). High compliance to the diet was reported (mean 90.4%) and it was somewhat challenging (mean 50.6%). Epigastric pain (median 54.1 to 0%, $p = 0.0002$), postprandial fullness (median 52 to 0%, $p < 0.001$) and nausea (mean 47.6 to 19.9%, $p < 0.05$) significantly reduced from baseline to 6w. SF-36 total score (mental health $p = 0.37$ and physical health $p = 0.07$). Hydrogen gas production (median 5558 to 2228ppm×min, $p = 0.0059$) significantly declined.
CONCLUSION: In this study, FODMAP-restricted diet significantly reduced FD-symptoms and hydrogen gas production in 6 weeks.
Disclosure of Interest: None declared

P1107 MALNUTRITION IN HOSPITALIZED IBD- A CALL FOR RECOGNITION AND TREATEMENT

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INTRODUCTION: Malnutrition is frequent in IBD patients. Protein-calorie malnutrition leads to fatigue, inability to carry on every-day life activities and make the patient prone to prolonged and complicated hospitalizations. Diagnosis of malnutrition relies upon integration of history taking, physical examination and laboratory results. Low Urea, Creatinine, CPK and lymphopenia are cornerstone laboratory findings of muscle wasting.
AIMS & METHODS: In this study, we set to check the frequency of recognition and treatment of malnutrition in hospitalized patients with IBD. Retrieval of data from electronic files of all hospitalized IBD patients 2012-2013. Screening criteria for risk of malnutrition included any two of the following: Weight loss > 5%; lymphopenia < 1000/mm^3; BUN≤5; Creatinine≤0.4; Uric acid≤2; CPK≤20
RESULTS: 134 patients, of whom 113 had complete data, 51% males, 73% with Crohn's disease; age 32.2 years+/-13.6. 55% lost > 5% weight; 58% diagnosed at risk for malnutrition, 53% of Crohn's and 73% of UC patients ($p < 0.05$). Length of stay (LOS) was 5.1 days and 8.1 days for well-nourished and malnourished patients ($p < 0.05$). On multivariate analysis, only nutritional state and hypoalbuminemia were independent factors for prolonged LOS. Only 15% of patients received the diagnosis of malnutrition, 38% were given nutritional therapy and 32% had recommendations to take nutritional therapy after discharge from the hospital.
CONCLUSION: Malnutrition is common in hospitalized patients with IBD and is associated with prolonged hospitalizationX1.5 times than patients who are well nourished. Assessment of patients at risk, recognition and treatment of malnutrition are suboptimal. Measures to optimize identification of patients at risk for malnutrition and provision of adequate treatment are needed.
Disclosure of Interest: None declared

P1108 HOW OFTEN DO WE RECOGNIZE MUSCLE WASTING AND MALNUTRITION IN HOSPITALIZED IBD PATIENTS

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INTRODUCTION: Malnutrition and an inflammatory state can combine to contribute to muscle wasting in IBD patients. Since muscle wasting is directly related to frailty and quality of life it is of utmost importance to diagnose. Low Blood Urea Nitrogen (BUN), Uric Acid, Creatinine, and CPK are cornerstone laboratory findings of muscle wasting (MW). Weight loss characterizes protein-calorie malnutrition.
AIMS & METHODS: In this study, we set to check the frequency of recognition of muscle wasting and malnutrition in hospitalized IBD patients. Retrieval of data from electronic files of all hospitalized IBD patients 2011-4.2014. Screening

criteria for risk of MW and malnutrition included: Weight loss > 5%; BUN≤5; Creatinine≤0.4; Uric acid≤2; CPK≤20. Suspected MW was defined as a combination of two or more of the following low BUN, Creatinine, Uric acid or CPK. Malnutrition risk if one of the above and weight loss was present.
RESULTS: 169 patients, with active IBD, 54%% males, 73% with Crohn's disease; age 35 years+/-14. 38% lost > 5% weight; 11% had laboratory findings compatible with MW, 16% of patients with MW lost weight. Length of stay (LOS) was longer for patients with MW irrespective of WL or age (15.2+/-23 vs. 5.3+/-4 ($p<0.0001$). None of the patients were diagnosed with MW, only 15% of patients received the diagnosis of malnutrition
CONCLUSION: MW is prevalent in more than 10% of hospitalized IBD patients and is associated with prolonged hospitalization X3 times than patients. MW is a known factor associated clinical deterioration. The data herein presented, manifests lacking diagnosis and calls for measures to raise recognition of this important clinical manifestation.
Disclosure of Interest: None declared

P1109 INTRAGASTRIC PRESSURE DURING DIFFERENT NUTRIENT DRINK INFUSIONS

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INTRODUCTION: Recent intragastric pressure (IGP) measurements, used to assess gastric accommodation[1], have shown that intragastric nutrient infusion induces an initial drop in IGP, followed by a gradual recovery, with significant correlation to satiation and the volume required to induce maximal satiation. The type of nutrient(s) that drive(s) these IGP responses have not been identified.
AIMS & METHODS: The objectives were to assess the role of specific nutrients in inducing IGP response and their contribution to satiation. A manometry and infusion catheter were positioned in the proximal stomach of 15 healthy volunteers. After a stabilization period, one of three nutrient drinks (high lipid [10% lipid emulsion], high protein [whey protein isolate], or high carbohydrate [glucose]) were intragastrically infused at 60 mL/min, three days to one week apart in a single-blinded randomised order. There were no differences in caloric or osmotic load between the drinks. The experiment ended when subjects scored maximum satiation. IGP was presented as change from baseline (mean ± SEM). Satiation scores were measured before, during and after the infusion at 10-minute intervals using a 100 mm visual analogue scale. Results were compared using a repeated measures ANOVA.
RESULTS: 15 eligible volunteers (21-52 y, 7 men) were randomised. Volunteers scored maximal satiation after a higher volume of the carbohydrate drink infusion (1231 ± 126 mL) compared to the other nutrients (protein 1049 ± 99 mL, lipid 1006 ± 49 mL; $p=0.0027$). In all subjects and with each nutrient infusion, the IGP decreased initially to gradually recover thereafter. Maximum IGP decrease (termed nadir) was 7.6 ± 0.9 mmHg after 8.1 ± 1.3 min, 9.4 ± 1.0 mmHg after 10.1 ± 1.2 min, and 7.7 ± 0.6 mmHg after 8.7 ± 1.2 min for carbohydrate, protein and lipid respectively (nadir $p=0.1461$; time to nadir $p=0.4422$). Overall, the area above the IGP curve was greater for the lipid (114.7 ± 14.7 mmHg/min) compared to the carbohydrate and protein (94.6 ± 19.3 and 81.0 ± 9.5 mmHg/min, respectively) ($p=0.1020$). Post hoc analysis showed significant correlations between IGP and satiation score increase, with slightly greater satiation induced with the lipid (84 ± 3.5 mm; carbohydrate 78 ± 5.2 mm, protein 76 ± 6.3 mm; $p=0.1764$).
CONCLUSION: This study indicates all three macronutrients induce an IGP response in the healthy state. The findings offer opportunities to objectively identify whether these specific nutrients drive the impaired gastric accommodation seen in functional gastroduodenal patients (e.g., functional dyspepsia).
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Disclosure of Interest: None declared

P1110 DIETARY ASSESSMENT AND EVALUATION OF MYCOTOXIN EXPOSURE IN CELIAC PATIENTS

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INTRODUCTION: Gluten free diet (GFD) is currently the only available therapy for patients with celiac disease (CD), the most common autoimmune enteropathy in Western Countries, occurring in genetically susceptible individuals and triggered by gluten ingestion. As gluten rich products are an important source of nutrients, it is not clear if GFD could have a negative effect on the nutritional status of CD patients and if GFD could expose to mycotoxins contained in gluten free flours.
AIMS & METHODS: Aim of the study was to estimate the nutrient intake and the dietary exposure to mycotoxins in treated CD *vs.* controls.
Sixty participants, thirty histologically proven CD and thirty sex-age matched, healthy control were enrolled. Total food and beverage consumption was assessed by means of a food record filled in every day for a total of 7 days. The nutrient intake was calculated using a Microsoft Access application linked to the food database of the European Institute of Oncology and integrated with the nutrient composition of sixty commercial GF (Gluten-Free) foods. Test for mycotoxins (fumonisin B1 and deoxynivalenol) biomarkers was carried out on 24 hour urine collection.
RESULTS: Compared to controls, CD patients on GFD consumed a lower percentage of energy as carbohydrates and a higher percentage of energy as fats (48 % *vs* 51% and 37 % *vs* 33%, respectively). Moreover, GFD has a higher intake of vitamin C, vitamin E and sodium than normal diet (142 mg *vs* 118; 18 mg *vs* 13 mg; 3340 mg *vs* 2959 mg respectively). Concerning mycotoxins exposure, preliminary results on urinary fumonisin B1 and deoxynivalenol excretion failed to evidence any differences between GFD and control diet.
CONCLUSION: Present data show a higher consumption of fruit and vegetables rich in micronutrients and an increased intake of fat and sodium (due to GF packaged product) in GFD.
Exposure to mycotoxins does not differ between CD patients and controls.
Disclosure of Interest: None declared

P1111 HYPERNATRAEMIA AND C REACTIVE PROTEIN ARE INDEPENDENTLY RELATED TO 1-,3-MONTH AND LONG TERM MORTALITY IN PATIENTS WHO UNDERWENT PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) FOR DYSPHAGIA - A SINGLE-CENTRE EXPERIENCE

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) is performed to provide enteral nutrition to patients with swallowing disorders. Previous studies demonstrated that advanced age, low BMI, low serum albumin and high levels of C reactive protein (CRP) are related to worst clinical outcomes. The aim of our study was to evaluate predictive factors of morbidity and mortality in patients who underwent PEG placement.
AIMS & METHODS: Data from all consecutive patients undergoing PEG placement for oropharyngeal dysphagia between March 1999 and December 2013, were collected; in particular indication for PEG placement, comorbidities, concomitant medications and lab-tests were recorded.
All patients received antibiotic prophylaxis; anti-thrombotic drugs were discontinued when possible. Coagulation defects and serum potassium alterations were corrected. All procedures were performed under deep sedation administered by anaesthesiologists. Enteral feeding was started at least 24 hours after the procedure.
Patients were followed up and periprocedural (within 48h) major complications, 1- and 3-month mortality rates were recorded. Cox-proportional hazard regression and Kaplan-Meyer analyses were used to identify prognostic indicators of mortality; ROC curves were used to identify the best cut-off points.
RESULTS: 438 patients (178 Male; 77.4 ± 12.1 years) were included; causes of dysphagia were stroke (149), dementia (137), neurodegenerative disease (81), coma (40) and cancer (31); mean follow-up was 14.6 months. No periprocedural complications or death were observed; 1- and 3-month mortality rates were 4.0% and 8.1%, respectively. Gender (male), underlying neoplasia, presence of diabetes, low serum albumin, thrombocytopenia, hypernatraemia, increased CRP and leucocytosis were significantly related to mortality on univariate analysis.
Cox-regression identified serum sodium ≥ 150 mmol/L (OR 25.4; 95%CI 7.4-86.8; $P<0.0001$) as factor independently related to 1- month mortality and CRP >4,34 mg/dL (OR 5.3; 95%CI 1.8-15.9; $p=0.003$) to 3-month mortality. On Kaplan-Meyer analysis patients with CRP>4,34 mg/dL (HR 3.5; 95%CI 1.5-8.3) and Na ≥ 150 mmol/L (HR 4.3; 95%CI 1.1-17.6) presented a significantly increased risk of long term mortality.
The presence of an underlying neoplasia (as indication for PEG placement or comorbidity) is an independent risk factor for 1-, 3-month and long-term mortality (OR 3.69, 3.30 and 2.32, respectively). Finally, we observed that dementia was not associated with an increased risk of mortality (HR 1.21; 95%CI 0.75-1.96; $p=0.42$).
CONCLUSION: Significant hypernatraemia (≥ 150 mmol/L) and high levels of serum CRP (> 4,34 mg/dL) are independent predictors of short- and long-term mortality. Improvement in patients' selection criteria and pre-procedural management could lead to better outcomes after PEG placement. Our results suggest that serum hypernatraemia, reflecting an underlying modifiable dehydration status, has to be properly assessed and even corrected.
Disclosure of Interest: None declared

P1112 EFFICACY AND COMPLICATION OF ENTERAL FEEDING AFTER LIVER TRANSPLANTATION

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INTRODUCTION: Adequate nutrition support for patients undergoing major surgery has been shown to impact significantly on postoperative recovery. Data on the enteral feeding after liver transplantation (LT) are scarce.
AIMS & METHODS: We tried to know about the efficacy and complication of feeding tube which was inserted by fluoroscopic assistance, endoscopic assistance or transperitoneal jejunostomy in patients who were underwent LT. Between January 2008 and August 2013, 2058 cases of LT were performed at Asan Medical Center, Seoul, Korea and enteral feeding tube was inserted in 155(7.5%) patients after LT. Among 155 patients fluoroscopic placement was performed in 81 patients (52%), endoscopic placement in 49 patients (32%), and

transperitoneal jejunostomy in 25 patients (16%). We retrospectively analyzed the efficacy and complication of enteral feeding tube.
RESULTS: Median age was 55 years (interquartile range [IQR] 49-60years). Indication of enteral feeding were high risk of gastric aspiration (n = 90), gastric stasis (n = 27), pneumonia (n = 23), gastrointestinal bleeding (n = 12), and bowel rest (n = 3). Duration of enteral feeding was 14.5 days (IQR 8.0-30.7 days) in fluoroscopic placement, 20.0 days (IQR 8.0-40.0 days) in endoscopic placement, 37.5 days (IQR 18.2-86.2 days) in transperitoneal jejunostomy. Time to establishment of oral feeding was 13.0 days (IQR 6.2-25.7 days) in fluoroscopic placement, 24.0 days (IQR 10.5-43.5 days) in endoscopic placement, 37.0 days (IQR 17.0-64.2 days) in transperitoneal jejunostomy. After tube insertion, dislocation of tube and blockage of tube were found on 34 patients (22%) and 16 patients (25%). Most common enteral feeding related complications were diarrhea (n = 68, 44%).
CONCLUSION: Enteral feeding tube insertion to the patients who cannot maintain nasogastric tube or start oral intake for a long time is important for the nutritional support after LT. Each methods of tube insertion by fluoroscopy, endoscopy, or surgery show its own advantage and disadvantage. Proper selection of feeding methods according to the patient's condition can improve the prognosis of patients by better nutritional support after major surgery such as LT.
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Disclosure of Interest: None declared

P1113 GLUCOSE HOMEOSTASIS IN CRITICALLY ILL PATIENTS IS NOT AFFECTED BY DIFFERENT ENTERAL NUTRITION FORMULAS

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INTRODUCTION: Hyperglycemia is common in critically ill patients and associated with increased mortality. It has been suggested that different nutrition formulas may beneficially influence glucose levels in surgical ICU patients. We investigated glucose homeostasis in response to different enteral nutrition formulas in medical critically ill patients.
AIMS & METHODS: A total of 60 patients were randomized to receive continuous fat-based (group A, n = 30) or glucose-based enteral nutrition (group B, n = 30) for seven days. Indirect calorimetry was performed to determine energy demand at baseline and repeated on days 3 and 7 to evaluate substrate oxidation. Glucose levels, insulin demand, insulin/glucose ratio, calorie and substrate intake per 24 hours, as well as nutrition related side effects were assessed for 7 days.
RESULTS: Patients presented with similar age (60±12 vs. 58±16 years, p = 0.657), Body Mass Index (26.2±5.2 vs. 27.5±4.4 kg/m^2, p = 0.294) and SAPS II score (58±14 vs. 63±13, p = 0.147). At baseline patients did not differ with regard to energy demand (1542±382 vs. 1485±384 kcal, p = 0.566) or fasting glucose levels (149±65 vs. 139±68 mg/dl, p = 0.571). Over the course of 7 days patients had similar glucose AUC (710±172 vs. 763±122, p = 0.193), similar average glucose concentrations per 24 hours (repeated measures ANOVA p = 0.655), similar overall insulin demand (187±165 vs. 186±125 IE, p = 0.991), and a similar insulin/glucose ratio (repeated measures ANOVA p = 0.962). Furthermore they received similar amounts of enteral nutrition per 24 hours and showed no difference in nutrition related side effects such as gastric reflux, vomiting, diarrhea, and hyperlipidemia.
CONCLUSION: Patients showed similar glucose homeostasis and insulin demand regardless of whether continuous enteral nutrition was fat-based or glucose-based. Special nutrition formulas do not seem to influence glucose homeostasis in the acute phase of illness in medical critically ill patients.
Disclosure of Interest: None declared

P1114 HEALTHCARE PROFESSIONALS' KNOWLEDGE ON THE INSERTION & BASIC CARE OF NASOGASTRIC FEEDING TUBES

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INTRODUCTION: In the UK, thousands of nasogastric (NG) feeding tubes are inserted each day to administer enteral feeds and medication. The main risk associated with NG tubes is misplacement into the respiratory tract. Between 2005-2010, the National Patient Safety Agency (NPSA) reported 100 serious incidents relating to the misplacement of NG tubes, with 21 resulting deaths. Guidelines set by the NPSA aim to ensure that thorough checks are carried out to minimise patient risk.
AIMS & METHODS: The aim was to evaluate the knowledge of healthcare professionals on the basic principles behind inserting and caring for NG tubes. NPSA guidelines were analysed and a multiple choice questionnaire was created. Questions covered contraindications to NG tubes, basic safety checks to confirm correct placement (pH of aspirates and interpretation of chest x-rays) and basic care of NG tubes once sited. 120 questionnaires were distributed on one day to all available doctors and nurses in the ED, medical, surgical & intensive care wards in a South Wales hospital. Questionnaires were completed without time constraints and collected the same day. They were then marked against a prescored questionnaire.
RESULTS: 120 questionnaires were distributed. 73% were returned. 45% were completed by doctors & 55% by nurses. 38% were able to identify all contraindications to NG tube insertion. Participants were asked to estimate the length an NG tube should be inserted. A NEX (Nose-Ear-Xiphysternum) measurement should be taken prior to insertion. 32% of participants were able to identify the 3 correct anatomical landmarks. Questions regarding safety checks following insertion of an NG tube were answered well. 79% were able to identify the first line test (pH paper) that should be used to confirm correct placement. 82% were aware that chest x-ray is a second line test. Only 42% were aware of the correct pH which confirms correct NG placement. No participants were able to identify all situations requiring immediate re-confirmation of NG tube site. Worryingly, 16% did not identify that NG tube position should be reconfirmed before administering enteral medication/feeds. 14% were unaware that NG tube position should be reconfirmed after vomiting. 10% did not identify new signs of respiratory distress as a situation requiring reconfirmation of site. Participants trained to interpret chest x-rays were asked to identify chest x-ray features seen with a correctly sited NG tube. 29% correctly identified all features. The remaining participants did not identify one or more features that are essential to look for when checking NG placement on a chest x-ray. 56% did not identify bisecting the carina as a feature, and 15% did not select "clearly identifiable NG tube" as a required feature.
CONCLUSION: Amongst clinical staff there is poor knowledge on NG tubes. Many participants were unable to identify absolute contraindications and were unaware of the NEX measurement. Less than half the cohort were aware of the aspirate pH that confirms correct positioning. There was poor knowledge of situations requiring immediate re-confirmation of NG site and chest x-ray features confirming placement. These results highlight the need for improvement in training staff receive on NG tubes, to ensure that patent safety is not compromised.
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Patient Safety Alert NPSA/2011/PSA002: Reducing the harm caused by misplaced nasogastric feeding tubes in adults, children and infants.
Disclosure of Interest: None declared

P1115 FACTORS INFLUENCING MORTALITY FOLLOWING GASTROSTOMY INSERTION

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INTRODUCTION: High mortality rates have previously been reported following gastrostomy insertion, particularly among certain patient groups (e.g. dementia). With the increasing use of prophylactic gastrostomy for head and neck cancer (HNC), our group aimed to examine survival in this cohort compared to other referral indications and assess risk factors.
AIMS & METHODS: Gastrostomy insertions were examined from two hospitals in Sheffield between 2004 - 2013. Data was prospectively collected from all referred patients including demographic data, biochemical parameters, referral indications and gastrostomy type. Statistical analysis was performed with Chi-squared or Fishers exact tests.
RESULTS: 1733 patients were included (1004 male, mean age = 65). 30 day and 1 year mortality was 9.66% and 44.98% respectively. Indications for gastrostomy included; HNC (n = 591), neurological disease (n = 429), dysphagic stroke (n = 393), dementia (n = 9) and other (n = 311). The lowest mortality was seen in patients with HNC (30 day mortality = 5.2%, 1 year mortality = 32.6%). In comparison, 30 day mortality in all other groups was significantly higher (8.47% in neurological diseases, 15.86% in dysphagic stroke, 33.3% in dementia and 11.25% in 'other' indication, p < 0.01). Mortality was also significantly higher at one year (p < 0.01). There was no significant difference in mortality when comparing radiologically inserted and percutaneous endoscopic gastrostomies. Higher mortality rates were seen in patients aged 60 years or above at 30 days (OR 2.439 (1.666 – 3.731) p < 0.0001) and also at 1 year (OR 3.140 (0.268 – 0.600) p < 0.0001). Albumin less than 30g/L was also associated with significantly higher 30 day (OR 4.486 (3.067 – 6.561) p < 0.0001) and 1 year mortality outcomes (OR 2.319 (1.830 to 2.939) p < 0.0001). In accordance with recent published data, our findings would support an elevated CRP (> 5mg/L) being a factor associated with 30 day mortality (OR 8.930 (1.199 to 66.51) p = 0.006).
CONCLUSION: Referral indication for gastrostomy significantly impacts 30 day and 1 year mortality outcomes, with lowest rates demonstrated in patients with HNC. Identification of factors associated with mortality as seen in this study could help improve patient selection and be of relevance in the decision making process for gastrostomy.
Disclosure of Interest: None declared

P1116 20 YEARS EXPERIENCE OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN A PORTUGUESE TERTIARY CENTER

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INTRODUCTION: Gastrostomy may be indicated in several situations usually when oral intake is not adequate. It can be done surgically or with endoscopy: percutaneous endoscopic gastrostomy (PEG). PEG placement allows adequate nutrition, in dysphagic patients of different etiologies.

AIMS & METHODS: The aim of this study was to characterize the patients in whom a PEG was placed and the complications associated with the procedure. Retrospective study of all patients in whom a PEG was placed between November 1993 until April 2014 in a referral center, based on data prospectively collected, including follow-up visits. All PEGs were performed using the pull-through technique by one experienced endoscopist.
RESULTS: 865 patients were included; 515 were male with a mean age of 63.28 years. The mean follow-up time was 19.21 months (0-158).
The most common indication for the procedure was motor dysphagia. Most patients were referred from neurology: 309 (35%), otorhinolaryngology: 227 (26%), and internal medicine: 94 (11%).
507 patients had neurologic disease and 292 had cancer. Of the neurologic diseases the most common were amyotrophic lateral sclerosis (216; 43%); stroke (87; 17%); dementia (58; 11%); Parkinson (32; 6%); traumatic brain injury (21; 4%) and cerebral palsy (17; 3%). The most common malignancies were pharyngeal-laryngeal (207; 71%); esophagic (40; 14%) and central nervous system (30; 10%. In 5 patients the procedure was not done because there was no gastric transillumination (4 had previous abdominal surgeries).
The most frequent complication in our series: Minor: inadvertent PEG tube removal (about 100, difficult to be exact), mucosal extrusion (150), significant peristomal leakage (20); Major: pneumoperitoneum with abdominal pain, leucocytosis and elevated C reactive protein (5), wound infection (4), buried bumper syndrome (4), small bowel perforation during PEG/PEJ placement (1), interposed bowel (3) and cardio-respiratory arrest (3), one during the procedure and the other 2 in the 48 h after the procedure. Only one patient needed surgical intervention.
There were three other procedure related deaths. One patient refused surgery after small bowel perforation during the procedure; other had peritonitis after inadvertent PEG tube removal and the other patient in the sequence of an abscess after buried bumper syndrome.
CONCLUSION: In our series PEG was quite a safe procedure that was more commonly used in patients with neurologic disease and cancer.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00
PAEDIATRIC: UPPER GI – POSTER EXHIBITION – HALL XL

P1117 ARE DILATATIONS OF ESOPHAGEAL STRICTURES IN CHILDREN EFFECTIVE?

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INTRODUCTION: Esophageal strictures in children are most of the time acquired and benign. Although they have multiple etiologies, they all respond to the same treatment: instrumental dilatations.
Our objective is to specify the etiology of esophageal strictures and to assess their response to dilatation treatment depending on the etiology.
AIMS & METHODS: The study covers all the cases of esophageal strictures treated in our pediatric digestive explorations unit, that benefited from dilatations between January 1996 and December 2011. Out of 1,022 cases of diagnosed esophageal strictures, 422 benefited from dilatations. The dilatations were performed using Savary-Gillard bougies in an outpatient setting, under heavy sedation, or general anesthesia for complex strictures. Three to four bougies are passed per session. The response to treatment is judged good when obtaining a quasi-normal oral feeding without food hangings.
RESULTS: 422 children, aged between 2 months and 15 years, benefited from repeated dilatations, performed at short intervals in the beginning, then at longer intervals depending on the results. The strictures were caustic (330 cases of which 16 presented an anastomotic stricture after oesophagoplasty), peptic (48 cases), and anastomotic (operated eosophagal atresia (25 cases), congenital (9 cases), thermal (2 cases), caustic plant ingestion (1 case), and unknown nature (9 cases)).
The response to the treatment, all causes combined, is good in 345 cases out of 422 (82%). The results are better for the peptic strictures (98%) compared to anastomotic (90%), caustic (79%) and congenital (78%) strictures.
The 422 patients required 2,711 dilatation sessions. The average number of sessions is higher in caustic strictures than in other etiologies: 8 sessions versus 4 respectively.
Complications consisted in 5 cases of perforation (4 caustic strictures and 1 congenital), 1 case of digestive bleeding and 1 case of septicemia that responded well to medical treatment.
CONCLUSION: Caustic esophageal strictures are the most frequent cause in our practice. Globally, the response to dilatations is relatively good but their future, on the long term, remains a subject of preoccupation and an endoscopic surveillance of these children in adulthood is necessary in order to detect a possible dysplasia.
Disclosure of Interest: None declared

P1118 THE CHARACTERISTIC OF GASTROESOPHAGEAL REFLUX IN CHILDREN WITH CYSTIC FIBROSIS

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INTRODUCTION: Previously published studies have indicated that gastroesophageal reflux disease (GERD) is very common in patients with cystic fibrosis (CF), also in paediatric population. However, it hasn't been well characterized so far.
AIMS & METHODS: The aim of the study was to assess the frequency of GERD and characterize gastroesophageal reflux episodes (GER) in children with cystic fibrosis.
This was a multicenter, prospective study of children with cystic fibrosis older than 12 months of age. All children underwent 24 hour multichannel intraluminal pH-impedance (MII-pH) monitoring. The characteristic of GER was made with BioVIEW analysis software and manual revision made by single investigator.
RESULTS: 44 consecutive patients (22 boys, median age 10.65± 3.6, range 6.3-17.8) were enrolled into the study. GERD was diagnosed in 26/44 (59.1%) patients. A total of 1585 reflux episodes were detected by MII-pH. 1199 (75.6%) of them were acid, 382 (24.1%) – weakly acid and 4 (0.3%) weakly alkaline. 691 (43.6%) GER episodes reached the proximal oesophagus. In only 14/44 (31.7%) patients typical GERD symptoms were present.
CONCLUSION: It was the largest study characterising GERD in children with CF with a use of MII-pH performed so far. The frequency of GERD in children with CF is very high, similar to previously raised. Majority of GER episodes were acid, so proton pump inhibitors may be an effective therapeutic option in this population. Number of proximal GER was relatively high, which may increase the risk of aspiration. In children with cystic fibrosis GERD should be diagnosed regardless of presence of its typical symptoms.
Disclosure of Interest: None declared

P1119 TRAVERSING DIFFICULT ESOPHAGEAL STRICTURES IN CHILDREN

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INTRODUCTION: Esophageal stricture (ES) may arise in children from a number of etiologies, mainly as a primary anomaly, after esophageal surgery and as a result of chemical injury. Esophageal balloon or bougie dilation is a nonsurgical method for treatment of most esophageal strictures in children. Some strictures may be complex and require a divergent treatment approach.
AIMS & METHODS: The aim of this study was to determine the efficacy and safety of esophageal dilatations for symptomatic esophageal strictures in children.
A retrospective longitudinal study was carried out on children with ES who were submitted to esophageal dilatation in two pediatric hospitals in Rio de Janeiro over a median follow-up period of 6 years. The data collected were age, sex, type of ES, type of dilatation treatment, number of dilatations, intralesional injection of corticosteroid, use of rigid scope and dilatation with different accessories for endoscopes. All the procedures were under general anesthesia. The objective of each dilatation session was to break the stricture or to increase the esophageal diameter.
RESULTS: 63 patients were included in this study. Patients age ranges one month-old to 10 years-old and 54% were male. The most common stricture cause was postoperative (after esophageal atresia repair) in 46 patients (73%), followed by caustic stricture in 17% patients. A total of 453 bougie dilatations were carried out with the mean number of dilatations per patient being 7. Eighteen patients (29%) had complex strictures and require a special treatment. In 9 (14.3%) patients only the ERCP guide-wire pass the ES, 4 patients (6.3%) were treated with intralesional triamcinolone, 3 (4.8%) were first dilated with ERCP balloon, 2 (3.2%) require rigid esophagoscopy to the first dilatation, 2 were submitted to gastrostomy and retrograde positioning of the guide-wire, 2 were first dilated with biopsy forceps, 1 patient (1.6%) had been treated by electrocautery therapy and 1 with total esophageal occlusion were treated by anterograde-retrograde Rendez-vous approach. Dilatation was successful in 39 patients (62%), 13 patients (21%) are still being submitted to dilatation, 6 (9.5%) were referred to surgical treatment and 5 (8%) abandoned the treatment.
There were one (0.2%) anesthetic complication and 3 (0.6%) endoscopic perforations (2 treated clinically and 1 surgically).
CONCLUSION: Savary-Gilliard bougie dilatation is a safe and effective procedure in the management of the most ES in children. In ours series the most children (90%) had been treated endoscopically with low number of complications. Complex ES may require different treatment. The creativity of the endoscopist using different accessories for endoscopes allow many patients with complex stenosis to be treated in non surgical method.
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Disclosure of Interest: None declared

P1120 PRIMITIVE PEPTIC ULCER DISEASE: A 5-YEAR RETROSPECTIVE STUDY IN A CHILDREN'S HOSPITAL FROM NORTH-EASTERN ROMANIA

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INTRODUCTION: Primitive peptic ulcer disease is still frequent in children from middle income countries with a high incidence of *H. Pylori* infection and a large amount of population with impaired socioeconomic status.
AIMS & METHODS: To investigate the prevalence, clinical features and risk factors of primitive peptic ulcer disease (PUD) in a pediatric population from North-Eastern Romania. We examined retrospectively all endoscopy records from 2009-2013. Demographical, clinical, laboratory, endoscopical and therapeutic data were analysed.
RESULTS: We report an incidence of 6.09/100.000 individuals for primary PUD and a frequency of 4.61%. 49.36% of children were 14-16 years old (range: 7-18 years), male to female ratio was 1.46:1 and 77.41% of patients were living in urban areas. Clinical features included chronic abdominal pain (50.89%), followed by vomiting (34.18%) and upper digestive bleeding (11.39%). We found 65 douodenal ulcers (DU) and 9 gastric ulcers (GU). Family history was positive in 55.33 % of DU patients with group O and found type O blood in 55.56% of the patients. 71.42% were HP-related PUD; from these, 77.42 % were DU. Non HP-PUD was found in 28.58 % children We identify an improper diet (63.16%), smoking (57.39%), alcohol consumption (15, 78 %), psychological stress represented by school difficulties (27.27%), family conflicts (22.73%) and conflicts with entourage (13.64%) as additional risk factors for the disease. We noticed a significant correlation between a high number of family members ($r = 0.63$, $p = 0.002$), low socioeconomic status ($r = 0.87$, $p = 0.0003$) and *H.pylori* infection. We used standard triple therapy in 73.33% of the patients, bismuth-based quadruple therapy in 16.66 % children and sequential therapy in 10% of the cases. The global eradication rate was 66.66 % on all series of patients; we didn't have technical conditions to search antibiotic resistance of the bacteria but previous studies indicate a resistance to clarithromycin around 33 % in Romania.
CONCLUSION: In North-Eastern Romania, primitive PUD affects mainly teenagers from urban areas, originating from large families with a low socioeconomic status and a high incidence of *H.pylori* infection. DU were more frequent, associated with blood type O and family history; we also identified associated risk factors for the disease as diet, smoking, alcohol consumption and stress. Since we obtain a moderate eradication rate using the first line recommended therapies we considered this as an indirect proof of high clarithromycin resistance in romanian children due to the wide-spread practice of empirical antymicrobial therapy in our country.
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Disclosure of Interest: None declared

P1121 PRIMARY ANTIBIOTICS SUSCEPTIBILITY AND EFFICACY OF SUSCEPTIBILITY-GUIDED TRIPLE THERAPY FOR HELICOBACTER PYLORI AMONG JAPANESE CHILDREN WITH HIGH CLARITHROMYCIN RESISTANCE RATE IN THE LAST DECADE - A MULTI-CENTER OBSERVATION STUDY

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INTRODUCTION: Recently, the prevalence of *Helicobacter pylori* infection in Japanese children has been reduced to 3-5%. The drug susceptibility is different depending on the country or region, so that it is necessary to consider the regional characteristics to eradicate *H. pylori*. We are inspired to re-evaluate the eradication therapy among Japanese chidlren by high eradication rate of sequential therapy in European children.
AIMS & METHODS: The present study aimed to evaluate the drug resistance rate and the eradication rate of *H. pylori* in the last 10 years in Japanese children. From April 2003 to March 2012, in Japanese three facilities, total 74 (mean age 12.3 ± 3.2, male 47.3%) children and adolescents under 18 years old, who had no history of eradication therapy in the past, were included in this study. *H. pylori* was cultured using biopsy specimens from gastric antrum and corpus then the drug susceptibility was evaluated. Patients were treated with susceptibility-based triple therapy and were examined the rate of eradication. Successfulness of eradication was evaluated by the 13C-urea breath test and/or stool antigen test at least 8 weeks later after the end of treatment.
RESULTS: *H.pylori* susceptibility test showed that 47.2% were resistance (MIC = >1) to clarithromycin (CAM), 30.1% (MIC = >16) to metronidazole (MNZ). Susceptibility of amoxicillin (AMPC) (MIC = >0.06) was 21.3 %, but MIC = >1 was only 2 strains. The MIC 50 of CAM during the first five-years of study period was 0.12 and resistance rate was 44.4%. On the other hand, in the last five-years period, MIC of CAM was 2.0 and resistance rate was 52.2%, so it was speculated to be in the increasing trend in CAM-resistant strain. The overall eradication rate was 89.4%(59/66) by intention-to-treat analysis (ITT) and 96.7% by per-protocol analysis (PP). The PPI, AMPC and CAM regimen was the first choice for CAM susceptible strain. The ITT and PP eradication rates were 91.7% (33/36) and 100% (33/33), respectively. The PPI, AMPC and MNZ regimen was the first choice for CAM resistant strain and the ITT and PP eradication rates were 91.3% (21/23) and 100% (21/21), respectively.
CONCLUSION: An antimicrobial susceptibility-guided triple eradication therapy for *H. pylori* is effective in Japanese children with very high, approximately 50%, CAM resistance rate and it was comparable to or greater than the previously described sequential therapy in western countries.
Disclosure of Interest: None declared

P1122 ARE ESPGHAN 2011 GUIDELINES FOR CELIAC DISEASE ALSO SUITABLE FOR ASYMPTOMATIC PATIENTS?

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INTRODUCTION: In 2011, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) has released its updated guidelines on celiac disease (CD) diagnosis.1 According to these new guidelines, symptomatic children with anti-transglutaminase (anti-tTG2) antibody levels ≥ 10 times upper limit normal (ULN) could avoid duodenal biopsies if the HLA test and serum anti-endomysial antibodies (EMA) are positive.1 So far, both symptomatic patients with anti-tTG2 titer <10 times ULN and those asymptomatic should undergo upper endoscopy with multiple duodenal biopsies to confirm a suspected CD.
AIMS & METHODS: The aim of this study was to assess the accuracy of serological tests in asymptomatic patients to diagnose CD. We retrospectively assessed 286 children and adolescents (mean age: 8.3 years; age range: 10 months-17 years) who had received a CD diagnosis based on elevated titer of anti-tTG2, EMA positivity, histology and HLA typing. All patients (95 boys, 191 girls) were positive for anti-tTG2 and EMA. Patients were distinguished between symptomatic and asymptomatic while histological lesions were graded according to the Marsh-Oberhuber (MO) criteria. Statistical evaluation was made with the Fisher exact test.
RESULTS: Among the 286 EMA positive biopsied children, 196 (68.53%) had anti-tTG2 titers ≥ 10 times ULN. Among them, a group of 156 (86.02 %) children also had symptoms suggestive of CD (namely "high-titer" symptomatic children); of these, 142 (91.02%) showed severe lesion degree (3a, 3b, 3c MO). On the contrary, 40 out of 196 (13.98%) children were asymptomatic (namely "high-titer" asymptomatic children); 37 (92.5%) of them showed severe lesion degree (3a,3b, 3c MO). No difference was found between "high-titer" symptomatic children and "high-titer" asymptomatic children with regards to histological damage (Fisher exact test $p = 1.000$).
CONCLUSION: Our results indicate that the absence of symptoms in children with anti-tTG2 titers >10 times ULN and positive EMA antibodies does not undermine a "biopsy-sparing" CD diagnosis. The "biopsy-sparing" protocol seems to be applicable to both symptomatic and asymptomatic patients with anti-tTG2 titer >10 times ULN, positive EMA and HLA-DQ2/DQ8.
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Disclosure of Interest: None declared

P1123 SOCIOECONOMIC VARIATION IN THE INCIDENCE OF CHILDHOOD COELIAC DISEASE IN THE UNITED KINGDOM

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INTRODUCTION: Socioeconomic status has been proposed as a potential risk factor for coeliac disease (CD), but the few studies that have investigated this possible association report conflicting results. We aimed to estimate the current diagnostic patterns among children in the United Kingdom (UK) and how they vary by socioeconomic status.
AIMS & METHODS: All children aged 0-18 years who were actively registered with a large population-based general practice database between 1993 and 2012 were identified. The incidence of CD was evaluated in each quintile of the Townsend Index of Deprivation, a measure of socioeconomic status, and stratified by age, sex, country of residence and calendar year.
RESULTS: Among 2.063,421 children we identified 1.247 coeliac disease diagnoses, corresponding to an overall CD incidence of 11.8 per 100.000 person-years, which was similar across the UK countries and higher in girls than in boys. We found a gradient of CD diagnosis across socioeconomic groups, with the rate of disease being 80% higher in children from the least socioeconomically deprived areas than in those belonging to the most deprived areas (Incident Rate Ratio (IRR) 1.80, 95% CI 1.45-2.22). This pattern held for both boys and girls and across all ages. Across all four countries of the UK, we found similar associations between CD incidence and socioeconomic status. Whilst CD incidence up to age 2 remained stable over the study period, diagnoses at older ages have doubled over the past 20 years.

Table 1. Incidence rates and Incidence rates ratios of Coeliac Disease across socioeconomic status
Table to abstract P1123

Socioeconomic deprivation (Quintile of Townsend Index)	Rate per 100.000 person-years (95% confidence interval)	Unadjusted Incidence Rate Ratios (95% confidence interval)
1 (least deprived)	14.1 (12.7-15.7)	1.80 (1.45-2.22)
2	14.5 (12.9-16.2)	1.85 (1.48-2.30)
3	10.8 (9.5-12.3)	1.37 (1.09-1.73)
4	10.4 (9.0-11.9)	1.32 (1.05-1.67)
5 (most deprived)	7.8 (6.5-9.4)	reference

CONCLUSION: Despite a doubling in childhood coeliac disease diagnoses over 20 years, children from the most socioeconomically deprived areas are half as likely to be diagnosed as those from less deprived areas. Awareness campaigns and implementation of national guidance may help to implement strategies for case-finding in all children and reduce this inequality. Moreover, future studies should explore the possible association between exposures to different specific risk factors and the risk of CD across socioeconomic groups.
Disclosure of Interest: None declared

P1124 NARROW BAND IMAGING (NBI) COMBINED WITH WATER IMMERSION TECHNIQUE (WIT): ANY DIAGNOSTIC YIELD FOR CELIAC DISEASE? A PEDIATRIC PROSPECTIVE STUDY

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INTRODUCTION: Upper GI endoscopies are still required to diagnose the majority of children with celiac disease (CD), notwithstanding the recently updated ESPGHAN criteria.[1] The ''multiple-biopsy'' approach both in the duodenum and in the bulb has been suggested by several guidelines as the best strategy to confirm the diagnosis of CD; however, this approach increases the invasiveness of the endoscopic procedure itself and is fairly time-consuming
AIMS & METHODS: Our aim was to evaluate the diagnostic yield of a single biopsy guided by narrow-band imaging (NBI) combined with water immersion technique (WIT), in a prospective study of children with CD. We enrolled 43 children (12 males; mean age: 7.2 years; age range: 1.25-15.25 years) with suspected CD undergoing upper GI endoscopy to compare single ''NBI plus WIT''-guided biopsy versus the standard, duodenal and bulbar, ''multiple-biopsy'' approach (2 random biopsies in the bulb, 4 random biopsies in the 2nd-3rd duodenal portion). ''NBI-plus-WIT'' endoscopic severity was classified on a Likert scale as normal, altered with mild modifications (nodular mucosa, scalloping) or clearly altered (reduction and flattening of ''plicae''); inter-observer variability between two different physicians was also assessed with regards to endoscopic judgments. Histology was graded according to the Marsh-Oberhuber classification.
RESULTS: Diagnosis of CD was confirmed in 40 out of 43 children. ''NBI plus WIT'' approach correctly diagnosed 35 out of 40 celiac children, with a diagnostic sensitivity of 87.5 % (C. I.: 77.3-97.7); none among the studied patients showed an exclusive, ''NBI plus WIT''-detected histological damage. Clearly altered pattern at ''NBI plus WIT'' endoscopic visualization was significantly associated to villous atrophy both at ''NBI plus WIT''-guided biopsy and at multiple biopsy sampling (Spearman Rho 0.637 and 0.496). High anti-transglutaminase antibody titer ($\geq$10 times upper limit normal) was also associated to clearly altered pattern at ''NBI plus WIT'' endoscopic visualization. Concordance of ''NBI plus WIT'' endoscopic assessments was fairly high between two different operators (K: 0.884). After the passage through the pylorus of the endoscope, mean NBI plus WIT procedure time was 53.6 sec (DS: 12.7 sec), whereas mean time for multiple biopsy sampling was 218.2 sec (DS: 38.3 sec) ($p \leq 0.0001$).
CONCLUSION: Albeit time- and resource- saving, single ''NBI plus WIT''-guided biopsy is not as effective as the well established ''multiple-biopsy'' approach in confirming the diagnosis of CD. However, in presence of an altered ''NBI-plus-WIT'' pattern coupled to high anti-transglutaminase antibodies, a single ''NBI plus WIT''-driven biopsy might suffice to diagnose CD.
When no altered mucosal pattern is visible even at ''NBI plus WIT'', multiple bulbar and duodenal biopsies must be obtained to confirm diagnosis.
Disclosure of Interest: None declared

P1125 ANTI-TRANSGLUTAMINASE TITER, MARSH-OBERHUBER GRADING AND BONE MINERAL DENSITY IN CHILDREN WITH CELIAC DISEASE AT DIAGNOSIS

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INTRODUCTION: Metabolic bone disease remains a significant and common complication of celiac disease (CD). Several studies have demonstrated low bone mineral density (BMD) at the time of celiac disease diagnosis in both children and adults.[1] Low bone density in children and adolescents is defined as an areal BMD (aBMD) less than 2 SD below the age-adjusted mean value (Z-score < -2 SD).[2] The pathogenesis of bone loss in celiac disease has not been completely elucidated: two major causal factors are malabsorption and inflammation. Calcium and Vitamin D might be poorly absorbed substances in celiacs.1 Several studies demonstrated an increased RANKL/OPG ratio in vitro and an increased osteoclastogenesis in untreated celiac patients due to chronic release of pro-inflammatory cytokines.[3,4]
AIMS & METHODS: Aim of our study was to correlate Z-score value and anti-tissue transglutaminase type 2 (anti-tTG2) antibody titer and Z-score value and Marsh-Oberhuber grade (MO) in children with celiac disease at diagnosis. We enrolled 99 celiac patients (M 35; F 64; age-range: 4-15 years). All patients had positive test results for anti-tTG2 antibodies, histological lesions graded according to MO classification; all of them underwent lumbar DXA performed by Lunar Prodigy Advance (GE Healthcare, USA). Bone mineral density was estimated by Z-score. The linear correlation between the anti-tTg2 titer and Z-score value and between MO grade and Z-score was evaluated by the Pearson product-moment correlation coefficient (Pearson's *r*).
RESULTS: Anti-tTG2 antibody titers $\geq$10 times the upper limit of normal were found in 65 of 99 patients. 84 patients showed severe lesion degree (3c + 3b + 3a) in Marsh-Oberhuber classification, 3 patients showed MO2, 4 MO1, 4 no lesions and 4 didn't undergo conventional upper GI endoscopy (diagnosed according to the ''biopsy-sparing'' ESPGHAN 2012 criteria). Low BMD (Z-score ≤ -2DS) was found in 13 (13.13%) patients; 20 (20.20%) patients showed $-2 <$ Z-score < -1; 43 (43.43%) patients showed -1$\leq$ Z-score < 0 and Z score ≥ 0 was detected in 23 (23.23%) patients. No correlations were found between Z-score value and anti-tTG2 title (Pearson's r = -0.06) and between Z-score value and MO degree (Pearson's r = 0.07). Low bone mineral density does not correlate to the anti-tTG2 title and to Marsh-Oberhuber degree in a cohort of Italian children at CD diagnosis.
CONCLUSION: Our results indicate that there is no clear clinical predictor to identify children with low BMD and who should undergo DXA at the diagnosis. A follow up evaluation after few months of GFD might be more reasonable.
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Disclosure of Interest: None declared

P1127 EFFICACY OF DEAMIDATED GLIADIN PEPTIDE-BASED POINT-OF-CARE TEST (SIMTOMAX®) FOR THE EARLY DIAGNOSIS OF COELIAC DISEASE IN PAEDIATRIC PATIENTS

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INTRODUCTION: Coeliac disease (CD) is currently under diagnosed. It is estimated that 90% of patients remain undiagnosed. Early diagnosis is essential to avoid complications.
AIMS & METHODS: The objective of the study is to assess the effectiveness of a rapid, minimally-invasive point-of-care test (POCT) that detects both IgA and IgG anti-DGP antibodies and total IgA (Simtomax®) in the early detection of coeliac disease in paediatric patients.
A prospective study was conducted in which children (£18a) under suspicion of CD (risk groups and/or symptomatic patients) were selected, including brothers of coeliac children under gastroscopy for other gastrointestinal conditions. Those with severe disease, gluten-free diet, gastrointestinal bleeding, coagulopathy and/or infections during the last month were excluded. All children were evaluated with Simtomax®. A further genetic HLA-DQ study was performed in patients under suspicion of CD. Results were compared against the detection of tissue transglutaminase antibodies ELISA IgA or IgG-tTG (EliATM Celikey®, cut-off 10U/ml) and/or EMA as well as results of duodenal biopsy (DB), used for CD diagnosis according to the current ESPGHAN criteria.
RESULTS: 100 children were studied; including 6 brothers of CD diagnosed patients. 18 children were under 2 years-old, and 14 were found CD positive (1 missed with Ttg). Prevalence of CD found in the present study was 47% (confidence interval of 95% (CI95%): 37.9 – 58.2%). The results of the rapid test

were highly concordant with the diagnosis established to CD: a sensitivity of 95.8% (CI95%: 85.7 – 99.4%), specificity of 98.1% (CI95%: 89.7 – 99.7%), positive predictive value of 97.9% (88.7 – 99.6%) and negative predictive value of 96.2% (87.0 – 99.4%). Positive and negative likelihood ratios were, respectively, 49.8 (CI95%: 72 – 347.5) and 0.04 (CI95%: 0.01 – 0.17). We found two false-negative patients and a false-positive (the latter with a coeliac brother).
CONCLUSION: Taking into account its high diagnostic accuracy in the pediatric population, this rapid test could be considered an effective tool for the early diagnosis of CD, especially in primary care High LR+ and low LR- imply Simtomax® is a suitable tool for ruling in and ruling out CD and results suggest that this POCT could potentially replace standard serology for CD diagnosis in children. Further studies should also cover potential cost savings with Simtomax.
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Disclosure of Interest: None declared

P1128 UNVEILED. THE HIDDEN SHAPE OF NUMBERS. DATA MINING TECHNIQUES APPLIED TO HYDROGEN LACTOSE BREATH TEST

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INTRODUCTION: Informatics applied to clinical data collection provide huge sets of data. Interpretation of these sets with classical descriptive techniques can miss relevant conclusions. Clustering is a method to discover hidden groups or patterns in big sets of data. No initial groups are provided but the clustering is allowed to form groups to maximize the similarity of the patients in each group.
AIMS & METHODS: Application of data mining techniques to identification of hidden patterns in data from hydrogen breath test with lactose. The goal was to identify non evident groups of patients than can potentially share common characteristics not easily evident. Secondarily, we conducted a classic descriptive study of our data set.
Mathematical review with use of clustering techniques of hydrogen breath test. Time range of 4 years, from June 2009 to June 2013. Cluster analysis as such is not an automatic task, but an iterative process of knowledge discovery or interactive multi-objective optimization that involves trial and failure. Measures were, taken at 0 minutes (baseline), 30, 60, 90, 120, 150, 180. Test with an increased level of 20 ppm over baseline were considered "positive".
RESULTS: Data sets from 2751 lactose hydrogen breath test were included. A set of 6 different typologies of data curves were identified:1. Straight line, non-ascending, linked to baseline minor than 20 ppm.2. Straight line, non-ascending, linked to baseline bigger than 20 ppm.3. Curved line, ascendant before 90 minutes.4. Curved line, ascending after 90 minutes.5. Curved line, with doubly ascendant, before and after 90 minutes.6. Curved line, ascendant only at 180 minutes 839 children (32.63 %) were "positive", when increase in 20 ppm was considered independently from the net value of baseline. Otherwise when"positive" is defined strictly as patient with baseline bigger 20 ppm result is similar, showing 32.61 % of children with positive test. 166 patients (6.5 %) had showed high vallues only at 180 minutes.
CONCLUSION:
Although data mining is being incorporated into clinical practice, there is currently no literature on the same test in hydrogen. Using clustering techniques, we have identified a total of 6 curves type in our patients undergoing the test. As 6.5% shows elevation at 180 minutes,test should be always extended up this duration in any case. Early interruption of test is an usual practice in some institutions. A future research option will be to link these 6 groups to different sets of symptoms or metabolic activity of gut flora. Data mining provide an identification of groups not decided in advance, providing less selection bias in clinical research.
Disclosure of Interest: None declared

P1129 EVALUATION OF METHANOGENIC FLORA THROUGH BREATH TEST IN CHILDREN WITH SUSPECTED LACTOSE INTOLERANCE

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INTRODUCTION: Several studies evaluate the efficacy of the Hydrogen (H_2) breath test as a non-invasive study with high sensitivity and specificity to diagnose lactose intolerance. Moreover, it has been reported that an increase in breath CH_4 excretion occurs in children with lactose intolerance. Several papers used different methods to evaluate CH_4 on expired air.
AIMS & METHODS: The aim of the study is to evaluate the importance of CH_4 measurements in the diagnosis of lactose intolerance using different cut-off.
We evaluated 133 children with symptoms suggestive of lactose intolerance. All patients underwent a Lactose H_2 and CH_4 Breath Test (LHMBT). Lactose was administered orally (dose of 2 mg/kg, max 50 mg) diluted in max 250 ml of water. The expired air was collected in specific syringes with a capacity of 20 ml. One breath sample was taken before the intake of lactose and breath samples were taken after the ingestion of lactose every 15 min for 3 hours. The expired H_2 and CH_4 was measured with a specific analyzer (Microlyzer DP; Quintron Instruments, Milwaukee, Wis.). The result was considered positive when a H_2 peak exceeded 20 part per milion (ppm) over the baseline value. Whilst, CH_4 was considered positive using three different cut-off, 20 ppm above the baseline (Method 1), 12 ppm above the baseline (Method 2) or 5 ppm above the baseline (Method 3). A clinician, blinded for the results of the breath test, registered the symptoms of the patients during the test. Statistical evaluation was considered statistically significant for a $p<0.05$).
RESULTS: Fifty-four patients (40.6%) out of 133 resulted positive with methods 1 and 2. Whilst, 63 patients (47.4%) out of 133 can be defined positive with method 3. The percentage of patients positive for hydrogen only (H_2+CH_4-) was 57.4% using method 1 and 33.3% using method 2. No patients showed H_2-CH_4+ values using these methods. Contrary, using method 3, 47/63 (74.6%) patients were positive for both the gases (H_2+CH_4+) and 9/63 (14.3%) children resulted H_2-CH_4+. The peak level of H_2 in H_2+CH_4+ patients was significantly higher than in H_2+CH_4- patients using method 1 and 2 ($P<0.0001$; $p<0.007$, respectively); but not using method 3 (P 0.09). Twenty-seven (50%) out of 54 symptoms was registered in positive patients using method 1 and 2 (p 0.0006); using method 3 we registered 28/63 symptoms in positive children (44.4%) (p 0.008). Sixteen/28 symptoms appeared at the same time of the maximum level of H_2 ($p< 0.001$), and in 13/28 symptoms appeared at the same time of the maximum level of CH_4 ($p< 0.001$). Patients positive only for methane did not respond to the free-lactose diet, showing different disease that explain the symptoms.
CONCLUSION: Our results show that CH_4 had no added value to a simple H_2 breathtest. Moreover, low cut-off of methane may reduce the specificity of the test.
Disclosure of Interest: D. Ummarino: no conflict of interest, B. Hauser: no conflict of interest, A. Staiano: no conflict of interest, Y. Vandenplas: no conflict of interest

P1130 CAN BLOOD CITRULLINE LEVEL IN INFANTS, WITH GLUTEN INDEPENDENT ENTEROPATHY, SCREENING TEST FOR SMALL INTESTINE MUCOSA ATROPHY?

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INTRODUCTION: Blood citrulline level is subject of several investigations but majority concern celiac disease. Can citrulline be a universal indicator of intestinal atrophy?
AIMS & METHODS: Inclusion criteria were: children with histological confirmed intestinal (duodenal) atrophy. Biopsy specimen was taken endoscopically before age 6 months. Endoscopy was provide on the EXERA III with an endoscope GIF - N180 «Olympus». Group A ($N=4$) have to be gluten independent enteropathy or congenital atrophy (presumably), with diarrhea and progressive malnutrition resistant to intensive treatment. Two cases of tufting enteropathy were detected prospectively. Age at time of biopsy sampling: median - 2.9 (10-90th percentile = 0.4-5, 6) months. Control group (B, $N=11$) were included children without symptom of diarrhea, with normal weight, height and head circumferential. Endoscopy wasn't done. Blood samples were taken 5.9 days (CI 95% = 4, 5 - 7, 4). Such age was chosen based on data that citrulline is a indicator of mass enterocytes and this group will have lowest citrulline level per life.
Serum level of citrulline, threonine and taurine was detected by standard validation method -high performance liquid chromatography (HPLC) by AGILENT 1100 chromatograph on the column Zorbax Eclipse C18 with the fluorimetric detector.
RESULTS: Significant difference in citrulline level between two groups atrophy/not atrophy was detected. Group A ($n=4$) median citrulline level 12.2 mmol/l (CI 95% = 6.1 - 12.9), group B 24.1 mmol/l (CI95% = 22.0-40.6), $p=0.002$ (Mann-Whitney U or Wilcoxon rank-sum for difference in median).
CONCLUSION: We can assume that the level of blood citrulline in infants can be used as a screening test to assess the risk of the small intestine mucosa atrophy. Endoscopy with biopsy sampling must be followed after low blood citrulline was detected. Further studies are required to clarify.
Disclosure of Interest: K. Marakhouski Other: "Olympus" CIS expert, I. Pauk: None declared, S. Kletski: None declared, A. Portianko: None declared, D. Bulyga: None declared, T. Gnedzko: None declared, O. Popova: None declared, Z. Kuvaeva: None declared

P1131 RISK FACTORS FOR NECROTISING ENTEROCOLITIS IN PRETERM INFANTS WITH GESTATIONAL AGE ≤ 32 WEEKS

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INTRODUCTION: Necrotizing enterocolitis (NEC) is an acute inflammatory necrosis of small bowel, being the most common neonatal gastrointestinal emergency, that mainly affects preterm low birth weight. NEC incidence is inversely proportional to gestational age (GA), only 10% of term infants develop this disease. Because the etiology and pathogenesis of NEC are still incompletely understood, therapeutic options, morbidity and mortality were not significantly improved in the last decade of time. NEC is a major cause of mortality (up to 25%) and morbidity including recurrent sepsis, dependence on parenteral nutrition, need for surgery and survival with short bowel syndrome. Taking into account the catastrophic development of this disease, it is necessary to focus research on prevention strategies and identify predictive risk factors for its occurrence.
AIMS & METHODS: To identify the risk factors for NEC in preterm infants with GA≤32 weeks in a third level maternity in Romania, using data registered in the National Registry of Respiratory Distress. **Methods:** We retrospectively studied 442 preterm infants ≤ 32 weeks of gestation, born in a third level maternity in Romania between 2010-2013. GA was between 23-32 weeks (with a medium of 29.60 ± 2.26, birth weight was between 480g-2350 g (1309.86 ± 369.44), gender: female 230 (52.0%); male 212(48.0%). Incidence of NEC was 2.7% (12 preterm infants with GA ≤ 32 weeks, stage II and III of disease). The risk factors were selected in four categories: maternal factors, fetal factors, therapeutic factors and factors related to newborns diseases. Statistical analysis of data was performed using Independent Samples T-test and Pearson Chi-Square correlation. p was calculated for confidence interval of 95% (statistical significance $p < 0.05$). To establish NEC predictors we used binominal logistic regression, the Wald model of regressive elimination**.** There were anlysed the characteristics that differentiates preterm babies who developed NEC of those who did not developed this condition.
RESULTS: The final model of regression indicates the fact that the higher risk in developing NEC have had those who presented: mother with ruptures membranes over 18 hours and nosocomial infections. Other most frequend factors implicated in the development of NEC, are, in order of frecvency: maternal-fetal infections, sepsis, maternal hipertension, corioamniotitis, persistent ductus arteriosus, ventilation in CPAP system, lack of antenatal corticotherapy, oxigenoteraphy. There was a statistically significant correlation between NEC and birth weight ($p = 0.003$), chorioamnionitis ($p = 0.02$), bronchopulmonary disease ($p = 0.02$), ruptures membranes over 18 hours ($p = 0.03$).
CONCLUSION: In this study the incidence of NEC was 2.7%, similar to that reported in the literature.
The variability depends on the diagnostic possibilities of each center. The most predictive factors for NEC in our study are: nosocomial infections, ruptures membranes over 18 hours and materno-fetal infections. The knowledge of risk factors for NEC can allow healthcare providers to assess and adjust care practices for preterm infants who presents a higher risk for NEC, based on empirical data.
Disclosure of Interest: None declared

P1132 EFFICACY OF PROBIOTICS IN PATIENTS WITH LACTOSE INTOLERANCE – A PRELIMINARY STUDY

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INTRODUCTION: Lactobacillus bulgaricus and Streptococcus thermophilus produce lactase enzyme. Probiotics may alleviate lactose intolerance by modifying the intestinal flora into one which contains lactase-producing bacteria.
AIMS & METHODS: To assess the efficacy of probiotics in improving lactose intolerance.
Patients were treated with a unique probiotic formulation (Bio-25, Ambrosia - SupHerb, Israel) for 6 months. All patients completed a demographic questionnaire as well as a visual analog scale (VAS) for the assessment of the intensity and frequency of bloating, flatulence, abdominal pain and change in bowel habits, at entry, every 8 weeks and at the end of treatment period. Measurement of hydrogen levels (parts per million - ppm) at each of these time points was also performed. Study end points were: Improvement in symptom intensity or frequency, and the decrease below cut off point of 20ppm of the breath test. The Wilcoxon signed-rank test was used to compare symptom intensity and severity before and after treatment.
RESULTS: The study group comprised eight symptomatic female patients with a positive lactose intolerance breath test. Mean age and mean body mass index (BMI) (kg/m^2) were: 36.4±18.6 years and 25.2, respectively. Treatment with probiotics was associated with a significant improvement in the reported intensity of bloating ($z = 2.55$, $p = 0.11$) and flatulence ($z = 2.21$, $p = 0.027$); frequency of bloating ($z = 2.06$, $p = 0.039$) and flatulence ($z = 2.04$, $p = 0.041$); abdominal pain ($z = 2.06$, $p = 0.039$), and constipation ($z = 2.07$, $p = 0.039$). Lactose breath test was successfully normalized in two (25%) patients.
CONCLUSION: Treatment with probiotics may lead to symptomatic improvement in patients with lactose intolerance. A larger study is warranted to confirm our findings.
Disclosure of Interest: None declared

P1133 IMPAIRED SECRETION OF SATIATION HORMONES IS ASSOCIATED WITH INSULIN RESISTANCE IN OBESE ADOLESCENTS

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INTRODUCTION: The role of gastrointestinal (GI) hormones in the pathophysiology of obesity is unclear, although they are involved in the regulation of satiation and glucose metabolism. The objectives of this study were i) to examine glucagon-like peptide 1 (GLP-1), amylin, ghrelin and glucagon responses to a test meal in obese adolescents and ii) to test which GI peptides are associated with insulin resistance.
AIMS & METHODS: A total of 16 obese (8 male and 8 female; mean age: 12.8 ± 0.6 yr; mean BMI 31.2 ± 1.0 kg/m^2) and 14 control (5 male and 9 female; mean age: 14.2 ± 0.4 yr; mean BMI 20.7 ± 0.6 kg/m^2) adolescents were included. Subjects were instructed to eat a test meal (490 kcal). Plasma samples were collected before and after meal ingestion for hormone and glucose analysis.
RESULTS: Obese adolescents were insulin resistant as expressed by the HOMA index and had significantly increased fasting glucagon and amylin levels compared to the control group ($P = 0.003$ and 0.044, respectively). In response to the test meal, the increase in GLP-1 levels was reduced in obese adolescents ($P < 0.001$). In contrast, amylin secretion was significantly increased in the obese population compared to the control group ($P < 0.005$).
Bivariate analysis for HOMA index and post-prandial GLP-1 levels showed a negative correlation ($R^2 = 0.343$, $P < 0.001$). Amylin post-prandial levels and amylin basal concentration demonstrated both a significant positive correlation (R^2 AUC = 0.42, R^2 basal = 0.46, both $P < 0.001$). Fasting glucagon showed a positive correlation to HOMA (R^2 0.46, $P < 0.001$).
CONCLUSION: We conclude that hyperglucagonemia, hyperamylinemia and reduced post-prandial GLP-1 secretion are important pathophysiological steps in the development of metabolic syndrome in adolescents.
Disclosure of Interest: None declared

P1134 USE OF THE PROBIOTIC LACTOBACILLUS REUTERI DSM 17938 IN THE PREVENTION OF ANTIBIOTIC-ASSOCIATED INFECTIONS IN HOSPITALIZED BULGARIAN CHILDREN: A RANDOMIZED, CONTROLLED TRIAL

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INTRODUCTION: Antibiotic-associated diarrhoea (AAD) occurs in up to 25% of all individuals receiving antibiotics. In hospitalized patients, AAD is related to significant increases in mortality, length of stay, and cost of medical care. Twenty-nine percent of hospitalized patients may develop diarrhoea after antibiotic use; therefore, identifying strategies to minimize antibiotic-associated diarrhoea could be of significant medical and economic advantage.
AIMS & METHODS: Objective:
To evaluate the effectiveness of *Lactobacillus reuteri* DSM 17938 for the prevention of antibiotic-associated diarrhoea and *Clostridium difficile*-related infections in hospitalized children in a Bulgarian hospital.
Study design:
Children ($n = 100$, aged 3 to 12 years) admitted to the hospital for acute infections were enrolled in a randomized, double- blind, placebo-controlled trial. They were assigned to receive either a probiotic supplement containing 1 x 10^8 CFU *Lactobacillus reuteri* DSM 17938 in the form of one chewable tablet once per day ($n = 49$) (BioGaia AB, Stockholm, Sweden) or placebo ($n = 48$). The probiotic or placebo was taken 2 hours after lunch each day, during the entire period of antibiotic treatment at the hospital and for additional 7 days.
RESULTS: Data from 97 children were included in the final analysis. The incidence of diarrhoea (defined as at least 3 loose or watery stools per day in a 48-hour period that occurred during or up to 21 days after cessation of antibiotic treatment) was unexpected low in both groups-L. reuteri ($n = 1$) versus placebo ($n = 1$): 2.04 vs 2.1 per 100 ($p > 0.05$, risk ratio 1.02, 95% CI 0.7-1.4). *L reuteri* DSM 17938 did not significantly affect the incidence or severity of AAD diarrhoea and *Clostridium difficile* infection. We found unusually high colonisation rate of non-symptomatic *C. difficile* measured by toxin-specific ELISA. There was no difference between the probiotic and placebo groups for any of the other secondary outcomes (i.e., incidence of mild diarrhoea, frequency of stool samples positive for *C. difficile* toxin A and B at the beginning and at the end of study period, frequencies of other gastrointestinal symptoms in the same study period) ($p < 0.05$). No adverse events were reported.
CONCLUSION: Due to the low incidence of antibiotic-associated diarrhoea in both groups, no conclusion can be made on the efficacy of *L. reuteri* DSM 17938 on AAD in hospitalized Bulgarian children. The probiotic did not affect the non-symptomatic high rate of *C. difficile* colonisation (33.3% in the placebo and 38.8% in the *L. reuteri* group at baseline) in this population. There was also no difference between groups regarding different gastrointestinal side-effects.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 21, 2014 9:00–17:00

THE IMMUNE SYSTEM: A DRIVING FORCE IN DIGESTIVE HEALTH AND DISEASE II – POSTER EXHIBITION – HALL XL

P1135 EFFECT OF DNA TREATMENT AND PHYSICAL ACTIVITY ON TUMOUR GROWTH ON C57BL/6 – C38 COLORECTAL ADENOCARCINOMA MICE MODELL

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INTRODUCTION: Numerous studies have investigated the positive effect of physical activity in cancerous diseases regarding disease-free survival, presence of recidive tumours and lower risk of metastasis. In physiological and pathological conditions as well, circulating free DNA (cfDNA) level increases. During physical activity higher cfDNA was detected however the risk of malignancies decreased. Effect of cfDNA may depend on its origin.
AIMS & METHODS: Our aim was to study the influence of elevated cfDNA level on tumour progression using animal model. DNA was isolated by our standard method using Zymo DNA columns (DNA Clean & Concentrator™-500, Zymo Research). We had five groups with fifteen C57BL/6 mice in each. C38 non-necrotic colorectal adenocarcinoma tissue was implanted subcutaneously in every group at the same time. Group I got high concentration subcutaneous healthy C57BL/6 spleen-derived DNA (sdDNA), pretreatment started three weeks before tumour implantation and was continued until the end of the study. Group II got the same DNA treatment started at the date of tumour implantation. Treatment of group III started at the same time than in group II, but we used C38 tumour derived DNA (tdDNA). Group IV was used as a control group injected with PBS. Group V was subjected to five hours long physical activity five times per week in a rodent wheel started three weeks earlier than tumour implantation. On the 22nd day mice were slaughtered, peripheral blood, fresh frozen and paraffin embedded tumour tissue and colon samples was collected. Hematoxylin-eosin, cytokeratin, Ki-67, CD3 markers were used to investigate the cell proliferation, necrosis and T-cell invasion. RNA was isolated from tumour tissue (MagNA Pure 96 Cellular RNA LV Kit, Roche) and real-time PCR validation was performed of tumour growth and cell proliferation-related genes.
RESULTS: The size of the tumour in group V was 51%, in group I was 71% and in group II was 48% compared to control group IV. Investigation of implanted tumour tissue showed that proliferation increased in tdDNA treated group III and tumour tissue was less differentiated. CD3 expression was lower in group III than in control group IV, and group V showed strong positivity. The mucosa in colon samples of group III was destruated and showed IBD-like morphology. The number of lymphoid tissue plaques decreased as well. A group of genes showed expression alteration between group I and group V.
CONCLUSION: Plasma cfDNA level may regulate gene expression. The physical activity and DNA treatment has similar preventive effect. The ratio of tumour cell derived and healthy cells derived cfDNA in plasma may regulate immunitiy and tumour progression.
Disclosure of Interest: None declared

P1137 BRAF MUTATION AND IGFBG7 HYPERMETHYLATION IN COLORECTAL SERRATED POLYPS, TUBULAR ADENOMA AND HYPERPLASTIC POLYP

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INTRODUCTION: In colorectal cancer carcinogenesis, serrated neoplasia pathway is characterized with BRAF mutation and aberrant DNA methylation. The aim of this study was to compare serrated polyps to conventional tubular adenoma in BRAF mutation and DNA methylation.
AIMS & METHODS: For DNA extraction, 146 paraffin embedded tissue samples including 47 tubular adenomas (TAs), 53 traditional serrated adenomas (TSAs), 17 sessile serrated adenoma/polyp (SSAs) and 29 hyperplastic polyps in proximal colon (HPs) were collected in Yonsei University Wonju College of Medicine. BRAF V600E mutation was identified through polymerase chain reaction and pyrosequencing assay, and methylation of LINE1, IGFBP7, hMLH1, and CD133 was evaluated through disulfite conversion, polymerase chain reaction, and pyrosequencing assay.
RESULTS: BRAF V600E mutation was found in 2.1% of TA, 47.2% of TSA, 41.2% of SSA, and 20.7% of HP. TSA and SSA had higher BRAF mutation than TA ($P<0.0001$). TSA had higher BRAF mutation than HP ($p=0.018$). IGFBP7 hypermethylation was found in 17% of TA, 37.7% of TSA, 88.2% of SSA, and 37.5% of HP. TSA and SSA had higher hypermethylation of IGFBP7 than TA ($p=0.021$ and $P<0.0001$, respectively). SSA had higher hypermethylation of IGFBP7 than HP ($p=0.002$). hMLH1 hypermethylation was found in 2.1% of TA, 5.7% of TSA, 0% of SSA, and 0% of HP. CD133 hypermethylation was found in 21.3% of TA, 9.4% of TSA, 35.3% of SSA, and 17.4 % of HP.
CONCLUSION: TSA and SSA had different expression of BRAF mutation and IGFBP7 hypermethylation from TA. HP in proximal colon had different expression of BRAF mutation from TSA, and IGFBP7 hypermethylation from SSA. These findings suggest that TSA and SSA have different genetic alterations from TA or HP.
Disclosure of Interest: None declared

P1138 DNA ORIGINATED FROM TUMOROUS COLONIC EPITHELIUM SEEMS TO BE A MORE POTENT IMMUNOMODULATOR ON PBMCS THAN THOSE OF NORMAL DNA

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INTRODUCTION: In case of tumorous and inflammatory conditions, the amount of self-DNA is elevated in the serum The methylation pattern of genomic DNA fragments may related to its organ and disease origin. Self-DNA sequences are recognized by TLR9 on human immune and other types of cells.
AIMS & METHODS:: We compared the immunostimulatory effect of DNA originated from normal and tumorous colonic tissue using isolated peripheral mononuclear cells (PBMCs) from healthy volunteers.
DNA was isolated from fresh-frozen colonic epithelium samples. PBMC was isolated from healthy volunteers by Ficoll-Paque (Sigma). After isolation the viability of PBMCs was determined by Trypane blue dying. PBMCs were incubated for 6 hours with 15-15 μg of self-DNA either of normal and tumorous origin. The expression level of the pro-inflammatory cytokine-related genes was measured by qPCR. Changes of PBMC-associated mRNA expression level of 84 genes were determined by qPCR-based Qiagen T and B cell activation arrays. After 24h incubation with DNA Affymetrix U133 2.0 whole-genome expression analysis was performed.
RESULTS: Incubation with normal DNA resulted in higher IL-2 mRNA expression of PBMCs (dCt of non-treated controls: 11.74 ± 0.1650; dCt of tumorous DNA-treated samples: 10.18, $\pm$ 0.1900; dCt of normal DNA-treated samples: 9.45 ± 0.2900). After incubation either with normal or tumorous DNA IL-6 mRNA expression increased (dCt of non-treated controls: 4.67 ± 0.2800 dCt of tumorous DNA-treated samples: 3.45, $\pm$ 0.1150 dCt of normal DNA-treated samples: 3.55 ± 0.1450).
Based on the results of whole-genome array (Affymetrix U133 2.0) analyses upon treatment with normal DNA overexpression of several matrix metalloproteinases (MT1E, MT1X, MT1G, MT1H, MT1M) and that of phosphatidic acid phosphatase (PPAP2B) were observed. Moreover, the fold changes of several other genes, like EEA1, IL1A, KCNJ2, NLRP3, THBD, OSM were also increased ($p \leq 0.05$). However, following tumorous-DNA treatment no expression changes of these genes were detected.
CONCLUSION: Overexpression of IL-2 on PBMCs induced by normal-DNA treatment may affect T cell maturation and differentiation along with T cell reactivity. IL-6 overexpression in cases of normal and tumorous DNA-treatments may indicate the activation of pro-inflammatory mechanisms leading finally to the overexpression of MMPs.
Disclosure of Interest: None declared

P1139 EFFECTS OF MODIFIED SELF-DNA SEQUENCES ON CELL KINETIC PARAMETERS AND DIFFERENTIATION OF HT29 CELLS

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INTRODUCTION: We have reported that Toll-like receptor 9 (TLR9)-signaling pathway activiation by modified self-DNA depends on the structural characteristics of DNA sequences. However, no concrete data exists on how the characteristics of TLR9 activating self-DNA fragments influence the viability, proliferation, death, and differentiation of cancer cells, which all may have important immunobiologic consequences in inflammatory and tumorous colonic disorders.
AIMS & METHODS: To understand the biologic role of modified self-DNA bound to TLR9, we assayed its effect on cell viability, proliferation, death and differentiation in HT29 cells. HT29 cells were incubated separately with type-1 (normally methylated / non-fragmented), type-2 (normally methylated / fragmented), type-3 (hypermethylated / non-fragmented), or type-4 (hypermethylated / fragmented) self-DNAs for 24, 48 and 72 hours. Cell viability was examined by MTT-assay, cell proliferation by TUNEL method, cell proliferation by Ki-67 assay, while cell differentiation by pancytokeratin (CK) immunohistochemistry.
RESULTS: Treatments with type-1, -3 and -4 DNA sequences resulted in remarkable decrease of cell viability and proliferation, and increase of apoptosis after 72h. The effects of type-3 DNA incubation were the most significant. Type-2 DNA treatment resulted in a slight decrease of cell viability after 48h, but at 72h all parameter of cell kinetics were similar to that of control cells. Regarding cell differentiation, CK expression was only increased after type-3 DNA treatment.
CONCLUSION: Activation of TLR9-signaling pathways by modified self-DNA sequences may display significant effects on cell kinetic parameters like viability, proliferation or death, moreover may influence cell differentiation, which may have clinical importance in the future.
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alterations in HT29-cells to DNA fragment length and methylation status. *Sci World J* 2013; 2013: 293296.
Disclosure of Interest: None declared

P1140 DNA ORIGINATED FROM NORMAL AND TUMOROUS COLONIC TISSUE ACTS DIFFERENTLY VIA TLR9 SIGNALING ON HT29 CARCINOMA CELLS

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INTRODUCTION: Within tumorous and chronic inflammatory conditions self-DNA is released to the extracellular compartment. The Toll-like receptor 9 (TLR9)-mediated immunobiologic effects of self-DNA however are not fully clarified
AIMS & METHODS: Using HT29 carcimoma cells we compared the effects of self-DNA originated from normal and tumorous colonic tissue on the expressions of TLR9- and pro-inflammatory cytokine-related genes. DNA was isolated from fresh-frozen normal and tumorous colonic epithel tissues. HT29 cells were then incubated with DNA samples for 6 hours. After total RNA isolation Affymetrix U133 2.0 microarray analysis and qRT-PCR were performed regarding the genes of the TLR9 signaling pathway. CK20, E-cadherin and DNMT3A immunocytochemistries were also performed for cell differentiation analysis.
RESULTS: After treatment either with normal or tumorous DNA IL-1beta overexpression was observed (dCt in controls vs. tumorous DNA-treated vs. normal DNA-treated samples: 25.87 ± 0.1627 vs. 23.54 ± 0.2613 vs. 24.28 ± 0.2253, $p < 0.05$).
Based on the results of whole-genome expression analyses overexpressions of 3 types of metalloproteinase genes (MT1X, MT1F, MT1H), 3 of metastasis associated genes (TACSTD2, MACC, MALAT1), 1 differentation-associated gene (CEACAM), and 2 metabolism-associated genes (INSIG1, LIPG) were detected. Following incubation with tumorous DNA expressions of CK20, E-cadherin and DNMT3A proteins were increased.
CONCLUSION: Incubation with tumorous DNA binding to TLR9 may promote cancer cell invasion via increased activity of MMPs and other pro-metastatic proteins. Moreover, our results suggest a possible link between TLR9-signaling and DNMT3A regulation.
Disclosure of Interest: None declared

P1142 DIAGNOSIS AND CLASSIFICATION OF REFRACTORY CELIAC DISEASE IN CELIAC PATIENTS DESPITE STRICT ADHERENCE TO A GLUTEN FREE DIET

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INTRODUCTION: Patients with celiac disease (CD) are defined as suffering from refractory celiac disease (RCD) when clinical and histological symptoms persist or recur, despite strict adherence to a gluten free diet (GFD). Intraepithelial T lymphocytes (IETLs) may show normal phenotype and are attributed to RCD type 1 (RCD-1). The IETLs that present an aberrant and even clonal phenotype are attributed to RCD type 2 (RCD-2). These IELs are associated a high risk for development of enteropathy associated T lymphocytes lymphoma (EATL). EATL is the main cause of death in these patients and has a 5 year survival of only 8%. Without detailed phenotyping of IELs, diagnosis of RCD could be missed.
AIMS & METHODS: To establish a diagnostic scheme, in Israel, for RCD diagnosis in CD patients with persistence of CD related symptoms and reported adherence to a GFD based on previously described diagnostic systems. RCD type was determined by performing flow cytometry analysis (FCA) and T-Cell receptor rearrangements PCR (TCR) on small duodenal biopsies, obtained from 11 distinct CD-GFD patients. In addition, Peripheral blood was also obtained and assessed from these patients and served as an internal control.
RESULTS: FCA exhibited RCD-1 phenotype in the duodenal biopsies of 10 patients – all IETLs were normal although abundant. Furthermore no IETLs clonality was demonstrated in these patients by TCR. RCD-2 phenotype was diagnosed in the biopsy of 1 patient who demonstrated a high presence of aberrant IETLs and distinct clonality observed by TCR. Peripheral blood samples, in both RCD-1 and RCD-2 patients, showed no presence of IETLs, nor clonality of T lymphocytes implying duodenal locality of the IETLs.
CONCLUSION: Characterization of IETLs as normal and aberrant by FCA, in CD patients with persistent symptoms despite adhering to a GFD is important for the diagnosis of RCD. Using FCA as an RCD diagnostic tool is as good as exploring IETLs clonality by TCR. Moreover, FCA is preferable and may be solely used for differentiating RCD patients at risk for EATL development. In these patients TCR serves as a complementary instrument for a complete diagnosis.
Disclosure of Interest: None declared

P1143 ACTIVATION OF TOLL-LIKE-RECEPTORS (TLR) ON ISOLATED KUPFFER CELLS (KC) AND SINUSOIDAL ENDOTHELIAL CELLS (SEC) OF THE LIVER: OPPOSING EFFECTS ON THE PRODUCTION OF THE VASOCONSTRICTOR THROMBOXANE B2

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INTRODUCTION: The role of TLR-dependent formed Thromboxane (TX) for portal hypertension in cirrhosis, we have already shown in previous work (including Steib CJ et al., Hepatology 2010). To develop risk stratification ratifications and targeted new therapeutic strategies for patients in the future, the aim of this study was to determine, which liver cells play a relevant role for TX-production and which TLR are involved in this process.
AIMS & METHODS: KC and SEC were isolated from mouse livers (male C57/Bl6) and stimulated over 24h with various TLR-agonists (Pam3CSK4 [TLR 1/2] 0.1g/ml; HKLM [TLR 2] $10e^8$ cells/ml; Poly (I:C) [TLR 3] 10ng/ml; LPS-EK [TLR 4] 10ng/ml; ST-FLA [TLR 5] 10ng/ml; FSL-1 [TLR 6/2] 1ng/ml; ssRNA40 [TLR 7] 0.25µg/ml; ODN1826 [TLR 9] 5µM; $n = 6$). Thromboxane B_2 (TXB_2) efflux before and after stimulation into the cell media was measured by ELISA (mean±SD, $*p < 0.05$).
RESULTS: In KC TXB_2-efflux increases differently (before stimulation vs. after stimulation in pg/ml; **TLR 1/2**:212±90 vs. 242±43; **TLR 2**:251±24 vs. 1271±255*; **TLR 3**:302±96 vs. 400±139; **TLR 4**:231±75 vs. 717±363*; **TLR 5**:254±46 vs. 640±250*; **TLR 6/2**:271±32 vs. 2291±1446*; **TLR 7**:213±91 vs. 296±206; **TLR 9**:229±34 vs. 704±232*), however in SEC after stimulation increasingly there is a decrease in TXB_2-secretion (**TLR 1/2**:544±187 vs. 42±27*; **TLR 2**:477±89 vs. 82±45*; **TLR 3**:408±204 vs. 107±62*; **TLR 4**:497±70 vs. 88±53*; **TLR 5**:238±150 vs. 284±306; **TLR 6/2**:301±191 vs. 100±53*; **TLR 7**:420±131 vs. 111±35*; **TLR 9**:324±207 vs. 84±55*).
CONCLUSION: The activation of TLR 2, 4, 5, 2/6, and 9 on isolated KC of healthy livers lead to a significant production of vasoconstrictive effective TXB_2, whereas the activation of SEC through TLR 1/2, 3, 4, 6, 7 and 9 led to a decrease of TXB_2 production. These findings are important to identify relevant early stage microbial products for the formation of TXB_2 in the future and to develop new targeted therapeutic strategies.
Disclosure of Interest: None declared

P1144 UNIQUE PROFILE OF LIVER PERFUSATE MONONUCLEAR CELLS TRANSFERABLE TO LIVER TRANSPLANTATION RECIPIENTS -ANALYSIS OF THE LIVING DONOR LIVER PERFUSATE BY MULTICOLOR FLOWCYTOMETRY

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INTRODUCTION: Liver transplantation induces relative immune tolerance than the other organ transplantation. The mechanisms responsible for this phenomenon have been acknowledged as the liver resident tolerant immune cells that could be transferred to donor. In living donor liver transplantation, the effluent solution passing through the graft livers during perfusion before transplantation has been shown to be useful to characterize the leukocytes. Recent advances in multicolor flowcytometry enabled us to investigate the character of the leukocytes in detail. We analyzed the perfusate cells with multicolor flowcytometry, revealed the characteristics of the cells, and detected them after an early period post transplantation.
AIMS & METHODS: Liver perfusates were collected from 11 human liver grafts. During the backtable procedure, the grafts were perfused through the portal vein with 1-2L of Univeristy of Wisconsin solution under hydrostatic pressure, and the perfusate was collected from the vena cava. Mononuclear cells (P) were isolated within 12 hrs by density gradient centrifugation. Peripheral blood mononuclear cells (B) were drawn on the same day from peripheral vein. After isolation, cells were stained with cell surface antibodies collecting the population of B cell, CD4+ T cell, CD8+ T cell, NK cell, plasmacytoid dendritic cell (DC), myeloid DC, Programmed death (PD)-1 positive cells, CD45RA+ CCR7+ naïve T cells, CD45RA+ CCR7- effector T cells, CD45RA- CCR7-effector memory T cells, and CD45RA- CCR7+ central memory T cells, and CD4+ CD25+ CD127- regulatory T (Treg). To reveal the perfusate involvement in recipient after transplantation, we studied peripheral blood donor cell microchimerism in human leucocyte antigen (HLA) mismatched 17 patients.
RESULTS: Results: CD8+ T cells (P: 27.8%, B: 16.6%), CD14+ cells (P: 2.13%, B: 0.156%), NK (CD56+) cells (P: 82.9%, B: 66.8%), plasmacytoid DC (CD123+) (P:10.3%, B: 2.16%) and myeloid DC (CD11c+) (P: 6.38%, B: 0.926%) were increased and CD4+CD25+CD127low/- regulatory T cells (Treg) (P: 3.37%, B: 6.75%) was decreased in perfusate compared with peripheral blood. Furthermore, naïve subsets of T cells were lower, and effector memory subsets of T cells and PD-1 T cells were higher in perfusate lymphocyte than peripheral blood. The microchimerism was found in CD14+ cells (0.8%), CD8+ T cells (1.7%), CD4+ T cells (1.5%), B cells (0.95%) and NK (CD56+) cells (4.5%) as the perfusate pattern likely.
CONCLUSION: The perfusate contains CD4+T cells, CD8+ T cells, with higher exhaustion marker PD-1 and plasmacytoid DC, myeloid DC with lower activation marker CD86, probably not to react with many antigens flow into the liver via portal vein. This might explain one reason why liver transplantation exhibit more tolerant than other organ transplantation.

Disclosure of Interest: None declared

P1145 INTERLEUKIN-10 EXPRESSION IS REGULATED BY TOLL LIKE RECEPTORS 2 AND 4 IN INTESTINAL EPITHELIUM

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INTRODUCTION: Intestinal epithelium constitutes a physical and functional barrier which is essential for intestinal immunological activity. In fact, Toll-like receptors expressed in intestinal epithelium are responsible for microbiota recognition, and they also contribute to both intestinal homeostasis and inflammation. The balance between pro and anti-inflammatory cytokines seems to be crucial for homeostasis, and also for the development of inflammation. In this context, interleukin-10 (IL-10), a prototypical anti-inflammatory cytokine mainly produced by immune cells, has been shown to inhibit immune activation (1), and to be essential in tolerance to self (2) and mucosal antigens (3). In addition, deficient IL-10 expression seems to contribute to gut inflammation (4). Intestinal epithelium has been well documented as a rich source of proinflammatory cytokines, however little is known about the relation between intestinal epithelium and IL-10. Several studies have described IL-10 production mediated by TLR2 and TLR4 activation in immunological cells, however the role of TLRs expressed in intestinal epithelium in the modulation of molecular expression and release of IL-10 remains unknown.
AIMS & METHODS: The purpose of this work has been to assess the involvement of intestinal epithelium and TLR2 and TLR4 activation in the expression and release of IL-10. To carry out the study, we have used the human enterocyte-like cell line Caco-2 and intestine from WT, $TLR2^{-/-}$ and $TLR4^{-/-}$ mice. IL-10 release levels were measured by ELISA, and IL-10 mRNA and protein expression were analyzed by RT-qPCR and Western Blot respectively.
RESULTS: Caco-2 cells have shown to express and release IL-10. In addition activation of TLR2 or TLR4 in these cells showed to increase IL-10 mRNA and release. Surprisingly, IL-10 mRNA levels in $TLR2^{-/-}$ and $TLR4^{-/-}$ ileum and colon resulted increased, and IL-10 release levels were also augmented in $TLR4^{-/-}$ ileum whereas in $TLR2^{-/-}$ colon resulted decreased. TLR4 expression was increased in $TLR2^{-/-}$ ileum and reciprocally, TLR2 expression was augmented in $TLR4^{-/-}$ ileum, thus suggesting a cross talk between TLR2 and TLR4 which may maintain IL-10 release in the epithelium.
CONCLUSION: The present work shows that intestinal epithelial cells were able to synthesize and release IL-10, and that the activation of TLR2 or TLR4 stimulated IL-10 expression in these cells. In addition, IL-10 expression and release in mice intestine might be guaranteed by cross- regulation between TLR2 and TLR4. In summary, the results of the present work suggest that intestinal epithelial cells might contribute to the immune response by modulating IL-10 expression, and demonstrate cross-talk regulation of IL-10 expression between TLR2 and TLR4 in the intestine.
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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
POSTER PLUS VIDEO III – POSTER EXHIBITION – HALL XL

P1146 CLINICAL IMPACT OF THE SEQUENTIAL USE OF EUS ELASTOGRAPHY FOLLOWED BY CONTRAST-ENHANCED EUS IN PATIENTS WITH FOCAL PANCREATIC MASSES AND NEGATIVE EUS-GUIDED FNA

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INTRODUCTION: It is well known that EUS-guided FNA has a high sensitivity (over 85%) and specificity (100%) for diagnosis of pancreatic cancer. EUS elastography and contrast-enhanced EUS (CE-EUS) are useful methods for the assessment of patients with pancreatic masses, with high sensitivity and specificity reported in recent meta-analyses. In most of the cases, pancreatic adenocarcinoma is a hard (low strain), hypoenhanced (hypovascular) tumor.
AIMS & METHODS: The aim of the study is to establish an EUS based diagnostic algorithm in patients with pancreatic masses and negative cytopathology after EUS-FNA, based on previously published results and cut-offs of elastography and contrast-enhancement (CE-EUS).
We included in the study a subgroup of 50 consecutive patients with focal pancreatic masses who underwent an EUS examination with negative EUS-FNA for malignancy: 19 patients with pancreatic cancer and 31 patients with pseudotumoral chronic pancreatitis. Real-time elastography and contrast-enhancement during EUS were performed sequentially in all patients. The sensitivity, specificity and accuracy of these methods were calculated separately. Moreover, we established a clinical decision making algorithm based on real-time elastography (for characterization of tissue hardness), followed by contrast-enhanced EUS (for characterization of vascularity).
RESULTS: For the diagnosis of possible malignancy, the sensitivity, specificity and accuracy of EUS elastography were: 97.7%, 77.4% and 84% respectively, while CE-EUS has similar results: 89.5%, 80.7% and 84%, respectively. Subsequently, we selected the subgroup of 25 patients with soft/mixed appearance in elastography for sequential assessment using contrast-enhanced EUS. Thus, the sensitivity of CE-EUS in this set of patients was excellent (100%) while the specificity was 75%, with 76% accuracy. Overall, for the sequential evaluation with elastography, followed by contrast-enhanced EUS, there were no false negative results for possible malignancy, while the negative predictive value of this method was 100%.
CONCLUSION: The proposed algorithm of sequential use of real-time elastography, followed by contrast-enhanced EUS could be a good clinical tool to help select the patients with possible pancreatic adenocarcinoma in the setting of patients with negative EUS-FNA results.
Disclosure of Interest: None declared

P1147 PILOT STUDY TO ASSESS THE POTENTIAL GASTRIC-DUODENAL TRACT EXAMINATION USING A MAGNETICALLY CONTROLLED CAPSULE ENDOSCOPY

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INTRODUCTION: CE progresses inside the gastrointestinal tract only using intestinal motility and several approaches to actively guide the capsule have been proposed. Currently, the most promising solution seems to be the magnetic steering. Up to now the only system of CE magnetic steering available on the market is the Mirocam Navi CE. Aim: To evaluate the feasibility of exploring the gastric cavity and duodenal bulb using the guided CE Mirocam Navi system.
AIMS & METHODS: A small group of patients (18 pts, 9 females, mean age 65.5 yrs, range 52-81 yrs) undergoing CE was included in the study. The indications for CE included 13 pts with occult gastrointestinal bleeding (OGIB), 2 pts with suspected Crohn's disease, 2 pts with polyposis syndrome and 1 suspected ileal neoplasia. Patients with cardiac pacemakers or other implanted metallic devices were excluded. After the patient swallowed the capsule in a sitting position, the external controller was placed in the abdomen over the cardia in order to block the capsule and visualize the Z line. Then the aim of the study was to navigate the capsule through the stomach visualizing the gastric fundus, gastric body, and antrum. Each author moved the external controller and steered the capsule under direct vision through a real time view system. No specific movements were suggested and the attempts to visualize the gastric cavity lasted no more than 20 minutes. The authors reported if the gastric cavity visualization was satisfactory or not. Finally the authors tried to crawl the capsule through the pylorus using the external controller to visualize the duodenal bulb. Patients were asked to judge the tolerability of the procedure using a visual analogical scale (VAS) and any adverse event was registered.
RESULTS: A positive finding was observed in 11/18 of CE (diagnostic yield 61%). A complete visualization of the Z line, antrum, body, fundus and duodenal bulb was registered in 1/18 cases (5.5%), 18/18 cases (100%), in 12/18 (66.6%), 5/18 (27%) and in 6/18 (33%) of the cases, respectively. The crawl of the capsule into the bulb under external magnetic control was obtained successfully in 8/18 of the cases (44%). The mean score of the VAS scale was 9.3 cm (well tolerated). No adverse event was reported.
CONCLUSION: The Mirocam navi system is a promising method for controlled locomotion of CE; it is well tolerated and safe but the ability to control the movement in the upper gastro-intestinal tract is still unsatisfactory.
Disclosure of Interest: None declared

P1148 SUPCAM EUROPEAN PROJECT: PRELIMINARY PROTOTYPING AND TEST OF A NEW GENERATION ACTIVE ENDOSCOPIC COLON CAPSULE

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INTRODUCTION: Optical colonoscopy is currently the diagnostic gold standard for colic diseases, however it is also invasive, risky and embarrassing and minimally invasive diagnostic procedures are required. Market available video endoscopic capsules (VCE) explore the GI tract proceeding by means of visceral peristalsis and gravity. Higher diagnostic accuracy, more extensive clinical application and shorter times of investigation would be achieved by controlling the VCE locomotion. Some authors demonstrated that magnetic fields allow controlling the VCE movement. However the cylindrical shape, while may be suitable for the small intestine, esophagus and stomach, in the colon, due to its anatomical features, has intrinsic disadvantages as regard to VCE propulsion, surface friction and cleaning. Other limits of the previous solutions depend on the movement control precision, or in the use of a very cumbersome and expensive external instrumentation. The SUPCAM concept is based on the development of an innovative Active VCE (AVCE) whose design allows to safely and accurately guide it along the colonic lumen from the outside, using an innovative electromagnetic approach and an external compact assisted handle adapted to be transported and suitable for common outpatient setting. The SUPCAM EU Project is

aimed at developing a new generation of AVCE able to investigate the colon, ensuring a high level of navigation and diagnostic accuracy.
AIMS & METHODS: The aim of this study is to present a new mechanical configuration of a colon capsule and to demonstrate its precise locomotion in the colon from the anus to the cecum and vice versa through external magnetic fields generated by an external low-cost and assisted magnetic handle. An external electromagnetic handle and a capsule prototype were developed within the SUPCAM Project. Experimentally the prototype locomotion capabilities were assessed with motion control tests inside an insufflated human-sized plastic phantom colon.
RESULTS: A prototype of a double sphere colon capsule and external low-cost and assisted magnetic handle for magnetic fields generation and capsule propulsion have been fabricated. The prototype has been inserted transanally into the phantom colon. The endoscopist, moving manually the external handle, drove and accurately oriented the SUPCAM capsule within the phantom colon from the anus to the cecum and vice versa.
CONCLUSION: Our study demonstrated the development and test of a capsule prototype with a completely new double sphere mechanical configuration and an innovative electromagnetic approach. SUPCAM mechanical prototype allowed a precise, effective and safe propulsion and orientation in a phantom model through a low-cost, compact and easily manageable external assisted magnetic handle. In our opinion, SUPCAM endoscopy represents a highly innovative and disruptive solution for colon diseases diagnosis and screening. The further development of this innovative magnetically controlled AVCE, reducing clinical risk, improving tolerance, acceptability, territory availability and adherence to colorectal cancer screening programs, will provide significant benefits for patients and the whole healthcare system. Other studies are planned to test performance of more advanced SUPCAM prototypes in ex-vivo and in-vivo settings.
Disclosure of Interest: A. Tozzi Other: Supcam Patent co-owner, G. Ciuti: None declared, G. Lucarini: None declared, M. Mura: None declared, C. Quaglia: None declared, A. Menciassi: None declared, G. Battaglia: None declared

P1149 ACCURACY OF COLON CAPSULE FOR THE DETECTION OF COLONIC TUMORS

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INTRODUCTION: Colon capsule has shown to be a safe and accurate procedure for the study of colonic pathology. Previous studies have been focused on the diagnostic yield of colonic polyps and, to date, there is scarce data regarding its ability to detect colon cancer. We describe our experience in this field.
AIMS & METHODS: From December 2007 to February 2014 we have performed 211 colon capsules. We describe our experience regarding colon cancer detection.
RESULTS: In our study population, there were 14 colon cancers (12 male, mean age 63 years old). All but one were detected by the capsule. The one not detected by the capsule was due to battery life, as it expired before reaching tumor location. The main reason for referral was colorectal cancer screening in 61.5% of cases, followed by rectal bleeding in 23.1%. Regarding tumor location, 3 tumors were located in the rectum, 3 in sigmoid, 4 in descending, 2 in transverse, 1 in ascending and 1 in cecum. 3/14 patients had a stenosing tumor, in those patients the capsule was retained although it did not cause any obstructive symptoms. In two of these three cases capsule excretion took place after chemotherapy treatment and in the other case we retrieved the capsule with a Roth Net.
Colon cleansing level was adequate in 92.3% of cases.
CONCLUSION: According to our experience, colon capsule is accurate also for colon cancer detection. Despite the theoretical risk of obstructive symptoms associated to stenosing tumors, we haven't found any obstructive complication.
Disclosure of Interest: C. Carretero Lecture fee (s) from: Given Imaging, C. Prieto: None declared, M. Muñoz-Navas: None declared

P1150 CAN MAGNETIC ASSISTED CAPSULE ENDOSCOPY (MACE) REPLACE GASTROSCOPY?

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INTRODUCTION: Attempts in employing a simple technique of capsule endoscopy for visualisation of the upper GI tract has, thus far, been experimental, cumbersome and potentially expensive. We describe the first human series for comprehensive visualisation of the upper GI tract using the simple Intromedic MiroCam-Navi system. Our aim was to demonstrate the manoeuvrability of this magnetic capsule and evaluate its ability to completely visualise and maintain views in the upper GI tract.
AIMS & METHODS: 26 volunteers observed a 12hr overnight fast. 30mins before the examination volunteers drank a preparation mixture of 20mg of maxalon syrup with simethicone and pronase. After capsule ingestion, volunteers were allowed sips of water during the procedure. The MiroCam-Navi magnet was placed at strategic points on the body surface and rotated to hold and manoeuvre the capsule. Control was assessed by moving and holding the capsule for 1 minute to visualise each of the following stations: lower oesophagus, cardia, fundus, body, incisura, antrum and pylorus and also traversing across the stomach and through the pylorus. Total procedure time was taken from the moment of ingestion of the capsule to either reaching the duodenum, or after attempting a maximum of 10mins to traverse the pylorus. All the procedures were performed on the same day in Seoul Konkuk University Hospital by 6 endoscopists (experts in capsule endoscopy). All volunteers subsequently underwent a standard upper GI endoscopy within 3 days.
RESULTS: Volunteers' median age was 38yrs (range 26-45), median BMI 24 (range 19-38), median volume of water consumed 800 mls (range 200mls-1500mls) and median procedure time 24 minutes (range 12-39 minutes). Table 1 shows the success of clear visualisation of landmarks

	Landmark Visualised	Landmark Not Visualised
GOJ	**92%** *(n = 24)*	**8%** *(n = 2)*
Cardia	**88%** *(n = 23)*	**12%** *(n = 3)*
Fundus	**96%** *(n = 25)*	**4%** *(n = 1)*
Body	**100%** *(n = 25)*	**0%** *(n = 0)*
Incisura	**96%** *(n = 25)*	**4%** *(n = 1)*
Antrum	**96%** *(n = 25)*	**4%** *(n = 1)*
Pylorus	**100%** *(n = 26)*	**0%** *(n = 0)*

The capsule could be held overall in 88% of designated stations for 1 minute. The capsule could be moved from the fundus to the antrum in all cases and traverse the pylorus in 50% (n = 13). Age ≥40 was associated with successful pyloric traversing (p = 0.04).
There was positive concordance for 8 out of 9 minor pathological findings with standard upper GI endoscopy. A small 4 mm submucosal lesion was missed by capsule endoscopy in the cardia of one volunteer where views were obscured.
CONCLUSION: This is the first convincing demonstration of the potential value of MACE in the upper GI tract. There is a high degree of visualisation and control, with some improvement required for optimising fundal views and traversing the pylorus.
Disclosure of Interest: None declared

P1151 NON-EXPOSED ENDOSCOPIC WALL-INVERSION SURGERY (NEWS) AS A NOVEL FULL-THICKNESS RESECTION TECHNIQUE FOR GASTRIC TUMOR

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INTRODUCTION: Non-exposed endoscopic wall-inversion surgery (NEWS) is a new advanced method of endoscopic full-thickness resection without transluminal communication, causing intra-abdominal contamination or possible tumor dissemination, applying endoscopic submucosal dissection (ESD) technique.
AIMS & METHODS: The aim of this study is to investigate the efficacy, safety and advantages of NEWS for gastric submucosal tumors (SMT). Between July 2011 and March 2014, 12 patients (5 females, 7 males; mean age 65.8 years, range 49-79 years) underwent NEWS for intragastric-type gastric SMT within 4cm in size at the University of Tokyo Hospital. After marking around a tumor on both the mucosal and serosal surfaces and submucosal injection of sodium hyaluronate, circumferential seromyotomy and sero-muscular suturing were made laparoscopically, followed by circumferential muco-submucosal incision endoscopically. The resected specimen was perorally retrieved. Clinical data and pathological features were analyzed.
RESULTS: The mean resected specimen and tumor size were 23.9 mm (range, 10-45 mm) and 35 mm (range, 25-50 mm), respectively. All lesions were successfully resected in an en-bloc fashion. The mean operation time was 229.5 minutes (range, 140-397 minutes), and the mean estimated blood loss was 41.7 g (range, 0-250 g). Patients started oral intake on mean postoperative day 2.1 (range, 2-3), and the mean length of postoperative hospital stay was 7.9 days (range, 6-13 days). Micro perforation occurred in the three cases due to technical inadequacy, which were treated successfully without open surgery. There were no severe complications, such as hemorrhage, anastomosis insufficiency, delayed gastric emptying or surgical site infection. Histopathological examination of the tumors showed GIST (n = 11) and schwannoma (n = 1).
CONCLUSION: NEWS enabled en bloc full-thickness resection effectively and safely with minimum possible margin without contamination and tumor dissemination into the peritoneal cavity. This treatment may be promising not only for gastric SMT but also for node-negative early gastric cancer difficult to resect by ESD.
Disclosure of Interest: None declared

P1152 MUCOSAL-INCISION ASSISTED BIOPSY FOR SUSPICIOUS GASTROINTESTINAL STROMAL TUMORS

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INTRODUCTION: Tissue sampling is necessary for definitive diagnosis of GIST. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has been developed for tissue sampling of suspected GIST and is generally accepted to be a very useful for the diagnosis of this lesion, but the success rate for histology does not seem to be satisfactory (62%).
Recently Eikichi et al has published of retrospective review of mucosal incision assisted biopsy (MIAB) of suspected GISTs. So we performed prospective study of MIAB associated with suspicious GISTs.

AIMS & METHODS: To evaluate the diagnostic yield of the procedure, mucosal-incision assisted biopsy (MIAB), for the histological diagnosis of gastric gastrointestinal stromal tumor (GIST),and to know the complications of MIAB, we performed prospective study of the 14 patients with suspected gastric GIST who underwent MIAB in our hospitals.
RESULTS: Tissue samples obtained by MIAB were sufficient to make a histological diagnosis (diagnostic MIAB) in 12 out of the 14 patients (86%), where the lesions had intraluminal growth patterns. Histologic diagnosis were GIST (9, 64 %), Leiomyoma (2, 14 %) and inflammatory change (1.7 %). Locations were fundus (3, 21 %), cardia (3.21 %), body (5, 36%) and antrum (3, 21 %). Mean size 15.3 ± 0.8.
1patient had significant bleeding after MIAB but well controlled by endoscopic hemostasis.
CONCLUSION: Although it is generally accepted that EUS-FNA is the gold standard for obtaining biopsies for histological and cytological analysis of suspected gastric GIST, MIAB may be chosen as an alternative diagnostic modality only when the lesion has an intraluminal growth pattern. Further studies will be required to further assess MIAB, including randomized controlled trials to compare MIAB with EUS-FNA.
REFERENCES
World J Gastrointest Endosc 2013; 5: 191–196.
Disclosure of Interest: None declared

P1153 DETECTION OF SESSILE SERRATED ADENOMAS IN IBD SURVEILLANCE COLONOSCOPY BY ELECTRONIC VIRTUAL CHROMOENDOSCOPY AND DYE CHROMOENDOSCOPY

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INTRODUCTION: In IBD sessile serrated adenomas/polyps (SSAs) are difficult to detect by standard white light colonoscopy. We aimed to determine the frequency of finding SSAs during surveillance colonoscopy in IBD and to define the characteristics and endoscopic findings of SSAs developed in a background of IBD.
AIMS & METHODS: Biopsies from a cohort of 87 patients (male 43, female 44, median age 53, range = 23-82 years), with long-standing (8 years or more median duration of the disease 13 years) colonic IBD (UC = 42, CD = 42, IC 3) undergoing surveillance colonoscopy were reviewed. The lesions of dysplasia (ALM or DALM), SSAs, adenoma-like polyps (ALPs), hyperplastic polyps (HPs), and inflammatory polyps (IPs) were identified. Detection procedures were as follows:- Twenty five were assessed by high definition colonoscopy, Thirty four by high definition –iscan virtual chromoendoscopy and 28 patient by high definition dye chromoendoscopy with methylene blue 0.1%.(Pentax EC-3490Fi; Pentax, Tokyo, Japan).
RESULTS: 14 SSAs were detected (16%). Two in the HD group (8%), seven in the HD-iScan virtual chromoendoscopy group (21%) and 5 in the HD dye chromoendoscoy with methylene blue (18%). These were predominantly in younger patients. The endoscopic characteristics of SSAs were: flat lesion predominantly localized in the right colon (11 in the cecum and ascending colon and 3 in the sigmoid colon), more than >5 mm in size, cloudy cover, Kudo pit pattern modified type IIO and irregular spiral vascular pattern. In comparison, 10 ALPs (11 %) were detected – 2 in HD group (8%), 3 in iScan-HD group (9%) and 5 in HD dye chromoendoscopy group (18%). Only 1 patient had a DALM lesion.
CONCLUSION: 16% of patients had sessile serrated adenomas detected at surveillance colonoscopy in longstanding IBD patients. This detection rate of SSAs was more than ALPs. SSAs can be detected more frequently by HD-iScan virtual chromoendoscopy and by dye chromoendoscopy than by HD endoscopy alone. Sessile serrated adenoma is a common finding at surveillance colonoscopy for IBD and may be missed if electronic virtual chromoendoscopy or dye chromoendoscopy are not used.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
LIVER & BILIARY III – POSTER EXHIBITION – HALL XL

P1154 DOES LEPTIN PROFILE MODULATE OXIDATIVE STRESS AND DISEASE SEVERITY IN NON-ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Upregulated oxidative stress is recognized as important mechanism contributing to inflammation and fibrogenesis of the liver in non-alcoholic fatty liver disease (NAFLD). Leptin promotes oxidative stress and the fibrogenesis in the liver. Therefore, we aimed to evaluate the association between leptin levels, oxidative stress parameters and histopathological findings in NAFLD subjects.
AIMS & METHODS: Fifty-eight non-drinker patients with biopsy-proven diagnosis of NAFLD were studied (M/F: 31/ 27 mean age 47.4± 6.3 years). Histopathological examination was done using the system described by Brunt et al. For the determination of oxidative stress parameters malondialdehyde (MDA), and superoxide dismutase (SOD) activities were measured in serum and as well as in tissue specimens. Glutathione (GH) was measured in tissue homogenates. Nitric oxide (NO) and TNF-alpha receptor (TNF-sRp55) levels were measured in serum. Serum leptin levels were measured by radioimmunoassay. Statistical analysis was done using chi-squared test, Student's t-test, Mann-Whitney test, multivariate regression analysis and the area under receiver operating characteristic (ROC) curve. Comparison between the patients with non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH) were performed using Student's t test. Multivariate regression analysis and ROC curve were used to identify the independent predictors for NASH. All statistical analyses were performed using SPSS® statistical software program (Ver.10.0).
RESULTS: In bivariate analysis serum leptin levels didn't show any significant correlation with steatosis grade, necroinflammatory grade and stage. Serum leptin levels were neither significantly correlated with serum NO, SOD and MDA levels nor with tissue SOD, MDA and GH levels. The increases in TNF-sRp 55 levels correlated inversely with serum leptin levels (r = - 0.03, p = 0.04). Patients with NASH had significantly higher serum NO and tissue MDA and GH levels (p = 0.03, 0.04, 0.042, respectively). Using serum leptin levels the ROC curve for distinguishing between NASH and NAFL didn't show any respective sensitivity and specificity (AUROC = 0.48). In linear regression analysis serum NO ($\beta = 0.21$, p = 0.018), tissue MDA ($\beta = 0.06$, p = 0.01), and stage ($\beta = 2.6$, p = 0.01) were independently associated with increased leptin levels. In multivariate regression analysis increase of tissue MDA (OR:1.8; %95 CI:1.04-4.25, p = 0.04) and serum NO levels (OR:1.9; %95 CI:1.02-4.6, p = 0.04) were risk factors for NASH and increase of leptin activity had preventive effect against NASH (OR:0.052; %95 CI:0.004-0.72, p = 0.04).
CONCLUSION: Serum leptin levels did not show any significant correlations between oxidative stress parameters and overall histological severity. Patients with NASH had enhanced oxidative stress. In patients with NASH oxidative stress parameters and stage were independently associated with increased leptin levels with a preventive effect against NASH.
These data indicate that leptin may have preventive effect against oxidative stress and progression of hepatic injury in NAFLD.
Disclosure of Interest: None declared

P1155 ROLE OF LEPTIN AND INSULIN RESISTANCE IN THE DISEASE SEVERITY AND HEPATOCYTE APOPTOSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Apoptosis and insulin resistance (IR) are major contributors in the pathogenesis and the disease severity of non-alcoholic fatty liver disease (NAFLD). Leptin plays a key role in insulin sensitivity. We aimed to evaluate whether serum leptin levels correlate with IR, apoptosis parameters and histopathological disease severity in NAFLD subjects with and without IR.
AIMS & METHODS: Sixty non-drinker patients with biopsy-proven diagnosis of NAFLD were studied (M/F:32/ 28; mean age 47.5±10.2 years). Thirty-six NAFLD patients with IR were compared with 24 subjects without IR. Insulin resistance index (HOMA IR) was calculated using the homeostasis model assessment method. Histopathological examination was done using the system described by Brunt et al. Serum leptin levels were measured by radioimmunoassay. For apoptotic activity immunohistochemistry was performed for caspase-3 and 8, transcription nuclear factor kB (NF-kB), and antiapoptotic Bcl-2 protein. Tumor necrosis factor receptor (TNF-sRp55) level was measured in serum. Statistical analysis was done using chi-squared test, Student's t-test, Mann-Whitney test, multivariate regression analysis and the area under receiver operating characteristic (ROC) curve. P-values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS® statistical software program (Ver.10.0).
RESULTS: HOMA-IR index correlated positively with the necroinflammatory grade, the stage, caspase-3 and 8 levels (p = 0.02, 0.002, 0.04, 0.021, respectively). The ROC curves revealed statistically significant discriminative power of HOMA-IR index for necroinflammatory grade,stage and non-alcoholic steatohepatitis (NASH) (AUROC = 0.7, 0.66, 0.65, respectively). Patients with IR had significantly higher steatosis grade, necroinflammatory grade, stage, caspase-3, caspase-8, TNF-sRp55, and serum leptin levels than those without IR.
In bivariate analysis serum leptin levels didn't show any significant correlation with fasting insulin, serum glucose, HOMA-IR index, steatosis grade, necroinflammatory grade and stage. Using serum leptin levels the ROC curve for distinguishing between NASH and simple steatosis didn't show any respective sensitivity and specificity (AUROC = 0.4). In linear regression analysis caspase-3 ($\beta = 0.11$, p = 0.002), caspase-8 ($\beta = 0.04$, p = 0.02), and stage ($\beta = 3.2$, p = 0.002) were independently associated with increased leptin levels In multivariate regression analysis caspase-3 (OR:2.2; %95 CI:1.06-5.26, p = 0.042) and caspase-8 levels (OR:2.3; %95 CI:1.06-5.72, p = 0.048) were risk factors for NASH and increase of leptin activity had preventive effect against NASH (OR:0.06; %95 CI:0.002-0.86, p = 0.043).
CONCLUSION: Insulin resistance in NAFLD is associated with enhanced hepatocyte apoptosis and histopathological disease severity. In patients with IR fibrosis severity and apoptosis parameters were independently associated with high leptin levels and increase of leptin activity showed preventive effect against NASH.
Our findings show that NAFLD patients with IR may have increased risk for disease progression and leptin has preventive effect against apoptosis and liver fibrosis.
Disclosure of Interest: None declared

P1156 LONG-TERM OBSERVATION OF WILSON DISEASE PATIENTS – EXPERIENCE OF A SINGLE CENTER

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INTRODUCTION: Wilson disease (WD) is an inherited copper metabolism disorder. If the patient remains undiagnosed and untreated, disease outcome may be fatal. Lifelong therapy provides normal WD patients' survival.
AIMS & METHODS: Aim: To evaluate the clinical course and long-term outcome of WD patients.
Material and methods: Sixty-five WD patients (22 females and 43 males) at a mean age of 37 years (range, 18-65 years) were analysed from January, 2003 to December, 2013. Survival analysis by Kaplan-Meier method and Logit model were used.
RESULTS: Twenty-eight patients (43.08%) were with liver disease alone, thirty-two (49.23%) - with hepatic and neurological presentation, three - with neurological features without any signs of a liver injury. There were two asymptomatic patients, too. The following hepatic forms were proved: steatosis (in 6.6%), hepatitis (in 41.7%), and cirrhosis (in 51.7% of the patients). There was a mean delay of diagnosis of 39 months. At the end of the study, 74.2% of cirrhotic patients were in Child A stage. Two patients developed acute liver failure after treatment discontinuation. We observed a hepatocellular carcinoma in one cirrhotic patient. Six patients with liver cirrhosis of Child C stage had fatal outcome during the observation. Three of them were with concurrent diseases – HBV and autoimmune cirrhosis. Kayser-Fleischer ring was detected in 35.4% of the patients being more common in those presenting with neurological symptoms. The cumulative survival rate of people with WD after first onset of symptoms was up to 76.38% at the end of 15th year, and that after diagnosis - 77.29%. It was estimated the impact of the lag in the diagnosis of WD on overall survival. At each year delay in the diagnosis the probability of death was increased by approximately 10%. There was a beneficial effect of D-penicillamine (D-p) treatment in almost all the patients. There were no complications during the pregnancies, with stable disease and normal birth.
CONCLUSION: Our observation showed a delayed diagnosis of WD. In most patients, the course of the disease was stable or even improved during the treatment. Mortality rate increased in the patients with cirrhosis. There was a favourable response after long-term treatment with D-p as first-line therapy in WD.
Disclosure of Interest: None declared

P1157 NON-INVASIVE PARAMETERS OF NASH AND LIVER FIBROSIS IN DAILY PRACTICE

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INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD) is a hepatic manifestation of metabolic syndrome. Risk of progression to cirrhosis is related to inflammatory reaction (NASH) and fibrosis. Despite all its limitations liver biopsy is still the gold standard in distinguishing NASH and staging of fibrosis, but non-invasive approaches are emerging.
AIMS & METHODS: The aim was to evaluate the usefulness of non-invasive laboratory parameters for detection of NASH and fibrosis in patients with NAFLD in routine clinical practice. Liver biopsy was performed in 56 patients with NAFLD (mean age 48.9 ± 15 years) and Kleiner score was used for histological staging and grading. Non-invasive parameters of fibrosis (hyaluronic acid, OELF, AST/ALT, BARD, APRI, NAFLD fibrosis score) and inflammation (M30 and M65 cytokeratin 18 fragments) were measured and calculated. The same parameters were applied to a group of other 56 patients not indicated to biopsy. 14 healthy individuals formed a control group.
RESULTS: NASH was bioptically diagnosed in 38 patients, simple steatosis in 18 patients. F0-F2 fibrosis was present in 39 patients; F3-F4 in 17 patients. Serum concentration of hyaluronic acid was significantly higher in patients with advanced fibrosis ($p = 0.01$), cut-off value 25 μg/l discriminated patients with F3-4 with 90% sensitivity and 84% specificity from those with F0-F2 (AUROC 0.94). AUROC for OELF score was 0.97; other parameters did not reach statistical significance. Serum concentrations of M30 a M65 in patients with NASH differed from subjects without NASH ($p = 0.01$). Examination of M65 discriminated patients with NASH with 80% sensitivity and 82% specificity (AUROC 0.89). Interestingly, when these non-invasive criteria were applied to a group of patients without biopsy, NASH would be diagnosed only in 15%, but the advanced fibrosis in 35% of them.
CONCLUSION: Non-invasive serum parameters in patients with NAFLD can differ with high accuracy those with steatohepatitis and advanced fibrosis. Among the patients not indicated for liver biopsy in the routine praxis a substantial part may have advanced fibrosis.
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Disclosure of Interest: None declared

P1158 ISOFLAVONES SUPPLEMENTATION ATTENUATES THE PROGRESSION OF NON-ALCOHOLIC FATTY LIVER DISEASE VIA THE DECREASE IN OXIDATIVE STRESS-MODIFIED PROTEINS

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INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD), a phenotype of metabolic syndrome in liver, is generally believed as a high-risk group in arteriosclerotic disease and type 2 diabetes. The progression of NAFLD is associated with oxidative stress; however, the proper treatment of NAFLD remains to be established. Recent studies have suggested that isoflavones have beneficial effects on metabolic syndrome-related disorders. Here we assessed the effects and mechanisms of isoflavones in Western diet (WD)-induced mice and NAFLD patients.
AIMS & METHODS: C57BL/6J mice were fed for 8 weeks on AIN93G (control) or WD (high in fat, cholesterol and sucrose) with or without 0.05% isoflavones (daidzein derivatives 50%, genistein derivatives 10%, and glycitein derivatives 40%). For human trial, nutrition survey was performed for 20 NAFLD patients and 20 healthy subjects. 25 mg of isoflavone aglycons were orally taken to 10 NAFLD patients for 28 days to evaluate blood tests and parameters related to oxidative stress.
RESULTS: The increases in ALT, blood glucose, liver fat accumulation and triglyceride in liver of WD-fed mice were improved by isoflavones treatment. The expression of hepatic genes related to steatosis, such as acetyl-coA carboxylase and peroxisome proliferator-activated receptor gamma, were also normalized by isoflavones. Further, isoflavones supplementation showed a tendency to improvement in the increases in oxidative stress (4-hydroxy-2-nonenal (HNE)-modified proteins) and glycation (methylglyoxal (MG)-modified proteins) in WD-fed mice. Nutrition survey showed that presumed oral intakes of daidzein and genistein in NAFLD patients were significantly lower compared to those in healthy subjects. Diet intervention trial indicated that isoflavones supplementation significantly reduced body weight and ALT as well as 7-ketocholesterol (7-KC) and hexanoyl-lysin (HEL)-modificed proteins in plasma.
CONCLUSION: Isoflavones supplementation attenuated liver function, and decreased oxidative stress or glycation in WD-fed mice and NAFLD patients. Further examinations are required due to low number of cases; however, isoflavones supplementation may be a treatment option for NAFLD.
Disclosure of Interest: None declared

P1159 NONINVASIVE DIAGNOSTIC OF NONALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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INTRODUCTION: It is known that in 72% of patients with type 2 diabetes mellitus diagnosed NAFLD. Patients with NAFLD are usually asymptomatic, high values of liver enzyme tests being the most common finding. The definitive diagnosis of NAFLD is based of liver biopsies. Although liver biopsy is the current gold standart for diagnosis of NAFLD, it is not a practical screening tool given the cost, time-consuming nature and potential mortality of this procedure. However, more attention is attracted to early diagnosis NAFLD by using a special set of design formulas biochemical parameters, data Fibroscan or respiratory tests with 13C-methacethine (C13-MBT)
AIMS & METHODS: A comparative analysis of methods for diagnostics of clinical forms NAFLD using specially developed formulas 13C-methacethine breathe test (MBT), biochemical parameters.
The study involved 131 patients with type 2 diabetes mellitus (DM) (male 48, female 83, aged 43 to 82 years, mean age 60.94 ± 0.82 years). Control group, 106 patients without diabetes, men 47, women 59, aged 35 to 69 years (mean age 60.26 ± 1.27). Biochemical tests were performed: total bilirubin (TB), AST, ALT, AST / ALT, GGTP, lipidogram, carried ultrasonographic examination, the calculation formulas of Angulo, Forns, Fib-4, Apri. Defining the antitoxic function of the liver by 13C- MBT.
RESULTS: Total cholesterol (TC) ($p = 0.00127$), HDL ($p = 0.0001$), triglycerides ($p = 0.0001$), AST / ALT ($p = 0.09594$) were reliable indicators between the main and control groups. Among the patients of the main group were detected 91 patients with NAFLD, control -32. There were higher TB, AST, ALT and AST / ALT levels among patients with NAFLD, none of the indicators does not exceed the upper limit of normal. Formula Forns correlated with the clinical form NAFLD. Marked strong negative relationship between the Forns and ALT levels ($r = -0.944$) and TB ($r = -0.967$) with fibrosis, and TC ($r = -0.805$) and LDL ($r = -0.846$) with steatosis. 13C-MBT was conducted on 32 patients. In patients with steatosis and steatohepatitis, index MDT replied a moderate decrease liver (10-20%), marked reduction with fibrosis (< 10%). A strong negative correlation was noticed between LDL ($r = -0.878$) and TG ($r = -0.933$) and MBT in fibrosis.
CONCLUSION: In the resulting formula Forns over 4.25, 13C-MBT least 10%, lower levels of ALT but TB, and TC more than 2.6 mmol / L, triglycerides more than 2.6 mmol / l - high probability of fibrotisis. The result of the Forns least 4.25, 13C-MBT between 10-20% TC more 5.2 mmol / l and LDL more than 2.6 mmol / L indicates liver steatosis.
Disclosure of Interest: None declared

P1160 SOMATOSTATIN ANALOGUES IMPROVE HEALTH RELATED QUALITY OF LIFE IN POLYCYSTIC LIVER DISEASE

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INTRODUCTION: Polycystic liver disease (PLD) is characterized by progressive hepatomegaly resulting from liver cysts and is associated with an impaired physical dimension of Health Related Quality of Life (HRQL). Somatostatin analogues reduce hepatomegaly in PLD.
AIMS & METHODS: We pooled data of two randomized placebo controlled trials (NCT00565097/NCT00426153) that evaluated HRQL with the short-form Health survey (SF-36) in 96 PLD patients treated 6-12 months with somatostatin analogues or placebo. SF-36 contains a summarizing physical component score (PCS) and was administered at baseline and end of treatment. We used multiple linear regression analysis with correction for trial (random effect) and baseline PCS (fixed effect) to delineate the effect of somatostatin analogues. As a secondary analysis, we determined the effect of severe hepatomegaly ($>75^{th}$ percentile), delta liver volume, underlying disease, gender, age and occurrence of adverse events on PCS change independent of treatment. Results are given as estimated mean score ± standard error. The PCS is standardized to the healthy population with a score of 50 points.
RESULTS: We included 87 patients (89% female, mean age 48 yrs) with a baseline PCS of 44.32 points and median liver volume of 4504 mL. PCS improved with somatostatin analogues, but remained unchanged with placebo (3.41 ± 1.29 vs. -0.71 ± 1.54, $p<0.05$). Severe hepatomegaly and adverse events significantly contributed to PCS decrease, while delta liver volume, gender, age and underlying diagnosis did not impact PCS.
CONCLUSION: Somatostatin analogues improve the physical dimension of HRQL in polycystic liver disease patients after 6-12 months of treatment. Besides treatment, severe hepatomegaly is independently associated with a decline in HRQL during follow up.
Disclosure of Interest: None declared

P1161 FEATURES OF UPPER GASTROINTESTINAL ABNORMALITIES IN NON-ALCOHOLIC STEATOHEPATITIS (NASH) PATIENTS

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INTRODUCTION: Non-alcoholic steatohepatitis (NASH), hepatic manifestation of metabolic syndrome has been considered the most common liver disease today. NASH patients are reported to have higher incidence of colon polyps, however, features of their upper gastrointestinal findings have not been reported.
AIMS & METHODS: The aim of this study is to clarify the upper gastrointestinal abnormalities of NASH patients by comparing with those of health check subjects.
This is a retrospective study. We diagnosed 94 patients as NASH in our hospital from March 1998 to July 2012. 1) Among them, 36 who underwent esophagogastroduodenoscopy (EGD) were enrolled in this study. 2) From 118 subjects who underwent health-check at our hospital from January 2012 to September 2012, 73 were selected as healthy control (group) excluding those with obesity (body mass index; BMI > 25), hepatic dysfunction, fatty liver, and diabetes, and 3) 14 obese subjects without hepatic dysfunction were selected as obesity group. Following findings in EGD were compared among 3 groups; esophageal hernia, reflux esophagitis, Barrett's esophagus, atrophic gastritis, superficial gastritis, erosive gastritis, gastric ulcer including scar, and gastric polyp.
RESULTS: Age, sex, and BMI of NASH/health/obesity groups were 65 ± 12/ 64 ± 14/ 65 ± 12 (mean ± SD); 22, 14/ 35, 38/ 10, 4 (male, female); 26.6 ± 3.8/ 21.6 ± 1.8/ 26.2 ± 1.0, respectively. Age was comparable among three groups. BMI of NASH and obesity group was significantly higher than that of healthy group ($p<0.0001$), while that of NASH and obesity was not different. Among NASH group, 6 (17%) were cirrhosis. Esophageal hernia and reflux esophagitis were significantly more observed in NASH group than in healthy group (77.8/50.7% and 50/26%, $p=0.01/0.01$), while prevalence of these findings were not different between healthy and obesity group. Prevalence of Barrett's esophagus, atrophic gastritis, superficial gastritis, gastric ulcer, and gastric polyp showed no significant difference among three groups. Prevalence of erosive gastritis in NASH patients was significantly higher than that in healthy group (44%, 16/36; 12%, 9/73; $p=0.0002$), while no significant difference of this finding was observed between NASH and obesity group. Only in NASH group, portal hypertensive gastropathy and esophageal varices were found in 2 cirrhotic patients.
CONCLUSION: NASH patients have higher risk of esophageal hernia and reflux esophagitis than healthy subjects.
Disclosure of Interest: None declared

P1162 HYPERHOMOCYSTEINEMIA AS A PREDICTOR OF THE DEVELOPMENT AND PROGRESSION OF NONALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Studied the influence of the pathogenetic mechanisms of hyperhomocysteinemia on the formation and progression of nonalcoholic fatty liver disease (NAFLD) by inducing oxidative stress. It is shown knots in the degree of hyperhomocysteinemia depending on the stage of the disease.
AIMS & METHODS: Examine the degree of hyperhomocysteinemia (HHcy) in patients with non-alcoholic steatosis and steatohepatitis (NASH). Determine the correlation between homocysteine serum level and indicators of oxidative stress (nitric oxide (NO) and TBA-active metabolites in blood plasma). We observed 65 patients with NAFLD. The first group included 33 patients with hepatic steatosis. In the second group there were 32 patients with NASH.
RESULTS: HHcy were revealed in patients with disease severity: normal levels of homocysteine (Hcy) were reported in 6 patients (18.2%) in the first group (12.44 ± 1.6 μmol/L), while in the second group, only 2 patients (6, 2%) patients (12.96 ± 0.74 μmol/L). Mild degree HHcy was detected in 13 (39.4%) and 8 (25%) patients in the first (21.65 ± 3.93 μmol/L) and the second group (20.03 ± 3.24 μmol/L) respectively. HHcy moderate detected in 14 (42.4%) patients in the first group (42.19 ± 16.96 μmol/L) and 18 (56.3%) in the second (62.88 ± 22.24 μmol/L). Heavy HHcy occurred in 4 (12.5%) patients in the second group (113.22 ± 14.96 μmol/L), while the first group of patients had no evidence of violations. Significant correlation between the level of Hcy and NO: the first group - $r=0.79$; $p<0.05$; second group - $r=0.89$; $p<0.05$.
CONCLUSION: Our results show that the degree of HHcy increases with the severity of NAFLD. There are positive correlations between the Hcy and indicators of oxidative stress in patients with NAFLD.
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P1163 LIVER SPECIFIC SERUM MICRO RNA122 AS A PROGNOSTIC MARKER IN PATIENTS WITH LIVER CIRRHOSIS

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INTRODUCTION: Recent research has shown that miRs are emerging as important regulators of cellular differentiation and undifferentiation. The miR-122 accounts for approximately 70% of all miRs in the liver, whereas other organs express much lower amounts of this miRs. And due to almost exclusive expression of miR-122 in the liver the presence of it in the serum is highly indicative of liver processes.
AIMS & METHODS: was to study the role of miR-122 as a prognostic new marker in patients with liver cirrhosis. MiR-122 that was detected by quantitative real-time reverse transcription (RT)-PCR technique. Eighty patients with liver cirrhosis were included in our study, we divided them into 4 equal groups according to the complications of liver cirrhosis (1-compensated cirrhotics, 2- ascites, 3-spontanious bacterial peritonitis SBP, and 4- hepatorenal syndrome HRS group) to evaluate if the serum level of miR-122 might be a suitable parameter for disease severity and prognosis in such patients.
RESULTS: miR-122 was statistically significantly higher in group 1 "compensated" compared to both groups 2 "ascites" and 3 "SBP" ($p=0.001$), while the difference was highly significant when compared to its level in group 4 ''HRS'' ($P<0.001$). Serum miR-122 levels were positively correlated with serum albumin, PC, and serum Na levels while it was negatively correlated with creatinine, urea, and INR. Also there was strong negative correlation between serum miR-122 level and MELD score ($p=0.001$), and very strong negative correlation between serum miR-122 level and Child score ($p<0.001$).
CONCLUSION: Lower serum miR-122 levels are associated with ascites, spontaneous bacterial peritonitis and hepatorenal syndrome. Therefore, serum miR-122 could be a new potential parameter for liver function and a prognostic parameter in patients with liver cirrhosis.
Disclosure of Interest: None declared

P1164 THE NEUTROPHIL CAUGHT BETWEEN CIRRHOSIS, GUT PERMEABILITY AND VIRAL HEPATITIS C

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INTRODUCTION: Cirrhosis has been linked to high risk for infection and dysfunctional neutrophil granulocytes have been proposed to be one of the reasons for this ineffective immune response. However, contradictory reports have emerged regarding the nature and direction of their dysfunction, leaving the pathophysiological mechanism and underlying causes yet to be discovered.
AIMS & METHODS: Therefore we aimed to explore neutrophil granulocytes in cirrhosis as well as the role of aetiology, opsonisation, gut permeability and underlying diseases in neutrophil functionality.
Neutrophil function (oxidative burst, phagocytic and opsonisational capacity), gut permeability and hepatitis C virus infection (HCV) parameters of 98 liver cirrhosis patients of different aetiologies (56 alcoholic, 20 HCV, 22 other) and 72 controls (33 healthy, 39 HCV infected without cirrhosis) were analysed. Neutrophil function was assessed by flow cytometry, gut permeability by high performance liquid chromatography (differential sugar absorption) or ELISA (diamine oxidase, soluble cluster of differentiation 14) and HCV parameters by routine methods.
RESULTS: Compared to healthy control values, phagocytic capacity (Phagoindex, PI) is decreased in patients with HCV induced cirrhosis (0.7-fold), not significantly influenced in alcoholic cirrhosis (1.1-fold), and increased in cirrhosis of non-viral/non-alcoholic aetiologies (1.5-fold). In addition, the amount of neutrophils without measurable phagocytosis shows a significant increase in HCV induced cirrhosis but is not as prominent in alcoholic and other cirrhosis (5.0-, 1.9- and 1.2-fold, respectively). The progression from Child's A to B cirrhosis decreases PI approximately 30% regardless of the aetiology. Furthermore, alcoholic cirrhosis is accompanied by high amounts of primed neutrophils in the bloodstream, and HCV induced cirrhosis results in impaired production of reactive oxygen species after bacterial stimulation. However, opsonisation is sufficient in all cirrhosis groups and shows no differences compared to controls. Gut permeability is elevated in all aetiologies, most pronounced in alcoholic cirrhosis which shows a significant increase in every marker. High permeability is associated with neutrophil dysfunction but explains only partially the observed alterations. In HCV induced cirrhosis a part of the phagocytic dysfunction originates from HCV infection itself. Before the onset of cirrhosis and with normal gut permeability, HCV infected controls already display a 2.5-fold increase in neutrophils without phagocytosis and a slight non-significant decrease in PI, compared to healthy controls.
CONCLUSION: Aetiology, gut permeability and HCV infection impact strongly and diversely on neutrophil function in cirrhosis. Still, causal links between already published and well established explanations need to be explored.
Disclosure of Interest: None declared

P1165 INCREASING PREVALENCE OF MULTIDRUG-RESISTANT INFECTIONS IN PATIENTS WITH CIRRHOSIS

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INTRODUCTION: Bacterial infections are an important complication of liver cirrhosis. Moreover, they represent a common motive of its descompensation, hospitalization and health-care related costs. Recently, infections caused by gram-positive and multidrug-resistant bacteria have become more frequent, with a significant impact on patientś morbidity and mortality.
AIMS & METHODS: Aim: To asses the rate of infections caused by multidrug-resistant bacteria in hospitalized patients with liver cirrhosis. The most frequent infections (pneumonia, urinary tract infection, SBP, bacteriemia) were included. Methods: We evaluated 277 cirrhotic patients admitted to our center between Junuary 2012 and July 2013 due to a bacterial infection.
RESULTS: 340 infections were evaluated in 277 patients. Their mean age was 64.6 years (range 31 - 91). The etiology of the cirrhosis was: due to alcohol abuse (50%), hepatitis C infection (43.3%), hepatitis B infection (14%). 56 (20.2%) patients had hepatocellular carcinoma, 61 (22%) chronic renal insufficiency, 96 (34.7%) were diabetic and 127 (45.8%) were on beta blockers. The mean MELD on admission was of 14.6, and Child-Pugh score of 7.8 points.
The most frequent infections were UTI in 155 patients (56%), followed by SBP in 84 patients (30%), pneumonia (70%) and bacteriemia in 54 (19.5%). The infections were community-adquired in 104 patients (37%), health-care related in 120 (43%) and nosocomial in 83 (30%). We obtained microbiological isolation in 187 of the 277 patients, 73 of those had 2 or more different bacterial isolations, i.e. in total 290 isolations, 39.8% by gram positive bacteria and 60.2% gram negative bacteria, being *E. coli* the most frequent one. 42 (15%) of the bacteria were multidrug resistant, 32 BLEEs and 10 MRSA, and in 10 *Enterobacteriaceae*, Amp C betalactamase was identified. Risk factors for a multiresistant infection were: hospital admission and use of antibiotics during previous 90 days.
Global mortality rate during the episode was of 15.2 % (15 patients), with accumulated mortality of 30% during the following 6 months. In the univariate analysis, the factors associated to mortality were: acute renal insufficiency, microbiological isolation in control bacterial cultures, sepsis or septic shock, and diagnosis of pneumonia. The independent risk factors were: acute renal insufficiency (p: 0.022, OR 1.73 IC95: 1.15 – 2.58), and isolations in control cultures (p: 0.002, OR 1.98 IC95: 1.3 – 3.25).
As for the antibiotics, the third-generation cephalosporines remained the treatment of choice in 45.5% of patients, followed by carbapenems (23.8%). 54.5% of patients requiered the use of more than one antibiotic, mainly carbapenems or vancomycine.
CONCLUSION: In our group of cirrhotic patients with bacterial infections a relatively high rate of multidrug resistant infections were observed, especially as far as BGN are concerned. Treatment with broad-spectrum antibiotics is recommendable in high-risk group of patients.
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Disclosure of Interest: None declared

P1166 COMPARISON OF THE LIMON SYSTEM TO ICG-CLEARANCE MEASUREMENT BY HPLC

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INTRODUCTION: Indocyanine green (ICG) elimination is a test to evaluate hepatic function in patients with liver disease and to quantify liver perfusion. Conventional ICG clearance is dertermined by measuring the rate of elimination of the synthetic dye using several venous samples after its intravenous administration. With the new infrared-based transcutaneous pulse spectrophotometry (LIMON^{TM}) a plasma disappearance rate (PDR) and a calculated remaining concentration after 15 minutes (R15) are provided. Several studies have suggested that the LIMON^{TM} system is able to measure ICG-concentration accurately, however a direct comparison to conventional ICG clearance measurements in patients with liver cirrhosis has not been performed yet.
AIMS & METHODS: In a randomized controlled double-blind study to test the effect of Udenafil, a new phosphodiesterase-5-inhibitor, in patients with liver cirrhosis a conventional ICG clearance measurement as well as a determination by the LIMON^{TM} system was performed. Included patients had a proven compensated liver cirrhosis. After enrolment, two visits to evaluate hemodynamics and ICG kinetics before and after ingestion of a placebo or Udenafil were scheduled within 7 days. 0.3 mg/kg ICG were administered via an antecubital vein. Blood samples were drawn from the opposite cubital vein before and exactly 3, 6, 9, 12, 15, 18, 21, 30 and 40 minutes after ICG injection.
All samples were centrifuged immediately and stored at -80°C until analysis. Calculation of PDR and R15 were done by P. Thomann (Kineticon, Freiburg, Germany). In parallel, with transcutaneous spectrophotometry PDR and R15 were are measured with the LiMON^{TM}-device (PULSION Medical Systems AG, Munich, Germany). For this analysis, the results of the ICG determination via blood samples and LIMON before the drug ingestion on both study days are compared.
RESULTS: 20 patients with liver cirrhosis were included (4 female, age 54.9±10.8 years, Child-Score 6.7±1.3). One female patient stopped the study after Visit 1 because of side effects (dizziness, malaise) a few hours after application of ICG and 100mg Udenafll. 20 analyses were performed at Visit 1 and 19 analyses at Visit 2. In 2 patients a stable transcutaneous signal was not obtained at Visit 1 so the LIMON^{TM}-system failed. The plasma disappearance rate at Visit 1 was 9.82±5.68% for blood analyses and 10.34±5.54% for the LIMON device, respectively. The results for the R15 were 35.26±22.66% for blood analyses and 27.47±18.71% for the LIMON device. At Visit 2 the PDR results were 8.79±5.64% versus 10.37±6.58%, respectively. The results for R15 were 37.64±22.49% versus 29.20±21.34%, respectively. The correlation between the two methods was high (r for PDR Visit 1: 0.938, r for R15 Visit 1: 0.968; r for PDR Visit 2: 0.892, r for R15 Visit 2: 0.921).
CONCLUSION: This is the first analysis to compare conventional analysis of ICG clearance with a transcutaneous spectrophotometry in patients with compensated liver cirrhosis. ICG plasma disappearance rate and R15 estimated with the LIMON^{TM} device correspond well to conventional ICG clearance. With the LIMON^{TM} device the ICG kinetics can be obtained in an easy way within 5 minutes with only minor effort.
Disclosure of Interest: None declared

P1167 OSTEOPOROSIS IN PRIMARY BILIARY CIRRHOSIS: TWO BIPHOPHONATES COMPARED

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INTRODUCTION: Osteoporosis characterized by loss of bone strength leading to fragility fractures is a common event in women who have Primay Biliary Cirrhosis (PBC). Although its pathogenesis is not well known it results mainly from low bone formation. At present the treatment of osteoporosis in patients with PBC mostly relies on oral biphosphonates,particularly in weekly 70 mg alendronate,but there are a concern because of poor compliance. The efficacy,adherence and safety of monthly 150 mg ibandronate were compared in a 2-year study in 20 postmenopausal women with osteoporosis and PBC.
AIMS & METHODS: Bone mineral density (BMD) of the lumbar spine and proximal femur by dual-energy x-ray-absorptiometry (DXA),liver function and bone markers were measured at entry and every 6 months at entry and every 6

months over 2 years. Adherence to therapy was assessed by the Moriski score. At enrollment the two groups were similar with respect to age,BMD,cholestasis,previous fractures and bone markers. Eighteen patients,nine in the alendronate group and nine in the ibandronate completed the study.
RESULTS: At 2 years both treatments resulted in a significant increase in BMD at the lumbar spine,the mean percentage change was 4.5% in alendronate and 5.7% in ibandronate group (p = not significant) BMD increased at the total hip by 2% and 1.2% respectively. Change in bone markers were similar in both groups and one patient with alendronate developed a new vertebral fracture. Adherence to the therapy was higher with ibandronate. Neither treatment impaired liver function or cholestasis. One patient in the alendronate group discontinued treatment because of gastrointestinal adverse effects such as dyspepsia,nausea and vomiting.
CONCLUSION: Both regimens,weakly alendronate and monthly ibandronate,improve bone mass and are comparable in safety for osteoporosis therapy in patients with PBC,although adherence is higher with the monthly regimen. Further larger studies are needed to assess fracture prevention.
Disclosure of Interest: None declared

P1168 HFE GENE C282Y AND H63D MUTATIONS ARE ASSOCIAED WITH LIVER CIRRHOSIS IN LITHUANIAN POPULATION

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INTRODUCTION: Liver cirrhosis is an ultimate complication of different chronic liver disorders. Cirrhosis is commonly caused by alcohol use, viral hepatitis B and C and many other causes. The search for epidemiological, biological or genetic factors that could help to select patients at higher risk of developing cirrhosis is necessary. The literature data on impact of HFE-gene C282Y and H63D heterozygous mutations for liver cirrhosis risk in different populations and depending on cirrhosis etiology is controversial.
AIMS & METHODS: The aim of this study was to determine the association between the presence of HFE gene C282Y and H63D mutations and liver cirrhosis in Lithuanian population. A cohort of consecutive cirrhosis patients consisted of 209 individuals with different disease etiologies. The diagnosis of cirrhosis was confirmed by clinical features, liver biopsy and radiological imaging tests. Control group consisted of 1004 healthy blood donors. HFE gene mutations in cirrhotic patients and control group were detected using PCR-RFLP method. Statistical analysis were performed using statistical software for genetic association studies PLINK v2.050.
RESULTS: The presence of C282Y mutation was associated with higher risk of the liver cirrhosis when compared with controls (OR-2.07, p = 0.005). The carriage of C282Y/wt genotype increased the risk of liver cirrhosis compared with individuals having wt/wt genotype (OR-2.00, p = 0.012). A similar pattern was observed in a dominant model for C282Y mutation (wt/wt vs. C282Y/wt + C282Y/C282Y) which showed increased risk of developing liver cirrhosis (OR-2.07, p = 0.007). This link was even more evident in males as carriers of C282Y allele had increased risk of liver cirrhosis with an OR of 2.58 (p = 0.002). The presence of H63D mutation was not associated with cirrhosis risk in overall study population; however, after stratification into genders H63D allele was associated with higher risk of liver cirrhosis in males (OR – 1.5, p = 0.018), but not in females (OR – 0.84, p = 0.43).
CONCLUSION: HFE gene C282Y mutation is associated with liver cirrhosis irrespective of disease aetiology, while H63D mutation was linked with liver cirrhosis only in males. These genetic alterations might contribute to faster progression of chronic liver diseases of different aetiology to end stage in Lithuanian population.
Disclosure of Interest: None declared

P1169 AUTOLOGOUS BONE MARROW - DERIVED LIVER STEM CELLS REDUCE LIVER FIBROSIS AND IMPROVE LIVER FUNCTION IN CARBON – TETRACHLORIDE - TREATED HEPATIC CIRRHOTIC RAT

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INTRODUCTION: To determine the safety, feasibility and therapeutic effect of in vitro-expanded autologous bone marrow-derived liver stem cells (BMDLSC) transplantation in hepatic cirrhotic rats treated with carbon - tetrachloride.
AIMS & METHODS: Liver cirrhosis rat models were prepared and then divided randomly into three groups, 25 in each group. In rats, we analyzed the effect of different cells infusion in three experimental groups (group A, bone marrow cell infusion + CCl (4); group B, bone marrow - derived liver stem cell infusion + CCl (4); group C, bone marrow stem cell infusion + CCl (4)).
RESULTS: We observed significantly increased average serum albumin levels and higher expression of Differentiated liver cells, green fluorescent protein (GFP), matrix metalloproteinase 9 (MMP9), and proliferating cell nuclear antigen in the livers of group A. We observed MMP9/GFP double-positive cells in the cirrhotic livers. A significant decrease in the liver fibrosis areas was observed in group A. There were significant differences in ALT, ALB, TBIL and AFP in three groups, P < 0.05.
CONCLUSION: Infusion of bone-marrow-derived cultured liver stem cells improved liver function and liver fibrosis in rat with CCl4-induced cirrhosis.

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Disclosure of Interest: None declared

P1170 THE RISK OF MALIGNANT TRANSFORMATION OF THE COLORECTAL POLYPS- PROSPECTIVE STUDY

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INTRODUCTION: Because colonic polyps are highly prevalent in the general population (especially with increasing age), they confer an important predisposition to colon cancer
AIMS & METHODS: We performed a prospective study including 659 patients, with amean age of 60.1 ± 11.5 years, in which a number of 928 polyps were resected. We have evaluated the correlation between the dimension of the polyps and the risk of malignant transformation on the ground of the grade of epithelial dysplasia revealed by the histopathological examination.
RESULTS: From the total number of the studied polyps, 324 were without dysplasia, 514 with mild/moderate dysplasia and 89 with high grade dysplasia/malignant polyps. The mean dimension of the polyps without dysplasia was significantly lower in comparison to the dimension of the polyps with high grade dysplasia/malignant polyps: 8.69 ± 0.5978 mm vs. 15.64 ± 1.626 mm, p < 0.0001 ES. There were no statistically significant diferencies between the mean dimension of the polyps without dysplasia vs. the dimension of the polyps with mild/moderate dysplasia: 8.69 ± 0.5978 mm vs. 8.85 ± 0.3489 mm (p > 0.05). The mean dimension of the polyps with mild/moderate dysplasia was significantly lower in comparison to the dimension of the polyps with high grade dysplasia/malignant polyps: 8.85 ± 0.3489 mm vs. 15.64 ± 1.626 mm, p < 0.0001 ES. According to the dimension, the studied polyps were subdivided into two groups: polyps < 15 mm, and polyps > 15mm, respectively. In the first group there were 803 polyps included, from which 286 (35.6%) without dysplasia, 460 (57.2%) with mild/moderate dysplasia and 57 (7%) with high grade dysplasia/malignant polyps. The second group was formed by 121 polyps, from which 38 (31.4%) without dysplasia, 54 (44.6%) with mild/moderate dysplasia and 29 (23.9%) with high grade dysplasia/malignant polyps. Comparing these two groups, we noticed that high grade dysplasia was found in a significantly higher number of polyps > 15mm in comparison with those < 15 mm, p < 0.0001 ES, OR 3.829 95% CI (2.185 to 6.709), RR 1.470 95% CI (1.186 to1.822).
CONCLUSION: Our results demonstrate the existence of a statistically significant correlation between the dimension of the polyps and the risk of malignant transformation, namely, the bigger the polyps are, the higher the risk of malignant transformation is. Polyps over 15 mm diameter hold a risk of malignant transformation 1.5 times higher than the smaller polyps.
Disclosure of Interest: None declared

P1171 MANAGEMENT OF SPONTANEOUS BACTERIAL PERITONITIS IN A LARGE DISTRICT GENERAL HOSPITAL. ARE WE FOLLOWING EUROPEAN GUIDELINES?

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INTRODUCTION: Spontaneous Bacterial Peritonitis (SBP) is the most frequent and life-threatening infection in patients with liver cirrhosis. It requires prompt recognition and treatment. Mortality is high for patients admitted with decompensation which is a growing problem due to the increasing prevalence of cirrhosis. Hence early detection of complications such as SBP is critical to improve outcome. EASL (European Association for the Study of the Liver) released Clinical Practise guidelines on management of SBP in 2010. We have compared our data on managing SBP and determine if this is compliant with guidelines and if there is uniformity within our DGH.
AIMS & METHODS: Our aim was to assess whether we are managing SBP in our DHG in accordance with EASL guidelines from 2010. We collected data retrospectively from October 2011 to November 2012. Then we collected data for 1 year following intervention from November 2012- November 2013. We requested our pathology lab to supply patient details of any ascitic fluid samples with a white cell count > 500/mm^3. We Investigated and recorded the following data:
1. Did patients receive an ascitic tap on admission
2. Was a Neutrophil count >250/mm^3 recorded
3. Was a WCC > 500/mm^3 recorded
4. Positive culture results documented
5. Was Antibiotics started before culture results
6. Was Intravenous albumin given
7. Evidence of Hepatorenal syndrome (HRS) documented
8. Was a Repeat ascitic tap performed
9. Prophylactic antibiotics

RESULTS:

Outcomes measured	Oct 11 – Oct 12 (n = 15)	Nov 2012 – Nov 2013 (n = 12)	Percentage improvement
Ascitic tap on admission	47%	50%	3%
Neutrophil count >250/mm^3 recorded	0%	0%	0%
Positive culture results documented	40%	17%	-23%
Antibiotics started before culture results	93%	100%	7%
Intravenous albumin given	27%	83%	56%
Hepatorenal Syndrome	53%	33%	20%
Repeat Ascitic Tap performed	17%	67%	50%
Prophylactic Antibiotics	33%	33%	0%
Mortality	60%	17%	43%

CONCLUSION: It was alarming to see the variation in management amongst doctors, especially gastroenterologists and hepatologists. Following education there has been improvement in outcomes which hopefully has a positive impact on morbidity and mortality. It is unclear why ascitic neutrophil count is not done in this trust and many other trusts.
This audit highlights the need to ensure that there is a standardised approach to the diagnosis and management of SBP. By adhering to guidelines it may help mortality and morbidity.
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EASL clinical practise guidelines on the management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome in cirrhosis. *J Hepatol* 2010; 53: 397–417.
Disclosure of Interest: C. Kanagasundaram: nil

P1172 SYMPTOMATIC TREATMENT OF HEPATIC ENCEPHALOPATHY WITH CHOLINE ALPHOSCERATE

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INTRODUCTION: The treatment of hepatic encephalopathy (HE) involves multiple drugs that may lead to recovery of consciousness and thinking but therapeutic options are often limited.
AIMS & METHODS: The aim of our work now was to assess the efficacy of *choline alphoscerate* for the treatment of HE in patients with liver cirrhosis. In this prospective study, we included 34 patients with liver cirrhosis and HE, stage I-II. The control group comprised 17 patients receiving standard treatment. Patients from the intervention group received *choline alphoscerate* (L-alpha-glyceryl phosphorylcholine, Gliatilin; 800 mg per day) for one month in addition to the basic treatment. HE was assessed by clinical symptoms, number connection test, and electroencephalography (EEG).
RESULTS: In the intervention group vs. controls the normalization of sleep and movement disturbance improved in 88% and 72% of the patients, respectively. In the control group only 53% of the patients improved in sleep patterns and 40% in motor coordination. Of note on the 10th day of treatment, patients in the intervention group started to perform in the number connection tests 27.2 ± 1.2s faster, whereas in the control group the improvement was significantly ($P < 0.05$) less (12.7 ± 1.4s). Patients on choline alphoscerate showed a marked clinical improvement correlating with EEG changes. Before treatment, a reduction of α-rhythm was detected in 82% of the patients; after treatment this proportion was only 41% ($P < 0.05$), indicating normalization of brain function in the majority of patients. In the control group 73% of patients showed abnormal EEG findings before and after treatment. The presence of θ-waves was observed in 45% of patients before and 24% after treatment with choline alphoscerate ($P < 0.05$); in the control group the corresponding frequencies were 54% and 47% ($P > 0.05$).
CONCLUSION: *Choline alphoscerate* eliminates pathological neurological symptoms in 78% patients with cirrhosis, whereas improvement is only detected in 38% of patients with HE on conventional therapy. The natural choline supplement has a favorable safety profile and should be studied further in randomised controlled trials.
Disclosure of Interest: None declared

P1173 DIFFERENT SCORING SYSTEMS IN PREDICTING SURVIVAL IN CHINESE PATIENTS WITH LIVER CIRRHOSIS UNDERGOING TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

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INTRODUCTION: Transjugular intrahepatic portosystemic shunt (TIPS) is an established minimal-invasive procedure to treat complications of portal hypertension, and several scoring systems have been used to help choose suitable patients. But the accuracy remains controversial.
AIMS & METHODS: To compare the performance of the Child-Turcotte-Pugh (CTP) classification system, Model for end-stage liver disease (MELD) score, Emory score, Bonn TIPS early mortality (BOTEM) score, and serum bilirubin and platelet count (SB/PLT model) in predicting survival in Chinese patients with liver cirrhosis undergoing Transjugular intrahepatic portosystemic shunt (TIPS). The clinical data of patients undergoing TIPS in our department were retrospectively analyzed to compare the 5 scoring systems based on survival after TIPS.
RESULTS: A cohort of 159 patients was involved. The survival curves showed statistical significance between classification B and C of CTP ($\chi2 = 9.451$, $p = 0.002$), between MELD < 10 and MELD ≥ 10 ($\chi2 = 10.099$, $p = 0.001$) and between low risk and moderate risk groups of Emory score ($\chi2 = 4.656$, $p = 0.031$), indicating a better discriminatory ability. By ROC curves and logistic regression model, MELD score and CTP system had a better power to predict 3-month, 12-month, and 24-month survival. MELD score and CTP classification system had smaller values of -2Ln(L), Akaike Information criterion (AIC), and Schwarz-Bayesian criterion (SBC), respectively.
CONCLUSION: MELD score and CTP classification system provide better prognostic stratification for a cohort of Chinese patients with advanced cirrhosis undergoing TIPS. However, MELD score is not significantly superior to CTP system.
Disclosure of Interest: None declared

P1174 IN MELD FIT A PREDICTIVE FACTOR FOR IN HOSPITAL MORTALITY IN CHIRROTICS PATIENTS WITH OESOPHAGEAL VARICEAL BLEEDING?

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INTRODUCTION: The model for end stage liver disease (MELD) score is very accurate for predicting mortality in patients with end stage liver disease. Since 2002, MELD is used for patient allocation on liver transplant waiting lists. Oesophageal variceal bleeding (OVB) is a high mortality rate complication in patients with cirrhosis. The aim of this study was to compare the prognostic value of MELD and MELD fit for in-hospital mortality (IHR) in cirrhotic patients with OVB.
AIMS & METHODS: The study cohort consisted of 135 patients [mean age 54.9 (±12.2), 73.3% male] consecutively admitted to our hospital with OVB. All the patients were submitted to upper endoscopy within 12h, and sclerotherapy or band ligation was performed in case of active bleeding. Octeotride or terlipressin therapy was started at admission and continued for 5 days. In order to calculate MELD and MELD fit scores, data of the laboratory results from blood samples taken within 6h from admission were used. The level of significance was set at $p < 0.05$.
RESULTS: The IHM was 17.0% (23 patients). On univariate analysis the predictive factors for IHM were **rebleeding** (OR = 17.3 (5.6-53.35), **p < 0.001), antibiotic prophylaxis** (OR = 5.05 (1.7-14.7), p = 0.001), **MELD score ^{3} 15** (OR = 5.7 (1.8-17.8), p = 0.001) **and MELD fit score ^{3} 14** (6.9 (1.9-24.6), p = 0.001). On multivariate analysis all remain independently associated to IMH. Applying a receiver operating characteristic (ROC) analysis after multivariate logistic models, the area under the curve (AUC) derived from the MELD and MELD fit scores were, respectively, 0.87 (95%CI: 0.79-0.95) and 0.88(0.8-0.95) for IHM.
CONCLUSION: In cirrhotic patients with OVB MELD score (best cut-off of 15) and MELD fit score (best cut-off of 14) identifies a group of patients with a higher risk of IHM.
Disclosure of Interest: None declared

P1175 EFFICACY OF ENDOSCOPIC BAND LIGATION AS PRIMARY PROPHYLAXIS OF BLEEDING FROM ESOPHAGEAL VARICES

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INTRODUCTION: Endoscopic band ligation is a very effective procedure for the treatment of esophageal varices. Its use is recommended for primary prophylaxis as an alternative to beta-blockers, for the treatment of acute hemorrhage or for secondary prophylaxis.
AIMS & METHODS: The aim of this study was to evaluate our experience regarding elastic band ligation for primary prophylaxis of variceal bleeding.
Analysis of patients undergoing variceal eradication program as primary prophylaxis of variceal hemorrhage, from January 2010 until February 2014.
RESULTS: From a total of 213 patients, 93 were treated for primary prophylaxis; 79% of those were male, with a mean age of 60±12 years, with a median follow- up of 11.4 months. The main cause of portal hypertension was alcoholic cirrhosis (54%), followed by HCV (20%) and HBV (6%) infection. Most patients had a Child-Pugh score of A (48%), with the remaining scoring B (28%) or C (24%). In 55% of the patients it was possible to eradicate varices, with a median number of 2 sessions and 12 rubber bands. The presence of hepatocellular carcinoma was related to the inability to eradicate varices (p = 0.001), and concomitant use of propranolol did not influence the efficacy of eradication (p = 0.937). The mortality rate in one year was 15%. Five patients had variceal bleeding (5%), which was significantly related to mortality at one year (p = 0.022). No patients had bled from the scar. Patients with Child C had greater difficulty in eradicating varices than those with Child A (38% vs 60%, p = 0.101), and higher mortality during follow-up (24% vs 4%, p = 0.036).
CONCLUSION: Endoscopic band ligation was effective in preventing variceal bleeding, with an overall success rate of 95%.
Disclosure of Interest: None declared

P1176 THE SAFETY AND EFFECTIVENESS OF SEDATION WITH MIDAZOLAM IN CIRRHOTIC PATIENTS UNDERGOING ENDOSCOPIC VARICEAL LIGATION

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INTRODUCTION: Endoscopic variceal ligation (EVL) is the established treatment for acute esophageal variceal bleeding. Unlike other therapeutic endoscopic procedure, sedation is generally not used in a cirrhotic patient for fear of hepatic encephalopathy (HE). However, a successful procedure might not be guaranteed due to poor cooperation and/or delirious behavior. We study we evaluated safety and effectiveness of midazolam in cirrhotic patient undergoing EVL.
AIMS & METHODS: The medical records of 320 cirrhotic patients who underwent EVL between October 2003 and December 2012 were reviewed retrospectively. The main outcomes were treatment success and adverse drug reaction (ADR) that might be related with sedation. Also, risk factors for development of HE were pursued.
RESULTS: Midazolam was used in 151 patients and not in 161 and baseline characteristics were similar. The rates of treatment success were not differ in both groups (95.8% vs. 96.2%, p = 0.999). Although the incidence of ADR didn't differ (46.2% vs. 55.0%, p = 0.115), development of HE (6.6% and 0%, p = 0.001) and desaturation (23.2% vs. 7.7%, p = 0.001) were more common in the midazolam group. A patient from the midazolam group died due to uncontrolled bleeding. There were a total of 10 cases of HE. With logistic regression, ECOG score 2 turned out to be associated with ADR (OR = 2.69, 95% CI 1.68-4.29, p). However, age, body mass index, Child-Pugh classification and variceal grade were not related.
CONCLUSION: Because midazolam was associated with ADR including HE in a cirrhotic patient undergoing EVL, it should be used with extreme caution including appropriate intra- and post-procedural monitoring, especially when the ECOG score of a patient is not less than 2.
Disclosure of Interest: None declared

P1177 RESPONSE TO TERLIPRESSIN AND ALBUMIN IS ASSOCIATED WITH IMPROVED OUTCOME IN PATIENTS WITH CIRRHOSIS AND HEPATORENAL SYNDROME (HRS)

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INTRODUCTION: Hepatorenal syndrome (HRS) is a severe but potentially reversible complication in patients with cirrhosis, left untreated it is associated with a very poor prognosis. Several randomized controlled trials (RCT) have proven that treatment with terlipressin and albumin improves renal function, however the effect on overall survival has not been well established.
AIMS & METHODS: Aim of the study was to gain further insight into the effect of terlipressin treatment in patients with HRS on renal function, overall survival and renal-replacement-free-survival.
All patients presenting with HRS and treated with terlipressin in our tertiary referral liver and transplantation center between April 2013 and March 2014 were included, and clinically relevant parameters such as response to therapy, overall survival and renal-replacement-free-survival were prospectively investigated.
RESULTS: Overall 57 patients were followed-up over a median of 65 days. Cirrhosis was in an advanced stage in the majority of patients (Child-Pugh C: 46; 81%). Median cumulative terlipressin dosage and treatment duration were 20 mg and 5 days. Complete or partial response to terlipressin with recovery from HRS was observed in 20 and 3 out of 57 patients (51%; 5%). Median overall survival was significantly better in patients with response to terlipressin than in patients with non-response (167 vs. 27 days; p < 0.0001), as well as median survival free of renal-replacement-therapy (82 vs. 4 days; p < 0.0001). In univariate analysis, non-response was associated with a high baseline serum-bilirubin-concentration.
CONCLUSION: Terlipressin in combination with albumine is effective in a majority of patients with HRS. Response to therapy is associated with improved survival.
Disclosure of Interest: None declared

P1178 NON INVASIVE ASSESSMENT OF LIVER FIBROSIS WITH SIMPLE BLOOD PARAMETERS, MYRIADS OF MARKERS. . .. WHAT TO MIX AND WHERE TO MATCH!

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INTRODUCTION: There are many simple scores (that require only routine blood parameters) for non-invasive assessment of liver fibrosis. But there are only limited data comparing these scoring systems.
AIMS & METHODS: Our aim was to compare simple scores for non-invasive assessment of liver fibrosis with liver biopsy in patients with chronic hepatitis C virus (HCV) infection and validate the recently proposed fibrosis cirrhosis index (FCI)[1].
In 193 chronic HCV patients who underwent liver biopsy, we compared the liver biopsy (Scheuer classification) fibrosis scores with AAR (AST/ALT ratio), APRI (AST/Platelet ratio), FIB-4, Fibrosis Index (FI) and FCI.
These scores are calculated as; AAR = [AST(IU/l)/ALT(IU/l)], APRI = [{AST(IU/l)/ AST(ULN)(IU/l)} × 100]/ platelet count (10^9/l), FIB-4 = [Age (Years) × AST (IU/l)]/ [Platelet count (× 109/l) × ALT (IU/l)1/2], FI = [8.0 - 0.01 × Platelet count (109/l) - Albumin (g/dl)], FCI = [Alkaline phosphatase (IU/ml) × Bilirubin (mg/dl)] / (Albumin × Platelet count)
RESULTS: The mean age of patients was 41.4±9.6 years (160 males), genotype-4 (144, 74.6%) was the commonest followed by genotype-1 (66, 34.2%).
Liver biopsy showed stage-0 fibrosis in 19 (9.8%), stage-1 in 77 (39.9%), stage-2 in 69 (35.8%), stage-3 in 25 (13%) and stage-4 in 3 (1.6%) patients. Compared with liver biopsy, AAR, APRI, FIB-4, FI and FCI showed correlation coefficient indices of 0.144, 0.409, 0.414, 0.558, and 0.54 respectively. The AUROCs for these indices for advanced fibrosis (F0-2 v/s F3.4) were; AAR (for cutoff > 1) 0.52, APRI (cutoff > 1.5) 0.83, FIB-4 (cutoff > 3.25) 0.79, FI (cutoff > 3.3) 0.92, and FCI (cutoff > 1.25) 0.92.
The sensitivity and positive predictive value for FI (80% and 84% respectively) and FCI (82% and 83% respectively) was significantly higher than other indices.
CONCLUSION: The fibrosis index (FI) and fibrosis-cirrhosis index (FCI) accurately predicted advanced fibrosis stage in chronic HCV infected patients; they seem more accurate than other frequently used serum indices.
REFERENCES
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Disclosure of Interest: None declared

P1179 RISK FACTORS AND OUTCOME IN ICU PATIENTS WITH END STAGE LIVER DISEASE

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INTRODUCTION: Acute or chronic liver failure is associated with numerous complications which may occur in combination and patients may require intensive care unit (ICU) treatment. Therefore, it seems necessary to identify prognostic clinical parameters and risk factors at the time of ICU admission.
AIMS & METHODS: To estimate the frequency of mortality and cirrhosis morbidity among patients with end stage liver disease (ESLD) admitted to the ICU and to evaluate the relation between demographic, clinical and laboratory data (potential risk factors) of those patients and mortality.
120 patients with ESLD were enrolled [102 males (85%) and 18 females (15%)]. History taking,clinical examination,full investigations and classification of patients according to Child-Turcotte-Pugh (CTP) and MELD score were done.
RESULTS: Regarding clinical presentation, hepatic encephalopathy (HE) was found in 87.5%, jaundice in 60%, hematemesis in 41.7%, hepatorenal syndrome (HRS) in 35.8% and spontaneous bacterial peritonitis (SBP) in 20.8%. Mortality rate was 57.5%; the main causes of death were HRS (40.8%), HE (21.7), aspiration pneumonia (10%), septic shock (2.5%) and irreversible shock in only 1.7%. There was a significant relation between mortality and old age, CTP and MELD scores and a longer stay at the ICU. Increased white blood cell count, increased hemoglobin and decreased prothrombin concentration and raised creatinine were independent risk factors of mortality in ESLD patients in the ICU. Mortality rates were higher (86.2%) with 5-6 risk factors and (21.7%) with 1-2 risk factor(s).
CONCLUSION: The mortality rate in of ESLD patients admitted to the ICU was 57.5% and the most common cause of death was HRS. CTP, MELD score, HE, HRS and jaundice were significant predictors of mortality in ESLD patients. Mortality increased with increased number of risk factors. Creatinine level, white blood cell count, hemoglobin and prothrombin concentration were independent risk factors affecting the outcome of ESLD patients in the ICU.
Disclosure of Interest: None declared

P1180 SAFETY AND EFFICACY OF TOLVAPTAN FOR TREATMENT OF REFRACTORY ASCITES IN CIRRHOTIC PATIENTS

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INTRODUCTION: Since September 2013 in Japan, the vasopressin V_2 receptor antagonist tolvaptan (7.5 mg/day) has been approved for the treatment of cirrhotic patients with hepatic ascites and edema that do not respond to diuretics. Thirty-one patients with refractory ascites were given tolvaptan at two institutions.
AIMS & METHODS: We prospectively evaluated its safety and efficacy, and determined the predictive factors of a good response. From 14 September 2014 to 31 March 2015, among 31 (19 males, 12 females; 71 (range, 49–89) years) patients with refractory ascites treated with diuretics (furosemide 20–80 mg/day, spironolactone 0–100 mg/day), 29 patients were given tolvaptan at 7.5 mg/day and 2 patients were administered 3.75 mg/day. 15 patients were Child-Pugh class B and 16 were C in their hepatic function reserve. Underlying disease was constituted as follows, HCV was 24, HBV was 1, Alchohol was 4, NASH was 4. Correlations between pre-treatment data and decrease in body weight were determined using logistic regression analyses and scatter diagrams.
RESULTS: Pre-treatment parameters were: estimated glomerular filtration rate, 53.2 mL/min/1.73 m^2; serum osmolarity, 292.6 mOsm/L; albumin, 2.5 g/dL; serum sodium, 129.9 mEq/L; blood-urea-nitrogen, 34.9 mg/dL; hemoglobin, 10.1 g/dL. Twenty-two patients had a loss in body weight of 2 kg and were termed ''responders''. With regard to pre-treatment parameters, there were no

significant differences between responders and non-responders. There were no differences in the response rate for each Child–Pugh class. Responders had a higher rate of increase in urine volume in the first 24-h collection after tolvaptan administration than non-responders (183% *vs* 143%, p = 0.047). In six patients, the rate of change in urine osmolarity 24 h after tolvaptan administration was closely correlated with rate of change in body weight ($R^2 = 0.77$). Rupture of esophageal varices occurred in four patients in the observation period (three in G3 and one in G2). Hypernatremia (>150 mEq/L) was not experienced.
CONCLUSION: These data suggest that for cirrhotic patients with refractory ascites, tolvaptan is effective and safe. In the pre-treatment state, finding predictive parameters for responders is very difficult. However, 24 h after tolvaptan administration, the increasing urine rate and rate of change of urine osmolarity are useful guides to identify responders.
Disclosure of Interest: None declared

P1181 TREATMENTS OF ECTOPIC VARICES WITH PORTAL HYPERTENSION

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INTRODUCTION: Ectopic varices that are not esophagogastric are located predominantly in the duodenum, jejunum, ileum, colon, rectum, or enterostomy stoma. Bleeding from ectopic varices, which is rare in patients with portal hypertension, is generally massive and life threatening.
AIMS & METHODS: From January 1994 to September 2013, we performed endoscopic treatments or interventional radiologic treatments for 1530 portal hypertensive patients with esophagogastric varices. In this study, we evaluated the clinicopathological features and treatments of ectopic varices.
RESULTS: Seventy-seven patients were hospitalized in our ward for treatments of ectopic varices. The underlying pathologies of portal hypertension included liver cirrhosis in 46 patients, cirrhosis associated with hepatocellular carcinoma in 12, primary biliary cirrhosis in 6, idiopathic portal hypertension in 7, extrahepatic portal vein obstruction in 5, and the other disease in 1. The location of the ectopic varices were rectal varices in 58, duodenal varices in 9, intestinal varices in 4, urinary bladder varices in 2, stomal varices in 1, colonic varices in 3. Seventy-three of 77 patients (94.8%) with ectopic varices had previously received emergency or prophylactic endoscopic injection sclerotherapy (EIS) for esophageal varices. In 47 of the 58 rectal variceal patients, EIS was performed with no complications. In 9 of the 58 patients, endoscopic band ligation (EBL) was performed, and 8 of whom experienced no operative complications after EBL. Percutaneous transhepatic obliteration (PTO) was successfully performed for the remaining 2 large rectal variceal patients. We successfully performed the treatments for 9 duodenal variceal patients (the bulbs in 1, the second portion in 6, and the third portion in 2); balloon occluded retrograde transvenous obliteration (B-RTO) in 4, EIS using Histoacryl in 3, EIS plus B-RTO in 1, PTO in 1. Four small intestinal variceal patients (3 jejunal varices, 1 ileal varices) had undergone B-RTO in 2, PTO in 1, endoscopic treatments in 1. B-RTO was successfully performed for ileal varices and jejunal varices. One jejunal variceal patient died 3 days after PTO because of poor general condition, and endoscopies revealed the recurrence of varices in the other jejunal variceal patient after endoscopic treatments. PTO was successfully performed for 2 urinary bladder variceal patients. Endoscopic treatments or interventional radiologic treatments were successfully performed for remaining ectopic varices.
CONCLUSION: Hemorrhage from ectopic varices should be kept in mind in patients with portal hypertension presenting with lower gastrointestinal bleeding.
Disclosure of Interest: None declared

P1182 CANDIDATES FOR CONSERVATIVE TREATMENT AMONG PATIENTS WITH PORTAL VENOUS GAS

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INTRODUCTION: Although hepatic portal venous gas (HPVG) is a sign of poor prognosis, there have been recent reports of cases treated conservatively. However, it remains difficult to determine whether emergency surgery is required. The aim of this study was to clarify the indications for conservative treatment in patients with HPVG.
AIMS & METHODS: Of 107.787 cases in which computed tomography (CT) was performed between April 2009 and September 2013 at our hospital, HPVG was detected in 117 patients. Seventy three patients were excluded because they presented with cardiovascular arrest. Therefore, a total of 44 patients were included in this study. The patients were divided into two groups, group A (n = 26), patients treated conservatively, and group B (n = 18), patients who required surgery or died within 30 hospital days. The factors associated with conservative treatment were analyzed using Fischer's exact test, Mann-Whitney U test and logistic regression analysis. The variables included age, gender, comorbidities (hypertension, diabetes mellitus, ischemic heart disease, cerebrovascular disease, liver cirrhosis, renal failure and malignancy), subjective symptoms (abdominal pain, constipation, vomiting and diarrhea), physical findings (systolic blood pressure, pulse rate, body temperature, abdominal tenderness and peritoneal irritation sign), laboratory findings, including blood gas analysis, and CT findings (pneumatosis intestinalis, ascites and location of HPVG). A receiver operating characteristic curve was used to determine the cut-off value.
RESULTS: The study subjects were 23 men and 21 women with a median age of 78.5 (range, 20 - 102). The major etiologies of HPVG in group A were ileus and enterocolitis. On the other hand, the etiologies in group B were mesenteric ischemia and emphysematous cholecystitis. Idiopathic HPVG was seen in 7 patients in group A and 1 in group B. In the univariate analysis, there were significant differences between the two groups related to body temperature and level of C-reactive protein (CRP), lactate dehydrogenase, aspartate aminotransferase, creatine kinase, lactate and base excess (BE). In the multivariate analysis, CRP and BE were identified as independent risk factors associated with poor prognosis. The cut-off values were 12 mg/dl for CRP and -4.0 mmol/l for BE. When CRP ≤12 mg/dl and BE ≥-4.0 mmol/l were used to identify candidates for conservative treatment, the sensitivity and specificity were 91% and 89%, respectively.
CONCLUSION: CRP and BE might be useful markers to determine the conservative treatment of patients with HPVG.
Disclosure of Interest: None declared

P1183 PORTAL VEIN THROMBOSIS IN THE SETTING OF LIVER TRANSPLANTATION

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INTRODUCTION: The prevalence of portal vein thrombosis (PVT) in patients that have been undergone liver transplantation (LT) is 9.7%±4.5%. The factors associated with its presence and involvements in post-transplant prognosis are unknown. The aim of our study was to determine the prevalence, assess the factors that are associated with its presence as well as to clarify their association with the prognosis in patients with liver cirrhosis (LC) and LT.
AIMS & METHODS: From January 2005 to May 2013, laboratory, radiological and surgical data were retrospectively collected from patients with LC who had undergone LT in our center for the first time.
RESULTS: 165 patients who had (46.7%) or had not been diagnosed of hepatocellular carcinoma (HCC) were included, all of them without tumoral thrombosis. The mean age was 55 (SD9), male 73.3% and HVC 44.8%. Child-Pugh was (A/B/C:31.5/40.6/21.2%) and MELD 15 (SD6). Previous decompensations were: ascites 61.2%, hepatic encephalopathy 33.9%, variceal bleeding 26.1%, spontaneous bacterial peritonitis (SBP) 15.2%. The mean post-transaplant follow-up was 36 months (0-100).
TVP was diagnosed while LT in 16 (9.7%) patients. The TVP was previously diagnose with image tests in 4 patients (25%) (1(0.1% by Doppler ultrasound (DU) and 4(43.8%) by computed tomography(CT)). All patients had a DU in a mean time of 4 months prior the LT(0-10) and 7(43.8%) had a CT in a median time of 1 month before the LT(0-45).
TVP was significantly related to the presence of SBP (37.5 vs 13.1%;p = 0.01), high levels of creatinine (1.4(SD1.8) vs 1(SD0.6;p = 0.04), and low levels of albumin (3.1(SD0.9) vs 3.5(SD0.6);p = 0.03). MELD was higher in patients with TVP (16 (SD6) vs 14(SD5);p > 0.05). Surgery time was similar in both groups (6:05h vs 6:10h, p = 0.8), transfusion of blood products was higher in patients with TVP(plasma bags 15.5 vs 12.5, platelets pool 3 vs 4 and Red cells 7.5 vs 7.9), although the results were not statistically significant.
TVP was correlated with the mortality in the first 30 days (18.8 vs 8.4%;p > 0.05).
CONCLUSION: TVP is a common complication in patients with cirrhosis undergoing LT. Its presence is correlated with suffering from SBP, high levels of creatinine and low levels of albumin. The pre-transplant diagnosis rate is very low (25%) and its presence may have implications for short-term mortality.
Disclosure of Interest: None declared

P1184 COMPARISON OF PLATELETS FUNCTION USING MULTIPLATE® TEST IN CIRRHOTIC PATIENTS WITH AND WITHOUT PORTAL VEIN THROMBOSIS

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INTRODUCTION: Portal vein thrombosis (PVT) occurs significantly more often in cirrhotic patients, compared with total population. PVT diminishes survival in patients with cirrhosis, by increasing incidence of other complications such as bleeding from esophageal varices, loss of ascites responsiveness to diuretics or hepatic encephalopathy. Moreover, PVT complicates qualification for liver transplantation, in some cases preventing this procedure. Factors which influence development of PVT in cirrhosis as well as adaptive changes in coagulation system to this vascular complication are unclear.
AIMS & METHODS: Our study compares platelets function between cirrhotic patients with and without PVT.
Material and methods: 33 patients with liver cirrhosis were qualified for this study and PVT was diagnosed in 10 patients (spiral CT). Etiology of cirrhosis was: alcoholic (n = 18), HCV-infection (n = 6), HBV-infection (n = 4), autoimmune hepatitis (n = 3) and unknown (n = 2). The blood samples from all patients was collected for assessment of aggregation function using MultiPlate® system.
RESULTS: Cirrhotic patients with PVT had lower platelets aggregation activity related to stimulation with thrombin receptor activating-peptide (TRAPtest; 33.5±15.2 *vs* 59.8±22.9 U; $P < 0.05$), arachidonic acid (ASPItest; 25.1±13.4 *vs* 44.3±23 U; $P < 0.05$) and ADP (ADPtest; 21±12.5 *vs* 38.2±18.6 U; $P < 0.05$).
CONCLUSION: Our study showed decreased aggregation activity of platelets in cirrhotic patients with PVT that is probably an adaptive mechanism counteracting the expansion of thrombosis.
Disclosure of Interest: None declared

P1185 LOW-DENSITY LIPOPROTEIN CHOLESTEROL EXERTS A POTENT INFLUENCE ON RESPONSE TO TELAPREVIR-BASED TRIPLE THERAPY FOR CHRONIC HCV GENOTYPE 1 INFECTION

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INTRODUCTION: The aim of this study was to investigate the relation between baseline characteristics including the serum lipid levels and the treatment outcome from telaprevir (TVR) in combination with pegylated-interferon (PEG-IFN) α2b and ribavirin (RBV).
AIMS & METHODS: This prospective study consisted of 218 treatment-experienced patients infected with HCV genotype 1. All received 12 weeks of TVR in combination with 24 weeks of PEG-IFNα2b and RBV.
RESULTS: The SVR rate was 83.0% (181 of 218) by intention-to-treat analysis. In multivariable logistic regression analysis of pretreatment predictors of SVR, low-density lipoprotein cholesterol (LDL-C) level (odds ratio [OR], 1.02, $p = 0.0036$), IL28B TT genotype (rs8099917) (OR, 3.21, $p = 0.0139$), and prior relapse (OR, 4.77, $p = 0.0006$) were extracted as independent predictors of SVR. Receiver operating characteristic analyses to determine the optimal threshold values of the baseline LDL-C level for predicting SVR showed that the area under the curve was relatively high (AUROC 0.78, $P < 0.0001$, cutoff value 95 mg/dL). IL28B TT genotype (OR, 6.89, $P < 0.0001$), prior relapse (OR, 2.33, $p = 0.0289$), and platelet count ($x10^9$/L) (OR, 1.01, $p = 0.0048$) were extracted as independently associated with LDL-C $\geq$ 95 mg/dL. For patients with prior partial/null responses, the SVR rates of the groups with LDL-C $\geq$ 95 mg/dL were significantly higher than those of the $<$ 95 mg/dL groups with any IL28B genotypes and pretreatment platelet count ($\geq$ 150 or $<$ 150x10^9/L).
CONCLUSION: The baseline LDL-C level had a strong impact on outcome from TVR-based triple therapy, especially for patients with prior partial/null responses, irrespective of IL28B genotypes and platelet count.
Disclosure of Interest: None declared

P1186 TREATMENT OF PREVIOUSLY UNTREATED PATIENTS WITH CHRONIC HEPATITIS C GENOTYPE 1 (G1) INFECTION IN GERMAN REAL - LIFE: FREQUENCY AND SEVERITY OF HEMATOLOGICAL ALTERATIONS UNDER BOCEPREVIR TRIPLE THERAPY COMPARED TO DUAL THERAPY

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INTRODUCTION: Triple therapy of chronic hepatitis C G1 infection with the HCV protease inhibitor boceprevir is accompanied by hematological alterations such as anemia, leukopenia and thrombopenia. Data regarding the frequency and severity of these alterations caused by triple therapy in real-life are still scarce and were evaluated in the present analysis by comparison of two German real-life cohorts.
AIMS & METHODS: Data of treatment-naïve patients treated for G1 infection ($N = 1873$) with pegylated interferon (PegIFN) alfa-2b and ribavirin (RBV) in a large German observational study (Online-AWB) were compared with data of 153 treatment-naïve patients from the ongoing German NOVUS observational study who have started triple therapy with PegIFN/RBV together with boceprevir at least 8 months ago.
RESULTS: Hematologic alterations according to the WHO classification caused by dual or triple therapy are shown in the table. Patients undergoing triple therapy achieved a similar frequency of the most common hemoglobin (Hb) alterations grade 1 in contrast to significantly higher frequencies of grade 2 and grade 3 Hb alterations. Hb alterations during triple therapy were managed by RBV dose reductions in 51% while 2.5% received blood transfusions. Only one patient was treated with erythropoietin and one patient discontinued triple therapy because of anemia. Compared to dual therapy there was a higher frequency of alterations in leukocyte (grade 2 and grade 4) and platelet count (grade 1 and grade 3) in patients undergoing boceprevir triple therapy (table).

	Hematological alterations			
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Hb (g/dL)	**9.5- < 11.0** % (N)	**8.0 - <9.5** % (N)	**6.5 - <8.0** % (N)	**<6.5** % (N)
Online-AWB (N = 1873)	**33.5** (628)	**10.7** (200)	**0.8** (15)	**0.1** (1)
NOVUS (N = 153)	**39.9** (61)	**21.6** (33)	**3.9** (6)	**0.7** (1)
P	0.1115^	<.0001^	0.0035*	0.1454*
Leukocytes (10^3/μL)	**2.0 - <3.0** % (N)	**1.5 - <2.0** % (N)	**1.0 - <1.5** % (N)	**<1.0** % (N)
Online AWB (N = 1873)	**42.5** (795)	**13.8** (258)	**3.5** (66)	**0.1** (2)
NOVUS (N = 153)	**39.7** (60)	**21.9** (33)	**5.3** (8)	**1.3** (2)
P	0.5166^	0.0065^	0.2638^	0.0300*
Platelets (10^3/μl)	**70 - ≤ 100** % (N)	**50 - <70** % (N)	**25 - <50** % (N)	**<25** % (N)
Online AWB (N = 1873)	**17.0** (318)	**5.6** (105)	**3.4** (64)	**0.6** (12)
Novus (N = 153)	**26.3** (40)	**7.2** (11)	**8.6** (13)	**0.7** (1)
P	0.0037^	0.4053^	0.0015^	1.0000*

^ Chi-square test, * Fisher's exact test

CONCLUSION: Triple therapy with boceprevir results in a higher frequency of hematological alterations compared to dual therapy. Most alterations are mild to moderate. In German real-life Hb alterations are managed by RBV dose reductions without the use of erythropoietin and only few patient need blood transfusions.
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P1187 PERFORMANCE OF TRANSIENT ELASTOGRAPHY AND SERUM BIOMARKERS AS NON-INVASIVE METHODS FOR ASSESSMENT OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS C EGYPTIAN PATIENTS

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INTRODUCTION: Different non-Invasive methods for assessing stage of hepatic fibrosis had emerged in the last decade. Most popular methods include transient elastography and serum biomarkers panels.
AIMS & METHODS: We aimed at studying the diagnostic performance of transient elastography and five biomarker panels (APRI, FIB-4, Forns' Index, Egy-Score and Hepa-Index) in detecting different stages of hepatic fibrosis in chronic hepatitis C Egyptian patients. Hundred treatment naïve chronic hepatitis C patients were enrolled. They were subjected to liver biopsy and histopathological scoring of fibrosis according to METAVIR scoring system, transient elastography (using FibroScan), APRI, FIB4, Forns' Index, Egy-Score and Hepa-Index. Calculations and cut off values for biomarkers panels were done according to their original publications.
RESULTS: Significant fibrosis ($\geq$ F2 METAVIR) was best detected by transient elastography followed by Forns' Index, Hepa-Index, Egy-Score, FIB-4, and APRI respectively (AUROC: 0.947, 0.806, 0.803, 0.776, 0.645 and 0.589 respectively). Advanced fibrosis ($\geq$F3 METAVIR) was best detected by transient elastography followed by Egy-Score, Forns' Index, FIB-4, Hepa-index and APRI respectively (AUROC: 0.976, 0.875, 0.851, 0.828, 0.783, and 0.754). Cirrhosis was best detected by transient elastography followed by Egy-Score, FIB-4, Forns' Index, APRI and Hepa-Index respectively (AUROC: 0.958, 0.874, 0.841, 0.827, 0.795 and 0.744).
CONCLUSION: Transient elastography had the best performance for non-invasive assessment of hepatic fibrosis in chronic hepatitis C Egyptian patients compared to the studied serum biomarkers.
Disclosure of Interest: None declared

P1188 TREATMENT OF PREVIOUSLY UNTREATED PATIENTS WITH CHRONIC HCV GENOTYPE 1 INFECTION WITH BOCEPREVIR (BOC) IN GERMAN REAL - LIFE: BASELINE AND ON-TREATMENT PREDICTORS OF AN EARLY VIROLOGY RESPONSE

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INTRODUCTION: The achievement of early virologic response (EVR) during triple therapy of chronic HCV genotype 1 infection with BOC has been identified as predictor of high SVR rates of up to 90% and as predictor to shorten treatment to 24 weeks. The present interim analysis of the NOVUS observational study was aimed to investigate EVR during BOC triple therapy in German real-life and to identify factors associated with EVR.
AIMS & METHODS: From April 2012 until January 2014, 536 patients with G1 infection were recruited in the ongoing NOVUS study by 97 practices and hospitals in Germany. Patients were treated with pegylated interferons (PegIFN) and ribavirin (RBV) together with BOC for 24 to 44 weeks after a 4 weeks lead-in period with PegIFN/RBV. The present interim analysis was restricted to 203 untreated patients with documented HCV-RNA levels at treatment week 8.
RESULTS: The frequency of EVR was 73%. Achievement of EVR was significantly associated with age ≤50 years, baseline viral load ≤400.000 IU/mL, normal gamma-GT levels and ferritin levels ≤300 µg/L at baseline, but not with gender, ALT levels, glucose levels, platelet count or genotype 1 subtype (table). The significant differences above were confirmed by univariate logistic regression analysis. When a multivariate logistic regression model was used, viral load and gamma-GT levels at baseline were identified as independent predictors of EVR: baseline viral load (≤400.000 IU/mL vs >400.000 IU/mL): OR 2.99 (CI 1.13-7.93; p = 0.027); gamma-GT (normal vs elevated): OR 2.17 (CI 1.03-4.60; p = 0.042). In an expanded model that included virologic response at the end of the 4-week lead-in period a HCV-RNA decline $>1\log_{10}$ (vs $\leq 1\log_{10}$) was strongly predictive of an EVR: OR 6.63 (CI 2.88-15.26; p < 0.0001).

	EVR (N = 148) % (n/N)	**P***
Male/ Female	76.3 (87/114) / 68.5 (61/89)	0.2161
Age ≤50/ >50 years	78.6 (99/126) / 63.6 (49/77)	**0.0202**
Genotype 1a/1b	69.0 (49/71) / 70.7 (70/99)	0.8122
BVL: ≤/> 400.000/ IU/mL	88.9 (56/63) / 65.7 (92/140)	**0.0006**
GGT normal/ elevated	81.6 (84/103) / 60.7 (54/89)	**0.0013**
ALT normal/ elevated	78.4 (29/37) / 70.8 (114/161)	0.3539
Platelets ≤/> 150/nL	69.7 (23/33) / 71.9 (110/153)	0.7997
Glucose ≤/> 100 mg/dL	69.8 (67/96) / 71.9 (23/32)	0.8232
Ferritin ≤/> 300 µg/L	71.9 (46/64) / 47.6 (10/21)	**0.0419**

CONCLUSION: 73% of treatment-naïve patients with HCV G1 infection undergoing triple therapy with BOC in German real-life achieve an EVR. A low baseline viral load ≤400.000 IU/mL, normal gamma-GT values at baseline and a HCV-RNA decline $>1\log_{10}$ at the end of the 4-week lead-in period are independent predictors for an EVR.
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P1189 EFFICACY AND TOLERANCE OF ANTIVIRAL COMBINATION THERAPY (PEGYLATED INTERFERON, RIBAVIRIN AND TELAPREVIR OR BOCEPREVIR) IN HEPATITIS C VIRUS: COHORT STUDY OF 100 PATIENTS

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INTRODUCTION: Since 2011, the "standard of care" treatment of Hepatitis C Virus genotype 1 is a combination of pegylated interferon, ribavirin and protease inhibitor: telaprevir or boceprevir.
AIMS & METHODS: The aim of this study was to evaluate its effectiveness and tolerance "in real life". Single center retrospective study of 100 unselected and consecutive patients whose antiviral treatment started between March 2011 and March 2013.
RESULTS: The median age was 53 years and 72% of the patients were men; 46% were F4 and 15% were F3. Status regarding previous treatment was: naive 30%, responder-relapser 28%, partial responder 17% and null responder 24%. After 2, 4, 8 and 12 weeks of treatment with protease inhibitor, Hepatitis C Virus RNA was undetectable in respectively 12%, 52%, 60% and 64% of the cases. The overall rate of sustained virological response at week 12 (intention to treat analysis) was 57%: 70% in the naive patients, 75% in responder-relapser, 41% in partial responder and 33% in null responder. During the therapy, the rate of serious adverse events was 41%. Four deaths occurred. Initial platelets count <100.000/mm3 and age ≥ 53 years were associated with a higher risk of occurrence of serious adverse events.
CONCLUSION: The rate of sustained virological response to tritherapy "in real life" is approximately 10% lower than those observed in phase III trials. Tolerance issues are limiting the use of protease inhibitor.
Disclosure of Interest: None declared

P1190 NON-INVASIVE LIVER FIBROSIS EVALUATION IN PATIENTS WITH CHRONIC HCV AND HBV HEPATITIS

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INTRODUCTION: The role of non-invasive test to assess liver fibrosis is increasing and they are gradually introduced in clinical practice. FibroScan is dedicated tool for liver fibrosis evaluation. Aspartate aminotransferase to platelet ratio index (APRI) and FIB4 score are cheap and easy reproducable in daily praxis for liver fibrosis evaluation.
AIMS & METHODS: The aim of our study was to assess correlation between transient elastography (TE), aspartate aminotransferase to platelet ratio index (APRI), FIB4 score and histological stage of fibrosis (F). APRI index was assessed as (AST elevation/platelet count) x 100 and FIB4 index as age (yr) × AST (IU/L)/(platelet count (10(9)/L) × ALT^(1/2) (IU/L)). In this prospective study the correlations of TE, APRI and FIB4 score with fibrosis stage were assessed in 157 chronic HCV or HBV hepatitis patients. TE, APRI and FIB4 were measured at the same day before biopsy. Interquartile range/median <20% and success rate >60% were considered as good quality criteria during TE. Fibrosis was evaluated using METAVIR score. Pathologist was blinded to TE, APRI, FIB4 results. Cut-off values were established by ROC analysis.
RESULTS: We included 139 HCV, 16 HBV and 2 coinfected patients. Strong correlation of liver stiffness R - 0.76 (p < 0.01) and FIB4 R – 0.66 (p < 0.01), but moderate of APRI R – 0.59 (p < 0.01) with liver fibrosis stage were established. For histological F4 stage TE cut-off value 12.5kPa had sensitivity 0.90 and specificity 0.87; APRI cut-off value 1.4 had 0.87 and 0.82; FIB4 cut-off value 2.89 had 0.84 and 0.84 respetively. F≥3 10.7 kPa (0.89 and 0.88), 1.18 (0.80 and 0.76), 2.23(0.85 and 0.80); F≥2 8.5 kPa (0.79 and 0.77), 0.95 (0.74 and 0.72), 1.63 (0.80 and 0.75); F≥1 5.5 kPa (0.82 and 0.76), 0.54 (0.82 and 0.76), 0.98 (0.82 and 0.69). Summarized results are shown in the table below.

Fibrosis stage	TE in kPa (sensitivity/specificity)	APRI (sensitivity/specificity)	FIB4 (sensitivity/specificity)
4	12.5 (0.90/0.87)	1.4 (0.87/0.82)	2.89 (0.84/0.84)
>=3	10.7 (0.89/0.88)	1.18 (0.80/0.76)	2.23 (0.85/0.80)
>=2	8.5 (0.79/0.77)	0.95 (0.74/0.72)	1.63 (0.80/0.75)
>=1	5.5 (0.82/0.76)	0.54 (0.82/0.76)	0.98 (0.82/0.69)

CONCLUSION: Liver TE and FIB4 score are strongly while APRI moderately correlated with fibrosis and accurately predicts the stage of liver fibrosis in patients with chronic HBV and HCV hepatitis. More advanced stage of liver fibrosis are predicted more accurately. TE is more sensitive and specific than APRI or FIB4 for andvanced liver fibrosis and cirrhosis.
Disclosure of Interest: None declared

P1191 REGULATING B CELLS MOBILIZED BY ACUTE PHASE GRAFT INJURY PROMOTED TUMOR RECURRENCE AFTER LIVER TRANSPLANTATION FOR LIVER CANCER

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INTRODUCTION: Orthotopic liver transplantation (OLT) has been regarded as the best curative treatment for patients with end stage liver diseases including advanced liver cirrhosis and acute liver failure. It is also the alternative therapy for patients with early stage hepatocellular carcinoma (HCC). Because of the severe shortage of grafts from brain-death donors, and the importance of timely operation on recipients, living donor liver transplantation (LDLT) offers the unique opportunity of early transplantation with theoretically unlimited source of liver grafts. However, a liver graft from a living donor is frequently small-for-size for the recipient. Acute phase fatty graft injury after transplantation will exacerbate further when the graft is small-for-size. Such acute phase liver grafts injury will trigger a series of inflammatory cascades, which will mobilize the circulating immune cells leading to cancer invasiveness.

AIMS & METHODS: We aim to investigate the impact of acute-phase small-for-size graft injury on mobilization of circulating regulating B cells (Bregs) in HCC patients after liver transplantation and to explore the molecular mechanism.
There were 115 HCC recipients included in current study. The intragraft gene expression profile and Bregs infiltration of the grafts greater (Group 1) and less than 60% (Group 2) of standard liver weight (SLW) were detected by RT-PCR and immunostaining. Circulating Bregs ($CD19^{+}CD24^{hi}CD38^{hi}$) were also compared together with the clinical-pathological data including the incidence of tumor recurrence and metastasis. The direct roles of TLR4, CXCL10 and CXCR3 on circulating Bregs mobilization were investigated in TLR4-/-, CXCL10-/- and CXCR3-/- mice models, respectively. The association of intragraft Bregs infiltration and tumor invasiveness were also examined in a rat liver transplantation for liver cancer model. The role of Bregs on liver tumor growth and invasiveness were further studied in a series of in vitro and in vivo functional experiments with the application of in vivo imaging modalities and intravital confocal microscopy.
RESULTS: The patients were grouped into Group 1 ($>=60\%$ SLW, $n=37$) and Group 2 ($<60\%$ SLW, $n=78$). Much more patients in Group 2 developed tumor recurrence and lung metastasis [19/78(24.4%) vs 3/37(8%), $p=0.04$]. Level of circulating Bregs was significantly higher in Group 2 (Week1: 7.02 vs 1.31/10ˆ5PBMC, $p=0.03$; month3: 5.7 vs 1.3/10ˆ5PBMC, $p=0.03$). There was more intragraft Bregs infiltration in group 2 indicated by CD20/IL10 staining. Intragraft gene expression of TLR4, CXCL10 and CXCR3 were significantly higher in Group 2 at early phase after transplantation. In rat liver transplantation model, more Bregs infiltration at early phase after transplantation correlated with late phase invasive tumor growth. Levels of circulating Bregs were significantly lower in the mice model with major hepatectomy and hepatic I/R injury using TLR4-/-, CXCL10-/- and CXCR3-/- mice, respectively. Bregs also promoted liver cancer cell proliferation and migration in vitro, and tumor growth in vivo.
CONCLUSION: A significantly higher population of circulating Bregs, which are mobilized by small-for-size graft injury, may lead to a higher incidence of tumor recurrence and metastasis after LDLT. TLR4/CXCL10/CXCR3 signaling may play important roles on Bregs mobilization.
Disclosure of Interest: None declared

P1192 DE NOVO INFLAMMATORY BOWEL DISEASE AFTER ORTHOTOPIC LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS

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INTRODUCTION: For patients who develop end-stage primary sclerosing cholangitis (PSC), orthotopic liver transplantation (OLTx) is the only effective treatment currently available. PSC is commonly associated with inflammatory bowel disease (IBD), particularly with ulcerative colitis (UC) in 60-85% cases. De novo IBD after OLTx has been reported, the 10-year risk is estimated to be 14-30%. De novo inflammatory bowel disease activity and impact on the recurrent PSC and colorectal cancer (CRC) after OLTx is not yet fully clear.
AIMS & METHODS: A total of 944 liver transplants were performed in IKEM (Czech Republic) between 1995 and 2012. We analyzed 69 consecutive patients with PSC (50 men and 19 women) who survived more than 12 months and were regularly followed up in our center. IBD was confirmed in 49 (71%) patients pre-OLTx. Except 2 patients with Crohn's disease (CD) all other patients were suffering from UC. Colonoscopy was performed in all patients before OLTx and annually after OLTx. Patients were studied over median follow up period of 82 months (range 16-228) after OLTx.
RESULTS: The course of IBD was mild or in remission in 34/49 (69.4%) patients after OLTx. The remaining 15 patients (30.6%) were suffering from clinically active disease. De novo IBD was confirmed in 13 patients (UC 12, CD 1) after median of 3 years (1-8) after OLTx. Except 2 patients the course of IBD has been described as mild. Recurrent PSC (rPSC) was confirmed in total of 25 patients (36.2%). Risk of rPSC was higher in de novo IBD vs. pre-TX IBD group (9/13 vs. 17/49, $p< 0.05$). Low-grade dysplasia (LGD) of colonic mucosa was found in 3/49 (6.1%) patients in pre-TX IBD vs. 1/13 of de novo IBD patients. Advanced colorectal neoplasia was confirmed just in pre-TX IBD group, high-grade dysplasia (HGD) in 1 (2.0%) patient and colorectal cancer (CRC) was confirmed in 3 (6.1%) patients followed by colectomy.
CONCLUSION: The course of de novo IBD after OLTx is frequently mild but could have negative impact on recurrent PSC. Detection of dysplastic changes supports the usefulness of regular colonoscopic evaluations.
Disclosure of Interest: None declared

P1193 THREE-DIMENSIONAL CONFIGURATION AND IMPROVED OXYGENATION PROTECT HEPARG PROGENITOR CELL LINE-DERIVED HEPATOCYTES FROM HUMAN PLASMA CYTOTOXICITY IN THE AMC-BIOARTIFICIAL LIVER

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INTRODUCTION: The AMC-Bioartificial Liver (BAL) is a high-capacity bioreactor that facilitates the human liver progenitor cell line HepaRG in a non-woven polyester matrix, where cells in 3D configuration are directly oxygenated with 40% O2. The AMC-BAL is designed to bridge patients suffering from Acute Liver Failure (ALF) to transplantation or regeneration and has proven to be efficacious in prolonging survival in a rat model of total liver ischemia (1). A phase I clinical trial has been planned for 2015. During patient treatment, the cells in the BAL are exposed to human ALF plasma. It is therefore essential to investigate the performance of HepaRG cells in human plasma. We previously found that exposure to rat plasma reduced hepatic transcript levels and increased cell leakage in both monolayer (2D, 20% O2) and BAL cultures (2.3). The effect of healthy rat plasma was comparable to ALF-rat plasma. The effect of human plasma is, however, unknown.
AIMS & METHODS: The aim of the study was to assess human plasma cytotoxicity on HepaRG cells in monolayer and BAL culture, and to investigate the contribution of 3D arrangement and increased oxygenation to plasma tolerance. We compared monolayer cultures and static 3D cultures in non-woven polyester matrices under 20% (low-O2) and 40% O2 (high-O2), to BAL cultures.
At maximal differentiation, a baseline test was performed for ammonia elimination, urea synthesis, cell leakage, lactate elimination and transcript levels of the genes encoding hepatic nuclear factor 4a (HNF4a), enzymes involved in ammonia metabolism including urea cycle, and detoxification protein CYP3A4.
Cultures were exposed to 100% plasma +antibiotics (plasma group) or to standard culture medium (control group) for 16 hours, and subsequently tested again on the parameters mentioned above. The differences between baseline and post-exposure test were compared between groups.
RESULTS: After 16 hours of plasma exposure, in BAL cultures, HNF4a and urea cycle genes were decreased up to 50% compared to control, but CYP3A4 expression remained stable. No significant change in hepatic functionality or cell damage was observed.
In monolayers exposed to plasma under low-O2 all hepatic transcript levels and ammonia elimination were decreased by up to 95% compared to control.
In both the 3D configuration group and the high-O2 group, mRNA transcription of hepatic genes was less downregulated compared to the low-O2 monolayer group, up to 75% of the controls, but the cytotoxic effect remained stronger than in the BAL group.
CONCLUSION: Human plasma has a detrimental effect on HepaRG liver functionality and transcript levels, when cultured in 2D with 20% O2. However, BAL-cultured cells are significantly less susceptible to plasma toxicity compared to monolayer cultures, and both 3D configuration and increased oxygenation contribute to this resistance to plasma cytotoxicity. This suggests that the duration of effective BAL treatment may last at least up to 16 hours. These results should be confirmed with human ALF plasma.
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Disclosure of Interest: M. Van Wenum: None declared, R. Chamuleau Other: RC is CSO of the University spin-off company Hep-Art Medical Devices, which has the exclusive license of the AMC bioartificial liver. However, he owns no shares of the company., E. Hendriks: None declared, T. van Gulik: None declared, R. Hoekstra Financial support for research from: 50% of RH salary was paid by the University spin-off company Hep-Art Medical Devices. Funders had no role in study design, data collection and analysis, decision to publish, or preparation of the abstract.

P1194 DE NOVO HEPATOCELLULAR CARCINOMA IN 4 LIVER ALLOGRAFTS

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INTRODUCTION: De novo hepatocellular carcinoma (HCC) in liver allografts is rare, with only 11 cases previously published in the last 14 yrs.
AIMS & METHODS: Our hospital has performed 1906 liver transplants (LT) from 1991 to 2012. 914 (47.9%) were due to hepatitis C virus (HCV). 67 (7.3%) of these were re-transplanted due to HCV recurrence and graft loss without evidence of HCC in the explant. Induction and baseline immunosuppression was based on calcineurin inhibitor (CNI) and all patients received metylprednisolone bolus as treatment of early acute cellular rejection. The median time to HCC was 13.5 yrs (range 8-19); the median age at diagnosis was 66 yrs (range 58-74). Three patients had chronic renal failure (one had a kidney transplant).
CONCLUSION: With improved survival of LT-patients and use of older allografts, an increase in the incidence of de novo malignancies may be expected. There are no screening guidelines in this patient population. We should be aware of the high-risk population of cirrhotic patients with HCV-allograft recurrence and CNI based IS.
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Disclosure of Interest: None declared

Table to abstract P1194
Table 1 Clinical features and management of 4 cases of de novo HCC in liver allografts. ¥ Years

Year of LT / aetiology	Recipient sex / age¥ at diagnosis	Donor sex / age¥	Time¥ from LT to cirrhosis / to HCC	HCC characteristics	Diagnosis method	Diagnosis alfa-fetoprotein (ng/mL)	Treatment	Cause of death / survival time after diagnosis
2002 / HCV	Female / 72	Female / 70	7 / 10	MRI and CT scan: 3.6 cm (segment 8), 4.3 cm (segment 7) and 3.2 cm (segment 4) HCC	Routine US	196.2	Sorafenib (5 months)	Dead due to liver failure complications / 5 months
1993 / HCV	Male / 60	Female / 51	17 / 19	Multicentric and disseminated poorly differentiated HCC. Recurrent HCV cirrhosis. Peritoneal and pulmonary metastases.	Highly elevated alfa-fetoprotein & MRI. Routine US the previous month failed to detect the tumour	1283.6	Palliative	Dead of multiorgan failure / 2 weeks
1995 / HCV & HCC	Male / 74	Male / 45	2 / 17	CT scan: 2 cm HCC (segment 4)	Routine US	3	RF & transarterial chemoembolization. No HCC recurrence	Dead of pulmonary sepsis / 10 months
2005 / Multiple HCCs &OH	Male / 58	Female / 68	Chronic rejection 1 yr posLT / 8	MRI – HCC 1.5 cm (segment 4b)	Elevated alfa-fetoprotein & MRI. US failed to detect the tumour	203	RF	Alive / 4 months follow up

P1195 ACUTE LIVER FAILURE OF HYPOXIC CAUSE - AN OFTEN OVERLOOKED ENTITY

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INTRODUCTION: Hypoxic hepatitis or acute ischemic hepatocellular injury represents 1% of Intensive Care Units (ICU) admissions. In most cases, it is underdiagnosed due to a reduced awareness of clinicians to its complex etiopathogenesis, and association with hypotension in only about 40 % of patients.
AIMS & METHODS: Aims: Evaluation of the causes and prognosis of acute liver failure (ALF) in an Intensive Care Unit with particular analysis of hypoxic etiology.
Methods: Retrospective analysis of the period between 1992-2013, all patients admitted to the Gastroenterology and Hepatology ICU with ALF; review of the etiology, progression and outcome (survival, liver transplantation and death).
RESULTS: 90 patients studied, mean age 42 years, 59% men. Etiology: viral - 35.6 % (HBV + HDV - 60.0%); toxic - 33.3% (Amanita phalloides - 30.0%); hypoxic - 16.6%; other - 11.1%; unknown - 3.3%. Causes of hypoxic ALF were: atrial fibrillation - 6; drepanocytosis/thalassemia - 2; cardiomyopathy - 2; epileptic seizure - 2; acute myocardial infarction - 1; cor pulmonale - 1; neuroleptic malignant syndrome - 1.
ALF mortality was 38.8 % (35 patients): viral 54.3%; toxic 34.3%; hypoxic 8.6%. 21 patients were referred for liver transplantation (23.3%) of which 17.7% were transplanted (16 patients). The majority of transplants were due to toxic ALF (69%) and none was performed due to hypoxic causes. Although 47 % of patients with hypoxic ALF have had inotropic support, there was a good clinical outcome.
CONCLUSION: Hypoxia is an etiology of ALF, which in our series represented one sixth of admissions for ALF. The prognosis is good if the diagnosis is made early on.
Disclosure of Interest: None declared

P1196 METABOLIC RADIOTHERAPY IN CHOLANGIOCARCINOMA: IS THIS A VALID ALTERNATIVE?

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INTRODUCTION: The Cholangiocarcinoma (CC) is a tumour with limited therapeutic options. The natrium-iodide symporter (NIS) mediates the uptake of iodine by thyroid, representing a key component in the successful metabolic radiotherapy using iodine-131 (^{131}I) in the treatment of thyroid tumours. Recently it has been shown that the expression of NIS is increased in CC, opening the possibility of a new therapeutic approach for this type of tumour.
AIMS & METHODS: The aim of this study was to evaluate the therapeutic efficacy of ^{131}I in a human cell line of CC, the TFK1. Kinetic studies of influx and efflux were performed in order to determine the profile of uptake and retention of ^{131}I by the cell line. Subsequently, the cells were subjected to different doses of ^{131}I in order to evaluate and characterize the effects of metabolic radiotherapy. The effect on cell survival was evaluated by clonogenic assay using the crystal violet staining. Flow cytometry was used to assess the type of induced cell death, the effects on the expression of BAX, BCL2 and cytochrome c, changes on mitochondrial membrane potential, as well as the production of reactive oxygen species and anti-oxidant defenses. To determine the possible damages in the DNA it was also performed the comet assay. To assess the cellular expression of NIS, immunohistochemical methods were carried out using anti-NIS antibody.
RESULTS: Treatment with ^{131}I induced a decrease in cell viability dependent on the dose. The predominant type of cell death was apoptosis, and it was accompanied by a decrease in the BCL2 and increase in the BAX expressions. It also occurred release of cytochrome c and mitochondrial membrane depolarization. Irradiation with ^{131}I also induced breaks in DNA. Interestingly there were no differences in the production of intracellular peroxides, superoxide dismutase and reduced glutathione. The immunohistochemical study revealed a strong expression of NIS in this cell line, with a predominantly membrane localization.
CONCLUSION: The ^{131}I caused a decrease in the survival of the studied cell line (TFK1), inducing cell death by apoptosis, through the intrinsic pathway. The ^{131}I appears to be a promising option for the treatment of CC, considering the membrane expression of NIS and the type of induced cell death.
Disclosure of Interest: None declared

P1197 SERUM/BILIARY MMP–9 AND TIMP–1 CONCENTRATIONS IN THE DIAGNOSIS OF CHOLANGIOCARCINOMA

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INTRODUCTION: Cholangiocarcinoma is generally detected late in the course of disease, and current diagnostic techniques often fail to differentiate benign from malignant disease. We analyzed the roles of serum and biliary MMP–9 and TIMP–1 concentrations in the diagnosis of cholangiocarcinoma.
AIMS & METHODS: The 113 patients (55 males, 58 females) included 33 diagnosed with cholangiocarcinoma (malignant group) and 80 diagnosed with choledocholithiasis (benign group). MMP–9 and TIMP–1 concentrations were analyzed in serum and bile and compared in the malignant and benign groups.
RESULTS: Biliary MMP–9 concentrations were significantly higher (576 ± 209 vs. 403 ± 140 ng/ml, $p<0.01$) and biliary TIMP–1 concentrations were significantly lower (22.4±4.9 vs. 29.4 ± 6.1 ng/ml, $p<0.01$) in the malignant than in the benign group. In contrast, serum MMP–9 and TIMP–1 concentrations were similar in the two groups. Receiver operating curve analysis revealed that the areas under the curve of bile MMP–9 and TIMP–1 were significantly higher than 0.5 ($p<0.001$). The sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and accuracy were 0.94, 0.32, 0.36, 0.93, 1.40, 0.19 and 0.5 for biliary MMP–9, respectively, and 0.97, 0.36, 0.39, 0.97, 1.5, 0.08 and 0.54 for biliary TIMP–1, respectively (Table I).

Table I. Concentrations of MMP–9 and TIMP–1
Table to abstract P1197

	Sensitivity	Specificity	PPV	NPV	PLR	NLR	Accuracy
Serum MMP–9 (cut-off: 325 ng/ml)	0.7273	0.3625	0.32	0.7631	1.1408	0.7523	0.4690
Bile MMP–9 (cut-off: 350 ng/ml)	0.9394	0.325	0.3647	0.9286	1.3917	0.1864	0.5044
Serum TIMP–1 (cut-off: 205 ng/ml)	0.9697	0.1375	0.3168	0.9167	1.1243	0.2204	0.3805
Bile TIMP–1 (cut-off: 31 ng/ml)	0.9697	0.3625	0.3855	0.9667	1.5211	0.0836	0.5398

CONCLUSION: Serum and biliary MMP–9 and TIMP–1 concentrations do not appear to be useful in the diagnosis of cholangiocarcinoma.

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P1198 DEVELOPMENT OF A SWINE BENIGN BILIARY STRICTRURE MODEL USING ENDOBILIARY RADIOFREQUENCY ABLATION

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INTRODUCTION: An established and reproducible animal model of benign biliary stricture (BBS) has been indispensable to develop new devices or methods for endoscopic treatment of biliary stricture.
AIMS & METHODS: We studied how to make a porcine BBS model using endobiliary radiofrequency ablation (RFA). Fourteen-month-old, female mini pigs (*Sus scrofa*), each approximately 30 kg, were used. Endoscopic retrograde cholangiography (ERC) was performed in 12 swine. The animals were allocated to three groups (100 W, 80 W, and 60 W) according to the electrical power level of RFA electrode. Endobiliary RFA was applied to the common bile duct for 60 seconds using by RFA probe which could be endoscopically inserted. ERC was repeated two and four weeks respectively after the RFA to identify BBS. After the strictures were identified, the animals were euthenized and bile duct samples were achieved to evaluate the pathologic findings.
RESULTS: BBS were verified in all animals. Cholangitis were detected on endoscopic findings of day 14 in all the animals of 3 groups, but not significant. Bile duct perforations occurred in 1 swine (n = 1, 100%) for 100 W group, and 1 swine (n = 7, 14.3%) for 80 W group. There was no major complication (n = 4, 0%) in 60 W group. All benign strictures were proven pathologically. The pathologic findings resembled BBS in human.
CONCLUSION: The application of endobiliary RFA with 60 W-electrical power resulted in a safe and reproducible swine model of BBS.

Disclosure of Interest: None declared

P1199 INCREASING INCIDENCE OF CHOLANGIOCARCINOMA IN CRETE 2002-2013

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INTRODUCTION: Epidemiological data on cholangiocarcinoma in Greece is limited. Crete has a homogeneous population and environmental factors are uniform.
AIMS & METHODS: Patients with cholangiocarcinoma, resident on the island of Crete, diagnosed between 2002 and 2013 in the two reference centers, were studied. Periampullary tumors were excluded. Data were prospectively and retrospectively collected from the database of the 2 major hospitals of Crete. Crude incidence rates are presented. The statistical analysis was performed with the SPSS 19 software.
RESULTS: During the 12-year period a total of 89 patients (55.6% males, median age 74 years) were diagnosed with cholangiocarcinoma. 7 of them had cholangiocarcinoma of the intrahepatic ducts, 42 were hilar Klatskin tumors and 40 patients were diagnosed with extrahepatic ducts carcinoma. Diagnosis was radiologically established in 91% of the cases (40% MRCP, 28% CT, 20% ERCP, 3% PTC), while histological diagnosis was available in 8 (9%) patients. A steady incidence increase of cholangiocarcinoma, irrespective of location, was shown. The estimated incidence rate per three-year period progressively increased from 1.33 to 1.996 to 4.99 and 6.48 per 100.000 for the periods 2002-2004, 2005-2007, 2008-2010 and 2011-2013 respectively. Median survival time was 7 months [SE 1.76 95% CI 3.53-10.46]. Median survival times according to location were 3 months [SE 2.61] for intrahepatic, 6 months [SE 1.4] for Klatskin tumors and 11 months [SE 1.88] for bile duct carcinomas.
CONCLUSION: A steady incidence increase of cholangiocarcinoma cases in Crete during the time period 2002-2013 was shown. This is probably due to changing dietary habits since both the genetic background and other environmental factors in the island are more or less stable.

Disclosure of Interest: None declared

P1200 HELICOBACTER BILIS IS A RISK FACTOR ASSOCIATED TO EXTRAHEPATIC BILIARY CANCER IN A MEXICAN POPULATION

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INTRODUCTION: The biliary tract cancer (include gallbladder, common bile duct (CDB) and Vateŕs ampulla) is the sixth cause of death for all cancer in Western countries with a global incidence rate of 2-6/100.000 habitants. Approximately 178.101 new cases of gallbladder carcinoma and 142.813 deaths were recorded in 2012. Although etiology and pathogenesis remain unclear, genetic alterations, environmental, and infection with enterohepatic *Helicobacter spp* such as *H. bilis*, *H. hepaticus*, or *H. cholecystus* have been suggested as risk factors.
AIMS & METHODS: The aim of this work was to study whether *H. bilis* or *H. hepaticus* are associated with bile duct cancer.
Multicenter, case-control study performed in 18 states of Mexico between May 2012-December 2013, included adults diagnosed with malignant stenosis of CBD and patients with benign pathology of the bile duct matched by sex, age (± 5 years) and place of residence. The diagnosis was made by endoscopic retrograde cholangiopancreatography (ERCP). All cases were confirmed by brush cytology-histopathology and clinical course. Epithelial cells were obtained by scraping the biliary ducts during ERCP and brushes were suspended in buffer solution and frozen at -80°C until tested. DNA was extracted from brushed cells using QIAamp DNA easy kit (Qiagen, Hilden, Germany) and quantified using PicroGreen kit (Life technologies, Carlsbad, CA). A PCR reaction to amplify a 207 bp fragment from the 16S rRNA gene specific for *H. bilis* and *H. hepaticus* was performed. Differences between groups were analyzed by chi square test, and odds ratio determined using Epidat 3.1 programme.
RESULTS: The study included 194 Mexican patients, 103 samples corresponded to extrahepatic bile duct cancer: 66 CBD, 11 gallbladder and 26 of Vateŕs ampulla. Mean age of cases was 61.81±13.95 years, 41 were men and 62 women. As controls, bile duct samples were obtained from 91 patients: 64 choledocholithiasis, 6 cholecystolithiasis, 3 biliary leaking, 14 benign stenosis, 2 normal biliary duct, 1 biliary post-surgical stenosis and one choledochal cyst.
H. bilis was positive in 44 (42.78%) of the patients with extrahepatic biliary cancer and in 19 (20.88%) of controls and difference was statistically significant (p = 0.002). Odds ratio for extrahepatic biliary cancer with H. bilis in comparison with gallstones or another benign pathology was 2.83 (95% CI 1.49-5.32). H hepaticus was detected in 17 (16.5%) cases, and 13 (14.28%) controls, a difference which was not significant (p = 0.82)
CONCLUSION: Our results suggest that *H. bilis*, but not *H. hepaticus* might be a risk factor to develop extrahepatic biliary cancer in Mexican population.

Disclosure of Interest: None declared

P1201 LONG TERM FOLLOW-UP DATA OF PATIENTS WHO DEFERRED CHOLECYSTECTOMY AFTER SUCCESSFUL EST

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INTRODUCTION: Endoscopic sphincterotomy (EST) has been the optimal therapy for choledocholithiasis since it was introduced in 1974. And the cholecystectomy is generally recommended after EST in cases with gall bladder stone. But there are debates if the cholecystectomy is necessary for all of the patients, and lots of patients defer cholecystectomy for various reasons. We studied the natural courses of patients with gall bladder stone who deferred cholecystectomy after EST in our clinic.
AIMS & METHODS: There were 727 patients with gall bladder stone who received EST for CBD stone from 2004 to 2012 in Changwon Fatima Hospital. 605 patients received cholecystectomy soon after EST, and the other 122 patients who defered operation were analyzed retrospectively by chart review and phone calls. 43 patients were lost to follow up and 79 patients were finally enrolled.
RESULTS: The mean age was 72.88 years and the mean follow up duration was 39.73 months. 28 patients had biliary recurrence (35.4%) and 12(15.1%) patients

received emergent cholecystectomy later. All-cause death was occurred in 9(11.3%) patients. The mean interval to 1st biliary recurrence was 17.9(months) and the types of recurrence were mostly cholangitis (16 pts) followed by cholecystitis (15 pts) and uncomplicated biliary pain (3 pts). 34 patiens (43%) defered cholecystectomy for old age, 29 patients (36.7%) defered for personal reasons and 16 patients (20.2%) were high risk for operation. In 9 cases of death, cause of death was cancer in 4 patients and 3 patients were died of pneumonia. There were no biliary complication related death.
CONCLUSION: There was significant biliary recurrence who had gall bladder stone but defered cholecystectomy after receiving EST for CBD stone. Many patients defer operation because of old age and personal reasons. They should be warned enough about high incidence of biliary recurrence despite rare mortality of biliary complication.
Disclosure of Interest: None declared

P1202 PROTEOMIC ANALYSIS OF HUMAN BILE SAMPLES IDENTIFIES NOVEL MARKERS FOR CHOLANGIOCARCINOMA IN PATIENTS WITH, AS WELL AS WITHOUT, UNDERLYING PRIMARY SCLEROSING CHOLANGITIS

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INTRODUCTION: Cholangiocarcinoma is a cancer form that is often detected late, resulting in poor prognosis. Its diagnosis is challenging, particularly in the context of primary sclerosing cholangitis (PSC). The aim of this study was to identify potential novel bile biomarkers for cholangiocarcinoma in patients with/without PSC.
AIMS & METHODS: Bile samples were prospectively collected from 21 patients referred for ERCP: 6 patients with a clinical diagnosis of cholangiocarcinoma (3 with and 3 without underlying PSC), 5 patients with PSC without suspicion of cholangiocarcinoma, and 10 patients with other benign bile duct diseases. Following delipidation, samples (60µl) were prepared by the filter aided sample preparation (FASP) method (modified), and digested by trypsin, before analysis by nano-LC MS/MS on a Q-Exactive instrument. Data were searched against the UniProt/Swissprot database using the Mascot software. At least one peptide at the 99% significance level with a score of 20 or above was required for protein identification.
RESULTS: The on-filter digestion approach, performed, to our knowledge, for the first time on bile, appeared to work well. Up to 758 individual protein identifications were possible from one sample, and the total time for preparation and analysis for all aspirates was less than a week. Interestingly, there was little resemblance between the PSC-associated and non-PSC -associated cholangiocarcinoma samples. Several markers for non-PSC-associated cholangiocarcinoma were identified, including EPS8L2 (3/3 non-PSC-cholangiocarcinomas, 0/18 others; $p = 0.0008$ [Fisher's Exact test]) and SLC9A3R1 ($p = 0.003$). Promising markers for PSC-associated cholangiocarcinoma are PDE4DIP (Myomegalin) (2/3 PSC-associated cholangiocarcinomas, 0/18 others; $p = 0.01$), and ITGA6 (Integrin alpha-6) ($p = 0.04$). Importantly, neither of the latter markers was found in PSC patients without suspicion of cholangiocarcinoma.
Furthermore, several differences between PSC ($n = 8$) and non-PSC ($n = 13$) samples were detected including the upregulation of S100P ($p = 0.03$) and down-regulation of EZR (Ezrin) ($p = 0.02$) in PSC samples. These two proteins are previously known to interact with each other, and S100P has been implicated in carcinogenesis, through the activation of ERK and NFκB signalling pathways.
CONCLUSION: A novel preparation method for proteomic analysis of human bile was evaluated, and proved to be simple, fast, and generate a high number of protein identifications. Several promising markers for PSC-associated and non-PSC-associated cholangiocarcinoma, were tentatively identified.
Disclosure of Interest: None declared

P1203 AUTOCRINE VEGF SIGNALING IN EXTRAHEPATIC BILE DUCT CANCER: CORRELATION WITH PATIENTS' PROGNOSIS AND TUMOR CELL PROLIFERATION

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INTRODUCTION: Tumor cells express vascular endothelial factor (VEGF) that can activate VEGF receptors (VEGFRs) on or within tumor cells to promote growth in an angiogenesis-independent fashion, however, this autocrine VEGF pathway is not reported in extrahepatic bile duct cancer (EBDC) and the role of autocrine VEGF pathway in cholangiocyte pathophysiology and clinical significance is yet unknown.
AIMS & METHODS: Immunohistochemistry were used to characterize the expression of VEGF and phospho-VEGF receptors in EBDC patients. Using EBDC cell lines, we studied the mechanism of VEGF signaling on EBDC cell proliferation.
RESULTS: The number of VEGF-positive, pVEGFR1-positive and pVEGFR2-positive cases was 40 (55.5%), 26 (36.1%) and 24 (33.3 %), respectively. Comparison of clinicopathological characteristics and immunohistochemistry showed that the positive expression of pVEGFR1 and pVEGFR2 significantly correlated with the poorer survival. The positive expression of pVEFR1 was a significant independent poor prognostic factor in EBDC. The pVEGFR1 expression was positively correlated with cell proliferation marker pErk1/2 in EBDC tissues. In vitro, we showed that VEGF promoted phosphorylation of VEGFR1 and VEGFR2 in an autocrine fashion, which is pro-proliferative through a PLC-ERK pathway. Sorafenib treatment inhibited cell proliferation and reduced VEGF secretion by inactivating autocrine VEGF pathway.
CONCLUSION: In EBDC, the pVEGFR1 and pVEGFR2 expression are prognostic factors of the poorer survival. The activation of autocrine VEGF signaling promotes EBDC cell proliferation, supporting a role of autocrine VEGF signaling as potential therapeutic target for clinical treatment.
Disclosure of Interest: None declared

P1204 HISTOLOGIC EFFECT OF IN VIVO RADIOFREQUENCY ABLATION ON BILE DUCT IN SWINE MODEL: A PRELIMINARY EXPERIMENT

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INTRODUCTION: Radiofrequency ablation (RFA) exerts heat energy on target tissue to induce localized necrosis. It has been used for local control of liver cancer. We recently developed RFA electrode and RF generator which can monitor total emitted amount of heat energy in real time for endobiliary application.
AIMS & METHODS: We evaluated histologically injury depth and whether perforation occurs or not in bile duct according to thermal energy amount after *in vivo* biliary RFA experiment of swine model. 14-month-old, female mini pigs (*Sus scrofa*) were used. After laparotomy and duodenal incision, guidewire was inserted into the common bile duct (CBD) through the major duodenal papilla. RFA electrode was passed over the guidewire, and placed in the distal CBD. Then RFA was applied to the CBD in different total energy amount of laser (50, 100, 150, 200, 300, and 1000 joule) with different target temperatures (80 and 90 °C). All mini pigs were sacrificed right after the procedure and bile duct samples were achieved to evaluate the pathologic findings.
RESULTS: Total eight mini pigs were verified for pathologic analysis. Mean value of injury depth of the bile ducts were 50 μm, 125 μm, and 150 μm in 50, 100, and 150 joule-group, respectively. Bile duct perforations were observed in all 3 swine at 200 joules or more with 90 °C of target temperature.
CONCLUSION: The application of *in vivo* endobiliary RFA under 150 joules of total heat energy with less than 80 °C of target temperature may result in unperforated, dose-dependent thermal injury of the bile duct.
Disclosure of Interest: None declared

P1205 LIVER RESECTION IS A BETTER SURVIVAL THAN SORAFENIB IN HEPATOCELLULAR CARCINOMA PATIENTS IN BARCELONA CLINIC LIVER CANCER STAGE C WITH MACRO VASCULAR INVASION

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INTRODUCTION: Hepatocellular carcinoma (HCC) is one of the most common malignancies, with an increasing incidence and is the third leading cause of cancer-related mortality in the world. Liver resection remains the curative therapy for BCLC stage A. For BCLC stage C, the efficacy of sorafenib has been demonstrated in clinical practice. However, certain patients could still benefit from liver resection than sorafenib, especially in Asian.
AIMS & METHODS: This study aims to evaluate and compare overall survival in HCC patients in BCLC stage C with macro vascular invasion treated with liver resection and sorafenib.
We retrospectively reviewed the medical records of 138 newly diagnosed hepatocellular carcinoma patients between 2005 and 2013 in BCLC stage C with macro vascular invasion and Child-Pugh class A were analyzed and compared at E-DA hospital, Taiwan.
RESULTS: Sixty-two patients (45%) were treated with surgical resection and 76 patients were treated with sorafenib (55%). The average age is 57.9 and 60.8 years old in the resection and sorafenib group, respectively. The rate of male is 78.8% and 82.6% in the resection and sorafenib group, respectively. The rate of HBV is 56.8% and 60.2% in the resection and sorafenib group, respectively. Median survival was 30.3 months (range 1.5-90.2 months) in resection group compared with 7.6 months (range 1.1-15.2 months) in the sorafenib group ($p < 0.001$). The 1-year survival rate is 67.8% and 15.6% in the resection group and sorafenib group, respectively.
CONCLUSION: Liver resection gets a better survival than sorafenib in HCC patients at BCLC stage C with macro vascular invasion and Child-Pugh class A.
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Disclosure of Interest: None declared

P1206 PATIENT-TARGETED AND MULTIDISCIPLINARY MANAGEMENT IMPROVES SURVIVAL IN PATIENTS WITH HCC: THE HEPATOCATT EXPERIENCE

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INTRODUCTION: Hepatocellular carcinoma (HCC) is the sixth most common and the third cause of cancer-related death in the world. Due to its complex and heterogeneous nature, HCC could represent a real challenge for clinicians. The overall survival rate in West countries population is 63% at 1 year, 29% at 3 years and 33% at 1 year in untreated patients.
AIMS & METHODS: The aim of our study is to analyze the impact of a multidisciplinary approach on patients' survival, comparing survival of our centre with data published in literature. Since September 2008 to September 2013, medical records of 636 patients with primitive lesions of the liver (including benign tumors and dysplastic nodules) were collected in the archive of our centre's Multidisciplinary Group (HEPATOCATT) and were retrospectively reviewed. For the survival analysis we selected 463 HCC patients for whom an adequate follow-up was available. Therapeutic strategies for each patient have been decided after collegial discussion with different specialists according to the stage of disease, the liver damage and the patient's clinical state, also adopting BCLC international guidelines.
RESULTS: Data analysis showed an overall survival of 79% and 56% at 1 and 3 years respectively. 51% patients presented with early stage HCC (BCLC A), 27% with BCLC B, 17% with BCLC C and 5% with end stage HCC (BCLC D). The survival analysis according to BCLC stage showed a survival rate of 90% at 1 and 69% at 3 years for BCLC A, 78% at 1 and 52% at 3 years for BCLC B, 53% at 1 and 25% at 3 years for BCLC C, 59% at 1 and 31% at 3 years for BCLC D ($p<0.01$).
CONCLUSION: The current study shows that a patient-targeted and multidisciplinary management of patients with HCC allows similar or slightly better survival rates than data of literature. This was particularly evident for advanced stages. Furthermore, our study shows a better survival rate for BCLC D than for BCLC C stage, proving that a customized therapy of the underlying liver disease allows even patients with advanced HCC to access potentially curative treatments.
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Disclosure of Interest: None declared

P1207 VASCULAR ENDOTHELIAL GROWTH FACTOR AND HYPOXIA INDUCIBLE FACTOR IN HCC: PROGNOSTIC ROLE IN PATIENTS UNDERGOING CONVENTIONAL AND DEB-MEDIATED CHEMOEMBOLIZATION

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INTRODUCTION: Transcatheter arterial chemoembolization (TACE) is the conventional palliative treatment for HCC in the BCLC "intermediate" stage. Factors interfering with effectiveness include the neo-angiogenic reaction due to ischemia, with changes in circulating vascular endothelial growth factor (VEGF) and hypoxia-inducible factor (HIF) levels after TACE.
AIMS & METHODS: Our study sought significant differences in neo-angiogenesis before and after conventional TACE (C-TACE), compared to DC-Beads mediated TACE (DEB-TACE), measuring serum VEGF and HIF levels. VEGF and HIF levels (ELISA) were determined in the sera and plasma, respectively, of 129 consecutive HCC intermediate stage patients, before TACE (t0) and 4 weeks after (t1). C-TACE was administered to the first 86 patients and DEB-TACE to the next 43. Tumour vascularization was evaluated at t0 and response to treatment at t1, based on angiography and sCT scan (mRECIST criteria).
RESULTS: VEGF levels at t0 significantly correlated with lesion size (0.005) and number (0.004) in both C- and DEB-TACE. HIF levels at t0 significantly correlated with aetiology (0.02), in particular with HCV, and large size lesions (0.05) both overall and in patients undergoing DEB-TACE. VEGF showed a significant increase from t0 to t1 overall (0.002) and separately in C-TACE and DEB-TACE (0.02). The t0-t1 variation in HIF was not significant. The two markers showed opposite trends, with an increase in VEGF after treatment and a decrease in HIF (chi square 0.0001). An inverse significant correlation was observed between the two markers, with high VEGF at t0 corresponding with low HIF at t1 (0.03). VEGF t0 levels and tumour size were singled out in the Cox multivariate analysis as independent predictors of survival, with no significant results with respect to HIF. DEB-TACE and C-TACE effects in terms of mRECIST response to treatment did not differ, with similar severity of side effects and, finally, survival.
CONCLUSION: Our study confirms the evidence so far obtained for VEGF, that is confirmed as an independent predictor of survival, with higher levels identifying patients with worse prognosis. An unpredicted reduction after treatment of HIF was observed, in contrast with the few studies carried out so far, mostly oriental, which may suffer from small sample size and an ethnicity-related bias. The interesting correlation with viral aetiology, in particular with HCV, should be explored further, in order to search for possible viral and cellular molecular targets, involved in HIF-mediated carcinogenesis. The opposite behaviour of the two markers could be attributable to activation of alternative pathways, such as that involving VEGF, mediated by SP1 and PI3K/Akt, or it could depend on different transcription sites (VEGF being preponderantly produced in the pericancerous tissues and HIF in the tumour area). DEB-TACE and C-TACE seem equally effective as regards response to treatment, side effects and, most importantly, impact on survival.
Disclosure of Interest: None declared

P1208 ASSOCIATION OF IL-28B RS12979860 GENE POLYMORPHISM AND HEPATOCELLULAR CARCINOMA IN PATIENTS INFECTED WITH HCV GENOTYPE 4

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INTRODUCTION: Hepatitis C infection is a major global public health problem. Egypt has the highest prevalence of HCV worldwide with 9% countrywide and up to 50% in certain rural areas **[1]** and the highest prevalence of HCV-4, which is responsible for almost 90% of infections and is considered a major cause of chronic hepatitis, liver cirrhosis, hepatocellular carcinoma ***[2]***. Hepatocellular carcinoma (HCC) is the fifth most common tumor and the third most common cause of cancer-related deaths worldwide [3]. There are few and controversial data available on the association between IL-28B SNPs and severity of liver fibrosis, presence of cirrhosis or developing HCC **[4].**
AIMS & METHODS: The current study aimed to investigate the association between rs12979860 SNP of IL-28B gene and HCC in Egyptian patients infected with HCV genotype 4. This hospital-based study included 150 patients with HCV infection that were classified into three groups: 50 patients with chronic hepatitis, 50 patients with cirrhosis, and 50 patients with hepatocellular carcinoma. The plasma Human interleukin 28B levels, liver enzymes activities and serum levels of total proteins, albumin, and α fetoprotein were measured, spiral computed triphasic scanning in focal hepatic lesion for documentation of HCC diagnosis (vascular flush with rapid washout). Also, Genotyping of IL-28B rs12979860 C/T allele Polymorphism was carried out using RFLP-PCR.
RESULTS: Fifty patients (33.3%) were CC homozygous genotype, whereas, the other 100 patients were either TT or CT. The genotype TT was more frequent in HCC group in comparison to chronic hepatitis group. In addition, T-carriers increase significantly in HCC group than chronic hepatitis group. Also, IL-28B and α-FP were significantly different in T-carriers than CC genotype, and in HCC patients in comparison to either chronic hepatitis or cirrhosis patients.
CONCLUSION: This study suggests that in IL-28B rs12979860 C/T polymorphism, the T allele appears to be more prevalent in patients with end stage liver disease (liver cirrhosis and HCC). Furthermore, chronic HCV infection with end stage liver disease may be associated with a reduced IL-28B production. Further research is needed to reveal the cause-effect of these polymorphisms on host protective immunity against HCV infection.
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Disclosure of Interest: None declared

P1209 EFFICACY OF RADIO FREQUENCY ABLATION FOR ELDERLY HEPATOCELLULAR CARCINOMA PATIENTS

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INTRODUCTION: In Japan, the population of patients with hepatocellular carcinoma (HCC) is aging, and the use of radiofrequency ablation (RFA) to treat elderly patients with HCC is increasing. However, there are few studies

that compare elderly and non-elderly patients regarding the efficacy of RFA. Therefore, we evaluated the efficacy of RFA for elderly patients with HCC.
AIMS & METHODS: Two hundred and nineteen patients with primary HCC (tumor size ≤ 30mm and tumor number ≤ 3) treated with RFA between 2004 to 2012 were analyzed. Elderly patients (age 75 or over) accounted for 33% (73 patients) of the patients. We analyzed patient characteristics, recurrence free survival (RFS), factors related to RFS and overall survival (OS).
RESULTS: The baseline characteristics of patients were comparable between two groups with the exception of gender (male, 49% vs. 69%, respectively, $p<0.01$), ALT (median, 39IU/L vs. 45IU/L, respectively, $p<0.01$) and the presence of diabetes mellitus (12% vs. 27%, respectively, $p=0.01$). The median RFS times were 29.7 months and 29.8 months in the elderly group and non-elderly group. The RFS rates at 1, 3, and 5 years were 80.7%, 31.8%, and 21.2% in the elderly group compared with 76.6%, 40.0% and 29.7% in the non-elderly group, respectively ($p=0.43$). The times to local recurrence (TTLR) were not significantly different between the two groups ($p=0.12$). In multivariate Cox analysis, AFP > 20ng/ml (HR:1.84, 95%CI:1.2-2.8, $p<0.01$) and multiple tumor (HR:1.74, 95%CI:1.2-2.6,$p=0.04$) were significantly associated with recurrence. The 5-year OS rates in the elderly group were 51%, and 72 % in the elderly and non-elderly groups ($p<0.01$), respectively. There were 67 and 123 patients positive for anti-hepatitis C antibodies in the elderly and non-elderly groups, respectively. In patients with HCV who received anti-viral therapy (3 elderly, 29 non-elderly), none of the elderly and seven of non-elderly patients sustained viral response. When we restricted the analysis to patients who didn't receive anti-viral therapy (64 elderly group, 94 non-elderly group), the 5-year OS rates were not significantly different (50% and 65%, $p=0.13$), respectively.
CONCLUSION: Results indicated that RFA is equally effective for treating elderly and non-elderly patients with HCC.
Disclosure of Interest: None declared

P1210 RADIOFREQUENCY ABLATION FOR THE TREATMENT OF COLORECTAL LIVER METASTASIS: A CLINICAL OUTCOME REPORT

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INTRODUCTION: The 5 year-survival rate of patients with Colorectal liver metastases (CRLM) without treatment is < 5%, with a median survival time of 8-10 months. Radiofrequencyablation (RFA) is one of the loco-regional therapies that may be used as an adjunct to chemotherapy in treating these patients, and improve survival.
AIMS & METHODS: Data from patients diagnosed with CRLM and treated with RFA from 2003 to 2012 were gathered and analyzed: age, sex, number of lesions, size of the largest lesion, the treatment regimen and the number of RFA sessions. The overall survival rate, median survival time and the prognostic factors that affect survival were determined using Kaplan-Meier and Cox regression analysis.
RESULTS: From the period of March 2003 up to June 2012, a total of 69 RFA sessions were performed in 42 patients. All of the patients included underwent chemotherapy together with RFA. Three also underwent percutaneous ethanol injection therapy, while 1 patient also underwent liver resection. Majority of the patients (71%) underwent only a single RFA session. Eight patients underwent RFA twice to three times, while another 4 patients required 4 to 5 sessions of RFA. The overall 3- and 5-year survival rates of patients with CRLM treated with RFA were both 20.6%. There seems to be no significant difference in survival between age groups (p = 0.660), gender groups (p = 0.815), number of lesions (p = 0.055), RFA treatment combinations (p = 0.777), and number of RFA sessions (p = 0.141). The size (p = 0.011), and the number (p = 0.017) of lesions are significant predictors of survival. Median survival time is 25 and 11 months for lesions < 5cm, and > 5cm, respectively. Patients have a median survival time of > 54, 14, and 12 months for solitary, 2-5, and > 5 lesions, respectively.
CONCLUSION: RFA in conjunction with chemotherapy improves the overall survival rate of patients to 20.6%, and the median survival time to 26 months.
Disclosure of Interest: None declared

P1211 VALIDATION OF STAGING SYSTEMS FOR HEPATOCELLULAR CARCINOMA: A COMPARISON OF THE BM-JIS SCORE, THE JIS SCORE AND THE BCLC STAGING

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INTRODUCTION: The Barcelona Clinic Liver Cancer Staging system (BCLC) is the most widely used system and has been reported to have good stratification ability in patients with hepatocellular carcinoma (HCC). Similarly, The Japan Integrated Staging (JIS) score also has been reported to effectively stratify patients with HCC. The aim of this study was to examine which staging systems can predict the survival of patients with HCC.
However, the JIS score could not estimate malignant grade of HCC. The aim of this study was to evaluate the performance of a new staging system: the biomarker combined JIS (bm-JIS) which includes three tumor markers: alpha-fetoprotein (AFP), Lens culinaris agglutinin-reactive AFP and des-gamma-carboxy prothrombin with the conventional JIS score.
AIMS & METHODS: A total of 11.531 HCC patients were included in this retrospective study. We compared their overall survival, the stratification ability and suitability as a prognostic model according to the BCLC staging system and the JIS score.
RESULTS: There were significant differences between the survival curves for all JIS scores ($p < 0.0001$) and all BCLC scores ($p < 0.0001$). The independent homogenizing ability and the stratification value of the JIS score and the bm-JIS score determined by the likelihood ratio test using the Cox proportional hazard regression model showed the bm-JIS score to have a higher value (chi2 = 717.348) than the JIS score (chi2 = 668.91).
CONCLUSION: The bm-JIS score showed superior stratification ability and thus was found to be a better predictor of the prognosis than the conventional JIS score, especially for the patients with good prognosis.
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Disclosure of Interest: None declared

P1212 DOWNSTAGING THERAPY IN PATIENTS WITH INTERMEDIATE STAGE HCC (BCLC B) AS BRIDGE FOR TRANSPLANTATION: THE HEPATOCATT EXPERIENCE

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INTRODUCTION: At state of the art, patients with intermediate stage HCC (BCLC B) are suitable only of not curative treatment. Liver transplantation may potentially cure both the tumor and the underlying liver disease, but only patients with an early stage tumor disease (meeting Milan Criteria) could be evaluated for inclusion in the transplant list.
AIMS & METHODS: The aim of our study is to evaluate the efficacy of downstaging therapy in order to satisfy Milan criteria, in patients with intermediate stage of HCC (BCLC B) referred to our Center.
Since September 2010 to September 2013, among 463 HCC patients investigated at Multidisciplinary Group for the Treatment of Hepatocellular Carcinoma of our Center (HEPATOCATT), we retrospectively selected and reviewed medical records of patients younger than 65 years old, with intermediate-stage HCC (BCLC B) that underwent a downstaging treatment (liver resection, locoregional therapy, antiangiogenic drugs and/or combined treatments) and for whom an adequate follow-up was available. Tumor response was evaluated on 1-month follow-up multiphasic CT based on mRECIST criteria. CT scan was also performed on 3-month follow up to evaluate the persistence of the response.
RESULTS: We selected 20 patients with intermediate-stage HCC (BCLC B). In all patients more than one downstaging treatment have been performed (total of 41 treatments): 2 liver resections, 21 TACE, 10 PEI, 1 RFA, 7 combined treatments (5 TACE/RFA; 1 liver resection/antiangiogenic;1RFA/antiangiogenic).
On 1-month follow up CT scan, 14 out of 20 patients (70%) experienced an effective downstaging, satisfying Milan criteria. 3-months follow up CT scan showed a stability of disease in all patients. 9 out of 14 (64.3%) patients were listed for OLTx. Finally, 7/20 patients (35%) underwent liver transplantation.
CONCLUSION: Our results show that an effective downstaging strategy allows even patients with intermediate HCC (BCLC B) not suitable to liver transplantation, to access potentially curative treatments
Disclosure of Interest: None declared

P1213 TREATMENT OF HEPATOCELLULAR CARCINOMA MEETING THE MILAN CRITERIA. RETROSPECTIVE COMPARISON OF RADIOFREQUENCY ABLATION AND RESECTION FOR LESIONS TREATABLE BY BOTH TECHNIQUES

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INTRODUCTION: In patients with well-preserved hepatic function, hepatic resection (HR) is the most appropriate and effective treatment. In the last decade, local ablative therapies (mostly radiofrequency ablation -RFA) have obtained good results in term of efficacy. Whether ablation of HCC eligible

also for HR provides long-term disease control comparable to resection remains still in debate.
AIMS & METHODS: Aim. To compare the therapeutic outcome in terms of survival and recurrence of RFA and HR in the treatment of HCC lesions within Milan criteria treatable by both techniques.
Methods: Using inclusion and exclusion criteria, seventy-nine HCC patients treatable by both HR or RFA were included in this study. Thirty two patients were treated by HR and 47 by RFA. In the HR group, 22 lesions were located in the left lobe and 11 in the right lobe. In the RFA group 40 lesions were located in the right lobe and 7 lesions in the left lobe. Mean tumor size was 31.5 +/-7.55 mm in the RFA and 32.6 +/- 10 mm in the HR group. In the ARF group were included 41(88%) patients with Child Pugh A class and 6 (12%) patients were Child Pugh B class. In the HR group were included 30 (94%) patients with Child Pugh and 2 (6%) patients with Child Pugh B class. The outcome was considered in terms of overall survival (OS) and local recurrence rate. Survival curves were constructed with the Kaplan-Meier method and compared by using the log-rank test.
RESULTS: Even if in the first two years the RFA group presented a better OS, in the third year the survival rate was lower than HR (91%, 82%, and 35 % vs 81%, 65% and 57% at 1.2, and 3 years), respectively) ($p = 0.185$). The local recurrence was higher in the RFA group (38.2%) than in the HR group (3.1%)($p = 0.001$). There was one major complications in each group (death after surgical resection) and 1 case of haemoperitoneum after RFA.
CONCLUSION: RFA provides a better survival at 1 and 2 years than HR in patients with HCC within Milan criteria treatable by both treatments. The survival rate at 3 years is better for HR presumable due to the lower local reccurence rate.
Disclosure of Interest: None declared

P1214 ENDOSCOPIC RETROGRADE BILIARY DRAINAGE IN OBSTRUCTIVE JAUNDICE OF UNRESECTABLE HEPATOCELLULAR CARCINOMA: COMPARISON OF SELF-EXPANDABLE METALLIC STENTS VS. PLASTIC STENTS

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INTRODUCTION: Patency of self-expandable metallic stents (SEMS) known to be better than plastic stents (PS) in palliating malignant biliary obstruction. However, data were scarce for the obstructive jaundice caused by hepatocellular carcinoma (HCC). This study aimed to compare SEMS and PS in palliating obstructive jaundice of unresectable HCC.
AIMS & METHODS: A total of 96 patients who undergone endoscopic retrograde biliary drainage (ERBD) for obstructive jaundice of unresectable HCC and deployed either SEMS or PS successfully were included in this retrospective analysis. Successful biliary drainage rate, complication rate, stent patency duration and patient survival were compared between SEMS and PS groups
RESULTS: Thirty-six patients were SEMS group and 60 patients were PS group. Successful biliary drainage rate was not significantly different between SEMS and PS (69.4% vs. 65.0%, $p = 0.655$). Complication rate was 16.7% in SEMS vs. 21.7% in PS ($p = 0.552$). The median patency duration was also not significantly different between SEMS group and PS (68 day vs. 60 day, $p = 0.396$). Median patient survival was longer in PS group than SEMS group (123 day vs. 48 day, $p = 0.005$). Use of PS, lower total bilirubin level, earlier TNM stage, successful biliary drainage, and following anticancer treatment was significantly related with longer patient survival in multivariate analysis.
CONCLUSION: SEMS was not superior to PS for palliating malignant biliary obstruction of HCC with regard to successful drainage, patency and complications and patient survival was longer in PS group. Considering the lower cost of PS, ERBD with PS could be a favorable option for malignant biliary obstruction caused by HCC.
Disclosure of Interest: None declared

P1215 SURGERY OR EUS-GUIDED CHOLEDOCHODUODENOSTOMY FOR DISTAL BILIARY CANCER PALLIATION AFTER FAILED ERCP

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INTRODUCTION: Most patients with neoplasm in the biliopancreatic junction are diagnosed at an advanced stage. Endoscopic retrograde cholangiopancreatography (ERCP) is the method of choice for drainage of obstructed biliary tract. However, there is a failure rate of about 10%. In such cases, alternative techniques, such as, percutaneous transhepatic drainage and surgical drainage are applied.
AIMS & METHODS: To evaluate the technical and clinical success, quality of life and patient survival of biliary drainage by conventional surgery and endosonography-guided technique in patients with malignant neoplasm of the biliopancreatic junction.
From April 2010 to September 2013, 32 patients with malignant neoplasm of the biliopancreatic junction were studied. All patients included in this study had failed biliary drainage by ERCP. Three patients were excluded due to technical failure (failure in the construction of hepatico-jejuno anastomosis and formation of endosonography-guided choledochoduodenal fistula). Group I comprised of 15 patients who underwent Roux-en-Y hepaticojejunostomy (HJT) and gastrojejunal bypass. Group II consisted of 14 patients who underwent endosonography-guided choledochoduodenostomy (CDT). Clinical success was assessed by the decrease of more than 50% in total serum bilirubin in the first seven days after the procedure. Quality of life was assessed by SF-36 questionnaire and survival by Kaplan-Meier curve.
RESULTS: Technical success rate was 93.75% (15/16) in group I and 87.5% (14/16) in group II ($p = 0.598$). Clinical success occurred in 14 (93.33%) patients in group I and 10 (71.43%) patients in group II. There was no significant statistically difference ($p = 0.169$). The average quality of life score were statistically equal between the techniques during follow-up ($p > 0.05$ * Technical Moment). There were statistically significant mean changes during follow-up of functional capacity score, physical health, pain, social functioning, emotional and mental health aspects in both techniques ($p < 0.05$). The mental health score was, on average, statistically higher in group II (CDT) at all times ($p = 0.035$). The median survival time of patients in group I was 82.27 days and Group II patients was 82.36 days. Sixty percent of patients in group I died within 90 days after the surgical procedure. On the other hand, 42.9% of the patients who underwent CDT died in the same period. There was no statistically significant difference in survival time between the groups ($p = 0.389$).
CONCLUSION: Data relating to technical and clinical success, quality of life and survival were similar in both groups and there were no statistically significant differences.
Disclosure of Interest: None declared

P1216 APPROPRIATE THERAPEUTIC STRATEGY FOR BILIARY STENTING USING THREADED INSIDE STENTS BASED ON THE LOCATION OF THE MALIGNANT OBSTRUCTION

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INTRODUCTION: Although the use of endoscopic biliary stents in cases of malignant obstruction may be widespread, optimal endoscopic management remains controversial. We retrospectively evaluated the safety and efficacy of the placement of a threaded inside plastic stent above the sphincter of Oddi (threaded PS) and compared the results with those of other stent types with respect to the location of the obstruction.
AIMS & METHODS: Forty patients with malignant hilar obstructions (type I–IV; Bismuth classification) underwent endoscopic indwelling stent placements. These cases involved the use of threaded PS, conventional PS, and uncovered metallic stents (MS). To create a threaded PS, a nylon monofilament thread (size 3/0) was attached to a conventional PS (Flexima, Boston Scientific) using a puncher. The duration of patency and complications were retrospectively evaluated in each group. The patients with malignant hilar obstructions all underwent threaded PS placement as a salvage therapy after MS was obstructed due to tumour ingrowth. We compared the patency of MS and threaded PS in these cases. In cases with mid or lower bile duct obstruction, the duration of patency and any complications were retrospectively evaluated in the MS and threaded PS groups.
RESULTS: All procedures were successful in each group. The median duration of patency in the threaded PS group was significantly longer compared with the duration in the conventional PS group (126.3 vs 42.1 days, $P = 0.025$, Log-rank test) and was not significantly different compared with the MS group (126.3 vs 200.3 days, $P = 0.76$). The removal of threaded PS was simple because the attached thread was visible in the sphincter of Oddi except in one case. The stents did not migrate in any group. The median duration of the threaded PS patency was 123 days compared with that of the MS patency of 163 days ($P = 0.486$). In patients with mid or lower bile duct obstruction, the median duration of the threaded PS patency was significantly shorter compared with that of the MS patency ($P < 0.03$). In particular, the median patency of the threaded PS when there was no precedent endoscopic nasal bile drainage was significantly shorter (22 days).
CONCLUSION: The placement of threaded PS is safe and effective compared with conventional PS for the treatment of a malignant hilar obstruction; this procedure was not inferior to MS. In addition, the threaded PS patency was comparable with the MS patency even when used as a salvage therapy, suggesting that threaded PS may be useful not only for an initial therapy but also as a salvage therapy. On the other hand, the placement of threaded PS without a precedent ENBD was not superior to MS in cases with mid or lower bile duct obstruction. The type of stent should be decided in terms of both the location of the obstruction and the endoscopic therapeutic process.
Disclosure of Interest: None declared

P1217 AIR VERSUS IODINE CONTRAST CHOLANGIOGRAPHY FOR ENDOSCOPIC BILATERAL STENT-IN-STENT PLACEMENT OF METALLIC STENTS IN PATIENTS WITH MALIGNANT HILAR BILIARY OBSTRUCTION

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INTRODUCTION: Endoscopic biliary drainage is one of the major palliative treatments for unresectable malignant hilar biliary obstruction. However, post-endoscopic retrograde cholangiopancreatography (ERCP) cholangitis could occur frequently due to inadequate drainage, especially after contrast injection into biliary tree.
AIMS & METHODS: The aim of this study was to investigate the effect of air cholangiography on post-ERCP complications for endoscopic bilateral stent-in-stent (SIS) placement of self-expandable metallic stents (SEMS). This study was included 42 patients with unresectable malignant hilar obstruction who underwent endoscopic bilateral SEMS placement using SIS technique. They were divided into the two groups, air ($n = 21$) or iodine contrast ($n = 21$)

cholangiography, respectively. We retrospectively compared comprehensive clinical and laboratory data in both groups.
RESULTS: There were no significant differences in age, gender, stent type, liver function tests, type of tumor origin, and Bismuth classification between the two groups. Technical success was achieved for all 42 patients and functional success rate was 95.2% (20/21) in each group. Post-ERCP complications were occurred in 5 (23.8%) of the patients in air group and 8 (38.1%) of the patients in iodine contrast group ($P=0.17$). The rate of cholangitis in air group was significantly lower than that in the iodine contrast group (4.8% vs. 33.3%, $P=0.045$). The difference of 30-day stent occlusion and 30-day mortality between the two groups was not significant ($P=1.000$ and $P=0.232$, respectively).
CONCLUSION: Air cholangiography is a safe and effective method to visualize intrahepatic bile duct with low incidence of post-ERCP cholangitis. In addition, it could be considered for endoscopic bilateral SIS placement of SEMS in patients with malignant hilar biliary obstruction.
Disclosure of Interest: None declared

P1218 THE USEFULNESS OF NARROW-BAND IMAGING SYSTEM IN DIAGNOSING AMPULLARY LESION

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INTRODUCTION: The differentiation between ampullary tumors and benign ampullary lesions is challenging occasionally because endoscopic findings may be similar to each other. Narrow-band imaging system (NBI) can yield clear images of microvessel and surface structure, and it is widely used for the diagnosis of gastric or colonic cancer.
AIMS & METHODS: we evaluated the the usefulness of NBI for differentiating between the ampullary tumor and other benign diseases. 29 patients with 42 ampullary lesions were retrospectively analyzed between March 2010 and January 2011. Inclusion criteria were enlarged or protruded lesions that were suspected ampullary tumor during duodenoscopy. Abnormal NBI images were classified as follows: Irregular arrangement of villi; Irregular size of villi; Disappearance of ridged villi structure; Demarcation with normal villi; Abnormal microvasculature. The correlation between NBI images and histological findings was investigated.
RESULTS: In histological examination, there were 21 adenoma, 6 adenocarcinoma and 15 benign diseases. On NBI images, the abnormal findings according to our classification were: Irregular arrangement of villi (50%); Irregular size of villi (64%); Disappearance of ridged villi structure (40%); Demarcation with normal villi (55%); Abnormal microvasculature (67%). In multivariate analysis, irregular arrangement of villi (OR, 45.44; 95% CI, 2.87-604.34; $P<0.01$) and abnormal microvasculature (OR, 11.79; 95% CI, 2.24-235.67; $P<0.01$) were significant factors to identify ampullary tumor.
CONCLUSION: Our study suggested that Irregular arrangement of villi and Abnormal microvasculature on NBI image would be useful for detection of ampullary tumor.
Disclosure of Interest: None declared

P1219 THREE-MONTH SURVIVAL OF MALIGNANT OBSTRUCTIVE JAUNDICE PATIENTS: FACTORS AFFECTING MORTALITY

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INTRODUCTION: Understanding any related factors affecting mortality in malignant obstructive jaundice patients will better guide to an approriate and optimal planning in making diagnostic approach and proper treatment for each aetiological and relating factors thus improving survival and patients' quality of life.
AIMS & METHODS: To obtain survival and mortality-related factors of malignant obstructive jaundice patients, retrospective cohort study was conducted with medical records of obstructive jaundice inpatients from January 2010 to December 2013 were reviewed. Suggested mortality-related factors include age, gender, sepsis, hypoalbumin, serum bilirubin level, serum CA 19-9 level, billiary drainage, non ampula vater carcinoma, and comorbid factors were analyzed. Overall survival and survival related mortality factors were measured, bivariat and multivariat analysis was done with Cox Proportional Hazards Regression Model to obtain Hazard Ratio (HR) of each prognostic factor. Prognostic score from each mortality-related factor was calculated based on the last regression model.
RESULTS: A total of 181 (106 male/75 female) patients were enrolled in this study, with patients aged 50 years or above was 57.5%. The cox proportional hazards model demonstrated that sepsis (HR 2.462; 95% CI 1.552 – 3.906), unsuccessful / no prior billiary drainage (HR 1.604; 95% CI 0.988 – 2.603), and Charlson comorbid score ≥ 4 (HR 2.476; 95% CI 1.562 – 3.923) were independent prognostic factors for mortality. Patients with significant prognostic factors had shorter survival than overall survival (median survival 14 days; 95% CI: 9.66 – 18.34 vs 26 days; 95% CI: 20.82 – 31.19, respectively) ($p=0.01$). Score ≥ 2 identified as the highest prognostic score threshold with sensitivity 68%, specificity 75%, and AUC on ROC curve 0.769.
CONCLUSION: Patients with significant prognostic factors had shorter survival than overall survival. Sepsis, unsuccessful / no prior billiary drainage, and Charlson comorbid score ≥ 4 were main prognostic factors with significant difference affecting mortality rate in malignant obstructive jaundice inpatients. Prognostic threshold ≥ 2 quite good to classify malignant obstructive jaundice inpatients into high risk mortality population. Mortality of patients with those significant prognostic factors can be predicted in 76.9%.
Disclosure of Interest: None declared

P1220 CLINICAL USEFULNESS OF BILE CYTOLOGY OBTAINED BY TRANSPAPILLARY CATHETERIZATION OF THE GALLBLADDER FOLLOWED BY RUBBING WITH A GUIDEWIRE FOR GALLBLADDER WALL THICKENING

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INTRODUCTION: Although gallbladder (GB) diseases have been increasingly detected with the widespread use of ultrasonography, MRI, and multi-detector-row CT, it is sometimes difficult to distinguish malignant GB diseases from benign ones.
AIMS & METHODS: The aim of this study was to evaluate the clinical usefulness of bile cytology obtained by endoscopic transpapillary catheterization of the gallbladder (ETCG) followed by rubbing with a guidewire for GB wall thickening. Between January 2008 and December 2013, 67 patients with GB wall thickening who underwent ETCG cytology were enrolled in this study. Fifty-five patients underwent surgical treatment. Pathological findings of the resected specimen revealed GB cancer in 20 patients and benign GB diseases in 35 (20, chronic cholecystitis; 11, adenomyomatosis; 2, xanthogranulomatous cholecystitis; 1, acute cholecystitis; 1, cholesterol polyp). Five patients were diagnosed as inoperable advanced GB cancer by CT findings such as liver/lymph node metastases. The remaining seven patients were diagnosed as benign GB diseases after a follow-up period of at least 12 months. The method of ETCG cytology was as follows. A 5 Fr catheter with side holes was inserted into the GB over a 0.025 or 0.032-inch hydrophilic guidewire. The first aspirated bile was discarded. Fresh exfoliated cells were obtained after washing by saline solution and rubbing the target lesion with a guidewire. Cytology was performed by HE stain with the cellblock method. A rating of Class IIIb or more was defined as malignancy. The sensitivity, specificity, and accuracy of ETCG cytology were evaluated.
RESULTS: Of the 25 patients with GB cancer, 16 were defined as having malignancy by ETCG cytology (6, Class V; 6, Class IV; 4, Class IIIb). The causes of false-negative results included insufficient material in 2 patient, inability to rub the lesion with a guidewire in 1, and indeterminate causes in 6. Of 42 patients without malignancy, one patient was found to be false positive by ETCG cytology (Class IIIb). Sensitivity, specificity, and accuracy of ETCG cytology were 64%, 98%, and 85%, respectively. No procedure-related complications such as cholecystitis and cystic duct perforation occurred.
CONCLUSION: Bile cytology obtained by ETCG is a feasible and safe method for differential diagnosis of GB wall thickening.
Disclosure of Interest: None declared

P1221 CURRENT STATUS OF ENDOSCOPIC MANAGEMENT FOR AMPULLARY NEOPLASM

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INTRODUCTION: Endoscopic papillectomy (EP) is performed in selected patients with ampullary neoplasm. Accurate preoperative tumor staging is indispensable for making management decisions.
AIMS & METHODS: The aim of this study was to elucidate the current status of endoscopic management for ampullary neoplasm. Eighty-three patients with ampullary neoplasm (male, 51; female, 32; mean age, 68; mean tumor size, 21 mm) who underwent transpapillary intraductal US (IDUS) of the bile duct (BD) were enrolled in this study. The indication for EP was determined based on the following findings by IDUS: (1) no tumor infiltration into the BD or the pancreatic duct (PD) and (2) adenoma or T1 cancer. In cases of T1 cancer, additional surgery was considered when the tumor had invaded the Oddi's muscle because of the risk of lymph node metastasis.
RESULTS: Based on the results of IDUS, EP was performed in 37 patients. Twenty-one had adenoma and 16 had adenocarcinoma (T1, 14; T2, 2). The other 46 patients, whose tumors were contraindicated for EP by IDUS, were treated by pylorus-preserving pancreatoduodenectomy (T1, 19; T2, 10; T3-4, 17). Of these 19 surgical cases of T1, 9 had a tumor invading the Oddi's muscle and 8 had a tumor spreading into the BD or PD. Theoretically, the remaining 2 patients could have been treated by EP based on the histopathological findings.
In the 37 patients who underwent EP, the accuracy of IDUS in T staging was 95% (35/37). Of the two patients with T2, one underwent additional surgical treatment, which revealed neither a residual tumor nor lymph node metastasis by histopathological evaluation of the resected specimen. The other refused surgical therapy and received chemotherapy without evidence of recurrence for 48 months. One patient with T1, whose tumor invaded the Oddi's muscle, died in an accident one month after EP. In one patient with T1 (tumor depth, Oddi's muscle) who refused additional surgical treatment, lung metastases were detected by chest CT 11 months after EP without local recurrence. In the remaining 12 patients with T1 (tumor depth, mucosa), neither local recurrence nor distant metastasis was observed. Of the 21 patients with adenoma, 4 successfully underwent argon plasma coagulation for a residual tumor. At follow-up (mean duration, 38 months; range, 1-108 months), no local recurrence was observed in the

remaining patients. The sensitivity, specificity, and accuracy of determining the indication for EP by IDUS was 89%, 96%, and 93%, respectively.
CONCLUSION: IDUS can provide useful information for determination of the indication for EP. Detailed histological evaluation of the resected specimen and long-term follow-up are mandatory after EP.
Disclosure of Interest: None declared

P1222 RISK FACTORS FOR INTRAHEPATIC AND EXTRAHEPATIC CHOLANGIOCARCINOMA: A CASE-CONTROL STUDY IN JAPAN

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INTRODUCTION: The association between diabetes, smoking, obesity, and cholangiocarcinoma (CC) risk remain inconclusive. We evaluated the risk factors for both intrahepatic cholangiocarcinoma (ICC) and extrahepatic cholangiocarcinoma (ECC).
AIMS & METHODS: A case-control study in which cases were cholangiocarcinoma patients referred to Yokohama City University Hospital (YCUH) in Japan between 2009 and 2013 and controls were healthy individuals. Controls were randomly selected from an existing database of healthy individuals at YCUH. Data on family history, diabetes, smoking and drinking were collected by a retrospective review of the patients' records and health examination reports or by interview. The associations between potential factors and CC risk were determined.
RESULTS: A total of 111 patients (23 ICC; 88 ECC) and 547 age- and sex-matched controls were enrolled. Compared with controls, ICC patients had a higher prevalence of diabetes (34.8% vs 17.4%, $p = 0.04$). The adjusted odds ratio (OR) and 95% confidence intervals (CI) were 3.1 (95% CI: 1.08-9.19). ECC patients showed significant independent associations with diabetes (OR: 2.68; 95% CI: 1.36-5.29) and smoking (OR: 2.88; 95% CI: 1.57-5.30).
CONCLUSION: These findings strongly support the positive link between diabetes and the increased risk of ICC and ECC, and smoking were associated only with ECC.
Disclosure of Interest: None declared

P1223 THE ROLE OF CONFOCAL LASER ENDOMICROSCOPY IN THE MANAGEMENT OF PATIENTS WITH BILIARY STRICTURES: A CONSENSUS REPORT BASED ON CLINICAL EVIDENCE

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INTRODUCTION: Differential diagnosis of bilio-pancreatic strictures includes cholangiocarcinoma and benign lesions. The nature of biliary tumors remains very difficult to diagnose due to the difficulty of getting adequate tissue samples and to the lack of histopathological evaluation. Confocal Laser Endomicroscopy (CLE) has been shown to considerably improve the characterization of those lesions as compared with standard modalities thanks to a sensitivity and an NPV higher than 90%. This substantial evolution has the potential to provide a more informed diagnosis and to impact patient management.
AIMS & METHODS: The aim of this study is to develop up-to-date evidence-based consensus statements for the diagnosis of biliary strictures.
Initial statements on the use of CLE for the characterization of indeterminate biliary strictures were developed by a single CLE expert based on the available clinical evidence. Those preliminary statements were edited and submitted by an external group of 16 GI physicians using a modified Delphi approach. After two rounds of votes based on relevant data, quality of the evidence and strength of recommendation, statements were validated if the threshold of agreement was higher than 75%.
RESULTS: Out of 9 proposed statements, 6 were validated and 3 rejected. CLE can be used to evaluate biliary strictures, and the probe can be delivered via a catheter or a cholangioscope. CLE is more accurate than ERCP with brush cytology and/or forceps biopsy in determining malignant or benign strictures, using established criteria. The accuracy of CLE in indeterminate biliary strictures may be decreased by prior presence of plastic stent.
The Negative Predictive Value (NPV) of CLE is very high. The use of CLE can assist clinical decision-making such as excluding malignancy. CLE should be cited as a valuable tool for an increased diagnostic yield in official guidelines. The «black bands» that can be seen in pCLE images have been shown to be collagen fibrils that predictably increase in pathologic tissue.
CONCLUSION: According to the panel of 16 physicians, given its very high accuracy, Confocal Laser Endomicroscopy has the potential to improve the current diagnostic algorithm of biliary strictures. At centers where expertise is available, Confocal Laser Endomicroscopy used during ERCP in the evaluation of biliary strictures should be considered as a standard practice complementary to conventional tissue sampling.
Disclosure of Interest: None declared

P1224 BILIARY DRAINAGE FOR MALIGNANT BILIARY OBSTRUCTION CAUSED BY METASTATIC GASTRIC CANCER

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INTRODUCTION: Malignant biliary obstruction (MBO) is not a rare condition in advanced gastric cancer (AGC). However, the clinical outcome of this setting remains unclear. Moreover, the role of biliary drainage for this setting is not fully elucidated.
AIMS & METHODS: Between October 2004 and February 2014, 63 consecutive AGC patients (pts) with MBO who received biliary intervention were studied retrospectively.
RESULTS: Of 63 pts, 35 pts (%) had previous gastrectomy (B-1/B-2/RY reconstruction = 8/5/22). The primary tumor of differentiated adenocarcinoma in 23 pts (37%) and undifferentiated in 40 pts (63%), with liver metastases in 7 pts (11%) and ascite in 30 pts (48%). Portal vein stenosis and periportal collar sign were observed in 28 pts (44%) and 17 pts (27%), respectively. The causes of biliary obstruction were lymph node metastases in 8 pts, peritoneal metastases in 45 pts, and direct invasion in 10 pts, with the median lengths in biliary obstruction of 25 mm. Biliary drainage was performed via ERCP in 14 pts and PTBD in 49 pts, with technical and clinical success of 100% and 86% (ERCP/PTBD = 93%/84%), respectively. Periportal collar sign, emerged as a result of tumor infiltration to Glisson's capsule, was revealed as a risk factor for unsuccessful drainage (Odds ratio 9.2 (95% CI 1.5-78.0), $p = 0.02$). Nine complications were developed; 5 after ERCP (2 acute pancreatitis, 2 cholecystitis, and 1 cholangitis) and 4 after PTBD (1 stent migration, 1 pneumothorax, hemobilia in 1, and 1 pseudoaneurysm). After biliary intervention, 29 pts (46%) received systemic chemotherapy. Median survival after biliary intervention was 3.6 months. Clinical success of biliary drainage was prognostic of survival after intervention (4.9 vs. 1.1 months, $p < 0.01$).
CONCLUSION: Although the prognosis of AGC pts with MBO is poor, biliary interventions should not be considered as a contraindication because of its safety and efficay in selected pts.
Disclosure of Interest: None declared

P1225 THERAPEUTIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) in patients with altered gastrointestinal (GI) anatomy remains a challenging procedure. However, the progression of techniques and devices like a Double-balloon enteroscopes (DBEs) enables us to perform ERCP on these patients. The aim of this study is to assess the efficacy and safety of therapeutic ERCP, especially biliary drainage for malignant biliary obstructions, in patients with surgically altered GI anatomy (patients with Billroth-I anastomosis were excluded).
AIMS & METHODS: 2239 consecutive ERCP procedures were performed at Toranomon Hospital during a 5- year period (2009 to 2013). In these, a total of 19 patients with altered GI anatomy underwent 33 ERCPs for malignant biliary obstruction. We retrospectively investigated: (1) the success rate of reaching either the papilla of vater or the bilioenteric anastomosis; (2) the success rate of cannulation to deeper parts of a biliary tract; (3) the rate of successful therapeutic ERCPs; (4) complications.
RESULTS: The mean age was 72.5 years, range 58 to 82 years; 68% were male and 32% were female. Bile duct cancer 45.5%(n = 15), pancreatic cancer 18.2%(n = 6), hepatocellular carcinoma 18.2%(n = 6), and lymph node metastasis from the recurrence of gastric cancer, or esophageal cancer 18.2%(n = 6) were major indications. 10 cases underwent Roux-en-Y anastomosis, 4 cases underwent Billroth-II anastomosis, 4 cases underwent biliojejunal anastomosis, and 8 cases underwent bilioduodenal anastomosis. A plastic stent and self-expanding metal stent (SEMS) were positioned for biliary drainage in 39.4% of the cases (13/33) and 33.3% (11/33), respectively. The results of the above investigations were: (1)87.9% (29/33), (2)84.8% (28/33), (3)84.8% (28/33), (4)3% (1/33): respiratory suppression. There were no cases of the therapeutic ERCPs being stopped by an accident during this procedure. Procedure-related mortality did not occur. There were no incidences of hemorrhage and/or perforation. The median duration of hospitalization was 21 days (2-82 days) and 44% of patients could be discharged within 2 weeks. The median duration of survival after therapeutic ERCPs was 80 days (16-601 days).
CONCLUSION: ERCP in patients with surgically altered GI anatomy remains a challenging procedure. But due to using DBE or PCF, the number of the successful therapeutic ERCPs is increasing in these patients. Successful therapeutic ERCP was achieved in 84.8%, a relatively high figure in this study. The median duration of survival time is short, only 80 days, because the most patients are at the end stage of their diseases. To improve the QOL of patients with malignant biliary obstructions, therapeutic ERCP should be performed positively, even if it's a case of altered GI anatomy, because it's relatively safe procedure, less invasive, and possible to discharge patients earlier.

Disclosure of Interest: None declared

P1226 CHARACTERIZATION OF CHOLANGIOCARCINOMAS: CLINICAL AND TOPOGRAPHIC FEATURES OF A GROWING ONCOLOGICAL REALITY

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INTRODUCTION: Cholangiocarcinomas account for 3% of the malignant gastrointestinal neoplasms. The incidence of intra-hepatic cholangiocarcinomas has increased for unknown reasons [1.2].
AIMS & METHODS: To determine the clinical and analytical characteristics, the diagnosis approach and the treatment options for patients with cholangiocarcinoma according to its location. Retrospective analysis of patients with diagnosis of cholangiocarcinoma in the last 5 years in a tertiary referral center.
RESULTS: 89 patients (55% male) were followed for a median of 23 weeks (P25-75: 8-80). There was a progressive increase in the number of cholangiocarcinoma diagnosis since the beginning of the cohort (14 new diagnoses in 2008-2009, 31 in 2010-2011 and 44 in 2012-2013). The mortality rate at 6 months was 40.5% and the median survival was 164 days (P25-75: 61-566). Most patients (53%) presented perihilar, 24% extrahepatic and 24% intrahepatic cholangiocarcinoma (ICC). The median age at diagnosis was 71 years, being lower in the ICC (68 vs 74, $p = 0.014$). The diagnosis was obtained using imaging methods in 73% of cases, the abdominal computed tomography was the most common method (45%). There was a statistically significant correlation between the diagnosis of ICC and the need of histological methods to make a diagnose ($p < 0.001$). Serum levels of G-GT, alkaline phophatase and total bilirrubin at diagnosis were lower in ICC ($p < 0.001$). In 36% of cases there was metastatic disease at diagnosis, being hepatic metastization the most common disease (12%). In 56% of cases palliative treatment was decided at diagnosis and in 54% of the patients underwent surgery. Hepatectomy was the most common intervention and was performed in 20% of the cases.
CONCLUSION: ICC presents with less cholestasis at diagnosis. It is more frequent the need for a histological diagnosis in this type of cholangiocarcinoma. An increase of the incidence of cholangiocarcinoma was verified in this cohort.
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Disclosure of Interest: None declared

P1227 PREDICTIVE FACTORS OF SURVIVAL IN CHOLANGIOCARCINOMA: A 5-YEARS EXPERIENCE

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INTRODUCTION: Most patients with cholagiocarcinoma present an unresectable disease at diagnosis with an extremely poor prognosis, an average five-year survival rate of 5 to 10 percent. Those, who undergo potentially curative resection, tumor-free margins can be obtained in only less than half of the patients [1-2].
AIMS & METHODS: To analyze the survival of patients with cholangicarcinoma according to clinical and therapeutic options. Retrospective study of patients with diagnosis of cholangiocarcinoma between 2008 and 2013 in a tertiary referral center. The Kaplan-Meier survival curves were used, alpha = 0.05.
RESULTS: We included 71 patients (39 male) with a median age of 71 years at diagnosis. The mortality rate during the follow-up period was 79% (37% at 3 months, 42% at 6 months and 51% at 12 months). The median survival was 44 weeks (P25-75: 8-90). A higher level of survival at 3, 6 and 12 months was associated with chemotherapy treatment ($p = 0.002$, $p = 0.001$, $p = 0.003$, respectively), lower levels of CA-19.9 ($p = 0.001$, $p = 0.009$, $p = 0.013$), surgical treatment ($p < 0.001$), TNM-R0 ($p = 0.006$, $p = 0.031$, $p = 0.039$) and no metastization at diagnosis ($p < 0.001$, $p = 0.006$, $p = 0.002$). Survival in the first trimester was associated with TNM-N0 ($p = 0.022$). Survival in the first year was associated with higher levels of albumin ($p = 0.032$), lower levels of alkaline phosphatase ($p = 0.020$), younger age ($p = 0.038$) and fewer days between the beginning of the symptoms until the diagnosis date ($p = 0.029$). The analysis of the Kaplan-Meier curves showed an association between survival, absence of metastization at diagnosis ($p < 0.001$), surgical treatment ($p < 0.001$) and chemotherapy treatment ($p = 0.009$). In terms of survival at 3, 6 and 12 months, the therapeutic surgery and the mestastization were associated independently in the logistic regression.
CONCLUSION: The factors that determine a greater survival are surgical treatment and chemotherapy. Absence of metastization at diagnosis seems to be related to a medium-term survival.
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Disclosure of Interest: None declared

P1228 CLINICAL OUTCOMES OF ENDOSCOPIC SNARE PAPILLECTOMY OF DUODENAL MAJOR PAPILLARY NEOPLASM

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INTRODUCTION: The use of endoscopic snare papillectomy (ESP) for the treatment of duodenal major papillary neoplasm was increased. However, concerns about ESP included the risks of incomplete removal.
AIMS & METHODS: The aim of this study was to evaluate the clinical outcomes of ESP and the effectivity of argon plasma coagulation (APC) for the treatment of residual tissue.
Among the patients who received ESP for the treatment of duodenal major papillary neoplasm from November 2005 to march 2014, 33 patients were enrolled. These patients were followed for more than 3 months. We retrospectively reviewed the medical records of the patients.
RESULTS: Twenty eight patients had adenoma, 2 had adenocarcinoma, 1 had carcinoid tumor, 1 had paraganglioma and 1 had inflammation. Median follow-up periods was 12 months (range: 3-72 months). The overall rate of en bloc resection was 87.9% (29/33). Specimens with margin positivity after ESP were reported in 12 patients (9 lateral margin positivity, 3 lateral and vertical margin positivity). Among the 12 patients with margin positivity, 5 patients received additional treatment (4 APC, 1 hot biopsy and APC) and 7 patients with grossly no residual tissue were followed by close endoscopic surveillance with white light and/or narrow band imaging. Among all patients, local recurrence was detected in 4 patients (12.1%, 4/33). 3 cases (25%, 3/12) occurred in the patient with margin positivity and 1 case (4.8%, 1/21) occurred in the patient with margin negativity. Two patients with local recurrence were the patients who did not receive additional treatment of lateral margin positivity. There was no local recurrence in the patients who received APC for the treatment of residual tissue.
CONCLUSION: After ESP of duodenal major papillary neoplasm, additional treatment of margin positivity should be considered and close endoscopic surveillance should be performed. APC may be an effective method for the treatment of residual tissue.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
PANCREAS III – POSTER EXHIBITION – HALL XL

P1229 MUCUS SECRETION OF PANCREATIC DUCTAL EPITHELIUM INCREASES IN CHRONIC PANCREATITIS

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INTRODUCTION: Mucoprotein plug formation within the pancreatic ducts is one of the early events of chronic pancreatitis (CP), but little is known about its pathogenesis. Recent evidence suggests impaired ion- and fluid secretion of pancreatic ductal epithelial cells (PDEC) in CP, which together with increased mucus secretion may alter mucus hydration and subsequently lead to plug formation.
AIMS & METHODS: We aimed to invesigate mucus secretion of PDEC in CP. Human and mouse pancreata were investigated. Human CP tissue samples were collected from surgically resected pancreata, whereas CP was induced by administration of 6x50μg/kg cerulein, 3 series/week for 4 weeks in mice. Morphometric analysis of mucus was carried out by CellF software. Total RNA was isolated from human and mouse tissue. The mRNA levels of different mucin subtypes were analysed by quantitative RT-PCR.
RESULTS: We found that mucus volume density (Vd_{muc}) of human PDEC was significantly higher in CP than in controls, in case of smaller ducts (ductal diameter $<100\mu m$: $1.21\pm0.13 nl/mm^2$ and $0.37\pm0.05 nl/mm^2$, respectively). Similarly, mouse PDEC showed significantly higher Vd_{muc} in CP than in controls, especially in ducts with smaller diameter (ductal diameter $<80\mu m$: $0.72\pm0.06 nl/mm^2$ vs. $0.005\pm0.0002 nl/mm^2$, ductal diameter $>80\mu m$: $0.075\pm0.020 nl/mm^2$ vs. $0.016\pm0.004 nl/mm^2$). Mucin gene expression analysis showed, that muc6 was ~1000-fold upregulated in mouse and 17-fold upregulated in human CP.
CONCLUSION: There is a substantial mucus hypersecretion in CP localized to the small ducts. Obstruction of the small ducts by mucus in CP may contribute to the pathogenesis of the disease. Supported by EPC Travel Fellowship.
Disclosure of Interest: None declared

P1230 IMPACT OF ETHANOL ON METABOLIC ACTIVITY OF HUMAN PANCREATIC STELLATE CELLS

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INTRODUCTION: Alcohol consumption is the leading cause (70-90%) of chronic pancreatitis, which is known to be one of the major factors for pancreatic cancer pathogenesis. Pancreatic stellate cells (PSC) are known to play a key role in pathogenesis of chronic pancreatitis. It is known, that ethanol activates PSC

migration to pathological site of the pancreas. The effect of ethanol on PSC energy metabolism is unknown. The aim of our study is to investigate PSC growth change and energy metabolism under exposure to different alcohol concentrations.
AIMS & METHODS: Human PSC were extracted from pancreatic tissue obtained during pancreatic surgery. PSC were cultivated in Petri dishes in DMEM and F-12 media, containing 20% FBS with addition of Penicillin-Streptomycin. Immunofluorescence assay using beta-actin as primary antibody was performed for differentiation PSC from fibroblasts. Crystal violet test was performed using control cell group, 0.1%, 0.5% and 1% ethanol concentration. MTT assay was carried out to determine different alcohol concentration impact on the PSC viability. Oxygen consumption of PSC's was measured oxygraphically in cell media by using Oroboros-2K oxygraph (respiratory subtrates glutamate+malate).
RESULTS: Cultivated cells were beta-actin positive indicating presence of PSC, but not fibroblasts. Evaluating alcohol impact to the cell phenotype, we observed 0.5% alcohol induced cells were bigger compared to control. 0.1% and 1% ethanol concentration forced cell shrinking. MTT assay revealed that the best cell proliferation was achieved in PSC under pretreatment with 0.5% ethanol. Pretreatment of cells with 0.5% ethanol increased oxygen consumption by 34% as compared to control, i.e. activated energy metabolism, while low ethanol concentration (0.1%) had no effect. However, higher concentrations (1%) of ethanol decreased the pancreatic stellate cells respiration rate by 15% and 37% as compared to control and to 0.5% ethanol group, respectively. The 2.4-dinitrophenol uncoupled respiration rate was also found to be diminished (by 22%) after pretreatment with higher concentration (1%) of ethanol. Lower concentrations of ethanol (0.1-0.5%) had no effect on this parameter.
CONCLUSION: 0.5% ethanol concentration is the best PSC's promoter in the matter of growth and oxygen consumption, while other investigated concentrations seem to have opposite effect. Further studies are necessary to investigate the ways to reduce the activity of ethanol affected PSC's.
Disclosure of Interest: None declared

P1231 CIGARETTE SMOKE EXTRACT INHIBITS CFTR ACTIVITY AND PANCREATIC DUCTAL FLUID SECRETION IN GUINEA PIG

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INTRODUCTION: Smoking represents an independent risk factor for the development of chronic pancreatitis, however, the pathomechanism remains unknown. Secretion of fluid and bicarbonate plays a crucial role in maintaining the integrity of the gland.
AIMS & METHODS: The aim of this study was to investigate the effects of cigarette smoke extract (CSE) on pancreatic ductal fluid secretion and on cystic fibrosis transmembrane conductance regulator (CFTR) Cl^- channel activity. Intra/interlobular pancreatic ducts were isolated from guinea pig pancreas. Basal and forskolin stimulated fluid secretion were measured by videomicroscopy, whereas, CFTR currents were detected by whole cell configuration of the patch clamp technique. CSE was prepared by smoking of 3 cigarettes into 40ml distilled water by a smoking machine and 10x (21μg/ml), 40x (5.25μg/ml) and 400x (0.5μg/ml) dilution of the extract were studied.
RESULTS: Administration of 5μM forskolin activated CFTR currents by 10-15-fold in magnitude. 15 min administration of 0.5, 5.25 and 21 μg/ml CSE inhibited the currents by 44%, 64.6% and 79.4%, respectively (n = 2-4). Concerning the fluid secretion, the basal volume of isolated intact pancreatic ducts in bicarbonate-free solution was considered to be 1.0. Administration of 25mM bicarbonate increased the relative luminal volume up to 1.57±0.02 (n = 7). Administration of 5 μM forskolin further increased the luminal volume to 1.87±0.1 (n = 16). Simultaneous administration of 21μg/ml CSE decreased fluid secretion by 24% (1.42±0.06; n = 12).
CONCLUSION: CSE inhibits pancreatic ductal fluid secretion and the activity of the CFTR which may play role in the smoke-induced pancreatic damage.
This study was supported by OTKA, MTA and NFÜ/TÁMOP.
Disclosure of Interest: None declared

P1232 THE CONTRASTING EFFECT OF URSODEOXYCHOLATE AND CHENODEOXYCHOLATE ON PANCREATIC DUCTAL EPITHELIAL CELLS

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INTRODUCTION: We have recently shown that chenodeoxycholate (CDC) in high concentration strongly inhibited ion transporters through the destruction of mitochondrial function in intact guinea pig pancreatic ducts. Since ursodeoxycholic acid (UDC) is known to protect the mitochondria against hydrophobic bile acids and have antiapoptotic effect, we investigated whether UDC is able to prevent the CDC-induced cell damage.
AIMS & METHODS: Intra-interlobular ducts were isolated from guinea pig pancreas. Ducts were then pretreated with UDC (0.1 mM and 0.5mM) for 5 h and 24 h and changes in intracellular Ca^{2+}concentration $[Ca^{2+}]_i$, ATP level $[ATP]_i$, pH $[pH]_i$, mitochondrial permeability transition pore (MPTP) opening were measured by microfluorometry. Mitochondrial transmembrane potential (MTP) was studied by confocal microscopy. Morphological changes of mitochondria were investigated by transmission electron microscopy. Expressions of bile acid transporters were studied by reverse transcriptase PCR (RT-PCR).
RESULTS: 5 h pretreatment with 0.1 or 0.5 mM UDC and 24 h pretreatment with 0.1 mM UDC did not significantly influence the effect of 1 mM CDC on duct cells. However, 24 h pretreatment with 0.5 mM UDC significantly reduced the rate of ATP depletion, mitochondrial injury, MPTP opening and the decrease of MTP induced by 1 mM CDC. In addition, 0.5 mM UDC prevented the inhibitory effect of CDC on the acid-base transporters, however, had no effect on the CDC-induced calcium signaling. mRNA expression of Slc10A1 and A2 was detected in the ducts by RT-PCR.
CONCLUSION: Our results indicate that protection of mitochondria with UDC administration may represent a novel option against bile acid-induced ductal injury.
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Disclosure of Interest: None declared

P1233 GLUCAGON-POSITIVE ISLET CELLS CAN BE POSSIBLE SOURCE OF PANCREATIC ACINAR TISSUE REGENERATION IN COPPER-DEFICIENT MODEL

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INTRODUCTION: Liver and pancreas are supposed to have the common origin. There were publications by Rao et al. (1989) showing the possible appearance of hepatocyte-like cells in pancreas in copper-deficient diet model of pancreatic injury however the mechanisms of pancreatic regeneration in this model weren't described.
AIMS & METHODS: The aim of our work was to find out the possible sources of pancreatic tissue restoration in copper-deficient model of pancreatic injury. 24 white Wistar male rats (80-100 g weight) were maintained on copper-deficient diet (MP Biomedicals, USA) containing a relatively non-toxic copper-chelating agent, triethylenetetramine tetrahydrochloride (Tokyo Chemical Industry Co., Ltd, Japan) in final concentration of 0.6 % w/w and had unlimited access to water for 8 weeks, and then returned to normal rat chow for another 8 weeks (recovery phase). Control group animals were maintained on normal rat chow for the whole duration of experiment. Groups of 3 animals each were killed after 4, 6, and 8 weeks of copper-deficient diet and 4, 6, and 8 weeks after they returned to normal rat chow. Histological sections of pancreas were stained immunohistochemically using antibodies to insulin and glucagon.
RESULTS: After 4 weeks of copper-deficient diet we observed the signs of pancreatic acinar tissue injury, after 6 and 8 weeks of diet only few ducts and pancreatic islets were still present along with the almost total loss of acinar tissue. The same picture was observed 2 and 4 weeks after animals were returned to normal rat chow. Partial recovery of pancreatic acinar tissue was observed only at 6 and 8 weeks of recovery phase. In control group glucagon-positive cells were located predominantly on the periphery of pancreatic islets while insulin-positive cells occupied most central part of the islet. Staining with antibodies to glucagon after 2 and 4 weeks of copper-deficient diet revealed positive cells on the periphery of the islets; however there're some totally glucagon-positive islets as well as some separate glucagon-positive cells within the destroyed acinar tissue. Later on (6 and 8 weeks of copper-deficient diet and 2 and 4 weeks of recovery phase) few small totally glucagon-positive islets along with the larger islets with intense glucagon-positive staining on periphery and weaker staining in the central part of the islet were observed. Pancreatic acinar tissue seemed to be partially restored around the remaining/newly formed islets after 6 and 8 weeks of return to normal rat chow. Staining with antibodies to insulin was positive only in central parts of the islets at all terms of the experiment.
CONCLUSION: So we suppose that glucagon-positive progenitor cells can be probably the source of pancreatic islets and acinar cells restoration.
Disclosure of Interest: None declared

P1234 DIFFERENTIAL EFFECTS OF THE CENTRAL AND PERIPHERAL ADMINISTRATION OF OPIOIDS IN EXPERIMENTAL ACUTE PANCREATITIS IN RATS

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INTRODUCTION: Acute pancreatitis (AP) is often associated with severe pain, which causes discomfort and worsens the prognosis of the disease. Major analgetics (opioids) attenuate the pain associated with AP, but there are no experimental studies that investigated the effects and possible administration methods of analgesia on the severity of AP.
AIMS & METHODS: AP was induced by intraperitoneal (i.p.) administration of 3 g/kg L-ornithine in SPRD rats. Intrathecal (i.t.) catheter was implanted one

week before AP induction. 0.1-1 mg/kg i.p. or 0.01-0.03 mg/kg i.t. buprenorphine (or physiological saline) was administered one hour before AP induction. Control rats were injected i.p. or i.t. with physiological saline or buprenorphine one hour before the i.p. administration of physiological saline instead of L-ornithine. The animals were sacrificed after 24 hours. Laboratory (serum amylase activity, pancreatic dry/wet weight ratio) and histological (necrosis, oedema, inflammatory cell infiltration) parameters were measured.
RESULTS: I.p. and i.t. treatment with buprenorphine did not influence laboratory and histological parameters in the control group. In the AP groups, all of measured parameters were significantly elevated compared to control groups. Pretreatment of AP rats with i.p. administered buprenorphine significantly increased, whereas i.t. administration of the analgetic reduced all of the measured parameters compared to the AP groups pretreated with saline.
CONCLUSION: The different routes of opioid administration have varying effects on the pathogenesis of AP. Central administration of buprenorphine seems to have beneficial effects on the severity of experimental AP, however peripherally given opioids worsen the severity of the disease.
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Disclosure of Interest: None declared

P1235 REVISION OF THE L-ARGININE-INDUCED EXPERIMENTAL PANCREATITIS MODEL IN MICE

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INTRODUCTION: The pathogenesis of acute pancreatitis (AP) remains unknown and it has no adequate therapy. To investigate the pathomechanism, we rely on animal models such as L-arginine-induced AP, which is becoming increasingly popular. However, we found only mild inflammation in Balb/c and high mortality in FVB/n and C57BL/6 mouse strains with the originally published method (2x4 g/kg, 8% L-arginine).
AIMS & METHODS: We aimed to establish a basic amino acid-induced AP model with acceptable morbidity and mortality rate. AP was induced with different doses (2x4, 3x3, 4x2.5 g/kg) and concentrations (0-10%) of intraperitoneal L-arginine administration in Balb/c, FVB/n and C57BL/6 mice. Serum amylase-, pancreatic myeloperoxidase activity and oedema, necrosis, leukocyte infiltration were measured to determine AP severity. Our findings are represented as effectivity rate (ER = number of mice with AP/all treated mice).
RESULTS: In L-arginine treated groups, all parameters were significantly elevated compared to the control group. In all three strains, the injection with 3x3 or 4x2.5 g/kg L-arginine caused similar AP severity with lower mortality vs the 2x4 g/kg dose. In Balb/c mice, 10% L-arginine injection resulted in moderate morbidity and low mortality (ER = 90%). In FVB/n strain 5% L-arginine caused low mortality with severe AP (ER = 90%), while 10% L-arginine caused greater mortality (ER = 25%). C57BL/6 mice developed mild disease with low mortality due to 5% L-arginine (ER = 90%), however, disease severity and mortality were higher in case of 10% L-arginine administration (ER = 35%).
CONCLUSION: Mouse strains show different sensitivities to L-arginine and a fine borderline appears between effective and lethal doses and concentrations.
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Disclosure of Interest: None declared

P1236 THE EFFECTS OF HMG-COA REDUCTASE INHIBITOR ON LIPOPOLYSACCHARIDE INDUCED ACTIVATION OF PANCREATIC STELLATE CELLS

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INTRODUCTION: Pancreatic stellate cell (PSC) plays a crucial role in pancreatic fibrogenesis in chronic pancreatitis. Increased gut permeability has been described in acute and chronic pancreatitis with the effect of bacterial translocation across the mucosal barrier. Bacterial components such as lipopolysaccharide (LPS) may reach the bloodstream and pancreas. Islet cell dysfunction also develops during acute exacerbating stage and end stage of chronic pancreatitis. However little is known about the effect of LPS and hyperglycemia on PSC.
AIMS & METHODS: Aims: To investigate the effects of LPS and hyperglycemia on PSC activation and effects of simvastatin on LPS induced PSC activation.
Materials and Method: Primary cultures of rat PSCs were exposed to various concentrations of glucose and LPS with/without simvastatin. Quantification of proliferation was performed by Brd-U assay. PSC activation was assessed by expression of α-SMA and extracellular signal-regulated kinase (ERK) using Western blot.
RESULTS: Results: LPS induced activation and proliferation of PSC. However, glucose did not affect PSC proliferation. The proliferative effect of LPS on PSC was not affected by glucose concentration in culture media. Simvastatin inhibited LPS induced activation and proliferation of PSC. The proliferative effect of LPS was mediated by activation of Erk 1/2 pathway which was effectively inhibited by simvastatin.
CONCLUSION: Conclusion: This study shows that LPS is one of the activating factors toward PSC. Endotoxemia which is frequently encountered in the clinical settings of acute and chronic pancreatitis may act as a triggering factor for initiating and persisting pancreatic fibrosis. Simvastain could be a therapeutic agent for preventing pancreatic fibrosis.
Disclosure of Interest: None declared

P1237 THE ROLE OF HEAT SHOCK PROTEIN 70 IN PANCREATIC STELLATE CELLS

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INTRODUCTION: The role of heat shock protein 70 (hsp70) in acinar cells (acute pancreatitis) and ductal cells (pancreatic cancer) has been extensively studied. However, the role of hsp70 in pancreatic stellate cell (PSC), an important cell responsible for desmoplastic reaction, is less well understood.
AIMS & METHODS: Aims: To investigate the role of hsp70 in PSC activation and proliferation.
Materials and Methods: PSCs were incubated at 42°C for 2hr and recovered at 37°C for 24hr in order to induce hsp70 expression. Cultured PSCs were treated with heat, PDGF, TGF-β, and LPS to measure α-SMA and hsp70 expression by Western blotting. Cell proliferation was measured by BrdU assay. Simvastatin and quercetin were used in order to inhibit PSC proliferation and hsp70 expression, respectively.
RESULTS: Overexpression of hsp70 did not affect cytokine induced α-SMA expression. Hsp70 expression was significantly increased with PDGF and to a moderate degree with LPS, but not with TGF-β. Similarly, PSC proliferation was also significantly increased by PDGF and to a lesser degree by LPS, but TGF-β did not induce PSC proliferation. Simvastatin suppressed hsp70 expression and PSC proliferation induced by heat or PDGF. Quercetin completely inhibited PDGF-induced hsp70 expression and cell proliferation and partly inhibited heat-induced effects. However, heat preconditioning which induces hsp70 expression had no additional effect on PDGF induced cell proliferation.
CONCLUSION: Hsp70 expression was closely related to cell proliferation in PSCs. Inhibition of hsp70 expression abolished or decreased the effect of PDGF and heat on cell proliferation. Therefore, modulation of hsp70 expression could be an effective therapeutic target for inhibition of pancreatic fibrosis.
Disclosure of Interest: None declared

P1238 GRANULOCYTE COLONY-STIMULATING FACTOR REDUCES FIBROSIS IN A MOUSE MODEL OF CHRONIC PANCREATITIS

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INTRODUCTION: Chronic pancreatitis (CP) is a necroinflammatory process resulting in extensive fibrosis and loss of both exocrine and endocrine function. Granulocyte colony-stimulating factor (G-CSF), a hematopoietic stem cell mobilizer, has been shown an anti-fibrotic effect in liver partial through the enhancement of bone marrow (BM) cells into fibrotic liver[1]. In this study, we aim to test the effect of G-CSF on fibrosis in a mouse model of CP.
AIMS & METHODS: The BM from male green fluorescent protein transgenic C57Bl/6J mice was transplanted into irradiated female C57Bl/6J mice. CP was induced by consecutive caerulein injection (50ug/kg/day, two days a week) for 6 weeks. Mice were then treated with G-CSF (200ug/kg/day, 5 day a week) or normal saline for 1 week, and sacrificed at week 7 or week 9 after first caerulein injection. Pancreatic histology, collagen expression, myofibroblast and BM cells were evaluated to determine the effect of G-CSF in caerulein-induced CP.
RESULTS: The fibrosis was observed in the pancreatic tissues from mice with caerulein injection. The fibrosis was not induced by G-CSF alone. The degree of fibrosis and collagen were significantly decreased in the pancreas from mice with caerulein and G-CSF sacrificed at week 9, while there was no change observed at week 7. The number of myofibroblast in the pancreatic tissue was not changed between mice with or without G-CSF. However, the proportion of BM cells was significantly increased in the mice with G-CSF, suggesting a potential anti-fibrotic role of BM cells stimulated by G-CSF.
CONCLUSION: G-CSF administration contributes to the regression of pancreatic fibrosis at least partially through the enhanced migration of BM cells.
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P1239 THE NOVEL KYNURENIN ANALOGUE SZR-72 IS BENEFICIAL IN ACUTE PANCREATITIS IN RATS

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INTRODUCTION: The pathogenesis of acute pancreatitis (AP) is not well understood and the disease has no specific therapy. There is evidence that the L-kynurenic acid analogue SZR-72 has immune modulator roles in several inflammatory diseases. Therefore, we investigated its effects on experimental AP.
AIMS & METHODS: In the AP groups, male SPRD rats were injected intraperitoneally (i.p.) with 3 g/kg L-ornithine 1 hour after the administration of physiological saline (PS) or 30-300 mg/kg SZR-72 (n = 6-8). Control animals were injected i.p. with PS instead of L-ornithine and with 30-300 mg/kg SZR-72 or PS 1 hour afterwards (n = 6-8). Animals were sacrificed at 24 hours. Laboratory [serum amylase activity, pancreatic myeloperoxidase (MPO) activity, pancreatic dry/wet weight ratio (DW/WW)] and histological (necrosis, oedema, inflammatory cell infiltration) parameters were measured to evaluate disease severity.
RESULTS: The administration of 30-300 mg/kg SZR-72 did not influence serum amylase and pancreatic MPO activities, pancreatic DW/WW and histological parameters in the control groups. However, the injection of rats with L-ornithine significantly increased all parameters vs. the control groups. Pre-treatment of AP rats with 30 mg/kg SZR-72 did not have affect on disease severity. However, all measured laboratory and histological parameters were significantly reduced in AP animals in response to treatment with 300 mg/kg SZR-72.
CONCLUSION: Our experiments showed that SZR-72 has a dose-dependent effect on L-ornithine-induced AP. The administration of 300 mg/kg SZR-72 significantly ameliorated the severity of AP in rats. Further investigations are needed to determine the pathomechanism of SZR-72 action.
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P1240 IS TIMING OF EARLY ENDOSCOPIC INTERVENTION IN ACUTE BILIARY PANCREATITIS IMPORTANT?

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INTRODUCTION: The exact role and optimal timing for endoscopic retrograde cholangiopancreaticography (ERCP) for the management of acute biliary pancreatitis (ABP) remains a controversial topic.
AIMS & METHODS: The main aim of this study was to investigate any benefits early ERCP intervention may have in preventing the development of local and systemic complications due to ABP. Patients presenting to Türkiye Yüksek Ihtisas Teaching and Research Hospital (TYIH) between 1 January 2010 and 31 August 2011 with ABP, who underwent ERCP within 72 hours of the onset of symptoms were screened, and eligible patients were enrolled in the study. Patients were divided into 2 groups based on timing of ERCP (24 hour group: ERCP performed within 24 hours; 24-72 hour group: ERCP performed 24-72 hours after onset of symptoms), and comparisons between both groups were made in terms of patient characteristics, severity of pancreatitis, and local/systemic complications.
RESULTS: A total of 59 patients were included in the final analysis, for 32 of which ERCP was performed in the first 24 hours, while in the remaining 27 patients endoscopic intervention was undertaken 24-72 hours after the onset of symptoms. There was no difference between the 24 hour and 24-72 hour groups with regards to biliary stone detection rate (84.4% vs. 71.4% p = 0.196). However, impacted stones at the papilla were observed more frequently in the 24-hour group compared to the 24-72 hour group (50% vs. 11.1%; p = 0.006). Severity of pancreatitis, rate of pancreatitis-related complications, computed tomography severity index scores and durations of hospital stay were similar in both groups. The only deaths were observed in 2 (3.3%) patients in the 24-hour group.
Table 1. Comparison of disease severity between groups according to different scoring systems

	First 24 hours group n = 32 (%)	24-72 hours group n = 27 (%)	p-value
Ranson score			
≤2 – mild	25 (78.1)	22 (81.5)	0.750
3-5 – moderate	7 (21.9)	5 (18.5)	
mGPS			
≤2 – mild	25 (78.1)	21 (77.8)	0.974
>2 – severe	7 (21.9)	6 (22.2)	
CTSI*			
0-3	24 (92.3)	12 (85.7)	0.803
4-6	1 (3.8)	1 (7.1)	
7-10	1 (3.8)	1 (7.1)	
Organ failure**			
At least one organ	7 (21.9)	6 (22.2)	0.974
Hypotension	2 (6.3)	1 (3.7)	0.565
Acute renal failure	3 (9.4)	4 (14.8)	0.403
Respiratory failure	2 (6.3)	2 (7.4)	0.627
24-48. hour CRP, mg/L	59.95 (3.36-268	114.5 (6.26-271)	0.242
Length of hospital stay, days	5 (3-12)	7 (3-30)	0.122

MGPS, modified Glasgow prognostic score;CTSI, computerized tomography severity index; *calculated for 26 patients in the 24-hour group and for 14 patients in the 24-72 hour group, CRP, C-reactive protein,**based on Atlanta criteria
CONCLUSION: In our study, we could not demonstrate any added benefit of ERCP performed within 24 hours comparing with 24-72 hours of the onset of symptoms with regards to local and systemic complications of ABP. Undertaking early endoscopic intervention, however, increases the likelihood of detecting an impacted stone at the papilla, the delayed management of which may increase the risk for cholangitis. Early ERCP in patients with ABP is effective and safe, and may be recommended in the presence of cholangitis and persistent biliary obstruction.
Disclosure of Interest: None declared

P1241 PREDICTIVE FACTORS FOR, AND INCIDENCE OF RE-ADMISSIONS OF PATIENTS WITH ACUTE AND CHRONIC PANCREATITIS

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INTRODUCTION: While factors like older age and greater severity of the initial disease cannot be influenced to reduce the readmission rate for pancreatitis, variables like alcohol-, tobacco- and substance abuse should be addressed in outpatient programs to reduce disease recurrence and readmission rate for pancreatitis.
To study positive and negative predictive factors for hospital readmissions of patients after in-hospital treatment for pancreatitis.
AIMS & METHODS: Data from patient records and reimbursement information of the years 2006 – 2011 were evaluated for 606 hospital admissions for pancreatitis (373 patients). 973 patient variables, 611 secondary diagnoses, and 295 different procedures (OPS) were assessed by bivariate and multivariate analysis.
RESULTS: The readmission rate of pancreatitis patients during the first 30 days after discharge was 15 %, over the entire study period 29 %. The best predictors for readmission were, when present during the initial episode, concomitant liver disease (OR 12.8; C31.5-111), a suspected tumor of the pancreas (OR 10; C31.1-92), alcohol- (OR 5.4; C32-13), tobacco- or substance-abuse or mental illness. Patients with pseudocyst formation or who had undergone contrast enhanced CT were also more frequently readmitted. Lower than average readmission rates were found when pancreatitis was treated in connection with decompensated diabetes or gallstone disease.
CONCLUSION: While factors like older age and greater severity of the initial disease cannot be influenced to reduce the readmission rate for pancreatitis, variables like alcohol-, tobacco- and substance abuse should be addressed in outpatient programs to reduce disease recurrence and readmission rate for pancreatitis.
Disclosure of Interest: None declared

P1242 VALUE OF DIFFERENT PROGNOSTIC SYSTEMS AND BIOLOGICAL MARKERS FOR PREDICTING SEVERITY OF ACUTE PANCREATITIS ACCORDING TO THE REVISED ATLANTA CLASSIFICATION

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INTRODUCTION: Early identification of patients at risk for severe acute pancreatitis (SAP) is an essential step to guide an intensive care and to improve outcomes.
AIMS & METHODS: Because the severity of acute pancreatitis (AP) was reclassified, we aimed to compare the prognostic value of various predictors including procalcitonin (PCT), C-reactive protein (CRP), CT severity index (CTSI), and complex scoring systems (BISAP, Ranson's, APACHE-II score) according to revised Atlanta classification. Between March 2010 and September 2013, 152 patients with AP were prospectively enrolled. CRP and PCT were obtained on admission, and various scoring systems including Ranson's, APACHE-II, BISAP and CTSI were calculated.
RESULTS: There were 152 patients with AP (mean age 51.3 ± 18.5, 63.2 % male), of which 45 patients (30%) was classified as moderately SAP and 17 patients (11%) SAP. In patients with moderately severe to SAP, PCT (on admission, > 0.5 ng/ml, AUC 0.61, CI 0.51-0.70), CRP 2d (24 hours after admission, > 10 mg/dl, AUC 0.64 CI 0.55-0.67) BISAP (score ≥3, AUC 0.60, CI 0.51∼0.70), Ranson's (score ≥3, AUC 0.65, CI 0.56∼0.76), APACHE-II (score ≥8, AUC 0.61, CI 0.52∼0.70), and CTSI (score ≥3, AUC 0.79, CI 0.72∼0.87) were significant predictors compared to mild AP. Multivariate analysis showed that CTSI (sensitivity 63%, specificity 84%, OR 11.5, CI 4.7-27.8, $p<0.01$), APACHE-II (sensitivity 32%, specificity 88%, OR 3.7, CI 1.2-11.6, $p=0.028$), and CRP 2d (sensitivity 39%, specificity 90%, OR 4.6, CI 1.6-13.6, $p<0.01$) were strongly related to moderately severe and SAP. In patients with SAP compared with mild to moderately SAP, PCT (AUC 0.79, CI 0.67-0.92), BISAP (AUC 0.66, CI 0.50∼0.82), Ranson's (AUC 0.76, CI 0.65∼0.88), and APACHE-II (AUC 0.72, CI 0.57∼0.86) were significant predictors. On multivariate analysis using them, PCT (sensitivity 75%, specificity 82%, OR 5.8, CI 1.4-24.2, $p=0.015$) was only strongly associated with SAP.
CONCLUSION: According to revised Atlanta classification, various biological and structural scoring system had different prognostic value for predicting severity of AP. In patients with SAP, the best efficiency in the early prediction would be achieved by the measurements of PCT. However, in case of moderately to severe AP, CTSI, APACHE-II and CRP 2d act as a valuable predictors for severity of them.
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P1243 COMPLEX TREATMENT OF INTRAABDOMINAL HYPERTENSION IN PATIENTS WITH ACUTE PANCREATITIS

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INTRODUCTION: Abdominal compartment syndrome (ACS) is a serious problem in acute inflammatory diseases of the abdominal cavity. Causing severe changes in organs and tissues, this pathology is responsible for the up to 42% lethality (1). Acute pancreatitis (AP) occupies a special place among acute abdominal pathology. In case of wide-spread pancreatic and peripancreatic necrosis it can cause development of life-threatening complications, among which special subject of the interest is severe intra-abdominal hypertension (IAH)(2).
AIMS & METHODS: The purpose of this study was to use antiflatulents in complex treatment of IAH in patients with AP to prevent the development of ACS. We observed 35 patients with AP, in whom IAH of varying severity (according to classification of J. M. Burch et al.,1996) was identified at admission. Males were 21 (60%), females – 14 (40%). Age of the patients ranged from 24 to 58 years, averaging 38.6±1.2 years. We monitored intra-abdominal pressure (IAP) by measuring the bladder pressure (BP). First grade of IAH was detected in 12 patients (34.3%), second grade – in 18 (51.4%), third grade – in 5 (14.3%). With the help of ultrasonography liquid in omental bursa was found in all patients, in 13 of them – fluid in the abdominal cavity (enzymatic peritonitis). Complex conservative treatment of the 15 patients with AP (42.9%) corresponded to guidelines from the World Society of the ACS: insertion of nasogastric tube; prokinetic agents; intraabdominal catheter drainage (3 patients), epidural block; antisecretory and detoxification therapy and early enteral nutrition (Group 1). In 20 patients (57.1%) antiflatulent (50 Espumisan emulsion droplets in the probe for enteral feeding thrice daily) was added to diminish IAH (Group 2).
RESULTS: Complex conservative treatment in 60% of group 1 patients normalized bowel function (decreased bloating and flatulence, spontaneous defecation) during a week period. Monitoring of BP demonstrated significant decrease of IAP in 8 of them (53.3%): in 5 of the 7 patients (71.4%) with first grade IAH, 2 of 6 patients (33.3%) with II grade IAH and one of the two patients (50%) with IAH of III grade. Additional use of Espumisan emulsion allowed restoration of bowel function in similar terms in 90% of patients in group 2. In latter group normalization of IAP was achieved in 17 people (85%): in all 6 patients with first grade IAH, in 9 of 11 patients (81.8%) with second grade IAH and in 2 of 3 patients (66.7%) with third grade IAH ($p<0.05$). Conservative measures did not permit to normalize the IAP in 2 patients of every group whom then decompressive laparotomy was performed.
CONCLUSION: Complex conservative treatment of IAH including antiflatulents in patients with AP effectively normalizes bowel function, and thus decreases IAP in significantly more patients (85.0% versus 53.3% in the control group). The majority of patients could be avoided from the development of ACS.
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P1244 RISK FACTORS FOR INFECTION AFTER ENDOSCOPIC ULTRASONOGRAPHY-GUIDED DRAINAGE OF SPECIFIC TYPES OF PANCREATIC AND PERI-PANCREATIC FLUID COLLECTIONS

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INTRODUCTION: Endoscopic ultrasonography (EUS)-guided drainage is a widely-used treatment modality for specific types of pancreatic and peri-pancreatic fluid collections (PFCs). The complication of infection have been reported. It is recommended that the infection rate should be assessed by measuring risk factors.
AIMS & METHODS: Aims: The objectives were to measure whether the risk of infection after endoscopic ultrasound guided drainage was associated with (1) patient-related factors and (2) procedure-related factors.
Methods: A total of 83 patients were eligible for inclusion in this study from September 2005 through November 2012. EUS-guided drainage was performed in all patients. The complication of infection was observed. The data on patient-related factors, and procedure-related factors were collected. Patient-related factors mainly included age, sex, etiology of PFCs, location of the cyst, cyst diameter, and so on. Procedure-related factors mainly included approach of EUS-guided drainage and stent diameter. Separate multivariate logistic regression models for all EUS-guided drainage were carried out.
RESULTS: Complete EUS-guided drainage was achieved in all patients (100%). A definitive diagnosis of infection after EUS-guided drainage was made in seven patients. All seven patients had a history of acute pancreatitis, and the cyst diameters were all > 15 cm. Three patients suffered from diabetes mellitus.
CONCLUSION: Acute pancreatitis and cyst diameter were the relevant independent risk factors for infection after EUS-guided drainage. Furthermore, cyst diameter was an independent risk factor for infection. Additional stent placement or using double flanged metal stents may be useful to avoid infection.
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Disclosure of Interest: None declared

P1245 THE EFFECT OF ASPIRIN USE ON SEVERITY OF ACUTE PANCREATITIS IN HOSPITALIZED PATIENTS

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INTRODUCTION: Acute pancreatitis is a common gastrointestinal disease often seen in daily practice. Although the precise mechanism of pancreatitis is still not fully understood, it is believed that the inflammatory response via phospholipase A2, cyclogenase, and neutrophils plays a role. Aspirin is a commonly used NSAID, most notably prescribed for cardiovascular diseases such as stroke, myocardial infarction, and select groups of patients with atrial fibrillation. The aim of this study was to examine the effect of aspirin use on the severity of acute pancreatitis.
AIMS & METHODS: A total of 135 patients with the diagnosis of acute pancreatitis were included in this retrospective study. Relevant clinical data were collected. Patients were divided into two groups according to aspirin use or non-use and the severity of acute pancreatitis was compared. Severe pancreatitis was defined as a Ranson score at any time ≥ 3. Appropriate descriptive statistics

and statistical tests were performed. Statistical significance was defined as a p value < 0.05.
RESULTS: The cohort consisted of 58% (78 of 135) men with a mean (SD) age of 50 (18) years. Of the 135 patients, 4 (2.96%) had gallstone pancreatitis, 4 (2.96%) had alcoholic pancreatitis, and 127 (94.07%) had pancreatitis of unknown etiology. Median (interquartile range) Ranson score on admission and 48 hours afterwards were 2 (1.3) and 1 (0.2), respectively. On admission, there was no statistically significant difference in aspirin user group and non-aspirin user group between the mild-to-moderate acute pancreatitis group and the severe acute pancreatitis group (Table 1). Likewise, at 48 hours after admission, the percentage of patients with aspirin use was not statistically different ($p = 0.678$) between the two severity groups as shown on Table 2. Multivariable regression analysis showed that female gender was the only independent variable associated with a higher severity of pancreatitis ($p = 0.046$)
CONCLUSION: This pilot study demonstrates that aspirin use has no effect on decreasing the severity of acute pancreatitis. Female gender was associated with a higher severity of acute pancreatitis in the first 48 hours after admission. This association has never been identified in prior studies. Obesity, however, which has previously been found to be associated with a higher severity of pancreatitis was not identified as a predictor for the severity of acute pancreatitis in this study.
Disclosure of Interest: None declared

P1246 MEAN PLATELET VOLUME AND OTHER INFLAMMATORY MARKERS IN PATIENTS WITH ACUTE PANCREATITIS

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INTRODUCTION: Acute pancreatitis (AP) induced by different etiological factors is a pancreatic inflammation which is caused by the activation of pancreatic enzymes. The pancreas can usually heal itself without any local and systemic complications. No single laboratory markers are pathognomonic for AP. Mean platelet volume (MPV) has been investigated as an indicator of inflammation and related in several inflammatory diseases. In our study, we aimed to investigate the relationship between white blood cells (WBC) and C-reactive protein (CRP) which are the indicators of AP inflammation and MPV.
AIMS & METHODS: All the data from the 84 (male/female: 51/33) patients diagnosed by non-biliary acute pancreatitis (NBAP) were evaluated. The patients included in this study were diagnosed by clinically, laboratory methods (three times increase in amylase and lipase) and imaging. The symptoms of the patients at the first visit, the findings of the laboratory results and imaging were compared with the values at the time of discharge. The levels of MPV, WBC and CRP of the NBAP patients were compared with the control group (male/female: 53/47) at the first admission and discharge.
RESULTS: The mean age was 50.02 ± 17.69 years and 41.11 ± 10.46 years for NBAP and control group, respectively and there was no age and gender significant difference between groups ($p > 0.05$). WBC levels of the NBAP group at onset ($12.48 \pm 5.93/mm^3x10^3$) and remission ($7.54 \pm 2.4/mm^3x10^3$) were higher than the control group ($6.43 \pm 1.49/mm^3x10^3$) ($p = 0.0001$ for both groups). MPV levels of the NBAP group at onset (8.07 ± 1.07 fL) and remission (8.55 ± 1.05 fL) were lower than the control group (8.99 ± 0.94 fL) ($p = 0.0001$; $p = 0.003$). The mean CRP value was 10.46 ± 10.39 mg/dl at onset; however it dropped to the value of 3.48 ± 4.96 mg/dl at remission. CRP values of onset and remission were higher than the control group (0.47 ± 0.66 mg/dl) ($p = 0.0001$ in both groups) (Table 1). When the cut-off value of MPV was taken smaller than 8 fL in the ROC analysis, the sensitivity and specificity were found 54.7% and 86.8%, respectively (AUC: 0.74, $p < 0.001$).
CONCLUSION: In NBAP patients, the WBC and CRP values were higher at the initial phase of the disease than the healing phase. The MPV value was low at the first examination in which the inflammation was high; it was higher in the healing phase of the disease. In NBAP patients, the increase in MPV values during the healing phase shows that there is a decrease in the inflammation and the remission phase has started.
Disclosure of Interest: None declared

P1247 MARKED IMPROVEMENT IN PANCREATIC CANCER SURVIVAL – A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Pancreatic cancer has a poor prognosis with a 5-year survival rate of less than 5%. Most patients are diagnosed in a locally advanced or metastatic state. Chemotherapy regiments have changed since the introduction of survival prolonging polychemotherapies like FOLFIRINOX (5-Fluoruracil, Oxaliplatin, Irinotecan and Leucovorin). In this retrospective study we analyzed the overall survival of patients diagnosed with locally advanced or metastatic pancreatic adenocarcinoma who were treated at our community-based hospital during the past ten years. We compared patients diagnosed with pancreatic cancer before (historical control) and after the introduction of FOLFIRINOX in 2011.
AIMS & METHODS: We retrospectively identified patients with pancreatic cancer who were treated at our hospital from 2011 to July 2013 by our cancer center registry. Patients treated in the years 2003 to 2010 (historical control) were identified using the diagnosis-related group C25 (malignant neoplasm of pancreas). Patients were included if pancreatic adenocarcinoma in a locally advanced or metastatic state was diagnosed and if at least one cycle of chemotherapy was given. Survival was assessed until February 2014.
RESULTS: 107 patients met the inclusion criteria. Of the 74 patients in the historical control group 62 patients received Gemicitabine, 6 Gemcitabine combined with Erlotinib, 5 Gemcitabine combined with Oxalipaltin and one 5-Fluoruracil as the first line chemotherapy. Of the 33 patients diagnosed between 2011 and July 2013, 15 patients received FOLFIRINOX, 17 Gemcitabine and one patient Oxaliplatin as the first line chemo therapy. 45 out of the 74 patients in the historical control group died and 29 were lost to follow-up. 12 out of the 33 patients in the group diagnosed from 2011 died, 10 were lost to follow-up and 11 were alive until February 2014. Mean of combined time of survival and lost to follow-up revealed 9.2 months (95% CI, 7.4 to 11.0) in the historical control group and 12.7 months (95% CI, 9.8 to 15.6) in the group diagnosed from 2011. Estimated mean survival using Kaplan-Meier was 14.2 months (95% CI, 10.4 to 17.9) in the historical control group and 20.1 months (95% CI, 16.1 to 24.1) in the group diagnosed from 2011. Comparison of the survival curves between the two groups using the log-rank test showed $p = 0.005$.
CONCLUSION: This retrospective study presents a marked improvement in survival of patients diagnosed with locally advanced or metastatic adenocarcinoma of the pancreas in a community-based hospital during the past three years. A possible contributing reason is the use of new polychemotherapies.
Disclosure of Interest: None declared

P1248 EXOCRINE PANCREATIC INSUFFICIENCY IN PATIENTS WITH PANCREATIC OR PERI-AMPULLARY CANCER: A SYSTEMATIC REVIEW

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INTRODUCTION: Exocrine pancreatic insufficiency may occur due to loss of pancreatic parenchyma or obstruction of the pancreatic duct. This may occur in pancreatic or peri-ampullary cancer, both before and after resection. The prevalence and natural course of exocrine pancreatic insufficiency in these patients has not been thoroughly studied.
AIMS & METHODS: The aim of this study was to determine the prevalence of exocrine pancreatic insufficiency in patients with pancreatic or peri-ampullary cancer.
We systematically reviewed the literature published up to February 20th 2014, according to the PRISMA guidelines. We included studies reporting on exocrine pancreatic insufficiency in patients with pancreatic or peri-ampullary cancer. Studies reporting on exocrine pancreatic insufficiency due to other causes and focusing solely on a diagnostic test were excluded. Data on baseline characteristics, type of pancreatic resection, diagnostic test for exocrine pancreatic insufficiency and occurrence of exocrine pancreatic insufficiency were extracted. Prevalence of exocrine pancreatic insufficiency was calculated from these data.
RESULTS: After screening 3203 articles, 9 observational cohort (4 prospective, 5 retrospective) studies were included on a total of 664 patients. Of these patients 333 (50%) underwent pancreatoduodenectomy, 23 (3%) total pancreatectomy, 114 (17%) distal pancreatectomy and 194 (33%) no resection due to locally advanced pancreatic cancer. Median preoperative prevalence of exocrine pancreatic insufficiency was 44% (range 42-67%) before pancreatoduodenectomy; 20% (16-67%) before distal pancreatectomy; 63% before total pancreatectomy; and 50% in unresectable patients. The median prevalence of exocrine pancreatic insufficiency at least 6 months postoperative was 84% (36-100%) after pancreatoduodenectomy; 67-80% after distal pancreatectomy; and 100% after total pancreatectomy.
CONCLUSION: Exocrine pancreatic insufficiency is frequently seen in patients before resection for pancreatic or peri-ampullary cancer. The prevalence increases markedly following resection.
Disclosure of Interest: None declared

P1249 FACTORS ASSOCIATED WITH ABDOMINAL DISSEMINATION OF PANCREATIC CANCER: RETROSPECTIVE ANALYSIS OF SURGICAL PATHOLOGY FINDINGS

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INTRODUCTION: In pancreatic cancer, abdominal dissemination is one of the most important determinants of prognosis. To date, there have been few studies on which surgical findings are relevant to abdominal dissemination, so we retrospectively analyzed patients who underwent surgery for pancreatic cancer.
AIMS & METHODS: We included 145 patients who underwent surgery for pancreatic cancer at our institution between January 2006 and October 2013 in this study. The patients were divided into 2 groups based on whether abdominal dissemination was found during surgery. Abdominal dissemination was defined as the existence of disseminated nodules on the peritoneum or the surface of the liver and confirmed pathologically. We analyzed the 2 groups with respect to patient characteristics, cancer stage, washing cytology results, tumor location [head of pancreas (Ph) / uncinate process of pancreas (UP) or body of pancreas (Pb) / tail of pancreas (Pt)], vascular invasion [portal vein or its branches (PV invasion), superior mesenteric artery, celiac artery, or their branches (arterial invasion)], and whether preoperative endoscopic ultrasonography-guided fine needle biopsy (EUS-FNA) was performed.

RESULTS: Fourteen patients had abdominal dissemination (dissemination group), and 131 patients did not (non-dissemination group). In patients' background, the number of diagnostic laparoscopic procedures was significantly higher in the dissemination group than in the non-dissemination group ($p<0.001$), and there were significant differences in the 2 groups in cancer stage ($p<0.001$). Univariate analysis revealed that the number of positive washing cytology results, tumor located in Pb/Pt, PV invasion, and arterial invasion were significantly higher in the dissemination group than in the non-dissemination group ($p<0.001$, $p=0.002$, $p=0.035$, and $p=0.012$, respectively). The number of EUS-FNA procedures was similar in the 2 groups ($p=0.208$). Multivariate analysis revealed that more patients in the dissemination group had positive washing cytology compared to the non-dissemination group ($p<0.001$), and more patients in the dissemination group tended to have arterial invasion compared to the non-dissemination group ($p=0.059$).
CONCLUSION: We observed a significant relationship between abdominal dissemination and positive washing cytology. Arterial invasion may also be relevant to abdominal dissemination in pancreatic cancer.
Disclosure of Interest: None declared

P1250 SERUM CA 19-9 AS SCREENING TEST FOR PANCREATIC CANCER IN NEW ONSET DIABETIC PATIENTS

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INTRODUCTION: Patients with diabetes newly detected within 2 years have higher risk of pancreatic cancer than general population. The need of screening is suggested and CA19-9 is the only available biomarker for pancreatic cancer, however it is unknown in these patient.
AIMS & METHODS: The aim of this study was to evaluate the usefulness of CA 19-9 as a screening test for pancreatic cancer in the new onset diabetes patients. We retrospectively reviewed medical records of 9.584 patients with new onset (< 2yrs) diabetes from January 2004 to January 2013. Independent t-test, Kai square test, and ROC curve analysis were used to identify clinical features and usefulness of CA 19-9 as a screening test in diabetic patients.
RESULTS: Total 1465 patients were analyzed (male; female = 877;588, mean age was 62.1 yrs). Total 40 cases of pancreatic cancer (2.7%) were occurred but 1.425 patients did not show pancreatic cancer. Their mean age was 58.2 and 62.3 respectively ($p=0.019$). 279 patients were CA 19-9 high group and 1186 patients were low group. There was no significant difference in basal characteristics between two groups. In high group, 9.7% (27/279) developed pancreatic cancer and only 1% (13/1186) in low group. Compared with low group, a significant risk of pancreatic cancer was observed in CA19-9 high group ($p<0.001$). Pancreatic cancer patients with new onset diabetes showed higher CA 19-9 level than non-cancer patients (1744 vs. 33U/mL, $P<0.01$). When setting CA 19-9 cut off value as 37.05U/mL, sensitivity was 67.5% and specificity was 83.1%.
CONCLUSION: CA 19-9 is suggested as a screening test for pancreatic cancer in newly diagnosed diabetic patient.
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Disclosure of Interest: None declared

P1251 OUTCOME OF PANCREATECTOMY WITH ASSOCIATED ARTERIAL RESECTION

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INTRODUCTION: Pancreatic cancer is a leading cause of death in Europe with more than 100 000 deaths in 2012. Surgery remains the only curative option. Whereas extended surgery with venous resection have been demonstrated to be safe and may contribute to improvement of patient survival, arterial resection remains a controversy because of a high related morbidity.
AIMS & METHODS: Retrospective review of prospectively collected data on 18 patients who had pancreatectomy for malignant tumor with arterial resection between October 2008 and september 2013 at our institution. The main end point was postoperative outcome and secondarily the need for new interventional procedure.
RESULTS: The most common type of resection was total pancreatectomy (TP) in 10 cases, followed by pancreaticoduodenectomy (PD) in 8 cases and distal pancreatectomy in 2 cases. There were 15 arterial resection: 3 celiac trunk, 6 superior mesenteric and 9 hepatic artery. In 10 cases, resections were planned. Unplanned arterial resection was done in 8 cases, 3 because of intraoperative arterial injury and 5 because of tumour adhesions discovered intraoperatively. 2 patients had grade $\geq$ IIIb post operative complications including 1 pancreatic fistula. 4 patients required an interventional procedure, 3 were interventional radiology and 1 had surgery. Hospital and 30 day mortality was 0%. Mortality at 90 days occurred in one patient. Fifteen patient had pancreatic duct adenocarcinoma (pT3 = 14, pT2 = 1; R1 = 7), and 3 patients had neuroendocrine carcinoma (pT3N+ = 2, pT1N+ = 1; R1 = 0). In case of adenocarcinoma (n = 15), overall survival and disease free survival was respectively 24 months [2.6-63.5] and 14.3 months [2.6-61.2]. 10 patients had distant metastasis, 2 aptients had local recurrence.
CONCLUSION: In selected patients and after eventually neoadjuvant chemotherapy, pancreatectomy with arterial resection is associated to low morbidity. Overall survival and disease free survival are acceptable. In case of arterial resection, surgery is more radical with high rate of R0 and low rate of local recurrence.
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P1252 ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION OF SOLID PANCREATIC MASSES: IMPACT ON MANAGEMENT STRATEGY

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INTRODUCTION: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a safe and accurate technique for diagnosing pancreatic cancer. However, few studies investigated its impact for management of these patients.
AIMS & METHODS: AIM: To investigate the diagnostic yield and the impact of EUS-FNA in the management of solid pancreatic masses. METHODS: All patients who underwent EUS-FNA for a solid pancreatic mass between June 1st 2011 and December 31st 2013 were included. Aspirates were placed onto glass slides for cytological examination and microbiopsies were fixed for histology. The impact on clinical management was analysed prospectively according to different endpoints, such as its impact on indications for chemotherapy, surgery or appropriate follow-up modality.
RESULTS: Forty-five patients were included; two procedures were considered failures. A final diagnosis was obtained in 43 patients. The sensitivity, specificity and accuracy of combined cytology and histology for the diagnosis of malignant or potentially-malignant tumours were 89.2%, 100% and 90.7%, respectively. The sensitivity and accuracy of cytology alone were significantly higher than those of histology alone ($p<0.05$). There were no complications related to the procedure. By intention-to-diagnose analysis, EUS-FNA directly influenced the management strategy in 33 of 45 patients (77%).
CONCLUSION: In patients with pancreatic mass and suspected malignancy, EUS-FNA provides an accurate diagnosis in approximately 90% of cases. EUS-FNA can directly influence the management in three-fourths of patients.
Disclosure of Interest: None declared

P1253 DIAGNOSTIC ACCURACY OF ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION FOR PANCREATIC SOLID LESIONS – CYTOLOGICAL PREPARATIONS VERSUS CELL BLOCK SECTIONS

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INTRODUCTION: Endoscopic ultrasound (EUS) enables imaging of the pancreas with high resolution; however, it is not enough to distinguish between benign and malignant lesions. EUS-guided fine-needle aspiration (EUS-FNA) allows obtaining a tissue sample from pancreatic lesions for cytological or histological diagnosis.
AIMS & METHODS: The aim was to evaluate the diagnostic accuracy of EUS-FNA for solid pancreatic lesions, comparing the cytological preparations and cell block sections. We performed a retrospective study of EUS-FNA procedures for pancreatic solid lesions performed between January 2006 and December 2013. The diagnosis was established with cytology alone, cell block alone or both. Final diagnosis was based on clinical and imaging follow-up and/or surgical pathology.
RESULTS: Eighty-six EUS-FNA were performed in 84 patients (46 men; mean age 63 $\pm$ 11 years), using a 22-gauge needle. Median number of needle passes per procedure was 3. More than half of the lesions (56%) were located in the pancreatic head and median lesion size was 30mm [11-103]. Tissue samples were collected for both cytological preparations and cell block sections in 75 procedures (87%). Sensitivity, specificity and accuracy were 84%, 62% and 80%, respectively, for cytology alone, and 81%, 100% and 83% for cell blocks alone. EUS-FNA results that relied on both techniques had 90% sensitivity, 83% specificity and 89% accuracy.
Cytology revealed 5 malignancies not diagnosed on cell blocks, while cell blocks revealed 7 malignancies not diagnosed by cytology. There were 3 procedure-related minor complications (3.5%) but there was no mortality associated with the technique.
CONCLUSION: Our study revealed that EUS-FNA is a safe procedure with a high diagnostic accuracy for pancreatic solid lesions. Combination of cytological

preparations and cell block sections improved EUS-FNA accuracy, showing that collecting tissue samples for both techniques should be tried in every procedure.
Disclosure of Interest: None declared

P1254 FEEDING PATIENTS WITH GASTRIC OUTLET OBSTRUCTION UNDERGOING PANCREATODUODENECTOMY: ROUTINE TUBE FEEDING VERSUS EARLY ORAL FEEDING

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INTRODUCTION: Early oral feeding is nowadays considered the optimal routine feeding strategy after pancreatoduodenectomy (PD). However, 33-45% of patients develop delayed gastric emptying (DGE) after PD, usually requiring nutritional support. It is suggested that patients with preoperative symptoms of gastric outlet obstruction (GOO) have such a high risk of developing DGE that GOO represents one of the few remaining indications for routine postoperative tube feeding.
AIMS & METHODS: The aim of this study was to determine the association between preoperative GOO and postoperative DGE. We also compared routine postoperative tube feeding with early oral feeding in patients with GOO undergoing PD.
A multicentre retrospective cohort study was performed in all consecutive patients undergoing PD in two tertiary referral centres between 2010 and 2013. GOO was defined as two or more of the following preoperative symptoms: nausea, vomiting, loss of appetite, dysphagia, or postprandial complaints (abdominal pain, early satiation, or bloating). Patients with GOO were categorized into two groups based on the applied feeding strategy: routine postoperative tube feeding or protocolized early oral feeding (with on-demand tube feeding). Primary outcome was the time to resumption of an adequate oral intake.
RESULTS: Of 421 patients undergoing PD, 61 (15%) suffered from preoperative symptoms of GOO. DGE developed in 26 of 61 (42%) patients with GOO versus 113 of 360 (31%) patients without GOO ($p = 0.08$). Of 61 patients with GOO, 15 patients (25%) received routine tube feeding and 46 (75%) early oral feeding. Time to resumption of adequate oral intake (11 (4-69) vs.14 (7-11) days, $p = 0.80$), incidence of DGE (40% vs. 43%, $p = 0.81$) and length of hospital stay (17 (7-67) versus 14 (4-46) days, $p = 0.19$) did not differ between the two feeding strategies. Of the patients receiving early oral feeding, 24 of 46 (52%) patients with GOO ultimately needed postoperative tube placement as compared to 112 of 297 patients (37%) without GOO ($p = 0.06$).
CONCLUSION: In this retrospective study, the risk of DGE and need for postoperative tube placement tended to be slightly increased in patients with GOO, but outcomes were comparable between routine tube feeding and early oral feeding. Since almost half of patients with GOO tolerate early oral feeding, routine tube feeding may not be indicated in these patients.
Disclosure of Interest: None declared

P1255 IRREVERSIBLE ELECTROPORATION IN LOCALLY ADVANCED PANCREATIC CANCER: A SYSTEMATIC REVIEW

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INTRODUCTION: Ablative techniques are being explored as a new treatment option for locally advanced pancreatic cancer (LAPC). Unlike radiofrequency ablation, irreversible electroporation (IRE) is a non-thermal ablation technology and might preserve vascular and ductal structures.
AIMS & METHODS: The aim of this study was to evaluate the safety and potential benefits of IRE in patients with LAPC.
A systematic search was performed in PubMed, Embase and Cochrane Library for English articles published until March 2014 and subsequently reviewed according to PRISMA guidelines. Included were clinical studies reporting on outcomes of IRE in LAPC. Exclusion criteria were: 1) studies that did not report morbidity and mortality; 2) case reports; 3) conference abstracts. Baseline characteristics as well as study characteristics were extracted. Outcomes expressed as morbidity, mortality and overall survival were extracted from the articles.
RESULTS: After screening 143 studies, 4 clinical studies were included. These studies involving 176 patients, reported overall morbidity of 21-59%, IRE-related morbidity of 7-18.8%, and mortality of 0-3%. The IRE-related complications consisted of pancreatic fistula, portal vein thrombosis, duodenal leak and acute pancreatitis with reported rates of up to 3.7%, 7.4%, 7.4% and 7.1% respectively. Only one clinical study ($n = 139$) reported median survival of 20.2 months.
CONCLUSION: IRE for LAPC seems feasible and safe based on clinical studies. However, the number of complications does not seem improved in comparison with RFA, except for pancreatic fistula. A large prospective, preferably randomized study should establish whether morbidity, overall survival and quality of life are improved by IRE as compared to alternative established treatments.
Disclosure of Interest: None declared

P1256 INTRAABDOMINAL DRAIN VERSUS NO DRAIN FOR PANCREATIC RESECTION: A META-ANALYSIS

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INTRODUCTION: Routine placement of intraabdominal drains has been challenged for distinct abdominal surgical procedures. Studies for abdominal drains after pancreatic resections are inconsistent. The aim of this meta-analysis was to investigate morbidity and mortality of patients with and without abdominal drains after pancreatic resections.
AIMS & METHODS: According to the PRISMA guidelines, a literature search of medical data bases was performed for eligible studies reporting on patients with any kind of pancreatic resection, and comparing a group with abdominal drainage to a group without abdominal drainage. The quality of studies was assessed according to MINORS and STROBE criteria. Morbidity, mortality, and the length of hospital stay were compared by random effects models.
RESULTS: Overall, eight studies with 2.773 patients were included in this meta-analysis. Patients without intraabdominal drainage had a significant reduced rate of any kind of complications ($p < 0.001$). However, no significant differences were detected when separated into minor complications, major complications, pancreatic fistulas, intraabdominal abscesses, need for radiological interventions, need for re-operations, postoperative mortality, and length of in-hospital stay. Study heterogeneity made the results difficult to interpret.
CONCLUSION: The meta-analysis of the current literature does not allow explicit recommendations for or against the routine placement of intraabdominal drains after pancreatic resections. At least, omitting drains seems not to increase the rate of complications and should be considered for unproblematic pancreatic resections. Systematic review registration number CRD42014007497. No funding.
Disclosure of Interest: None declared

P1258 HEPATIC METASTASES OF GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS: A 17-YEAR SINGLE CENTER PROSPECTIVE STUDY

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INTRODUCTION: Gastroenteropancreatic neuroendocrine tumors (GEP NET) with hepatic metastases (HM) have a poorer prognosis in comparison with localized GEP NET.
AIMS & METHODS: Primary endpoints of the study are overall survival from the diagnosis of liver metastases (OS), progression-free survival (PFS) and treatment effectiveness. Among 186 consecutive patients with diagnosed GEP NET from 1995 to 2012, 74 had HM. Prognostic factors and survival times of GEP NET with HM with different treatments were calculated using Kaplan-Meier method and regression analysis.
RESULTS: Median OS (range) was 96 (3-201) months. Prognostic factors for OS were grading, presence of extrahepatic disease (EHD) and treatment ($p < 0.0001$). Ten patients (14%) achieved complete remission, 18 (24%) partial remission, 18 (24%) stable disease, and 28 (38%) progression of disease. Among responsive patients median PFS was 84 (4-180) months. Prognostic factors for PFS were grading and presence of EHD ($p < 0.001$). Five- and 10-year survival rate were 86% and 71% for radical surgery (RS), 82% and 58% for palliative surgery (PS) with radioreceptor therapy (RT), 58% and 37% for PS and medical treatment (MT), and 23% and 8% for MT alone.
CONCLUSION: Overall survival of GEP NET with HM resulted high, as described from other authors. Interestingly, we found that OS and PFS of patients treated with RS are similar to those of patients treated with PS and RT. Main prognostic factors for GEP NETs with HM are grading and EHD.
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Disclosure of Interest: None declared

P1259 DIABETES, SMOKING, ALCOHOL AND FAMILY HISTORY OF CANCER AS RISK FACTORS FOR SPORADIC PANCREATIC NEUROENDOCRINE TUMORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: The identification of environmental risk factors for sporadic pancreatic neuroendocrine tumors (PNETs) may suggest mechanisms of pathogenesis and allow the identification of groups at high risk of disease.
AIMS & METHODS: The aim of this systematic review was to assess if diabetes, smoking, alcohol and/or a family history of cancer are risk factors for sporadic PNETs. MEDLINE and abstracts from the ENETS and NANETS were searched for studies published until October 2013. Eligible studies were selected according to the PRISMA statement.
RESULTS: Four studies were included (study accrual period 2000-10) in a meta-analysis, involving 518 (range, 160-196) cases and 1805 (range, 233-924) controls. All studies were case-control studies and described regional cohorts. The pooled and adjusted OR was 3.512 (95% CI 2.188-5.638; $p \leq 0.001$) with a history of diabetes, 1.401 (95% CI 1.082-1.814; $p = 0.011$) with a history of ever smoking, 1.371 (95% CI 0.986-1.906; $p = 0.061$) with a history of heavy smoking, 1.397 (95% CI 1.075-1.816; $p = 0.013$) with a history of ever alcohol consumption, 3.206 (95% CI 2.038-5.043; $p \leq 0.001$) with a history of heavy alcohol consumption, and 2.160 (95% CI 1.639-2.847; $p \leq 0.001$) with a first degree family history of cancer. There was some heterogeneity in the results that was most apparent with regard to the risk of heavy smoking and heavy drinking.
CONCLUSION: Diabetes, smoking, alcohol and first degree family history of cancer are associated with an increased risk of developing sporadic PNET. There is a need for larger international case-control studies with homogenous study populations to draw definitive conclusions with regard to heavy smoking and heavy drinking and other potential risk factors for sporadic PNETs.
Disclosure of Interest: None declared

P1260 THE ROLES OF EUS-FNA AND 68GA-SOMATOSTATIN ANALOGUES PET/CT IN PATIENTS WITH PANCREATIC LESION(S) IDENTIFIED BY COMPUTED TOMOGRAPHY AND SUSPECTED TO BE NEUROENDOCRINE TUMORS

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INTRODUCTION: Pancreatic neuroendocrine tumors (PNETs) are diagnosed by multidetector computed tomography (MDCT) with increasing frequency: the roles of EUS-FNA and PET/CT in the diagnostic algorithm of these lesions has not been established yet.
AIMS & METHODS: We aimed to investigate the role of EUS-FNA and PET/CT in the evaluation of pancreatic lesions suspected to be PNETs, on the basis of MDCT. We retrieved from our institution databases all patients, who underwent both EUS-FNA and PET from Jan 2007 to Mar 2014, for diagnosis and staging of pancreatic lesions identified by MDCT. Only patients having a MDCT suspected for PNET, were considered in the analysis. We compared 1) the accuracies of EUS-FNA and PET in confirming the diagnosis of PNET and 2) the detection rates of MDCT and PET for suspected secondary lesions. The reference standard for the diagnosis of PNET was histology or cytology (confirmed by at least 6 month follow-up - mean 30 months).
RESULTS: 34 patients were identified (lesions diameter: 27 mm;8-98). The final diagnoses were: PNET ($n = 31$; $G1 = 20$; $G2 = 10$; $G3 = 1$); duct cells pancreatic carcinoma (1) and clear cell carcinoma metastases (2).
Table 1 shows results of the methods, according to the diagnosis:

	True positive	True negative	False positive	False negative
EUS-FNA	28	3	0	3
EUS-FNA (overall)	30	3	0	1
MDCT	31	0	3	0
PET/CT	27	0	3	4

In patients with clear cell metastases PET/CT showed a high tracer uptake, while only a faint uptake was found in the patient with duct cell carcinoma. EUS-FNA results were inconclusive in 3 patients; in 2 of them the diagnosis of PNET was confirmed by performing EUS-FNA again. In 5 patients with PNET, EUS and/or PET/TC identified additionally primary lesions. MDCT did not show any pathological lymph node, neither distant site metastases in 26 patients affected by PNET; PET identified a suspected secondary metastasis in one of these patients, but at a retrospective review of the MDCT findings the lesion was confirmed as visible, but missed during initial evaluation. MDCT diagnosed secondary lesions in 2 patients and these diagnoses were confirmed by PET/CT. In the other 3 patient the results of MDCT were doubtful; in all of them PET/CT identified secondary lesions, but these findings were later found to be false positive diagnoses in 2/3.
CONCLUSION: Although the majority of PNET identified by MDCT resulted positive using PET/CT, EUS-FNA remains necessary to confirm suspected PNET. In patients affected by PNET, in whom MDCT suggests the presence of secondary lesions, PET/CT may be useful providing additional clinical information. On the other hand, the probability of diagnosing secondary lesions by PET/CT in patients, without secondary lesions at MDCT is low.
Disclosure of Interest: None declared

P1261 DNMT1 OVEREXPRESSION IS A PREDICTIVE FACTOR FOR RECURRENCE OF PANCREATIC NEUROENDOCRINE NEOPLASM

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INTRODUCTION: Endoscopic ultrasound is used for precise preoperative evaluation of pancreatic neuroendocrine neoplasm. Endoscopic ultrasound-guided fine-needle aspiration provides safe, highly accurate cytologic confirmation. However, in contrast to adenocarcinomas, the degree of nuclear pleomorphism and architectural pattern do not correlate well with prognosis. It is desirable to find biomarkers that detect the malignant potential without morphological cytological changes. DNA methylation is important in transcriptional regulation, chromatin remodeling and genomic stability. DNA hypomethylation and regional DNA hypermethylation are commonly observed in various tumours, including pancreatic cancer, even in precancerous states, which lack obvious cytological atypia.
We investigated epigenetic alterations and clinicopathologic features of pancreatic neuroendocrine neoplasms using immunohistochemistry.
AIMS & METHODS: A case-control study of 38 patients with pancreatic endocrine neoplasm who underwent pancreatic resection and one case obtained from autopsy. The observation period was 3 to 192 months. We analysed correlations between clinicopathologic factors and immunohistochemical stains of DNMT1. DNMT1 was detected in nuclei of lymphocytes (positive control) and tumour cells. To discriminate definitely positive cases from cases, if more than 5% of cells in a sample exhibited nuclear staining the sample was considered to show immunoreactivity. Correlations between the incidence of DNMT1 immunoreactivity and recurrence were analysed using a chi-square test. A p-value < 0.05 was considered significant.
RESULTS: There were nine males and 30 females, including 23 cases of non-functioning neoplasms, nine of insulinoma, three of serotonin-producing neoplasms, two of gastrinomas, one of ACTH-producing neoplasm, one of VIP-producing neoplasm, and two of microadenomas. Multiple endocrine neoplasia type 1, invasive ductal adenocarcinoma of the pancreas, and gastric cancer were seen in each case. Tumour size was 10–44 mm. From 2010 WHO classifications, 76% of tumours were G1, 20% were G2, and 4% were G3. From 2000 classifications, 30 patients had well-differentiated endocrine neoplasms and nine had well-differentiated endocrine carcinomas. One patient died from liver metastasis 9 years after surgery. Six patients were alive with liver metastasis and had undergone chemotherapy. In one case, liver metastasis occurred 15 years after surgical resection. The remaining 17 cases were alive without recurrence. DNMT1 protein overexpression was significantly associated with liver metastasis ($p < 0.0006$). There was one case with metastasis 15 years after surgery and DNMT1 tested positive in the resected primary specimen.
CONCLUSION: Increased DNMT1 expression correlated to the metastatic potential of pancreatic endocrine neoplasm.
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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
ENDOSCOPY AND IMAGING III – POSTER EXHIBITION – HALL XL

P1262 USE OF THE GLASGOW BLATCHFORD SCORING SYSTEM FOR EVALUATION OF UPPER GASTROINTESTINAL BLEED IN AN IRISH POPULATION; CAN WE PUSH THE GB SCORE TO TWO FOR DISCHARGE AND FOLLOW UP ENDOSCOPY AS AN OUTPATIENT

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INTRODUCTION: Upper Gastrointestinal bleed (UGI Bleed) is very common cause for presentation to the emergency department often leading to unnecessary admission and prolonged length of stay, whilst awaiting in-patient endoscopy

AIMS & METHODS: To validate GBS in our population and to determine if those with GBS up to two can be managed with outpatient OGD
This was a prospective single-centre observational study of patients presented to our centre between December 2012 to June 2013. We recruited those with a working diagnosis of upper gastrointestinal bleeding (UGIB) including those who were discharged from the emergency department (ED) for outpatient OGD. Patients younger than 18 years of age and those who did not give consent were excluded. Data collections include patients' demographics, GBS, hospital admissions, OGD findings (normal or abnormal). Analyses were performed to determine the correlation between GBS and OGD findings (using the Forrest Classification) emphasizing on those with GBS score up to two
RESULTS: Seventy out of 93 patients who presented during the recruitment period had an OGD performed. The mean age of patients was 62.6 years and 53 patients were males (57.0%). The mean GBS was 6.2. Forty-six patients had a normal OGD and their mean GBS was 3.5.
11 had Forrest Classification III, 3 had Forrest IIc, 1 had Forrest IIb, 2 had Forrest IIa, 4 had Forrest Ib and 3 had Forrest 1a. 14 patients were re-admitted within four weeks but none for UGIB. There is a statistically significant correlation between the GBS and Forrest Classification in our cohort ($r = 0.431$, p-value < 0.001). Four patients with variceal bleed were included in the abnormal OGD group as well. Thirty four patients have GBS of 0 to 2 ('0' = 15, '1' = 12, '2' = 7) and all have normal OGD findings.
Ten of the twenty three not having OGD, had GBS score of zero, Three had score 1 and Two had GBS score 2. Patients with score zero and one were discharged from the emergency department for follow OGD but they never returned back to the endoscopy or represented to the hospital within 4 weeks with any symptoms of upper GI bleed. Three of the patients were very unwell with other co morbidities and they had GBS score of more than 8; in that case looking after physicians decided not to go for the OGD. Five of the patients had GBS score of more than 6 but their OGD record was not available in the notes as they may have endoscopy in the operation theater under surgical team.
CONCLUSION: Our study validates the GBS as per previous studies and suggests that we can push the score up to two at which it is safe to discharge and offer out-patient endoscopy.
Disclosure of Interest: None declared

P1263 PROBE BASED CONFOCAL ENDOMICROSCOPY TO DETERMINE THE EXTENT OF MYOTOMY DURING PERORAL ENDOSCOPIC MYOTOMY

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INTRODUCTION: Peroral endoscopic myotomy (POEM) achieved myotomy for treatment of achalasia through submucosal tunnel. The determination of extent of myotomy depends on preoperative high resolution manometry and endoscopic measurement. Endoscopic observation of the inner circular muscles showed a difference in appearance between the tight lower esophageal sphincter (LES) and normal muscle fibres. This study aimed to determine the criteria for observation through probe based confocal endomicroscopy (pCLE) in determining the pathological extent of LES during POEM.
AIMS & METHODS: This is a prospective clinical trial on the use of probe based confocal endomicroscopy to determine the extent of pathological LES. Prospective patients who underwent POEM for treatment of achalasia were recruited. After development of the submucosal tunnel from 15cm above gastroesophageal junction (GEJ) to 5cm below, the pCLE was applied to observe for changes at 2cm intervals from 10cm above to 5cm below GEJ. The criteria for changes during confocal endomicroscopy in pathological LES included – 1. Non-distinct vasculature; 2. No visible normal muscular fibres; 3. Increased cellularity; 4. Presence of thick dark bands. The patients received intravenous fluorescin 2 minutes before the observation. The pCLE was performed using a catheter type confocal probe (Cellvizio MKT) with a diameter of 2.0mm. All the procedures were video recorded for reassessment.
RESULTS: Four patients who underwent POEM for treatment of Achalasia received pCLE for determination of the extent of pathological LES. The mean operative time for POEM was 94.1 mins, and the mean duration for confocal observation at 8 different levels was 10.4 minutes. All the features employed for distinction between pathological LES and normal inner circular muscles were observed for all patients with Achalasia after development of submucosal tunnel. The corresponding length of abnormal pCLE findings was generally longer than that reported in preoperative manometry.

	Patient 1	Patient 2	Patient 3	Patient 4
Age / gender	75/M	M/78	F/76	F/62
Abnormal pCLE	40 – 45cm	39 – 42cm	38 – 45cm	37 – 45cm
Preop Abnormal LES	44 – 47 cm	40 – 42cm	41 – 44cm	42 – 46cm
Preop LES pressure	60 – 70 mmHg	8 – 12mmHg	26 – 32mmHg	30 – 40 mmHg
IRP4s	48.6mmHg	-	21.6mmHg	17.8mmHg

CONCLUSION: In this preliminary study, we were able to establish preliminary criteria to differentiate between pathological LES and normal inner circular muscle fibres during POEM. These changes shall serve as guidance to determine the extent of myotomy during POEM.
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Disclosure of Interest: None declared

P1264 ENDOSCOPIC MUCOSAL RESECTION OF SPORADIC DUODENAL POLYPS IS ASSOCIATED WITH A HIGH RISK OF COMPLICATIONS

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INTRODUCTION: Endoscopic mucosal resection (EMR) is an established technique for the treatment of early neoplastic lesions in the colon, esophagus and the stomach. Sporadic duodenal adenomas (SDA) are a rare finding on endoscopy. Little data is available about the safety and efficacy of EMR for SDA in larger case series.
AIMS & METHODS: The aim of this study is to report our experience with regard to the safety and efficacy of duodenal EMR for SDA.
Methods: Prospectively collected data of fifty nine patients (31 men, 28 female, mean age 61) referred for duodenal EMR to our center between 2006 and 2013, were analyzed. Only duodenal polyps were included in the study. Data regarding polyp size, location, endoscopic morphology, EMR technique, procedure time, complications, pathology result and periodical follow up were recorded. All patients underwent day after endoscopy to detect and treat delayed bleeding.
RESULTS: Seventy-one duodenal EMRs were performed in fifty nine patients during the study period. The median polyp size was 15mm (range 7-40 mm). The success rate of complete endoscopic removal after a single EMR was 83%. Complete remission was achieved with 2 and 3 EMRs in 9 and 3 patients respectively. Complications occurred in 26% of the procedures. We encountered 10 cases of early bleeding (<4 hours after EMR) and 10 cases of delayed bleeding (>4 hours after EMR) with need of additional hemostatic measures, transfusion or radiological intervention and admission to intensive care. In one patient a small perforation could be managed conservatively with clips. No patients were referred for rescue surgery. Except for 2 neuro-endocrine tumors, all lesions were adenomas with low grade dysplasia in 82% and high grade dysplasia in 18%. Long term histological follow up (median: 18 months, range 12-50 months) was available in 30 patients, complete histologic remission was achieved in 25 patients (83%). Five patients revealed histologic arguments of residual adenomatous tissue, all showing low grade dysplasia. No tumor related deaths were reported.
CONCLUSION: This study is one of the largest available series confirming the efficacy of EMR for SDA. Duodenal EMR is efficient *(83%)* in achieving long term complete histological remission. However morbidity (26%) seems higher for duodenal EMR as compared to EMR in other location within the gastrointestinal tract and in comparison to other smaller series. Our systematic approach of day after follow-up endoscopy could contribute to the higher morbidity rate with detection of late bleeding.
Disclosure of Interest: P. Martens: None declared, I. Demedts: None declared, S. Van Gool: None declared, H. Willekens: None declared, R. Bisschops Financial support for research from: Covidien, Ipsen, Pentax, Lecture fee(s) from: Covidien, Pentax, Fujifilm, Olympus, Consultancy for: Covidien

P1265 ENDOSCOPIC RESECTION OF DUODENAL ADENOMAS-COMPARISON OF SAFETY AND EFFICACY BETWEEN SPORADIC ADENOMAS AND ADENOMAS IN FAP

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INTRODUCTION: Although there is a low risk of malignant conversion of duodenal polyps in FAP, EMR is often considered. However, few studies have looked at the safety and efficacy of EMR. We compared the outcome of duodenal EMR's in patients with FAP vs sporadic adenomas. To our knowledge, this is the largest series of duodenal EMRs that is published so far (1)
AIMS & METHODS: We looked at Clinical records of all patients who underwent endoscopic resections for duodenal adenomas at Leeds in a 10 year period.
RESULTS: A total of 49 sporadic adenomas were resected (in 51 patients) and 44 FAP related (in 22 patients). Most lesions appeared either sessile (43) or flat elevated (48). The average size of the FAP related polyps was 16.9mm vs. 20.7mm in sporadic lesions. Most were removed by standard EMR ($n = 82$) rather than the strip biopsy technique ($n = 9$). Two procedures failed and no follow-up data was available after the resection of 2 sporadic polyps.
The final histology of the lesions were; TA+LGD (76), TA+HGD (13), adenocarcinoma (2) and 2 polyps were not retrieved. In 11 lesions, there was a change in the histological grade after resection.
There were 4 perforations (4.3%), 3 were managed surgically. 12 patients (13%) were readmitted with significant late GI bleeding and 8 patients required endoscopic therapy and transfusion.
There was no significant difference in the success rates in the two groups (19/44 vs 32/49) p value 0.94). However, the resection of polyps ≥2cm were significantly more likely to be associated with a complication (7/59 vs. 8/19 $p = 0.02$). There was no difference in the risk of complications with the polyp location, ASA status, Spigelman score or patient age.
Amongst the FAP polyps, polyps > 20 mm were significantly more likely to have local recurrence (3/6 vs 3/31 p value 0.04). There was no difference in the chances of success of the resection with the growth pattern, the location of the polyp or the Spigelman score.
CONCLUSION: Duodenal EMR is hazardous, particularly when lesions 2cm or larger are resected. However, there was no significant difference in the hazards or success rates between the two groups. Most FAP patients had further neoplasia

on follow up, but this is due to the fact that many of the adenomas were not resected /treated in the first sitting.

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Disclosure of Interest: None declared

P1266 WHAT IS THE OPTIMAL TIME TO DO ENDOSCOPY IN ACUTE CAUSTIC INGESTION?

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INTRODUCTION: Early (<24 h) upper GI endoscopy (UGIE) is used to prognosticate mucosal injury after caustic ingestion.

AIMS & METHODS: To evaluate the usefulness of day 5 UGIE over day 1 UGIE in prediction of cicatrisation and other outcomes after acute caustic ingestion.

Consecutive adult patients of caustic ingestion seen by us between 2009-2013 were subjected to upper GI endoscopy after informed consent within 24 hours and on fifth day of caustic ingestion. Upper GI mucosal changes were graded using Zargar's classification. Patients with changes of grade ≤IIa were classified as mild and those with ≥IIb were classified as severe. Patients were regularly followed up for development of complications. Management of cicatrisation included endoscopic dilatation followed by surgery if the former failed. Comparison was made between day 1 and 5 endoscopy changes for development of cicatrisation and complications.

RESULTS: A total of 63 patients had presented to us within 24 h of caustic ingestion of who 51(mean age 32±13.3yrs, 31 males) had day 1 and day 5 UGIE. Acid intake was seen in 43(84.3%), alkali in 6(11.8%) and unknown substance in 2(3.9%). The cause of caustic intake was suicidal in 24(47.1%), accidental in 20(39.2%) and unknown in 7(13.7%). Esophageal stricture developed in 12(23.5%) and antro-pyloric stricture developed in 18(35.3%) patients. 1(2%) patient died, emergency surgery was done in 1(2%) patient and definitive surgery for cicatrisation was done in 7(13.7%) patients. 42 (82.3%) patients recovered on conservative management requiring only dilatation in those with cicatrisation. Endoscopic grading on day 1 significantly overestimated severity of mucosal changes compared to day 5 grading **(table.1)**. Endoscopic grading on day 1 overestimated esophageal injury severity by 23.5% compared to day 5 grading. Endoscopic grading on day 1 overestimated gastric injury severity by 29.4% compared to day 5 grding. Day 5 endoscopic grading of esophageal injury correlated with stricture formation ($p = 0.019$) better than day 1 endoscopic grading ($p = 0.287$). For gastric injury both day 1($p = 0.005$) and day 5 ($p = 0.000$) endoscopic grading correlated with gastric cicatrisation. Day 5 endoscopic grading correlated better with need for surgery and recovery as compared to day 1 endoscopic grading ($p < 0.05$).

Table 1: Endoscopic grading on day 1 and day 5

	Mild changes grade ≤IIa	Severe changes grade ≥IIb	Day 1 vs day 5 (significance)
Esophagus day1(n = 51)	**19(37.3%)**	**32(62.7%)**	
Esophagus day5(n = 51)	**31(60.8%)**	**20(39.2%)**	**p = 0.008**
Stomach day 1(n = 51)	**11(21.6%)**	**40(78.4%)**	
Stomach day5(n = 49)	**25(51%)**	**24(49%)**	**p = 0.006**

CONCLUSION: Endoscopic assessment on day 1 significantly overestimates the grade of injury. Endoscopic grading of injury on day 5 is a better predictor of esophageal and gastric cicatrisation and need for surgery. We suggest that relook endoscopy on day 5 should be done in all patients of caustic ingestion.

Disclosure of Interest: None declared

P1267 A RANDOMIZED CONTROLLED TRIAL OF WHITE LIGHT ENDOSCOPY VERSUS BLUE LASER IMAGING ENDOSCOPY FOR THE DETECTION OF FOCAL GASTRIC LESIONS; A PRELIMINARY REPORT

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INTRODUCTION: White light endoscopy (WLE) may miss subtle mucosal changes of stomach. Blue laser imaging (BLI) (Fujifilm Co., Japan) is a novel bright illumination with high definition resolution diagnostic tool that may improve mucosal surface contrast and facilitate visualization of mucosal details.

AIMS & METHODS: To evaluate the detection rate of focal gastric lesions between WLE and BLI system. From November 2013 to March 2014, 110 patients were recruited (55 in each). Inclusion criteria: 1) aged > 50 years undergoing UGI endoscopy with indications; for instant, chronic dyspepsia, unexplained weight loss, iron deficiency anemia, etc. Exclusion criteria: 1) presence of active gastrointestinal bleeding; 2) presence of coagulopathy; 3) past history of partial gastrectomy. Patients were randomized to either WLE or BLI. The presences of focal gastric lesions, the morphology based on the Paris classification and real-time diagnosis were recorded. All lesions were biopsied for histological confirmation. The difference in the detection rate of focal lesion was analysed.

RESULTS: There was no significant difference in mean age (64 vs. 66 years) and gender distribution (41% vs. 50% male) between patients undergoing WLE and BLI. WLE and BLI could detect gastric polyp, erosion, ulcer, intestinal metaplasia (IM) and advanced gastric cancer (**Table 1**). BLI provided a trend of better focal gastric lesions detection when compared to WLE (52% vs. 41%, $p = 0.082$). All IM lesions were detected only by BLI, whereas WLE did not detect any IM. These five cases of IM were classificed as 0_IIa at 80% and 0_IIb at 20%. However, no early gastric cancer was detected in this study.

Table 1

	Gastric polyp	Gastric erosion	Ulcer	Intestinal Metaplasia (IM)	Advanced gastric cancer	Total
WLE	7	9	4	0	2	22
BLI	6	8	9	5	1	29

CONCLUSION: WLE and BLI are both potentially a promising tool for detection of subtle focal gastric lesions. However, BLI may have more advantage than WLE on detecting IM lesion. Additional cases should be recruited to determine the usefulness of BLI.

Disclosure of Interest: None declared

P1268 PUSH-METHOD PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) FOR HEAD AND NECK (H&N) CANCER PATIENTS; OUR EXPERIENCE AT A LARGE GASTROENTEROLOGY UNIT

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INTRODUCTION: Nutritional support via gastrostomy is advocated in H&N cancer patients undergoing chemo-radiotherapy treatment.

These may be inserted either endoscopically (PEG) or radiologically (RIG; Radiologically Inserted gastrostomy). PEGs may be performed using a pull or push (Seldinger) method. BSG guidelines 2010[1] specify that push-PEG technique should be preferred where cure is the intention of treatment for H&N cancer to avoid risk of tumour seeding[2]. We have adopted this method and describe our experience at a large gastroenterology centre of using push-PEGs for this purpose.

AIMS & METHODS: The aim of this study was to audit safety and success rates of push-inserted PEGs for H&N cancer patients. We retrospectively audited case-records of all patients receiving push-inserted PEG procedures between January 2012 to December 2013

RESULTS: Push-PEGs were successfully placed in 95% (53/56) patients. Mean age was 57.2 years; male:female ratio 36:17. Preprocedure antibiotics were used in 98% (52/53) patients. 84% (46/55) received a combination of midazolam (mean dose 2.8mg) and fentanyl (mean dose 52.5mcg); rest 16% received single sedative (midazolam). Discomfort scores[3] were recorded as 65% (33/51) comfortable during the procedure and 35% had mild discomfort. 30-day mortality was 3.8% (2/52). Major complications occurred in 2 patients (3.8%): misplaced suture in the peritoneal cavity requiring laparotomy retrieval; suture-tension induced gastric perforation 3 days post-procedure in an obese patient. No gastrostomy site metastases were observed. Minor complications occurred in 2 patients (3.8%); balloon rupture resulting in dislodged PEG and skin hematoma after day1 post-procedure. Our complication rates were lower than published 4.8%[4]. Three patients required RIG, having failed intubation due to stricturing disease.

CONCLUSION: Push method PEG is safe, useful and a viable alternative to RIG with high success rate in H&N cancer patients. RIG or surgically placed gastrostomies should be reserved as second-line approach. We aim to provide push-PEG for all H&N cancer by 2015 by education and training,compared to 62.2% (56/90). We reflect that obesity leading to suture-tension may be a risk factor for major complication.

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Disclosure of Interest: None declared

P1269 EFFICACY AND SAFETY OF ENDOSCOPIC MUCOSAL RESECTION OF NONAMPULLARY DUODENAL POLYPS

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INTRODUCTION: Endoscopic mucosal resection (EMR) of nonampullary duodenal (NAD) polyps is an alternative to surgical treatment. The literature is quite poor about this subject and series often includes small sized populations.

AIMS & METHODS: This study aimed to evaluate efficacy and safety of EMR for NAD polyps. This is a retrospective cohort analysis of all consecutive patients referred between 2002 and 2013 for management of NAD polyps at a tertiary-care center by a single practitioner.
RESULTS: Between 2002 and 2013, 61 NAD polyps have been resected in 53 patients (22 females, 31 males). The mean age was 64.5 years (34.5-91.5). The mean polyp size was 23.4 +/- 14.1mm of wich 8.2% (n = 5) <10mm, 50.8% (n = 31) between 10 and 20mm and 41% (n = 25) >20mm.
Of 53 patients who underwent attempted endoscopic resection, complete resection was achieved in 52 cases (98.1%), during a single session in 48 patients (90.4%) and with double or triple sessions in 5 patients (9.6%). En bloc resection was performed for 36 polyps (59%) and piece meal resection for 25 polyps (41%). 37 of resected areas were closed by endoclips (60.7%) but closure failed or was incomplete in 8 cases (21.6%).
Histological findings revealed 50 adenomas (15 tubulars and 35 tubulovillous or villous with high degree of dysplasia in 5 (10%) of them), 11 non adenomatous lesions (5 Brunner's gland hyperplasias, 1 Brunner's gland hamartoma, 1 gangliocytic paraganglioma, 1 lipoma, 1 neuroendocrine tumor, 1 inflammatory fibroïd polyp and 1 ectopic pancreas).
Complications occured in 11 patients (20.8%): 8 haemorrhages (15.1%) of which a lethal one, with surgery needed in 2 cases, and 3 perforations (5.7%). In multivariate analysis, the only predictive factor of complication was the failure of resected area closure by clip (OR = 7.2; IC 95 [1.3-39.6]).
5 recurrences (17.2%) have been observed among 29 patients diagnosed with adenoma who benefitted from a follow-up (mean follow-up: 23.4 months). All recurrences were successfuully treated by EMR.
CONCLUSION: EMR of NAD polyps is an effective therapy but with significant morbi-mortality rate. However, in most of cases, complications have been successfully treated by medical or endoscopic therapies. Long term endoscopic follow-up is needed in adenomas with a recurrence rate of 17.2%.
Disclosure of Interest: None declared

P1270 ENDOSCOPIC SUBMUCOSAL DISSECTION CAN TRANSFORM THE MANAGEMENT OF PATIENTS WITH UPPER GASTROINTESTINAL SUBMUCOSAL TUMOURS: RESULTS FROM A UK SERIES

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INTRODUCTION: It is very difficult to establish an accurate diagnosis for upper GI submucosal tumours. Biopsy during endoscopy cannot go deep enough. EUS is unable to give a tissue diagnosis. The risks of surgical resection are higher than the benefits as the lesion may very well be benign. As a result most of these patients keep having endoscopic surveillance as 'possible' GISTs.
AIMS & METHODS: A retrospective cohort study of patients undergoing ESD for upper GI submucosal tumours. They were all referred to us as possible GISTs that were found to be growing in size on surveillance. ESD was carried out in all these cases. As these lesions are mostly bulky, gravity and patient positioning were utilized as traction during ESD to achieve deroofing and enucleation of these tumours. Any complications were recorded. Endoscopic follow up was performed to assess for incomplete resection or recurrence.
RESULTS: 21 submucosal lesions were resected by ESD between 2007 and 2013. 7 were oesophageal, 10 gastric and 4 duodenal. Sizes ranged from 10 to 35mm. Endoscopic clearance was achieved in all cases. Histology showed a wide range of diagnoses, mostly benign (table). There was 1 complication; a microperforation which was identified and clipped intraprocedurally, giving a complication rate of 4.7%. On follow up, there was 1 recurrence (recurrence rate 4.7%) which was managed endoscopically. 1 patient had surgery as the ESD specimen showed a synovial sarcoma. Endoscopic cure rate was 95.2%.
Table: Histological diagnosis of submucosal tumours resected by ESD

Diagnosis	number
Granular cell tumour	3
GIST	2
Leiomyoma, lipoma	2+2
Pancreatic acinar tissue	1
Carcinoid	6
Inflammatory fibroid polyp	1
Hyperplastic polyp	1
Synovial sarcoma	1
Gangliocytic paraganglioma	1

CONCLUSION: ESD is a safe and novel, minimal access therapeutic technique which has the potential to transform management of submucosal tumours. Patients go from the uncertainty of having repeated endoscopies for an unknown diagnosis, to having it completely removed and cured in the vast majority, without the need for continuing endoscopies. In the remaining cases, ESD specimens provide an accurate histological diagnosis based on which definite management plans can be made.
Disclosure of Interest: None declared

P1271 PER-ORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA CARDIA, CASE SERIES FROM SINGLE TERTIARY CARE CENTRE

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INTRODUCTION: Treatment for achalasia cardia includes endoscopic (balloon dilatation/botulinum injection) or surgical Heller's myotomy. Per-oral endoscopic myotomy (POEM) is an upcoming modality. This study reports preliminary results of POEM in patients suffering from achalasia cardia.
AIMS & METHODS: Patients with achalasia cardia confirmed on endoscopy (EGD), high-resolution manometry (HRM) and barium swallow and undergoing POEM were included. Associated co-morbidities & previous treatments for achalasia were recorded. Eckhardt dysphagia score was recorded before the procedure. Procedure time, technical success and complications were noted. Follow up was by EGD, with or without HRM and post procedure Eckhardt score at 4 weeks.
RESULTS: 20 patients were enrolled, Male: Female (1:1). Achalasia Type: I – 4, II – 12, III – nil, Not Done - 4. Significant comorbidities: 6 / 20(30%). Categories: naïve patients (n-10), previous therapies – Heller's myotomy (n-2), botulinum injection – (n-1) and Balloon dilatation – (n-6). Mean symptom duration: 24-420 weeks. Mean pre- procedure Eckhardt score – 6.5; mean LES pressure 43.3mmHg (Range – 17 -74 mmHg). Mean procedure duration (minutes) was 187.5 (60 – 330), clinical success in all (100%) and no complications encountered. Technical difficulties occurred in 4 / 20 (20%) patients. Follow up (mean 6 months) mean Eckhardt score was 1.5 ($p = 0.001$) and mean LES pressure 12.8 ($p = 0.018$). Relief in dysphagia was in all patients (100%) and occasional heartburn in – 8 / 20 (40%).
CONCLUSION: POEM is safe and effective treatment for achalasia cardia. It is effective in treating naïve, previously treated patients and also in those with comorbid illness that may preclude surgical treatment.
Disclosure of Interest: None declared

P1272 FACTORS RELATED TO NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR UNDIFFERENTIATED-TYPE EARLY GASTRIC CANCER

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INTRODUCTION: Intramucosal undifferentiated-type (UD-type) early gastric cancer (EGC) ≤ 2cm without ulceration has been treated by endoscopic submucosal dissection (ESD) as an investigational treatment. However, it is difficult to estimate the depth of invasion in UD-type EGC compared with differentiated-type. In addition, tumor margin is indistinct in some UD-type EGCs extending along the proliferative zone in the middle layer of the mucosa, leaving normal ducts covering the superficial epithelium.
AIMS & METHODS: This study aimed to evaluate factors related to non-curative ESD of UD-type EGC. 137 consecutive UD-type EGCs in 127 patients who underwent ESD met the inclusion criteria: i) they had a poorly differentiated adenocarcinoma or signet ring cell carcinoma histologically proven by preoperative biopsy, ii) the cancer was intramucosal and appeared on endoscopy to be ≤ 2 cm and without ulceration, iii) they had had no prior endoscopic treatment or surgery of the upper gastrointestinal tract. This study assessed short-term outcomes of ESD, factors related to non-curative ESD and width of tumor extension along the mucosal proliferative zone in 0-IIc lesions. Curative resection of ESD for UD-type EGC was defined as the presence of an intramucosal cancer ≤ 2 cm without ulceration or lymphovascular invasion and with clear lateral and vertical margins on histological assessment.
RESULTS: Of 137 lesions, en bloc resection was achieved in 99.3% and R0 resection 94.2%. The median procedure time was 65 (10-300) minutes. Delayed bleeding, perforation and delayed perforation rates were 2.9%, 2.9% and 0.7%, respectively. Macroscopic types (0-IIc/0-IIa or 0-IIa+IIc/0-IIb) were 133/3/1. Median tumor size was 11mm (1-45). Pure sig morphology was identified in 58.4% and por including with other component in 41.6%. Curative resection was 70.1% and was significantly higher with pure sig than por (81.3%/52.6%, $p < 0.0001$). Main causes of non-curative ESD in all patients were submucosal invasion (16.8%) (minute submucosa $< 500\mu m$/deeper submucosa $\geq 500\mu m = 8.0\%/8.8\%$), tumor size > 20mm (12.4%) and ulceration (7.3%) (with overlapping, shown in table). Submucosal invasion and resected tumor size >20mm were significantly more common in por than in pure sig (29.8%/7.5%, $p < 0.001$ and 19.3%/10.0%, $p = 0.009$). 43 lesions (31.4%) were preoperatively underestimated by more than 5mm in size. 75% (6/8) of the lesion which were preoperatively diagnosed as 20mm in size were over 20mm. Extension along the proliferative zone was found in 74 of 133 0-IIc lesions (55.6%) and median width of extension was 980μm (0-11650μm). Increasing lesion size was associated with more extension along the proliferative zone (preoperative tumor size and median width of extension: 1-5mm/6-10mm/11-15mm/16-20mm = 490μm / 960μm /1040μm /1960μm).

Submucosal invasion (SM1/SM2)	**23(11/12)**	**16.8% (8.0%/8.8%)**
>2cm in size	**17**	**12.4%**
Ulceration	**10**	**7.3%**
Lympho-vascular invasion	**4**	**2.9%**
Positive lateral/vertical margin	**5/4**	**3.6%/2.9%**
Piecemeal resection	**1**	**0.7%**

CONCLUSION: Careful preoperative assessment is needed for UD-type EGC, especially if tumor size is near 20mm.
Disclosure of Interest: None declared

P1273 HOW TO PREDICT DELAYED BLEEDING AFTER ESD FOR GASTRIC NEOPLASMS?

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is a major treatment option for gastric neoplasms. However, ESD causes Post-ESD delayed bleeding (PEDB), one of the significant complication. Few studies showed that risk factor of PEDB is large artificial ulcer. Known as ESD induced ulcer is different from Peptic ulcer disease healing mechanism. Major healing mechanism is muscle contraction. For preventing the PEDB, prophylactic coagulation during the ESD was performed. So, we want to probe the effect of prophylactic coagulation induced thermal injury to the delayed ESD bleeding. The primary end point of this study is the relations between the post dissection coagulation time (PDCT) and delayed post ESD bleeding.
AIMS & METHODS: A total of 288 lesions diagnosed with early gastric neoplasms and treated by ESD from March 2005 to February 2013 in Eulji Hospital, retrospectively. PEDB was defined as the time of the bleeding after 24hrs: early PEDB, and late PEDB. Also the lesion was categorized non bleeding visible vessel, oozing bleeding and spurting bleeding. We analyzed associations between bleeding and the following factors of the characteristics of the patients and the lesions: age, sex, pathology, macroscopic findings (elevated, flat and depressed lesion), location, size of the resected lesion, duration time of the procedure, the type of the resection methods; enbloc or piecemeal resection, and fibrosis or not. Also, we measured the PDCT.
RESULTS: PEDB which is in 3.0% lesions (16/288). Delayed bleeding which oozing and spurting bleeding is only 1.5% (9/288). The male sex ($P<0.001$), piecemeal resection was risk factor of delayed bleeding ($p=0.025$). Compared with non bleeding group, larger resected size (4.26/3.50(cm), $p=0.02$), and delayed procedure time (96.62/58.24(min), $P< 0.001$) to be risk factors for delayed bleeding. And the PDCT was longer delayed bleeding group, but there are not significant (9.86/7.33(min) $p=0.19$). The location and macroscopic finding, pathology and fibrosis were not significant also.
CONCLUSION: This study demonstrated risk factors for PEDB. The male sex, piecemeal resection, large resected size and delayed procedure time are increase PEDB risk. However, we don't clarify the relationship between PDCT as thermal injury variable and PEDB because of small volume size of study.
Disclosure of Interest: None declared

P1274 LIMITED VALUE FOR FOLLOW UP ENDOSCOPY IN SEVERE OESOPHAGITIS: FINDINGS FROM A LARGE LONDON DISTRICT GENERAL HOSPITAL

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INTRODUCTION: The American Society of Gastrointestinal Endoscopy recommends the practice of endoscopic follow-up for patients with gastro-oesophageal reflux disease (GORD) with oesophagitis after adequate medical therapy has achieved mucosal healing, specifically to exclude masquerading Barrett's oesophagus (BE) or underlying cancer. Historically, follow-up oesophagogastro-duodenoscopy (OGD) for patients with GORD with oesophagitis was reserved for patients whose symptoms failed to respond to medical therapy, those who had severe oesophagitis or an oesophageal ulcer, or for those who needed additional biopsies to clarify a diagnosis. It could be argued that repeat OGD is not necessary as it gives a low yield in cancer and BE detection especially if initial appearance is benign and not indicative of BE.
AIMS & METHODS: The aim of this study was to assess the findings in patients who underwent a follow-up OGD for severe oesophagitis.
A single centre (large district general hospital), retrospective analysis of patients diagnosed with severe oesophagitis (Los Angeles classification Grade C or D) who subsequently underwent follow-up OGD over 8 years from 2005 was performed. Data was obtained using the GI Audit tool from the Unisoft endoscopy reporting system. Patients were assessed for the presence of cancer or BE at repeat OGD.
RESULTS: 76 patients with severe oesophagitis (31 grade D oesophagitis, 45 grade C oesophagitis) were included in the study. At follow up OGD, findings were: normal in 43, grade A oesophagitis in 18, grade B oesophagitis in 12, BE in 3. Of the 3 patients with BE on review, all had Grade D oesophagitis at initial OGD, one had appearance of BE macroscopically at initial OGD and the other 2 were both of non circumferential short segment (<3cm) BE without intestinal metaplasia. No patients had oesophageal cancer at follow up OGD.
CONCLUSION: In this study, the pick-up rate of cancer or BE at follow-up OGD assessment in patients with Grade C or D oesophagitis is very low (0.3%). Those in whom BE is diagnosed at follow up endoscopy, had preceding grade D oesophagitis and BE is short segment and without intestinal metaplasia. This pick up rate of BE is much lower than that reported if all patients with symptoms of GORD were endoscoped suggesting that the presence of severe oesophagitis is not a marker for detection of BE. From this study, we concluded the practice of endoscopic follow-up in patients with severe oesophagitis adds to higher healthcare costs without improving patient outcomes. OGD is a valuable diagnostic tool and for endoscopy services to be effective it is essential that it is not overloaded with inappropriate referrals. If our findings are replicated at other centres then guidelines on follow up OGD in oesophagitis should be re-visited.
Disclosure of Interest: None declared

P1275 ODYNOPHAGIA AND ITS YIELD ON UPPER GI ENDOSCOPY - A SYMPTOM WORTH ASKING ABOUT

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INTRODUCTION: Odynophagia can be defined as a painful sensation in the oesophageal region that occurs in relation to swallowing. Unlike dysphagia, which has historically been an alarm symptom or warning sign of oesophageal cancer, odynophagia is not classified as an alarm symptom and does not form part of the suspected upper gastrointestinal (GI) cancer referral form in the UK. Endoscopy is the gold standard imaging modality for the diagnosis of mucosal lesions in the oesophagus. However, there is no clear data regarding the findings at endoscopy in patients scoped for odynophagia. Mucosal abnormalities even in the presence of typical symptoms of gastro-oesophageal reflux disease, namely heartburn and regurgitation are absent in up to 70%.
AIMS & METHODS: We hypothesise that the presence of odynophagia has a high predictive value of mucosal abnormality at endoscopy and aimed to assess the findings at endoscopy for patients scoped for odynophagia.
A retrospective analysis of all patients who underwent upper GI endoscopy for odynophagia as a primary symptom over an 8-year period (2005-2013) within an NHS Trust in north London was performed. Data was obtained from the Unisoft Endoscopy reporting software. The findings at endoscopy in patients with odynophagia were scrutinized.
RESULTS: 50 patients were endoscoped for odynophagia during the study period. 34 of 50 patients (68%) had oesophageal mucosal lesions (4 Barrett's mucosa, 2 candida oesophagitis, 14 reflux oesophagitis, 6 malignant tumour, 5 oesophageal stricture, 3 oesophageal ulcers). 12% (6 of 50) had oesophageal cancer. A further 10 had hiatus hernia, 1 had a motility disorder and 1 had oesophageal diverticulum.
CONCLUSION: From this study, 68% of patients endoscoped for odynophagia have a positive endoscopic mucosal abnormality. Odynophagia as a symptom has a high sensitivity for abnormal endoscopy. 12% of patients endoscoped for odynophagia had oesophageal cancer. This prevalence is similar to the diagnosis of cancer in patients referred on the 'two week wait upper GI cancer referral form'. We recommend the symptom of odynophagia be classified as an alarm symptom and those presenting with odynophagia all undergo upper GI endoscopy to define the exact mucosal abnormality and exclude oesophageal cancer.
Disclosure of Interest: None declared

P1276 EVALUATION OF SAFETY OF ENDOSCOPIC BIOPSY FOR GASTRIC LESIONS IN ACCORDANCE WITH THE REVISED JAPAN GASTROENTEROLOGICAL ENDOSCOPY SOCIETY GUIDELINES FOR GASTROENTEROLOGICAL ENDOSCOPY IN PATIENTS UNDERGOING ANTITHROMBOTIC TREATMENT

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INTRODUCTION: Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment published by Japan Gastroenterological Endoscopy Society has been revised recently. In the revised guidelines, endoscopic biopsy is allowed without interruption of antithrombotic agents but hemorrhagic risk of endoscopic biopsy for gastric lesions in the patients with continuous use of antithrombotic agents has not been evaluated. We investigated whether bleeding caused by biopsy is more likely to occur in patients with continuous use of antithrombotic agents.
AIMS & METHODS: The aim of this study is to evaluate a risk of bleeding caused by endoscopic biopsy for gastric lesions with continuous use of antithrombotic agents (ATA) in accordance with the revised Japanese guidelines. Subjects were 4197 gastric biopsies in 2059 patients between January 2012 and December 2013. Subjects were classified into three groups according to the status of administration of ATA. Multivariate analysis was performed to identify independent risk factors associated with biopsy-caused bleeding which needed endoscopic hemostasis.
RESULTS: Patients were classified into three groups; those who had not taken antithrombotic agents (no ATA group: 3253 biopsies), those who had stopped these agents completely (stop ATA group: 266 biopsies), and those who had received and continued antithrombotic agents (ATA group: 678 biopsies). Endoscopic hemostasis was performed in 5 biopsies in the no ATA group (0.15%), 9 biopsies in the stop ATA group (3.38%, $P<0.001$, compared with

no ATA group) and 3 biopsies in the ATA group (0.44%, p = 0.15, compared with no ATA group). In multivariate analysis using logistic regression analysis, ATA use ($P < 0.001$, RR 3.61), and biopsy from upper third region of the stomach ($P = 0.001$, RR 5.53) were risk factors for biopsy-caused bleeding but continuous use of ATA did not increase additional hemorrhagic risk even in continuous use of multiple ATA.

CONCLUSION: Use of antithrombotic agents increased risk of bleeding caused by biopsy for gastric lesions but continuous use of antithrombotic agents did not increase additional hemorrhagic risk. Interruption of antithrombotic agents is not necessary even in the use of multiple antithrombotic agents in the endoscopic biopsy for gastric lesion. This study was performed in a single center, and further studies in multiple centers are necessary.

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Disclosure of Interest: None declared

P1277 ENDOSCOPIC DISTINCT FINDINGS OF DIFFERENTIATED-UNDIFFERENTIATED MIXED TYPE EARLY GASTRIC CANCER WITH CONVENTIONAL ENDOSCOPY: COMPARISON WITH PURE DIFFERENTIATED AND UNDIFFERENTIATED TYPES

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INTRODUCTION: Mixed type early gastric adenocarcinomas, which have both differentiated and undifferentiated histopathological component, have been reported to have higher incidence of lymph node metastasis than pure differentiated or undifferentiated types. The endoscopic features to distinguish mixed type early gastric cancer from other subtypes have not been previously described.

AIMS & METHODS: We reviewed endoscopic findings of 1230 early gastric adenocarcinomas that were resected in the National Cancer Center Tokyo between January 2011 and December 2012. The following cases were excluded: lesions located at the esophago-gastric junction, specimens from patients who had received chemotherapy within 1 year before resection, cancers located in the remnant stomach after previous gastrectomy and specimens suspected to be recurrent cancers after previous endoscopic resection. After excluding, total of 1047 lesions were evaluated finally. Endoscopic findings that were evaluated include location in the stomach, relationship with atrophic mucosa, color, clarity of demarcation with surrounding mucosa and endoscopic morphology of the lesions. Histopathological findings were evaluated size, depth, presence/absence of an ulcer and evidence of venous/lymphatic invasion. Histopathologically, these lesions were divided into 3 subtype; pure differentiated type, pure undifferentiated type and mixed type.

RESULTS: One thousand and forty seven lesions were consisted of 156 mixed type, 738 differentiated type and 153 undifferentiated type. When compared to differentiated type early gastric cancer, mixed type is more commonly located in the middle third of the stomach (odds ratio = 1.636, 95% C. I. = 1.077-2.487), located in the atrophic border area or the unatrophic area (odds ratio = 4.237, 95% C. I. = 2.330-7.705), 0-IIc type in Paris classification (odds ratio = 4.282, 95% C. I. = 2.515-7.289), larger than 20mm (odds ratio = 4.226, 95% C. I. = 2.703-6.608), have ulcerative findings (odds ratio = 1.868, 95% C. I. = 1.146-3.043) and have submucosal invasion (odds ratio = 3.237, 95% C. I. = 2.042-5.131) in multivariate analysis. In comparison to undifferentiated type early cancer, mixed type is more commonly located in the atrophic area (odds ratio = 1.839, 95% C. I. = 1.062-3.183), reddish colored (odds ratio = 4.966, 95% C. I. = 2.595-9.504), and have submucosal invasion (odds ratio = 1.935, 95% C. I. = 1.121-3.341). Histopathologically, mixed type cancers have a higher incidence of lymphatic invasion than the other subtypes in univariate analysis (p-value < 0.001).

CONCLUSION: Mixed type early gastric cancers have distinct endoscopic findings.

Disclosure of Interest: None declared

P1278 USEFULNESS OF LAPAROSCOPIC AND ENDOSCOPIC COOPERATIVE SURGERY FOR GASTRIC SUBMUCOSAL TUMORS, INCLUDING ESOPHAGOGASTRIC JUNCTION TUMORS

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INTRODUCTION: A preoperative histopathological diagnosis of gastric submucosal tumor (gSMT) is not only difficult with a regular biopsy, but it often cannot be obtained even by endoscopic ultrasound/fine-needle aspiration (EUS-FNA). In most gSMT cases, treatment indications are determined on the basis of macroscopic signs visible on diagnostic imaging such as EUS or computed tomography, including growth in size over time or surface ulceration, and a definitive diagnosis is only reached after surgical resection. Recently, however, the use of endoscopic submucosal dissection (ESD) for gSMT and the development of laparoscopic and endoscopic cooperative surgery (LECS) have enabled either preservation of the stomach or minimization of the extent of partial resection, and an increasing number of hospitals are introducing it as less invasive, more reliable treatment. In this study, the outcomes following the recent introduction of LECS for gSMT are presented. We evaluated the feasibility and safety of the LECS for SMTs located at the esophagogastric junction (EGJ), compared with non-EGJ SMTs.

AIMS & METHODS: Treatment for gSMT at our hospital broadly follows the algorithm given in the clinical practice guidelines for gastrointestinal stromal tumor (GIST), in which lesions are classified as those for which surgery is absolutely indicated, those for which it is relatively indicated (including endoscopic surgery), and those that should be monitored. Among those lesions for which surgery is relatively indicated, LECS is indicated for lesions that have an intragastric growth pattern, or for which fundusectomy can be avoided despite an extragastric growth pattern. We retrospectively evaluated the outcome of LECS performed in 29 gSMTs, including 6 EGJ SMTs.

RESULTS: Partial gastric resection was performed for 29 patients in our hospital using LECS between its introduction in February 2011 and February 2014. The mean tumor diameter was 31.2 mm (12-72 mm), with a R0 resection rate of 100%, with no postoperative complications of suture rupture, obstruction, or stasis occurring in any patient. On pathology, the tumors were GIST in 20 cases (low 19, high 1), myoma in 5, aberrant pancreas in 2, schwannoma in 1, and cavernous hemangioma in 1. Endoscopic confirmation of the EGJ enabled the extent of resection to be minimized and the stomach to be preserved, And fundusectomy was successfully avoided in all 6 patients in whom tumors were within 2 cm of the cardia. Although there were significantly differences in tumor size and resected specimen size between EGJ SMTs and non-EGJ SMTs, there were no significant differences in outcomes of LECS procedure.

CONCLUSION: LECS for gSMT is easily performed through cooperation between experts in endoscopy and laparoscopy, with good results. LECS is a low-invasive treatment that is both organ-preserving and curative, especially for EGJ SMTs.

Disclosure of Interest: None declared

P1279 THE EFFICACY OF CARBON DIOXIDE INSUFFLATION IN UPPER GASTROINTESTINAL TRACT ENDOSCOPIC SUBMUCOSAL DISSECTION: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED PROSPECTIVE STUDY

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INTRODUCTION: Recently, endoscopic submucosal dissection (ESD) is one of important treatment modality for gastrointestinal tract neoplasm. ESD is performed with using air insufflations, and is associated with abdominal discomfort. It is well recognized that carbon dioxide (CO2) is absorbed quickly in the body than air. CO2 insufflation is expected to be reduces abdominal discomfort and pain after ESD.

AIMS & METHODS: This prospective study was designed to assess the efficacy of CO2 insufflation instead of air insufflation during upper gastrointestinal tract (esophagus: 1, stomach: 53) ESD. From May 2012 to April 2014, a total of 54 consecutive patients were randomly assigned to CO2 insufflation (CO2 group, n = 26) or air insufflation (Air group, n = 28). Abdominal pain after ESD was chronologically recorded on visual analogue system (VAS) score. Also, we recorded of both group that change of abdominal circumference, the amounts of sedatives, and complication rates.

RESULTS: Baseline patient characteristics (age, gender, tumor size, tumor location, tumor histology) were not different in both groups. The mean procedure time was 54.6 minutes in the CO2 group and 57.5 minutes in the Air group, with no statistically significant difference between both groups. Abdominal pain on VAS in the CO2 group vs. Air group was 0.0 vs. 0.3 before the ESD ($p = 0.210$), 3.4 vs. 4.6 one hour after the ESD ($p = 0.131$), 2.7 vs. 3.8 three hours after the ESD ($p = 0.141$), 1.7 vs. 3.3 six hours after the ESD ($p = 0.015$), and 0.8 vs. 2.3 one day after the ESD ($p = 0.002$). In the CO2 group, the abdominal pain on VAS (six hours after the ESD & one day after the ESD) was significantly lower than that of the Air group. The abdominal circumference change in CO2 group shows less variation than in Air group. However, there was no statistical difference between them (0.89 cm vs. 1.42 cm, $p = 0.422$). The amounts of sedative drugs did not differ between the groups ($p = 0.17$). Complication rates were not statistically different between both groups (CO2 group: 19.2%, 5/26; Air group: 28.6%, 8/28) ($p = 0.53$).

CONCLUSION: The amounts of sedatives or complication rates, there were no differences in the two groups. However, CO2 insufflation during upper gastrointestinal tract ESD is less painful for patients than air insufflation.

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P1280 LIMITATIONS OF ESD FOR EARLY GASTRIC CANCER: RETROSPECTIVE ANALYSIS OF FACTORS RELATED TO POSITIVE VERTICAL MARGINS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for early gastric cancer is widely used and contributes greatly to the preservation of gastric function. In clinical practice, however, for cases not indicated for ESD, we occasionally encounter treatments such as diagnostic ESD that are considered overindications. Some cases have incomplete resection because of positive vertical margins and deviate from the rule that ''tumors should be completely resected en bloc.'' In this study, we examined the limitations of ESD (conditions of lesions worthy of full-thickness resection) by identifying the clinicopathological factors involved in positive vertical margins (pVM1) among cases of early gastric cancer resected using ESD.
AIMS & METHODS: A total of 653 lesions of early gastric cancer resected en bloc with ESD at two institutions prior to 2013 were categorized into the pVM1 and pVM0 groups. Factors that influenced pVM1 were extracted by univariate analysis of factors such as patient background (age, sex) and pathological background (site, tumor diameter, macroscopic type, ulcerative findings, pathological invasion depth, degree of differentiation, and vascular invasion) followed by multivariate analysis of those factors.
RESULTS: The pVM1 group included 24 lesions (3.5%). On univariate analysis, tumor diameter ($p < 0.0001$), pathological invasion depth (pT1b; $p < 0.0001$), and degree of differentiation ($p = 0.007$) had a significant effect on pVM1. On multivariate analysis of those factors, pT1b was the only factor that had a significant effect on pVM1. The pVM1 rates in pT1a and pT1b lesions were 0.055% and 19.6% ($p < 0.0001$), respectively, and the diagnostic rate of invasion depth was 92.5% overall and 97% and 84.6% in M-SM1 and SM2, respectively.
CONCLUSION: Submucosal (SM) invasion depth had a significant effect on pVM1. When SM invasive cancer is suspected prior to surgery, full-thickness resection, which is more reliable, is desirable for cT1b gastric cancer not only because of possible lymph node metastasis but also because of the high possibility of incomplete resection when ESD is performed for the primary tumor. The future development of function-preserving or reductive surgeries that bridge the gap between ESD and standard surgery in such cases of potentially invasive gastric cancer is desired.
Disclosure of Interest: None declared

P1281 CONVENTIONAL ENDOSCOPY USING "NON-EXTENSION SIGN" AS A DIAGNOSTIC MARKER IS SUPERIOR TO ENDOSCOPIC ULTRASONOGRAPHY (EUS) FOR DIAGNOSING DEPTH OF INVASION IN EARLY GASTRIC CANCER

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INTRODUCTION: Precise diagnosis of depth of invasion is important for deciding upon the proper treatment for early gastric cancer. The authors previously investigated the possibility of diagnosing depth of invasion with conventional endoscopy using ''non-extension sign'' as a diagnostic marker, and reported that the diagnostic sensitivity, specificity and accuracy for submucosal massive invasion (SM2, 500 micrometers and over) by cancer were 89.7%, 97.7%, 96.6%, respectively [1]. However, it is not clear whether conventional endoscopy is superior to endoscopic ultrasonography (EUS) with regard to discriminating submucosal massively invasive cancer (SM2, 500 micrometers and over) from mucosal cancer (M)/submucosal micro-invasive cancer (SM1, less than 500 micrometers). The present study aimed to compare the diagnostic performance of conventional endoscopy and EUS for SM2 early gastric cancer.
AIMS & METHODS: Consecutive early gastric cancer lesions, in which both preoperative conventional endoscopy and EUS were conducted, were included in the study among 863 lesions (704 patients) treated with endoscopic or surgical resection in our hospital between 2005 and 2012. Lesions were excluded if a definitive diagnosis could not be made through histopathological examination of resected specimens. During conventional endoscopy and EUS, the depth of invasion was diagnosed as M/SM1 or SM2 and immediately recorded into a database. ''Non-extension sign'' was determined as ''positive'' when one of the following two findings is detected according to the conventional endoscopic findings: (i) massive surround elevation; or (ii) mucosal convergence with elevation [1]. The ''non-extension sign'' relate to the increased thickness and rigidity caused by massive submucosal invasion by the cancer. In order to obtain reproducible findings, the stomach was insufflated with a large volume of air to detect non-extensibility. Diagnostic criteria for SM2 were positivity for ''non-extension sign'' on conventional endoscopy and a rupture in the 2nd layer 2 with a tumor echo in the 3rd layer on EUS. Lesions negative for these findings were diagnosed as M/SM1. Histopathological examination was used as the gold standard for diagnosing depth of invasion.
RESULTS: A total of 341 early gastric cancer lesions (M/SM1:SM2 = 284:57) were included in this study. The following results were obtained for the diagnosis of SM2 with conventional endoscopy vs. EUS: sensitivity, 89.5% (95% confidence interval [CI]: 81.5–97.4%) vs. 68.4% (95%CI: 56.3–80.5%) [$p < 0.05$, chi-square test]; specificity, 99.3% (98.3–100%) vs. 83.5% (79.1–87.8%) [$p < 0.0001$]; and diagnostic accuracy, 98.4% (96–99.3%) vs. 80.9% (76.8–85.1%) [$p < 0.0001$].
CONCLUSION: Conventional endoscopy using ''non-extension sign'' showed superior diagnostic performance compared to EUS for the diagnosis of SM2 early gastric cancer. The diagnosis of depth of invasion in early gastric cancer by this conventional endoscopy method has the potential to omit EUS.
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Disclosure of Interest: None declared

P1282 THE STUDY OF LONG TERM OUTCOMES UTILIZING TISSUE-ENGINEERED CELL SHEET TRANSPLANTATION FOR THE PREVENTION OF OESOPHAGEAL STRICTURE

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INTRODUCTION: We reported a regenerative medical approach to prevent oesophageal stricture after endoscopic submucosal dissection (ESD) using **tissue-engineered oral mucosal epithelial cell sheets** in a short term. In this study, long-term outcome has not yet been determined.
AIMS & METHODS: The aim of our study is to reveal the long-term outcome of cell sheet transplantation. Epithelial cells, isolated from the patient's own oral mucosal tissue, were cultured for 16 days using temperature-responsive culture dishes. Then, the autologous cell sheets were endoscopically transplanted onto the bed of the oesophageal ulcer after endoscopic mucosal resection (EMR) and ESD. Results of 10 patients who underwent endoscopic transplantation of oral mucosal epithelial cell sheets from April 2008 through September 2010 were recoded. We analyzed the outcome, the cause, and the endoscopic findings.
RESULTS: All patients were being followed-up. No stricture was detected in any of the patients. The average period of observation was 1.600 days. One patient was deceased because of pancreatic cancer. One patient underwent chemo-radio therapy for farther treatment. One patient underwent surgery due to metastasis of lymph nodes. Only the lymph nodes were dissected, the oesophagus remained intact. From the endoscopic findings: Melanosis was found at the transplanted site in a patient. Strong iodine staining was shown at the transplanted site in a patient.
CONCLUSION: Transplantation of cell sheets has been proven to be a safe method. No patients showed any controlled oesophageal stricture. This study was only an exploratory research, further studies which involve prospective randomized control studies will be needed.
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P1283 LONG-TERM OUTCOMES OF NON-CURATIVE ESD FOR EARLY GASTRIC CANCER: A MULTICENTER RETROSPECTIVE STUDY BY THE OSAKA GUT FORUM

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is currently becoming the major treatment for early gastric cancer (EGC) without risk of lymph node (LN) metastasis. ESD showed better results to remove EGC with relatively high resection rate and low local recurrence rate. On the other hand, when the endoscopic resection (ER) is non-curative, surgical treatment is required. Some patients, however, do not undergo surgery after non-curative

ER, because of their comorbidity, refusal of surgery, and so on. Long-term follow-up data and prognosis factors are needed for the case of non-curative ER.
AIMS & METHODS: The aim of this study is to investigate long-term outcome and evaluate the factors related to prognosis of non-curative ER. This is a retrospective study in consecutive patients with EGC underwent ESD from March 2003 to November 2010 in 10 institutes in the Osaka Gut Forum. We defined curative resection as the lesions meeting expanded criteria with R0 resection. Expanded criteria is following; 1) specified mucosal cancer without ulcer findings irrespective of tumor size, 2) mucosal cancer without ulcers 3 cm diameter or smaller, and 3) minute submucosal invasive cancer 3 cm diameter or smaller. We studied the overall and relapse-free survival rate using Kaplan–Meier methods, and the prognosis factors using Cox's regression model.
RESULTS: We treated 1468 patients with EGC by gastric ESD. Of them, 174 patients (174 lesions) resulted in non-curative resection. One hundred seven patients were underwent surgical treatment and 67 patients were observed. These patients had median age of 72 years (mean, 71.2 years; range, 39-90 years), and a male/female ratio of 132:42. Seventy-two lesions were mucosal cancer and 102 lesions were submucosal cancer. Median follow-up period was 58.5 months. There was one gastric cancer-related death in the case of surgical treatment. The 5-year overall survival rate and relapse-free survival rate were 91% and 86%, respectively, and were not significantly different between surgical and non-surgical groups. The most important factor related to relapse-free survival was age (hazard-ratio: 3.37), followed by lymphatic-vascular invasion (2.90), and depth of tumor (2.45).
CONCLUSION: The patients with non-curative endoscopic resection for EGC generally require additional surgery to avoid recurrence. This study, however, showed no significant advantage of surgery within at least 5 years after ER, even though selection bias can exist. There may be no merit of an additional operation in the patients without lymphatic-vascular invasion.
Disclosure of Interest: None declared

P1284 MULTICENTER, PROSPECTIVE TRIAL OF MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING FOR STAGE DIAGNOSIS OF SUPERFICIAL ESOPHAGEAL CANCER

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INTRODUCTION: Among superficial esophageal squamous cell carcinoma (SESCC), cancer invading within the epithelium and the lamina propria mucosa (T1a-EP/LPM) is considered as the indication of endoscopic resection, while surgical resection or chemoradiotherapy is recommended for cancer invading beyond the muscularis mucosa (≥T1a-MM). Many retrospective studies have reported that magnifying endoscopy with narrow band imaging (ME-NBI) can predict invasion depth of SESCC well. However, the true additional effect of ME-NBI on white light imaging (WLI) for diagnosis of invasion depth is unclear because of a lack of prospective data. Thus, a prospective study of ME-NBI was conducted in the present study.
AIMS & METHODS: Patients with SESCC were prospectively enrolled from 7 Japanese institutions. Enrolled patients received primary WLI followed by ME-NBI and the report of primary WLI was completed before the start of ME-NBI by an assistant. Diagnoses of invasion depth by each tool were divided into T1a-EP/LPM and ≥T1a-MM and then collated with the final pathological diagnosis by an independent pathologist blinded to the clinical data. All endoscopists attended the consensus meeting and were trained before the trial to standardize diagnosis among examiners, and this trial was started after achievement of a mean k value ≥0.6 among all participating examiners. The primary end point was diagnostic accuracy for invasion depth.
RESULTS: In total, 55 patients with SESCC were enrolled from June 2011 to October 2013, and the results of WLI and ME-NBI were finally analyzed for a total of 49 lesions. Forty one patients underwent endoscopic submucosal dissection and 8 patients did esophagectomy as the initial treatment. Final pathological diagnosis of invasion depth was T1a-EP/LPM in 31 lesions and ≥T1a-MM in 18 lesions. The accuracy of invasion depth in WLI and ME-NBI was 71.4% and 67.3% ($P=0.661$), respectively. Sensitivity for ≥T1a-MM was 61.1% in both WLI and ME-NBI ($P=1.000$), and specificity for ≥T1a-MM was 77.4% in WLI and 67.7% in ME-NBI ($P=0.393$). Moreover, we will present other data of subset analyses in this meeting.
CONCLUSION: ME-NBI did not demonstrate the additional effect on WLI for diagnosis of invasion depth of SESCC. Further development of diagnostic tool is hopeful in the future.
Disclosure of Interest: None declared

P1285 A NOVEL SELF-ASSEMBLED PEPTIDE SOLUTION FOR PREVENTION OF POST PROCEDURE BLEEDING AND PROMOTING ULCER HEALING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC LESIONS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) can remove early stage gastric epithelial neoplasms *en bloc* those that are large, with scarring, however, post-ESD bleeding has been reported in 4-7% of patients. Gastric ESD-induced ulcer is generally treated with proton pump inhibitor (PPI) for at least 8 weeks after ESD. Recently, a self-assembled peptide solution, which has a function as an extracellular matrix scaffold material to replace collagen has been developed.
AIMS & METHODS: The aim of this clinical trial was to assess the safety and efficacy of a novel self-assembled peptide solution for ESD-induced ulcers. Consecutive patients who underwent gastric ESDs enrolled in this study. Patients receiving antithrombotic therapy were included, but such medications were no longer being administered prior to the procedures. Cases with perforation and coagulopathy (INR > 3) despite anticoagulation management after heparin bridge therapy (HBT) were excluded. For every 1 cm of tumor, 1 mm^3 of fully-synthetic peptide solution that self-assembles at physiological pH and forms a gel comprising a network of nanofibers (PuraMatrix™; 3-D Matrix, Ltd) was applied to the ESD-induced ulcer using a catheter immediately after the procedure. Single dose PPI was administered for 8 weeks beginning the morning of the procedure. Ulcer stages were evaluated by endoscopy as active, healing or scarring at 1, 4 and 8 weeks after ESDs. The primary endpoint was the rate of post-ESD bleeding. The secondary endpoints include the transitional rate to healing and scarring stages of gastric ESD-induced ulcers according to the Sakita-Miwa classification.
RESULTS: Of 47 patients recruited, 45 patients with 51 lesions were enrolled for outcome analysis and 2 patients were excluded due to 1 perforations and 1 with coagulopathy. Fourteen patients (31%) were previously on antithrombotic therapy including 5 (11%) requiring HBTs. The mean size of resected specimen was 40±16mm. The rate of post-ESD bleeding was 2.0% (1/51, 95%CI, 0.03 to 10.3). A post-ESD bleeding was successfully managed endoscopically without needed blood transfusion. Transitional rate to healing stage at 1 week was 96%. Follow up endoscopies demonstrated scaring stage in 17% and 98% at 4 and 8 weeks respectively. There were no adverse effects related with PuraMatrix use.
CONCLUSION: The use of this novel self-assembled peptide solution may help reduce post-ESD bleeding rate and promote ulcer healing. Further studies are needed to fully evaluate its efficacy. (UMIN Clinical Trials Registry: 000011548)
Disclosure of Interest: None declared

P1286 FEASIBILITY OF IN VIVO ENDOCYTOSCOPY IN THE DIAGNOSIS OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA: A MULTICENTER STUDY

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INTRODUCTION: The endocytoscopy system (ECS) enables observation of cell nuclei and real-time microscopic diagnosis. High-quality in vivo imaging and accurate diagnosis of ECS images are essential for the practical application of this modality.
AIMS & METHODS: This study sought to determine the diagnostic visualization capabilities of in vivo ECS in superficial esophageal squamous cell carcinoma (SCC) and to reveal the diagnostic accuracy of pathologists. Patients with superficial esophageal SCC or high-grade intraepithelial neoplasia (HGIN) larger than 10 mm were targeted. Endoscopists selected 3 ECS images each of cancerous and non-cancerous lesions in each patient, and central pathologists verified both sets of images and the corresponding parts in the specimens. The ECS images were randomly assigned in each case and subsequently evaluated by 5

pathologists blinded to individual cases. Diagnostic criteria were cellular or structural atypia, specifically nuclear enlargement, anisokaryosis, high nuclear density, and intercellular boundary. The primary endpoint was the diagnostic rate of cancerous lesions on ECS images determined by the pathologists (sensitivity). The secondary endpoints were the inter-observer agreement among the 5 pathologists (multi-rater κ coefficient), the percentage of ECS images useful for diagnosis, and the diagnostic rate of non-cancerous lesions (specificity). Using a prototype integrated endocytoscope, ECS diagnosis was made based on that previously reported by Inoue et al. that defined ECA1–3 as a non-cancerous lesion and ECA4–5 as a cancerous lesion.
RESULTS: Between May 2011 and January 2012, 72 patients were registered at 9 medical facilities. After excluding patients who declined to participate or patients without an available specimen, 68 patients were enrolled. Mean tumor diameter was 22.5 mm (range, 10–60 mm). Fifty-five lesions were squamous cell carcinomas and 13 were HGIN. The diagnostic sensitivity and specificity were 88% (95% CI, 77.2–94.5) and 100% (95% CI, 94.5–100), respectively. The multi-rater κ coefficient was 0.88 (95% CI, 0.80–0.96). In addition, 96% (95% CI, 87.6–99.1) of the ECS images were suitable for diagnosis.
CONCLUSION: In vivo ECS images provided high visualization, with high sensitivity and high specificity in the diagnosis of esophageal squamous cell carcinoma by pathologists. Given the high inter- observer agreement, ECS appears to be useful for the real-time endoscopic histological diagnosis of esophageal squamous cell carcinoma.
Disclosure of Interest: None declared

P1287 LONG TERM OUTCOMES OF ENDOSCOPIC RESECTION FOR SUPERFICIAL PHARYNGEAL CARCINOMAS AND EFFICACY OF DOUBLE SCOPE ESD

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INTRODUCTION: For recent advance in image enhanced endoscopy, such as Narrow Band Imaging (NBI), we have more frequent opportunities for early detection of superficial pharyngeal cancer (SPC). Endoscopic resection has been proposed as a safe and effective treatment for SPC. We previously reported endoscopic submucosal dissection (ESD) yielded higher rate of complete resection, and lower rate of local recurrence compared with endoscopic mucosal resection (EMR). But ESD was more time consuming and more frequently complicated by laryngeal edema.
AIMS & METHODS: This study includes consecutive 113 patients treated by endoscopic resection for SPC from October 2006 to December 2013 in one referral cancer center. We treated SPC in first period by EMR, in second period by conventional ESD (cESD) and in recent period by double scope ESD (dsESD), in which we use second thin endoscopy for good counter traction. We compared outcome of these three methods for short term outcome, and we also showed long term outcome after endoscopic resection for SPC.
RESULTS: A total of 166 SPCs in 113 patients (Male: 100, Female: 13) were treated by endoscopic resection (EMR: 55, cESD: 32, dsESD: 79). The size of tumor was 18mm in average, which invaded to CIS/SEP/MP 108/57/1 respectively. All lesions were diagnosed squamous cell carcinoma. In dsESD, the procedure time was shortened compared to cESD (82 min vs 111 min, $p<0.05$) although the rate of laryngeal edema was not decreased (16% vs 9%). It may be because we treat more complicated cases recently. En bloc resection rate and complete resection rate for EMR, cESD and dsESD were 38%, 91%, 97% ($p<0.01$) and 29%, 63%, 84% ($p<0.01$), respectively. Local recurrence was detected in 3 cases after EMR and in 1 case after cESD. We treated by re-EMR in 2 cases, by RT in 1 case and by surgery in 1 case. LN metastasis was detected in 2 patients who were treated by surgical neck dissection. All the salvage treatment was successfully performed. For long time outcome with median follow–up period of 30 months (range 2-86 months), the overall survival rate at 5 years was 88% (95%CI, 82-94), no patient died of SPC. The cumulative development rate of multiple cancers in pharyngeal mucosal sites at 5 years was 27% (95%CI, 18-35). The pharynx was preserved in almost all the patients except for one case who had surgery for local recurrence.
CONCLUSION: Here we showed dsESD was a superior method in treating SPC, for achieving both en bloc and complete resection and reducing the procedure time. Endoscopic resection for SPC is organ preserving with no loss of function and effective treatment with curative intent.
Disclosure of Interest: None declared

P1288 THE USEFULNESS AND COST-EFFECTIVENESS OF NON-TARGETED GASTRIC BIOPSIES: ARE WE TOO FORWARD WITH THE FORCEPS?

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INTRODUCTION: There are no agreed guidelines on indications for endoscopic gastric biopsies. Taking and reporting gastric biopsies is costly, and there is a shortage of trained pathologists in the UK. We investigated whether non-targeted gastric biopsies contributed to cost-effective and best patient management.
AIMS & METHODS: We retrospectively analyzed all endoscopic gastric biopsies taken across two teaching hospital sites in a 3-month period, 2/1/13-31/3/13; details were obtained from our histopathology database. For each set of biopsies taken we accessed our endoscopy database for patient demographics, reason for endoscopy, appearance of gastric mucosa, Urease-based Helicobacter test (UBHT) result if obtained, and the grade of endoscopist (Consultant, Registrar or Nurse Specialist). The electronic patient medical record was reviewed to assess whether the biopsy changed the patient's diagnosis or management.
A targeted biopsy was defined as the presence at OGD of a polyp, ulcer or other lesion documented in the report. Non-targeted biopsy was any other appearance, including gastritis. The cost of biopsy included histopathology manpower and processing costs. We looked separately at the cost of UBHT testing plus forceps use.
RESULTS: During the 3-month period 2.265 OGDs were performed. 408 patients had gastric biopsies taken, resulting in 419 biopsy sets (some had multiple endoscopies), an overall biopsy rate of 18.5%. The age range was 18-97 years (median 63 years). 22% of endoscopists were consultants, 33% registrars and 45% nurse specialists. Of the 419 biopsies, 43% were targeted (n = 181) and 57% were non-targeted (n = 238).
Of the non-targeted biopsies, 0.8% (n = 2) revealed an adenocarcinoma, both these biopsies being from the same man who was under surveillance for a strong family history of gastric carcinoma. 70% (n = 168) showed a form of gastritis, 16% (n = 37) showed *H.pylori*, and 13% (n = 31) had normal histology. Of the non-targeted biopsies, 94% (n = 223) had no change to their diagnosis or management based on histology. 1% (n = 2) had a gastrectomy, which was the one man under surveillance, 3% (n = 8) had eradication therapy based on histology as UBHT was not performed, and 2% (n = 6) had recommendation to GP to give eradication therapy if not already given, as result of the UBHT test was unclear. The cost of processing each biopsy set was £103.51. The annual cost of non-targeted biopsies where result did not change the management (n = 223) was £92.330. This compared to £6.90 for each UBHT which would amount to only £6.154 per annum, creating an annual potential saving of £86.177.
CONCLUSION: The majority of non-targeted gastric biopsies did not contribute to patient management. Limiting non-targeted gastric biopsies could save significant resources, as well as contributing to patient safety by limiting unnecessary biopsies.
Disclosure of Interest: None declared

P1289 A PILOT STUDY ON THE ENDOMICROSCOPIC ASSESSMENT OF TUMOR EXTENSION IN BARRETT'S ESOPHAGUS-ASSOCIATED NEOPLASIA PRIOR TO ENDOSCOPIC RESECTION

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INTRODUCTION: Barrett's esophagus (BE)-associated neoplasia can be treated by endoscopy, but accurate assessment of neoplastic lesions in BE is challenging.
AIMS & METHODS: This study aimed to investigate the role of confocal laser endomicroscopy (CLE) as an adjunct in the endoscopic treatment of BE-associated neoplasia by assessing lateral and sub-squamous tumor extension (SSTE). In the context of a prospective single arm clinical pilot trial patients referred for endoscopic resection of BE-associated neoplasia (high grade dysplasia and esophageal adenocarcinoma) underwent high-definition white light endoscopy with narrow band imaging (NBI), followed by CLE-mapping of suspected neoplastic lesions prior to endoscopic mucosal resection (EMR) or endoscopic submucosal resection (ESD) depending on lesion size and anticipated histology.
RESULTS: In 7/38 (18%) patients CLE revealed additional neoplastic tissue as compared to prior white light and NBI – two concomitant lesions, two cases of lateral tumor extension within the Barrett's epithelium and three cases of previously undetected SSTE. Overall, en-bloc resection (tumor-free lateral margin) was achieved in 28/34 neoplastic lesions (82%) and complete resection (tumor-free lateral and basal margins) in 21/34 neoplastic lesions (62%).
CONCLUSION: CLE-assisted endoscopic resection of BE-associated neoplasia was safe and effective in this study, proved by a high additional diagnostic yield of CLE (including visualization of occult SSTE) and a favorable en-bloc resection rate. The clinical value of CLE for assisting endoscopic therapy of BE-associated neoplasia deserves further evaluation in randomized controlled trials.
Disclosure of Interest: None declared

P1290 DIFFERENCE IN ENDOSCOPIC VACUUM-ASSISTED CLOSURE (E-VAC) AND ESOPHAGEAL STENTING IN POSTSURGICAL GASTROESOPHAGEAL LEAKAGE

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INTRODUCTION: After esophagectomy or proximal gastrectomy, the reported incidence of esophageal leakage ranges from 5% to almost 30%. Gastroesophageal leakage increases morbidity and mortality rates, and several treatments are used to control leakage such as approximation with endoclipping, injection with tissue adhesive agents of histoacryl or fibrin glue, and endoscopic implantation with self-expendable metal stents (SEMS). But these treatments included endoluminal esophageal stent always could not be successful. E-VAC therapy has recently been reported as an effective treatment modality for postsurgical anastomotic leakage.
AIMS & METHODS: The aims of this study are to show the relative differences therapy of between esophageal stenting and E-VAC in treating postsurgical gastroesophageal leakage.

From 2006 to 2014, 13 patients treated with postsurgical gastroesophageal leakage in one medical center were evaluated (Male: Female = 11: 2). Mean age were 71.4 ± 5 years in E-VAC group and 63.1 ± 6 years in stenting group. Among the patients, 7 patients were treated by E-VAC. It has been proceeded endoscopically placing drainage tube armed with size-adjusted sponge in the necrotic cavities, and then applied continuous suction of mean pressure 125 mmHg. We changed sponges and drain twice a week. On the other hand, 6 patients were treated by covered SEMS. In stenting group, we removed the stent after 6 to 8 weeks because of difficulty to remove stent due to tissue hyperplasia. The followings were compared: clinical success rate, recurrence, mean closure time and mean hospital stay.

RESULTS: The 7 patients treated with E-VAC were all treated successfully. Of the 6 patients treated with stenting, 5 patients of them were treated successfully. However, one patient in stenting group died of cancer progression without control of leakage by stenting. One patient in the stenting group after 69 days and one patient in the E-VAC group after 63 days recurred. They were treated with same method. Mean closure time was 17.8 ± 17 days in E-VAC group and 16.8 ± 14 days in stenting group. Mean hospital stay were 33 ± 30 days in E-VAC group and 50.5 ± 29 days in stenting group.

Table 1. Postsurgical gastroesophageal leakage treated by endoscopic vacuum closure (E-VAC) and esophageal stenting: characteristics and treatment in 13 patients.

	E-VAC Group	Stenting Group
Age (year), mean ± SD	71.4 ± 5	63.1 ± 6
Male / Female	5 / 2	6 / 0
Clinical Success Rate	100 %	83 %
Closure Time, mean ± SD	17.8 ± 17	16.8 ± 14
Hospital Stay, mean ± SD	33 ± 30	50.5 ± 29

CONCLUSION: E-VAC therapy might be effective treatment option for postsurgical gastroesophageal leakage.

Disclosure of Interest: None declared

P1291 PROPER MUSCLE LAYER DAMAGE AFFECTS ULCER HEALING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is the established therapy for superficial gastrointestinal neoplasms. As the larger ulcers associated with ESD, management of artificial ulcers has become more important. However, the relationship between ulcer healing factors and treatment is still unclear.

AIMS & METHODS: We aimed to evaluate the ESD-related artificial ulcer reduction ratio at 4 weeks to assess the factor associating with ulcer healing after ESD that may lead to optimal treatments.

Between January 2009 and December 2013, a total of 375 lesions fulfilled the expanded criteria for ESD. After exclusion, 328 lesions were divided into two groups based on the ulcer reduction rate and analyzed: Group A, rate <90% and Group B, rate ≥90%. These two groups were compared based on clinicopathological / endoscopic features, concomitant drugs, and treatments.

RESULTS: The ulcer reduction rate was significantly correlated with factors related to the ESD procedure, i.e., procedure time, submucosal fibrosis, and exposure of the proper muscle layer, in univariate analysis. Multivariate logistic regression analysis showed that submucosal fibrosis (F2) ($p = 0.03$; OR, 16.46; 95% CI, 1.31–206.73) and exposure of the proper muscle layer ($p = 0.01$; OR, 4.27; 95% CI, 2.04–8.92) were statistically significant predictors of delayed healing.

CONCLUSION: This single-center retrospective study indicated that ESD-induced artificial ulcer healing was affected by submucosal fibrosis and exposure of the proper muscle layer, which induced damage to the contraction of the muscle layer.

Disclosure of Interest: None declared

P1292 LENS COATING WITH LIQUID CERAMICS IS USEFUL TO MAINTAIN GOOD VISIBILITY FOR TRANSNASAL SMALL-CALIBER ESOPHAGOGASTRODUODENOSCOPY

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INTRODUCTION: Unsedated transnasal small-caliber esophagogastroduodenoscopy (TN-EGD) is used to examine the upper gastrointestinal tract and its feasibility as compared to conventional transoral EGD has been shown. However, a well-known limitation encountered with TN-EGD is poor image quality as compared to conventional endoscopy due to the small size of the CCD, while insufficient lens cleansing is related its small caliber water jet nozzle. Poor visibility may affect endoscopic diagnostic accuracy, thus maintenance of good visibility is very important. Liquid ceramics coating is known to be an effective means to keep glasses or lenses clean because of its hydrophilic characteristic. Using a randomized prospective double-blind trial, we evaluated the efficacy of lens coating with liquid ceramics for TN-EGD.

AIMS & METHODS: Basic *in vitro* (Study I) and randomized prospective clinical (Study II) studies were performed. Two groups of small-caliber endoscopes, with and without ceramics coating (C- and N-group, respectively), were prepared. For lens coating, we applied a very small quantity of liquid ceramics onto the lens, then completely wiped it off with gauze.

Study I: Endoscopic lenses in the C- and N-groups were soiled with lard oil and washed using a lens cleansing procedure that consisted of air and subsequent washing solution from the endoscopic jet nozzle, then photographs of a test chart were obtained with them. Image quality was judged by 3 experts who had no knowledge of grouping.

Study II: We randomly assigned 115 patients who underwent TN-EGD to the C- and N-groups. TN-EGD procedures were performed by 3 expert endoscopists, who judged the level of endoscopic visibility using a 5-grade visual analogue scale after TN-EGD. This study was approved by the ethics committee of Izomo City General Medical Center. Written informed consent was obtained from all participants.

RESULTS: In Study I, photographic image quality was significantly better in the C-group as compared to the N-group ($P < 0.05$). In Study II, the level of endoscopic visibility in the C-group was also significantly superior ($P < 0.05$).

CONCLUSION: For EGD with transnasal small-caliber endoscopy, lens coating with liquid ceramics may be useful to maintain a good visual condition and improve diagnostic accuracy.

Disclosure of Interest: None declared

P1293 THE EFFIECTIVENESS OF CHROMOENDOSCOPIC METHOD USING AN ACETIC ACID–INDIGOCARMINE MIXTURE FOR SUPERFICIAL FLAT-TYPE (0-IIB) EARLY GASTRIC CANCERS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been established as a standard treatment for early gastric cancer (EGC) in Japan. The advantage of ESD is that it enables the *en-block* resection of large lesions, thereby allowing the accurate pathological evaluation of the resected lesions and avoidance of recurrence after piecemeal resection. Therefore, it is important to accurately determine the extent of gastric cancer invasion and resect the cancer. However, in superficial flat-type gastric cancer (0-IIb type), it is often difficult to determine the extent of tumor invasion.

AIMS & METHODS: We previously reported the effectiveness of chromoendoscopic method using an acetic acid–indigo carmine mixture (AIM) in one hundred gastric cancer cases. The aim of the present study was to estimate the accuracy of this chromoendoscopic method using an acetic acid–indigo carmine mixture (AIM) in superficial flat-type cases.

Studied were 112 flat-type EGC lesions. EGC were initially observed by white light (WL) after which indigo carmine (IC) solution was sprinkled onto the gastric mucosa. Images by WL and IC observation were recorded by a digital filing system. After washing away IC solution with water, AIM solution was sprinkled onto the gastric mucosa and images were recorded. Margin lines of EGC determined by each observation were drawn on recorded images by graphic software for comparison with resected specimens. First, diagnostic accuracy of the endoscopic images with each modality was independently evaluated with regard to the recognition of the entire contact border around the lesions by two endoscopists who have extensive experience in the diagnosis and management of EGC. Second, the agreements between the endoscopic views with efficient modality were evaluated and, finally, the evaluations of the two endoscopists were compared and, in case of any conflicts in the findings, an agreement was reached through discussion, and margin lines of EGC determined by each observation were drawn on the recorded images by graphic software.

After lines were similarly drawn on images of resected specimens, the extent of the lesions was compared with that determined by endoscopic images.

RESULTS: We found that AIM chromoendoscopy enabled us to achieve a very clear enhanced visualization of flat-type EGC lesions. Diagnostic accuracy of WL, IC, and AIM observations were 23.0%(n = 26), 54%(n = 60) and 82%(n = 92), respectively. No adverse events occurred with the AIM method. Diagnostic accuracy of AIM observation was significantly higher than that by WL observation ($P < 0.0001$) and IC observation ($P < 0.0001$).

CONCLUSION: We can achieve clearer visualization of the tumor extent by the AIM chromoendoscopy than by the IC method.

Disclosure of Interest: None declared

P1294 THE RESULT OF GLASGOW-BLATCHFORD SCORE COMPARED TO OTHER SYSTEMS IN ACUTE UPPER GASTROINTESTINAL BLEEDING

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INTRODUCTION: Upper gastrointestinal bleeding has been a major cause of hospital admission and mortality throughout the world. Therefore prediction of the risk in the patients with acute upper gastrointestinal bleeding (AUGIB) is important subject. Several scoring systems have been used to identify patients with acute upper gastrointestinal bleeding who are at a high risk. Glasgow-Blatchford score (GBS) predicts the need for medical intervention (such as

blood transfusion or endoscopy) by using the results of blood tests and vital sign. Rockall score (RS) is calculated by endoscopic finding, age, comorbidity, vital sign and used to predict outcome. But this scoring system has disadvantage of complicated calculation.
Recently AIMS65 is the simple risk scoring system that identified five factors such as serum albumin, international normalized ratio, altered mental status, systolic blood pressure and age. We studied retrospectively the usefulness of these scoring systems and compared these systems. We hope that our study will help for assessing the need for clinical intervention, re-bleeding and death in cases of AUGIB.
AIMS & METHODS: We found 384 patients who underwent urgent endoscopy due to UGIB from December 2008 to August 2013 at Pusan national university Yangsan Hospital. Of these patients, 223 patients were satisfied with UGIB and included in this study. All 223 patients were assessed by GBS, RS and AIMS65. At the same time the patients who needed the clinical intervention or died in-hospital within 30 days were defined as unfavorable outcome patients. Then the result of each scoring system was compared with clinical outcome.
RESULTS: Overall in-hospital mortality was 2.2% (5/223). In our total 223 patients, 43.9% (98/223) were classfied as unfavorable outcome patients. The re-bleeding rate was shown as 9.4% (21/223). Compared to these scoring system, there was little significant difference in predicting the need of therapeutic intervention and death. But GBS was significantly elevated in unfavorable outcome patients ($p = 0.0119$). Also GBS was superior to the other scores for predicting the need for packed red blood cell transfusions ($p = 0.0134$).
CONCLUSION: In acute upper gastrointestinal bleeding, GBS, RS and AIMS65 scoring system can predict need for intervention and unfavorable clinical outcome in AUGIB. GBS was more advantageous to the prediction of blood transfusion. On the other hand, these systems were similar to predict clinical outcome.
Disclosure of Interest: None declared

P1295 EVALUATION OF SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITHOUT CESSATION OF ANTITHROMBOTIC AGENTS

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INTRODUCTION: New guidelines for gastroenterological endoscopy considering the associated risk of thrombosis were revised in 2012, by the Japan Gastroenterological Endoscopy Society. The new edition of the guidelines includes discussions of gastroenterological hemorrhage associated with continuation of antithrombotic therapy, as well as thromboembolism associated with withdrawal of antithrombotic therapy. Therefore, we aimed to assess the feasibility of endoscopic submucosal dissection (ESD) without cessation of antithrombotic agents.
AIMS & METHODS: This was a retrospective study from a single institution. This study enrolled 330 neoplasms (47 esophageal neoplasms, 161 gastric neoplasms and 122 colorectal neoplasms) in 310 patient who had ESD from April 2013 to May 2014. 75 patients who were receiving antithrombotic agents because of their high-risk status for a thromboembolic event (after implantation of coronary stent, after valve replacement, or a previous history of thromboembolic event or heart failure due to atrial fibrillation) were involved. We evaluated the rate of post-ESD severe bleeding complications (overt hematemesis/hematochezia, a drop of hemoglobin > 2g/dL from baseline, or requirement of endoscopic hemostasis, and/or transfusion).
RESULTS: Of 310 patients, 58 took antiplatelet agent, among whom 13 continued aspirin, 4 replaced with heparin. 26 took anticoagulant agent, among whom 22 replaced with heparin. Of 310 patients, 9 took antiplatelet agent and anticoagulant agent in combination therapy. This 9 cases was performed ESD with continued aspirin under replacement of heparin. Post-ESD bleeding occurred in 4 subjects (1.2%) including 2 from the continued aspirin group, 1 from the withdrawal antiplatelet agent group who had a renal dysfunction, and 1 from the no-antithrombotic agents group who was big specimen diameter. Univariate analysis revealed antiplatelet therapy (OR = 13.69, 95%CI: 1.24-348.24, $p = 0.0036$) was associated with post-ESD bleeding, but continued aspirin (OR = 8.00, 95%CI: 0.49-247.40, $p = 0.059$) was not statistically significant. All post-ESD bleeding cases were treated successfully by endoscopic hemostasis. Emergency surgery was not required in any of the cases. Blood transfusion was needed in 1 patient (0.3%). Among 75 subject who had antithrombotic therapy, 2 developed acute cerebral infection (2.6%) including 1 from the continued aspirin group, 1 from the withdrawal antiplatelet agent group. No event occur in the anticoagulant group replaced with heparin.
CONCLUSION: ESD without cessation of antithrombotic agents, can be acceptable if performed carefully for patients with antiplatelet therapy.
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Disclosure of Interest: None declared

P1296 DETECTION OF COLONIC POLYPOID LESIONS BY PET OR PET-CT IN PHYSICAL CHECK-UP POPULATIONS

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INTRODUCTION: A 18-Fluorodeoxyglucose positron emission tomography (FDG-PET) or PET-computed tomography (PET-CT) is used clinically detect malignant lesions. The efficacy of PET or PET-CT comparing colonoscopy to detect colonic polypoid lesions including premalignant adenomas and colon cancers is not well defined in large number of populations.
AIMS & METHODS: The aim of this study is to evaluate the efficacy of PET or PET-CT comparing standard colonoscopy to detect colonic polypoid lesions in physical check-up examinees.
Methods: A total of 4063 persons with synchronous evaluation of PET or PET-CT with colonoscopy were enrolled between 2003 and 2010 for the physical checkup at our single health promotion center.
RESULTS: Colonoscopy with biopsy confirmed the adenomas and cancers in 1212 of 4063 examinees. The focal FDG uptake by PET or PET-CT showed in 19 examinees of positive colonoscopic findings. Sensitivity, specificity, positive predictive value, and negative predictive value to detect colonic polypoid lesions including adenomas and cancers by PET or PET-CT comparing with standard colonoscopy were 1.6%, 99%, 82%, and 70%, respectively. The sensitivity of PET or PET-CT according to the adenoma size was increased (1.7% for 1-10mm, 3.3% for 11-20mm, 40% for $>$20mm). A total of 8 patients had high grade dysplasia ($n = 1$), rectal neuroendocrine tumors ($n = 5$) or colon cancers ($n = 3$). Among them, only 1 patient with 5cm sized advanced colon cancer showed FDG-PET uptake.
CONCLUSION: In physical check-up examinees, a PET or PET-CT comparing with conventional colonoscopy did not detect colonic advanced adenomas, rectal neuroendocrine tumor (rectal carcinoid) or early colon cancers smaller than 1 cm. Therefore, detection of colonic polypoid lesions except advanced colon cancers by PET or PET-CT was insufficient in physical check-up populations.
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Disclosure of Interest: None declared

P1297 WATER EXCHANGE ATTENUATES REAL-TIME INSERTION PAIN AND POTENTIALLY ENHANCES COST SAVINGS BY PROMOTING COMPLETION OF UNSEDATED COLONOSCOPY

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INTRODUCTION: We tested the hypothesis that water exchange (WE) produces significantly lower insertion pain scores than air insufflation (AI) and water immersion (WI).
AIMS & METHODS: A 2-center RCT stratified enrolment of diagnostic and screening patients given on-demand sedation. Primary outcome: real-time maximum insertion pain recorded by an unblinded observer. Before discharge patients reported recalled pain to a blinded observer and guessed the method used.
RESULTS: 576 patients were randomized to AI ($n = 193$), WI ($n = 197$), WE ($n = 186$). Patients' correct guesses were $<33\%$. Table 1 shows the primary outcome and recalled pain (Visual analogue scale: 0 = none, 10 = worst). Comparison of primary outcome and recalled pain in unsedated patients (Pearson correlation 0.6, $p < .0005$) confirmed its validation. Uniquely, WE has no significant investigator differences in mean pain score during insertion ($p < .48$), and lower standard deviation. Recalled pain did not reveal differences in the three groups. Individual colonoscopist's real-time pain scores, however, were susceptible to type II errors due to small numbers. Since adoption of WE, ~85% of colonoscopies are unsedated. Immediate return to routine activities after successful unsedated colonoscopy was feasible. Estimates of resources saved on-site: patients, € 2.074; nursing time € 3.121; pharmacy expenses, € 194. At home, patients € 89.731. Table 1: Investigators' real-time and recalled pain, mean (95% CI). M, maximum; R, recalled; CI, confidence interval; SD, standard deviation. ≠, ANOVA.

Table to abstract P1297

Investigators	Pain	WE	WI	AI	P ≠
1	M	2.2 (1.6-2.8)	4.8 (4.0-5.6)	5.5 (4.8-6.2)	<0.0005
	R	1.9 (1.4-2.4) n=46	3.3 (2.4-4.1) n=40	3.9 (3.2-4.6) n=47	<0.0005
2	M	3.0 (2.3-3.7)	3.5 (2.7-4.2)	4.3 (3.8-5.2)	0.048
	R	2.2 (1.7-2.8) n=46	2.8 (2.1-3.5) n=43	2.8 (2.0-3.6) n=48	0.386
3	M	2.3 (1.0-3.6)	2.3 (1.0-3.6)	4.0 (2.9-5.1)	0.096
	R	0.5 (0.4-1.4) n=14	0.1 (0.1-0.3) n=19	0.5 (0.1-1.0) n=13	0.486
4	M	2.2 (0.8-3.6)	2.3 (1.6-2.9)	2.8 (2.0-3.5)	0.574
	R	0.2 (0.1-0.6) n=28	0.1 (0.1-0.3) n=12	0.2 (0.1-0.4) n=29	0.766
5	M	2.9 (1.8-4.0)	3.7 (2.3-5.1)	3.5 (2.2-4.8)	0.699
	R	0.7 (0.1-1.5) n=13	0.8 (0.1-1.6) n=16	0.3 (0.1-0.8) n=20	0.509
6	M	2.4 (1.6-3.2)	2.6 (1.5-3.7)	3.4 (2.4-4.5)	0.255
	R	0.2 (0.1-0.4) n=23	0.2 (0.1-0.4) n=20	0.6 (0.1-1.2) n=33	0.066
Within group, *P* value≠ (SD)		M 0.48 (2.1) R <0.0005 (1.7)	M <0.0005 (2.6) R <0.0005 (2.3)	M <0.0005 (2.7) R <0.0005 (2.5)	– –

CONCLUSION: This head-to-head comparison shows WE to have the lowest real-time insertion pain score, high repeatability and reproducibility by endoscopists with otherwise significantly different pain scores during insertion when using AI or WI. WE equalizes differences in method-related real-time pain among investigators. Promotion of the unsedated option lessens the burden of sedation on patients on-site and at home. Direct (nursing staff time) and indirect (patients) cost savings appear to be plausible. (NCT01781650, 01780818)
Disclosure of Interest: None declared

P1298 SHOULD PATIENTS WITH RECTAL BLEEDING HAVING A FLEXIBLE SIGMOIDOSCOPY COME FULLY PREPARED FOR A COLONOSCOPY?

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INTRODUCTION: The vast majority of patients referred for investigation of rectal bleeding have benign anal disease or proctitis. Flexible sigmoidoscopy (FS) has been widely used for the investigation of patients with rectal bleeding with same day single phospho-soda enema preparation prior to the examination. However, conversion to full colonoscopy is warranted if adenomatous polyps or colon cancer is detected to exclude synchronous lesions. We hypothesise that as the patients age at presentation of rectal bleeding increases, the prevalence of adenomatous polyps and colon cancer increases and thereby the requirement for evaluation of the entire colon. If this is established then we should recommend that patients undergoing FS for rectal bleeding should be scoped with full bowel preparation and converted to a colonoscopy if polyp or cancer is detected at the time of FS.
AIMS & METHODS: The aim of the study was to assess the diagnostic yield of FS in detecting colon cancer/polyp in patients of different ages presenting with rectal bleeding. A single centre, retrospective analysis of patients with rectal bleeding investigated with FS in a district general hospital from north London was performed. The patients were identified using the Unisoft Endoscopy reporting software over a period from June 2006 to March 2014. Data obtained during the study period was scrutinised for diagnosis and whether further full colonic imaging was indicated as judged by diagnosis of colon cancer or adenomatous polyp.
RESULTS: 1406 FS were performed in the study period. The table below demonstrates the findings at FS in patients with rectal bleeding according to age category. 25% of patients over 45 years of age have a cancer or polyp diagnosed that requires further full colonic imaging.

Age (years)	**<45**	**>45**	**>55**	**>65**	**>75**	**>85**	**>95**
Number of procedures	224	1179	944	666	404	144	12
Normal	90	308	223	126	72	34	3
Normal (%)	*40*	*26*	*23*	*19*	*18*	*24*	*25*
Cancer	0	67	64	56	40	12	0
Cancer (%)	*0*	*5*	*7*	*9*	*10*	*8*	*0*
Polyp	27	220	192	144	85	21	2
Polyp (%)	*12*	*19*	*20*	*22*	*21*	*15*	*17*
Other benign cause eg colitis/haemorrhoids	91	677	554	419	237	89	7
Other benign cause (%)	*40*	*57*	*59*	*63*	*58*	*62*	*58*

CONCLUSION: 25% of patients over 45 years of age undergoing FS for rectal bleeding have a colon cancer or polyp diagnosed that require further colonic imaging. Preparing all patients for a full colonoscopy at the time of attendance for FS and conversion to colonoscopy if a polyp or cancer is detected would save reattendance in 25% of patients over the age of 45 for rectal bleeding. The prevalence of polyps and cancer however is low in patients under 45 years of age and these patients could continue to have FS with enema preparation just prior to the procedure.
Disclosure of Interest: None declared

P1299 IS THE LOCATION OF THE POLYP IN THE COLON A RISK FACTOR FOR THE OCCURRENCE OF COMPLICATIONS FOLLOWING ENDOSCOPIC MUCOSAL RESECTION?

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INTRODUCTION: Endoscopic mucosal resection (EMR) is a commonly used technique to remove colorectal polyps. Complications such as bleeding and perforation can occur, with rates reported reaching 10% in some series. Some risk factors for the occurrence of these complications have been identified in the literature, such as the size of the polyp, its shape (flat or sessile), the presence of comorbid conditions and the use of antiplatelet and anticoagulant drugs. Some studies also found that the location of the polyp can be a risk factor.
AIMS & METHODS: The aim of this study is to determine if the location of the polyp in the colon is a risk factor for the occurrence of complications after EMR of supracentimetric polyps. Clinical and endoscopic data were collected by retrospective methods for all patients who underwent endoscopic resection of polyps of one centimeter or more from January 2001 to march 2013 at the Georges Pompidou European Hospital in Paris. A univariate and a multivariate analysis were used to identify risk factors for the development of complications.
RESULTS: 378 polyps were resected in 263 patients (mean age: 65.2 years [29-92], 57.9% of men). The mean size of the polyps was 17.2 mm. 67.2% were sessile, 20.9% flat and 11.9% pedunculated. Polyps were located in the right colon (proximal to the left colic flexure) in 62.4% of cases and in the left colon and rectum in 37.6% of cases. Endoscopic clip placement after EMR was performed in 53.7% of cases. 7.9% of patients were taking anticoagulant drugs and 19.8% were taking antiplatelet therapy. Complications after EMR occurred in 7.6% (29/378) of cases; there was 4 perforations (1.1%) and 25 hemorrhage (6.6%). The clinical outcome was favorable with conservative or endoscopic treatment in 96.5% of cases; only one patient had a surgery following a perforation. No death occurred. A complication was observed in 8.4% (20/236) and 6.3% (9/142) of cases following polyp resection in the right colon and the left colon, respectively ($p = 0.6$). A perforation occurred in 1.3% (3/236) and 0.7% (1/142) in the right and in the left colon respectively ($p = 1$). The rate of bleeding after EMR was 7.2% (17/236) in the right colon and 5.6% (8/142) in the left colon ($p = 0.6$), respectively. The univariate and the multivariate analysis showed that the only factor that was significantly associated with the occurrence of complications following EMR was the use of anticoagulant drugs ($p < 0.0001$). However, the location of the polyp, its size, its shape, the use of clips, the age of the patient or the use of antiplatelet drugs were not predictive factors for complications.
CONCLUSION: In this study, the location of the polyp in the right or left colon doesn't seem to be a risk factor for the occurrence of complications following EMR of supracentimetric polyps.
Disclosure of Interest: None declared

P1300 THE UTILITY OF ENDOCYTOSCOPY, WHICH CAN PROVIDE ADDITIONAL DIAGNOSTIC VALUE TO MAGNIFYING CHROMOENDOSCOPY FOR PREDICTING A MASSIVELY INVASIVE COLORECTAL CANCER: A RETROSPECTIVE COMPARATIVE STUDY

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INTRODUCTION: Magnifying chromoendoscopy (MC) is a Japanese standard diagnostic method for endoscopically predicting a massively invasive submucosal colorectal cancer (SMm) which has the possibility of metastasis[1]. Recently developed ultra-magnifying (450-fold) endoscopy "endocytoscopy (EC)" was also reported to be useful for predicting SMm.[2]
AIMS & METHODS: The aim was to assess the additional value of EC to MC for diagnosing colorectal lesions. Consecutive lesions which were resected after colonoscopical examination with use of EC were enrolled in this retrospective study between May 2005 and March 2013 in Showa University Northern Yokohama Hospital. Advanced-type lesions were excluded from the analysis. At colonoscopy, the on-site endoscopists diagnosed each lesion on the basis of MC+EC findings after assessing it on the basis of MC findings alone. The diagnostic abilities of MC+EC were compared to those of MC alone with reference to the histopathology of the resected specimens. As main outcome measure, the diagnostic abilities of predicting both neoplastic change and SMm were evaluated according to Kudo's pit pattern classification[1] and the EC classification[2].
RESULTS: Overall, 524 patients with 578 specimens were available for analysis. Of them, there were 71 non-neoplastic lesions,279 dysplasias, 15 slightly invasive submucosal cancers, and 94 SMms. The main results were shown in the table.

Table to abstract P1300

	MC alone	MC+EC	Pvalue (McNemar'stest)
Diagnostic ability of predicting.neoplastic change			
Sensitivity	93.0%	93.0%	1.000
Specificity	97.4%	96.8%	0.343
Accuracy	96.9%	96.4%	0.032
deeper than SMm			
Sensitivity	75.5%	81.0%	0.070
Specificity	97.9%	99.2%	0.041
Accuracy	94.3%	96.4%	0.002

CONCLUSION: Though MC alone has feasible diagnostic ability for predicting both neoplastic change and SMm, observation with EC can provide additional diagnostic value to MC for predicting SMm with substantial reliability.

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Disclosure of Interest: None declared

P1301 COMPARISON BETWEEN CONVENTIONAL SCOPES AND SHORT TYPE DOUBLE BALLOON ENDOSCOPES WHEN USING ESD FOR THE TUMOR LOCATED IN THE PROXIMAL COLON

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INTRODUCTION: Endoscopic submucosal dissection (ESD) method for the colorectal neoplasm has been spread all over the world in recent years. However there aren't so many medical facilities where the method is carried out completely.
There are 4 reasons - First, there are a lot of various shapes of colons. Second, the colon wall is very thin. Third, the feces in the colon contain much bacteria. Fourth, sometimes there are adhesion or malformation in the patients colon.
Furthermore once perforation arises, there is a possibility of emergency open surgery. Moreover, with the tumor in the proximal colon, ESD method becomes more difficult. In order to solve those difficulties, we basically employ short type DBE.
AIMS & METHODS: Our purpose was to evaluate the efficacy and safety of ESD by using short type DBE for the tumor located in the proximal colon in a prospective, randomized trial.
We treated the tumor located in the proximal colon using two types of scopes, the Conventional Scopes (CS) and Double Balloon Endoscopes (DBE). CS we used were EC450RD5M (Fujifilm Co., Tokyo, Japan), and PCF-Q260JL/I (Olympus Co., Tokyo, Japan) and DBE we used was EC450BI5 or EN530BI (Fujifilm Co., Tokyo, Japan).
The period of the evaluation was from Nov.2012 to Mar.2014.
We divided 70 cases into two groups: Group A (treated by CS), and Group B (treated by DBE). We examined the reaching time, the treatment time, the completing rate, the negative rate of cut end (lateral and vertical), the average hospitalization, the average cost and the perforation rate.
RESULTS: There were 32 cases in Group A and 38 cases in Group B. The number of ESD in the Group A were 32 lesions and Group B were 40 lesions. The reaching time to the cecum were 8.4±3.9 min. in the Group A and 5.3±2.2 min. in the Group B. The treatment time were 41.3±14.4 min. in the Group A and 26.2±9.1 min. in the Group B. The negative rate of cut end (lateral and vertical) were 87.5% (28/32) in the Group A and 100% (40/40) in the Group B. The perforation rate was 3.1% (1/32) in the Group A and no cases in the Group B.
The average cost were 591.7 EUR. in the Group A and 657.7 EUR. in the Group B (converted by EUR.-JPY. as of April 19th)
CONCLUSION: The cost spent on DBE is slightly more expensive than that spent on CS. However, given the low rate of perforation, the shortened time spent on ESD, and the accuracy of en-block resection, ESD by using DBE is beneficial for the patients who have the tumor in his or her proximal colon.
Disclosure of Interest: S. Katsuki: None, T. Fujita: None, K. Takanashi: None, E. Waga: None, K. Kitaoka: None, Y. Komatsu: None, H. Ohta: None, Y. Sato: None

P1302 FEASIBILITY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LARGE COLORECTAL TUMORS

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INTRODUCTION: Recently, endoscopic submucosal dissection (ESD) has been applied for superficial colorectal neoplasms and the number of publications about it has been increasing, but little is known about the outcomes of colorectal ESD for the lesions over 50 mm.
AIMS & METHODS: In this study, we evaluated the feasibility and safety of colorectal ESD for the lesions over 50 mm compared to the lesions less than 50 mm. A total of 674 superficial colorectal neoplasms in 629 patients treated by ESD at Kobe University Hospital from July 2008 to July 2013 were included in the analysis. Among these lesions, 28 residual or local recurrent lesions after previous treatment were excluded, as result, 646 lesions were analyzed for this study. Resected lesions were divided into two groups, large lesion group (tumor size ≥50 mm) and small lesion group (tumor size <50 mm).
RESULTS: Of 646 lesions included in this study, 530 lesions were classified into the small lesion group and 116 were into the large lesion group. The median operation time (range) in the large lesion group was 109 (37-596) minutes, and it was 55 (6-248) minutes in the small lesion group. Median procedure speed (range) in the large lesion group was 0.28 (0.06-0.83) cm^2/minutes, and it was 0.19 (0.04-0.83) cm^2/minutes in the small lesion group. The en bloc resection rate and the curative resection rate in the small lesion group was 98.7% and 96.0%, and those were 95.7% and 91.4% in the large lesion group, respectively. In terms of adverse events, perforation, muscle damage and postoperative bleeding occurred at similar frequency in both groups. To investigate further, the outcome of ESD depends on the part of the bowel (rectum, left colon and right colon) was analyzed. The median operation time was significantly longer in the large lesion group and the median procedure speed was significantly faster in the large lesion group in all bowel parts. The en bloc resection rate and the curative resection rate were not significantly different between two groups in either locations. In terms of adverse events, significant differences were not found in either locations.
CONCLUSION: ESD on colorectal lesions over 50 mm takes longer operation time, however, it is resected time effectively without increasing the risk of adverse events compared to smaller lesions by ESD.
Disclosure of Interest: None declared

P1303 ENDOSCOPIC DIAGNOSIS AND CLINICAL MANAGEMENT OF SESSILE SERRATED ADENOMA/POLYP

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INTRODUCTION: Sessile serrated adenoma/polyp (SSA/Ps) are known to be precursors of sporadic cancers (CRCs) with microsatellite instability (MSI). Consequently, colonoscopic identification of SSA/Ps has important implications for preventing CRCs. Although we reported evaluation of magnifying colonoscopy in the diagnosis of serrated polyps (*World J gastroenterol* 2012 August 28; 18 (32)), accurate endoscopic diagnosis is often difficult.
AIMS & METHODS: Our aim is the establishment of more accurate diagnostic criteria and examination of the clinical management for the present.
This study examined 191 serrated lesions excised in our hospital as suspected serrated lesions after magnified observation between January 2008 and March 2014. Patient characteristics (sex, age), conventional colonoscopic findings (location, size, morphology, color, mucin) and magnified colonoscopic findings (pit pattern diagnosis) were compared with histopathological diagnosis. Surface microstructures were analyzed using magnifying endoscopy.
RESULTS: Lesions comprised 57 HPs (29.8%) and 134 SSA/Ps (70.2%: complicated with cancer in 8 cases).
Conventional colonoscopy showed that SSA/Ps were characterized by existence in the right side of colon [$P < 0.001$], flat-elevated lesion [$P < 0.001$], normal-colored or pale in color of mucosa [$P < 0.001$], and with large amounts of mucin [$P < 0.001$]. Magnified colonoscopy showed the type II-open shaped (type II-O) pit pattern as characteristic of SSA/Ps [PPV 92.4%, specificity 86%]. All cancer cases were observed only in female. Cancer was also present in 8 lesions, in all of which a type III or IV or V pit pattern was also present within the same lesion.
CONCLUSION: In our study, we have understood to be able diagnose as SSA/P, which indicated both flat shaped and type II-O pit pattern, and SSA/Ps which had malignant potential indicated another pit patterns other than type II-O pit pattern. Consequently, we should consider excise not only large lesions, also lesions that have Type II-O pit pattern including the Type III, IV, V pit pattern.
Disclosure of Interest: None declared

P1304 CLINICOPATHOLOGICAL CHARACTERISTICS OF LATERALLY SPREADING TUMORS WITH "SKIRT"

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INTRODUCTION: Many laterally spreading tumors (LST) are detected in the rectum while the frequency of hyperplasia is high and there are few conventional small adenoma lesions. A hardly elevated, flat lesion with wide pits has been often observed at the margin of LST. This lesion has been termed "skirt". We have reported that LST with skirt were located in the rectum, however, the clinicopathological characteristics of LST with skirt have not been clarified.
AIMS & METHODS: The aim of this retrospective study was to clarify the clinicopathological characteristics of LST with skirt. Between February 2006 and December 2013, a total of 986 LST in 806 consecutive patients were resected endoscopically or surgically in our hospital. LST were macroscopically classified into the following three groups: granular-homogeneous type (LST-GH), granular-nodular mixed type (LST-GM) and non-granular type (LST-NG). The location was divided into two regions: rectum (from upper rectum to lower rectum) and colon (from cecum to recto-sigmoid colon). The "skirt" was defined by three findings: 1) spreading at the margin of LST, 2) presenting as a hardly elevated lesion, and 3) presenting with wide-shape pits. We assessed the clinicopathological characteristics such as age, gender, location, size, macroscopic type of LST, histopathological findings. We also assessed the endoscopic findings of skirt regarding the characteristics of pit in tumor surface using chromoendoscopy with indigo carmine dye or crystal violet dye, and the characteristics of microvessels by magnifying narrow band imaging (NBI) endoscopy.
RESULTS: Of the 986 LST, skirt was identified in the peripheral region of 34 LST (3.4%). All LST with skirt were attaching LST-GM. Of the 34 LST with skirt, 25 LST (74%) were located in the rectum and 9 LST (26%) were located in the colon (4 in cecum, 3 in sigmoid colon, and 2 in recto-sigmoid colon). The mean sizes of LST with skirt and LST without skirt were 46.5 ± 19.3 mm and 30.0 ± 16.8 mm. While carcinoma components were found in 27 lesions (80%) of LST with skirt, 437 lesions (46%) of LST without skirt were carcinoma. Significant differences were seen in the location ($p < 0.001$), the size of tumor ($p < 0.001$) and the frequency of carcinoma ($p < 0.001$) between LST with skirt and LST without skirt. In contrast, there were no significant differences in age and gender. Of the 34 LST with skirt, 26 were available for the histopathological analysis of region of skirt and all were diagnosed as low-grade dysplasia. With regard to the endoscopic findings at the surface of skirt, 29 (85%) showed coral reef-like appearance pit (which was often visible in ulcerative colitis) and the others showed type II like or type IIIL like pit pattern. As for the surface microvessels of the skirt surface, all regions could not be detected as meshed capillary vessels showing feature of lo-grade dysplasia, and were identified as capillary pattern type I.
CONCLUSION: Significant characteristics of LST with skirt were more frequent in rectal LST-GM lesions, larger tumor size, and high frequency of cancers compared to LST without skirt. In the portion of skirt, there was dissociation between endoscopic and histological findings.
Disclosure of Interest: None declared

P1305 COLONIC PREPARATION BEFORE COLONOSCOPY: EVALUATION OF A NEW METHOD WITH INTRACOLONIC INFUSION OF WATER COMPARED TO CLASSICAL ADMINISTRATION OF PEG

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INTRODUCTION: Bowel cleansing before colonoscopy is currently based upon lavage solutions of polyethylene glycol (PEG) or NaP with large amounts of fluids ingested in a split manner. This prospective randomized study compared a PEG protocol with a new method of bowel cleansing based upon infusion of water into the colon at low pressure (Angel of Water, Lifestream, Austin, TX), named hereafter the Prepsystem.
AIMS & METHODS: The device for water infusion is made of a reservoir of water maintained at 37°C. The patient is installed on an adapted seat allowing easy evacuation of water and faeces. Water is infused by gravity through a cannula, into the rectum. Patients with an indication of colonoscopy and no history of colorectal surgery or IBD were randomly assigned to PEG preparation (2L PEG in the evening before and 2L in the morning of colonoscopy) or the Prepsystem. All patients followed a low residue diet for 5 days. In the Prepsystem group, sennosides (Pursennide 80 mg, Novartis, Rueil Malmaison, France) were administered in the evening before and patients underwent 2 cleansing cycles, by infusion of 35L tap water each, about one hour before the colonoscopy. Quality of bowel cleansing was assessed with the Boston score by an endoscopist blinded to the preparation type. Boston scores in both groups were compared with a non-parametric test, with a signifcance level of 5%.
RESULTS: 100 patients were included (62 males, 59±13 y.). Main indications for colonoscopy were colorectal cancer screening (n = 57) and abdominal pain with recent change in bowel habits (n = 32). 50 patients received the Prepsystem and 50 the PEG protocol. Groups were comparable for age, sex and colonoscopy indication. 6 patients were excluded from the analysis after an incomplete colonoscopy for anatomical reasons, preventing calculation of the Boston score: 4 in the Prepsystem and two in the PEG groups. Consequently, 46 and 48 patients were analysed in the Prepsystem and PEG groups respectively. The median Boston score was 7 in both groups, without statistical difference. In the Prepsystem group, the colonoscopy was not completed up to the caecum in 2 patients because of poor cleansing. Mild mucosal tears induced by the cannula were observed in the rectum in 5 patients of the Prepsystem group. Mean duration of the colonoscopy was not different in the Prepsystem (19±3 min) and the PEG (22±1 min) groups. Blood electrolytes were not significantly modified after bowel cleansing in both groups. Patient satisfaction was good to excellent in all cases in the Prepsystem group.
CONCLUSION: The Prepsystem water infusion protocol appeared as effective as the split PEG protocol for bowel cleansing before colonoscopy. Patient tolerance of the Prepsystem was good. Further studies should evaluate the benefit of this protocol in patients with contraindications or poor tolerance to PEG cleansing or in ambulatory patients.
Disclosure of Interest: None declared

P1306 COLONOSCOPIC WITHDRAWAL TIME IS BELOW THE RECOMMENDED 6 MINUTES IN UNOBSERVED ENDOSCOPISTS AND SIGNIFICANTLY INCREASES UNDER MONITORING

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INTRODUCTION: Six minutes are recommended as the minimum withdrawal time for screening colonoscopy. However, there is a lack of data regarding the question how well this recommendation is followed by gastroenterologists unaware of being monitored in daily practice.
AIMS & METHODS: We aimed to assess first the withdrawal times in endoscopists unaware of being monitored, second if they would change the withdrawal time when knowing to be monitored (with subsequent increase in adenoma detection rate), and third, whether they could subjectively guess their withdrawal times. Seven experienced gastroenterologists performed 558 screening colonoscopies in a tertiary referral centre. Colon retraction times were first measured without and then with the gastroenterologist's knowledge of being monitored.
RESULTS: The mean withdrawal time in endoscopists unaware of being monitored was 4.7 ± 1.6 min (range 1-13 min) without colonic intervention and 7.1 ± 3.9 min (range 2-25 min) with colonic intervention. In endoscopists aware of their being monitored the withdrawal time without intervention rose to 8.1 ± 2.8 min and with intervention to 9.3 ± 3.9 min ($p < 0.001$ when compared to the withdrawal times unaware of being monitored). Adenoma detection rate increased significantly ($p = 0.001$) in endoscopists aware of being monitored. The subjective estimate of withdrawal time with and without intervention was comparable to the measured withdrawal time (7.7 ± 2.7 vs. 8.1 ± 2.8 min, $p = 0.180$; 9.3 ± 3.9 vs. 9.2 ± 4.3 min, $p = 0.796$).
CONCLUSION: Colonic withdrawal time in unmonitored gastroenterologists is shorter than recommended and increases when being monitored. Adenoma detection rate increases in monitored endoscopists. Endoscopists are good in guessing the measured withdrawal time. Withdrawal time should be monitored using a watch in the endoscopy room.
Disclosure of Interest: None declared

P1307 USEFULNESS OF AN ENDOSCOPE WEIGHT-REDUCING AID DURING GASTROSCOPY AND COLONOSCOPY

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INTRODUCTION: In recent years, as the diagnostic/therapeutic endoscopic procedures continue to increase in numbers, the left-arm/-shoulder burden continues to increase for the endoscopists performing these procedures, resulting in their overuse injuries (upper extremity biomechanical overload).
AIMS & METHODS: To help relieve the biomechanical overload associated with endoscopic procedures. Following installment of an infusion rail, an infusion runner system, and an infusion stand from the ceiling, a highly retractable Teflon tube was connected to the infusion stand with its lower end clipped to an endoscope, so that the endoscope could be left hanging from the system. With this device weight-reducing aid, the infusion rail and the Teflon tube gave greater freedom to endoscopist movement during endoscopy. The endoscopes available at the clinic (GIF-XP260, GIF-Q260, PCF-Q240ZI, and CF-H260AZI; Olympus) were compared in a diagnostic setting, with the endoscope connectors attached to each system, for weight as well as for force exerted on each device, with or without the weight-reducing aid.
RESULTS: The weight of each device with/without the weight-reducing aid was 0.66 kg/1.17 kg (0.56) for GIF-XP260, 0.8 kg/1.3 kg (0.62) for GIF-Q260, 0.96 kg/1.49 kg (0.64) for PCF-Q240ZI, and 0.97kg/1.58kg [0.61) for CF-H260AZI, respectively. The force exerted on each device with/without the weight-reducing aid was 6.46 Newton (N)/11.46 N (0.56) for GIF-XP260, 7.84 N/12.74 N (0.62) for GIF-Q260, 9.4 N/14.6 N (0.64) for PCF-Q240ZI, and 9.5 N/15.48 N (0.61) for CF-H260AZI, respectively.
CONCLUSION: An endoscope weight-reducing aid was developed. Endoscope weight reductions with this aid may not only help decrease the physical burden on the endoscopist performing endoscopic procedures but allow him/her to maintain concentration during prolonged diagnostic/therapeutic procedures, thus leading to better diagnostic yield and clinical outcome.
Disclosure of Interest: None declared

P1308 STENOSIS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LARGE COLORECTAL TUMORS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) provides a high rate of curative resection for large superficial neoplasms, as it allows en-bloc resection. It allows relatively large tumors to be included as candidates for endoscopic resection in place of surgical resection. Resection of large tumors would leave large ulcers at the site of ESD, and a large size of the defect after ESD can influence the healing progress. Consequently, post-ESD stenosis is a major complication in stomach and esophagus. A circumferential extent of the mucosal defect (CEMD) of ≧3/4 was found as a major risk factor for postoperative stricture. On the other hand, the situation might be different in the colorectum.
AIMS & METHODS: The aim of this study is to investigate the risk factor of post ESD stenosis in the colorectum. From September 2003 to October 2013, 619 consecutive superficial colorectal tumors were treated by ESD. Among them, 34 cases in which CEMD was 3/4 or more, were thoroughly investigated. Only one case was whole circumferential resection. CEMD was classified endoscopically as being 3/4-9/10 or 9/10 < just after the ESD procedure. Post-ESD stenosis was diagnosed when a standard 11.5mm diameter colonoscope could not be negotiated through the colonic segment at the site of ESD. Follow-up endoscopy was performed 4 to 6 months later. If patients had any different clinical symptoms from those prior to the ESD, endoscopy was performed in order to check for post-ESD stenosis.
RESULTS: Post-ESD stenosis didn't occur in 585 cases which CEMD was under 3/4. In 34 cases in which CEMD was 3/4 or more, postoperative stricture developed in 3 of them. Two cases were controlled only by a few sessions of endoscopic balloon dilatation. The other which was whole circumferential resection case from lower rectum to dentate line required steroidal suppository and Finger bougienage as daily regimen for 90 days and three sessions of endoscopic balloon dilatation. There was significant difference in CEMD but no significant difference in circumferential and longitudinal diameter of the resected specimen and procedure time between presence and absence of postoperative stricture groups.
CONCLUSION: Post-ESD stenosis didn't occur among cases with a CEMD of less than 9/10. Even in cases that developed postoperative stricture, the symptoms could be controlled by a few sessions of endoscopic balloon dilatation and conservative treatment. Thus, we concluded that near and whole circumferential resection is acceptable for lesions of the colorectum.
Disclosure of Interest: None declared

P1309 ENDOSCOPIC EXAMINATION OF GASTROINTESTINAL LESIONS ASSOCIATED WITH MICROANGIOPATHY CAUSED BY IMMUNOSUPPRESSANTS

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INTRODUCTION: There is a concern within the scientific community that many iatrogenic diseases will increase and diversify as a result of the diversification and increasingly widespread use of immunosuppressants (calcineurin inhibitors). Patients often experience lower gastrointestinal tract symptoms such as diarrhoea, melena and lower abdominal pain after allogeneic hematopoietic stem cell transplantation (allo-HSCT). The cause is often attributed to transplantation associated microangiopathy (TAM); however, the differentiation of this from gastrointestinal graft-versus-host disease (GVHD) is difficult, which may lead to patients being mistakenly treated for severe gastrointestinal GVHD.
AIMS & METHODS: We performed lower gastrointestinal endoscopies in patients experiencing post-transplantation abdominal pain to investigate the effectiveness of this procedure. The subjects were 101 patients selected from a group of 824 patients who underwent allo-HSCT at this medical facility during the 16-year period from 1998 to 2013 because of leukemia, myelodysplastic syndrome, malignant lymphoma, or aplastic anemia. The selected patients had all experienced abdominal symptoms such as diarrhoea, abdominal discomfort and abdominal pain within 6 months of the procedure, had undergone lower gastrointestinal endoscopy and histopathological examination and had been diagnosed with TAM based on the presence of microangiopathy with ischemic (non-inflammatory) crypt loss in mucosa of the biopsy specimens.
RESULTS: (1) The major findings obtained from the endoscopic examination of TAM were edema, rubefaction, coarse mucosa, inflammation, ulcers and mucosal loss. (2) Endoscopic examination enabled the identification of findings in 100% of the cases, with the highest percentage of findings concentrated in the ascending colon, sigmoid colon and rectum. (3) Pathological diagnosis revealed that the number of severe cases had been decreasing in recent years and that a small percentage of cases were complicated with GVHD or cytomegalovirus (CMV) infection. (4) A correlation was observed between the endoscopic severity and the histologic severity of TAM. (5) Magnification endoscopy allowed for the accurate diagnosis of TAM, including its severity and stage.
CONCLUSION: The results of the present study showed that active use of endoscopy for gastrointestinal symptoms following allo-HSCT allows the clinical picture of TAM to be elucidated and is useful in determining subsequent treatment strategies.
Disclosure of Interest: None declared

P1310 COMPARING STANDARD COLONOSCOPY WITH ENDORINGS™ COLONOSCOPY: A RANDOMIZED, MULTICENTER TANDEM COLONOSCOPY STUDY – INTERIM RESULTS OF THE CLEVER STUDY

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INTRODUCTION: Adenoma miss rates during colonoscopy have become widely acknowledged. This is primarily due to inadequate visualization of the proximal aspects of colonic folds and flexures. EndoRings™ (EndoAid Ltd., Caesarea, Israel) is a silicone rubber device, that is fitted onto the distal end of the colonoscope. Its flexible circular wings engage and mechanically stretch colonic folds during withdrawal.
AIMS & METHODS: In this multicenter tandem colonoscopy study, we compared adenoma miss rates (per lesion analysis) between standard colonoscopy (SC) and colonoscopy using EndoRings™ (EC). Secondary aims were to compare polyp miss rates, cecal intubation time, withdrawal time and total procedure time. Subjects referred for screening, surveillance or diagnostic colonoscopy were randomly assigned to undergo EC followed by SC or SC followed by EC.
Both colonoscopies were performed on the same day by the same endoscopist. Polyps detected during the first procedure were immediately removed. Diminutive (1-2 mm), rectal polyps with hyperplastic appearance were not removed. The study sample size was calculated with a two-group chi-square test with 80% power and 0.05 two-sided significance level. Based on an expected adenoma miss rate of 35% with SC and 10% with EC, an expected mean number of adenomas per subject of 0.75 and a 10% drop-out rate, a total sample size of 126 subjects will be required.
RESULTS: To date, 96 subjects have been enrolled After excluding 8 subjects due inability to reach the cecum or other protocol violations, 88 subjects (59% male, mean age 58 ± 9 years) remained for analysis. Indications for colonoscopy were screening n = 25 (28%), surveillance n = 26 (30%) and diagnostic evaluation n = 37 (42%). Forty three subjects were randomly assigned to undergo EC first followed by SC and 43 subjects to undergo SC first followed by EC. In the study group, 43 adenomas were detected during first pass with EC and 7 additional adenomas during the second procedure with SC. In the control group, 14 adenomas were detected during the first pass colonoscopy with SC and 14 additional adenomas during the second procedure with EC. The adenoma miss rate (14%) in subjects undergoing EC first was statistically significantly ($p = 0.001$) lower compared to subjects who underwent SC first (50%). Similar results were found for polyp miss rates, i.e. 11% for EC and 59% for SC ($p < 0.001$). The adenoma detection rate was statistically significantly ($p = 0.01$) higher with EC (51%) when compared to SC (24%). Mean cecal intubation times (9.4 min. vs. 8.3 min., $p = 0.15$) and withdrawal times (7.3 min. vs. 6.9 min., $p = 0.12$) were not significantly different between EC and SC. Mean total procedure time was longer ($p < 0.001$) with EC (21.9 min.) compared to SC (17.8 min.) due to removal of more polyps.
CONCLUSION: The interim results of this study (inclusion of all patients expected in June 2014) demonstrate that colonoscopy with EndoRings™ results in significantly lower adenoma and polyp miss rates than standard colonoscopy.
Disclosure of Interest: V. Dik: None declared, I. Gralnek Consultancy for: EndoAid Ltd., O. Segol Consultancy for: EndoAid Ltd., A. Suissa: None declared, L. Moons: None declared, M. Segev Other: Employee of EndoAid Ltd., T. Belderbos: None declared, D. Rex Consultancy for: EndoAid Ltd., P. Siersema Consultancy for: EndoAid Ltd.

P1311 COMPARISON OF CECUM INTUBATION AND ADENOMA DETECTION BETWEEN HOSPITALS CAN PROVIDE INCENTIVES TO IMPROVE QUALITY OF COLONOSCOPY

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INTRODUCTION: Cecum intubation rate (CIR) and adenoma detection rate (ADR) are used as quality indicators for colonoscopy. Both parameters are easy to measure and have been found to be negatively associated with the occurrence of post-colonoscopy colorectal cancer (CRC). Comparing CIR and ADR between hospitals could provide useful incentives for quality improvement if possible inter-hospital differences depend at least to some extent on modifiable institutional and procedural factors.
AIMS & METHODS: The aim of this study was to compare the quality of routine colonoscopy between seven hospitals in the Netherlands to determine to what extent possible differences in CIR and ADR could be attributed to

procedural- and hospital-related factors. We prospectively registered all colonoscopies performed between November 2012 and January 2013 in two academic and five general hospitals in the Netherlands. Colonoscopies in patients with inflammatory bowel disease (IBD) or hereditary CRC syndromes were excluded. To correct for casemix variation, we performed adjusted multivariate analyses for age, gender, ASA score and indication.
RESULTS: A total of 3,129 patients were included (54% female; mean age 59±15 years). The majority of procedures (90%) were performed in adequately prepared colons, defined as a Boston Bowel Preparation Scale (BBPS) score ≥6. Mean CIR was 95% and ranged from 89% to 99% between hospitals ($p<0.01$). In multivariate analysis, independent predictors for CIR were BBPS ≥6 (odds ratio (OR) 23.3, 95%CI 13.5-40.1), and hospital ($p<0.01$), with ORs ranging from 1.1 to 9.7 (largest hospital as reference). Mean ADR was 32% and varied between hospitals, ranging from 23% to 43% ($p<0.01$). Nurse endoscopists and fellows detected adenomas more frequently than gastroenterologists (36% and 34% vs. 30%, $p<0.01$), but this difference was not significant in multivariate analysis ($p=0.21$). Independent predictors for ADR were a BBPS ≥6 (OR 1.8, 95%CI 1.3-2.5), use of conscious sedation (1.7, 95%CI 1.1-2.6), cecum intubation (OR 2.0, 95%CI 1.3-3.0) and hospital ($p<0.01$) with ORs ranging from 0.5 to 1.4 (largest hospital as reference). We combined the CIR and ADR per hospital in a scatter plot, providing an overview that can be used by hospitals to drive quality improvements.
CONCLUSION: Differences in quality of colonoscopy between hospitals can be depicted using CIR and ADR. As both CIR and ADR are affected by modifiable institutional and procedural factors that are independent of casemix, a comparison between hospitals can help improving quality of colonoscopy.
Disclosure of Interest: None declared

P1312 THE 'GOLDEN RETRIEVER' STUDY: IMPROVING POLYP RETRIEVAL RATES BY PROVIDING COMPETITIVE FEEDBACK

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INTRODUCTION: Colonoscopy surveillance is an essential part of screening programs aiming to prevent colorectal cancer. Recommendations on the adequate surveillance interval for patients with one or more colorectal polyps are predominantly based on the presence and grade of neoplasia found after histopathological evaluation. Therefore, it is important that resected colorectal polyps, especially right-sided lesions, are retrieved for histology. The internationally accepted standard for polyp retrieval rate is 90%.
AIMS & METHODS: The primary aim of this study was to evaluate the effect of education and competitive feedback on the overall polyp retrieval rate. The secondary aim was to investigate the association between polyp size or location and non-retrieval. We included consecutive colonoscopies in a single center between April 1, 2013 and April 1, 2014. Patients with inflammatory bowel disease or familial colorectal cancer syndromes were excluded for analysis. All gastroenterologists and trainees performing colonoscopy were educated on the importance of polyp retrieval and techniques to improve retrieval 6 months after the start of the study (end of September 2013). Then, the polyp retrieval competition was started by publicly providing feedback on the retrieval rate of all endoscopists and the monthly best performers (or 'golden retrievers'). We compared overall retrieval rates during six months prior to and after October 1, 2013.
RESULTS: Overall polyp retrieval rate improved from 88.6% (466/526) to 93.2% (923/990) when comparing consecutive colonoscopies performed in 6 months before and during the polyp retrieval competition ($p=0.002$). Non-retrieval occurred significantly more often in polyps ≤5 mm compared to polyps >5 mm (11.1% vs. 1.7%, $p=0.005$). The retrieval rate of left-sided polyps was higher compared to right-sided polyps during the 6 months previous to the competition (92.6% vs. 84.1%, $p=0.003$), but this difference was not significant anymore when the 6 months of competition were also taken into account (92.5% vs 91.1%, $p=0.334$).
CONCLUSION: A simple intervention to improve awareness and dedication is able to increase both overall and right-sided polyp retrieval rates in order to meet the international standard of 90%.
Disclosure of Interest: None declared

P1313 EFFICACY AND TOLERABILITY OF SODIUM PHOSPHATE TABLETS AND POLYETHYLENE GLYCOL SOLUTION IN BOWEL PREPARATION FOR COLONOSCOPY: A PROSPECTIVE STUDY

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INTRODUCTION: As the result of the increment of colorectal cancer, the importance of high quality screening colonoscopy has been rapidly increasing. Polyethylene glycol (PEG) solution and sodium phosphate (NaP) solution are effective for colon cleansing before colonoscopy. However, large volume and unpleasant taste reduce tolerability and acceptability. Recently, NaP tablet has been developed to improve patient compliance and tolerability.
AIMS & METHODS: The aim of this study was comparing the efficacy and tolerability of the two different preparations. We have performed prospective cohort study to compare the efficacy of bowel preparation and patient's acceptance between NaP tablets and PEG during May 2011 and February 2013. We assigned patient randomly to two groups. Group A (n=250) received NaP before colonoscopy. Group B (n=250) received PEG before procedure. We analyzed the effectiveness of bowel preparation by endoscopist's scoring based on the grading system and patient acceptance by patient's questionnaire. In the grading system, we classified the cleansing grade into 5 categories, and defined the favorable and effective cleansing group as grade 1 and 2.
RESULTS: 440 patients (217 NaP; 223 PEG) completed the study preparation and patient's questionnaire prior to colonoscopy. There were statistically no significant differences in (gender ($p=0.87$), age ($p=0.37$), height ($p=0.64$) and weight ($p=0.12$)) between the two groups. Effectiveness of bowel preparation was significantly higher in Group A (88.0% vs 80.7%, $p=0.035$). There were no significant differences in acceptance between the two groups (A; 81.9%, B; 78.6%, $p<0.05$). Among 133 patients who have experienced both NaP tablets and PEG, (57.1%), (25.6%), and patients (17.3%) preferred NaP tablets, PEG, and either of the two in future colonoscopy. There was no severe adverse event through this study in both groups.
CONCLUSION: In conclusion, NaP tablets preparation is easy to take, well tolerated, and more preferred by patients than PEG.
Disclosure of Interest: None declared

P1314 PATHOLOGICAL FEATURES OF LATERALLY SPREADING TUMOR OF THE COLORECTUM; REFERENCES AMONG SUBTYPES AND SUBMUCOSAL INVASION

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INTRODUCTION: Laterally spreading tumors (LSTs) are usually good indication for endoscopic treatment because they are rather benign in spite of their large diameter. There are four subtypes in LSTs; granular type [homogeneous type (H) / nodular mixed type (M)], and non-granular type [flat-elevated type (F) / pseudo-depressed type (PD)]. Their pathological features are different among subtypes.
AIMS & METHODS: The aim of this study is to evaluate the pathologial features of LSTs focusing on their subtypes and submucosal (SM) invasion. In a retrospective review of the colonoscopy database (Apr 2001 to Dec 2013) at our institution, we selected cases of colorectal neoplasms based on the following criteria; endoscopically diagnosed cases of LSTs that underwent subsequent endoscopic or surgical resection. We evaluated pathological features (size, rate of SM invasion) according to LSTs subtypes. Furthermore, we examined the LSTs with SM invasion which treated from Apr 2010 to Dec 2013 focusing on their locus of SM invasion. For analysis, we used chi-square test and one way ANOVA post hoc test for statistical analysis.
RESULTS: A total of 2226 LSTs were eligible for inclusion. The main results are shown in the table. As the three types of LST(G(M)/NG(F)/NG(PD)) became larger, the ratio of submucosal invasion became higher. But LST-G(H) showed low rate of that even when they were large in diameter. LST-NG(PD) had higher ratio of submucosal invasion (45.1%; 102/226) than the other types ($P<0.01$). LSTs with SM invasion which treated from Apr 2010 to Dec 2013 were 104 lesions. The locus of SM invasion at LST-G(M) was almost (78.8%; 21/27) under nodule. In LST-NG(PD), SM invasion was tend to occur multifocally (45.2%; 14/31) compared with the other type (12.3%; 9/73) ($P<0.01$).

	Total	LST-G(H)	LST-G(M)	LST-NG(F)	LST-NG(PD)	P-value
N	2226	573	450	977	226	
Size (mm)	25.1±15.9	26.3±16.8	37.4±20.4	19.7±9.8	21.3±8.8	P<0.01
Rate of SM invasion (%)	12.7 (282/2226)	0.7 (4/573)	17.6 (79/450)	9.9 (97/977)	45.1 (102/226)	P<0.01

CONCLUSION: Pathological features of LSTs are different among subtypes. To understand the way of SM invasion in LSTs is useful to choise the appropriate treatment method.
Disclosure of Interest: None declared

P1315 DISTINCT CLINICOPATHOLOGICAL AND MOLECULAR FEATURES OF LATERALLY SPREADING TUMORS IN THE COLORECTUM

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INTRODUCTION: Colorectal flat-elevated neoplasms can be classified into small-flat adenoma and laterally spreading tumor (LST). LSTs are subcategorized into granular-type LST (LST-G) and nongranular-type LST (LST-NG). LSTs tend to extend laterally and circumferentially rather than vertically along the colonic wall and seem be found at an early stage tumor such as adenoma. However, LSTs with large nodules or depressions tend to invade the submucosa. These observations suggest that there may be biological differences between LST-Gs and LST-NGs.
AIMS & METHODS: We examined the clinicopathological and molecular features of 24 granular-type laterally spreading tumors (LST-Gs) and 57 nongranular-type LSTs (LST-NGs) that were resected endoscopically at Showa University Hospital from July 2007 through December 2011. We investigated the frequency of *KRAS* and *BRAF* mutations, and DNA methylation of seven genes or sequences (MINT1, MINT2, MINT31, *p16*, *MLH1*, *SFRP1* and *ESR1*) by pyrosequencing. We also examined the methylation level of *SFRP1* and *ESR1* in

normal adjacent mucosa. A tumor was considered to be CpG island methylator phenotype (CIMP) -positive if 2 or more CIMP markers (MINT1, MINT2, MINT31, *p16* and *MLH1*) were methylated.
RESULTS: We observed significant differences in the tumor size (30 mm vs. 15 mm), the frequency of *KRAS* mutation (75%, 18/24 vs. 5%, 3/57) and CIMP (35%, 8/23 vs. 5%, 3/57,) between LST-Gs and LST-NGs ($P < 0.001$). The frequency of *TP53* mutation tended to be higher in LST-NGs than LST-Gs (14%, 8/57 vs. 0%, 0/24, $P = 0.05$). However, we found no significant differences in the frequency of *BRAF* mutation between two groups. For LST-NGs, the histological grade was increased with an increase in the tumor size. The frequency of Dukes' A cancer was significantly higher in tumors larger than 20 mm or equal than tumors less than 20 mm in size ($P < 0.05$). In contrast, LST-G showed no correlation of a size-dependent increase in the histological grade. No significant differences in the frequency of KRAS mutation and CIMP in LST-Gs and LST-NGs were observed by tumor size. Although the methylation levels were relatively low, we observed *SFRP1* and *ESR1* methylation in normal adjacent mucosa as well as tumor tissues of LST-G and LST-NGs (median methylation density: *SFRP1* methylation, 18% and 22%; *ESR1* methylation, 19% and 20%, respectively).
CONCLUSION: Our results suggest that different molecular mechanisms may exist in these subtypes of colorectal flat-type neoplasms. Furthermore, *SFRP1* and *ESR1* methylation in normal adjacent mucosa might be associated with field effects defined by epigenetic changes as early events predisposing to laterally spreading manner of LSTs.
Disclosure of Interest: None declared

P1316 IMPROVING THE QUALITY OF COLONOSCOPY BOWEL PREPARATION USING A SMART PHONE APPLICATION

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INTRODUCTION: Bowel preparation for colonoscopy is a complex undertaking, involving diet modifications and laxative choice according to patient needs. An adequate level of cleansing is critical for the efficacy and the quality of colonoscopy. Bowel preparation is inadequate in an up to 30% of patients undergoing colonoscopy, and has been associated with patient characteristics, previous failure to adequately prepare colon and noncompliance with cleansing instructions. Education of patients before colonoscopy is very important to ensure compliance. Early data have shown a significant improvement in bowel preparation quality in patients who used the smart phone application (SPA). Therefore, we created a novel SPA aimed to increased bowel preparation quality and patient satisfaction, using different educational tools.
AIMS & METHODS: To determine whether SPA could improve proper bowel preparation in patients undergoing colonoscopy, and to evaluate the effect of SPA on patient satisfaction.
We performed a randomized, double-blind, pilot study with two parallel arms from January to April 2014. Outpatients submitted for colonoscopy, owners of a smart phone and able to manage a SPA, were included. We enrolled 194 consecutive patients (104 female, 90 male, age range 26-75 yrs) that were randomnly allocated by nurse assistant to one of the following bowel preparation protocols: a) SPA Group (n = 95): patients downloaded this free SPA onto their smart phone. The app provides to patients timed alerts and explains the procedure providing tips, examples of low fiber diet, and educational video to explain how to prepare the purgative solution; and b) Control Group (n = 99): written instructions for bowel preparation, with visual aids explaining the procedure and how to prepare the solution, was given to each patient. All procedures were performed in afternoon time, and patients received the same purgative regimen (2-L PEG solution plus ascorbic acid), in a full-dose same-day regimen. The study was powered to detect an improvement in quality of bowel preparation using the Herefield Cleansing Scale (HCS) scale. To evaluate the effect of SPA on patient satisfaction were assessed with a specific questionnaire at time of the colonoscopy. Patients were asked if they used the application and their satisfaction with the app. Endoscopists were blinded to the actual treatment given to each patient and to the answers. Results are expressed as median (CI 95%)
RESULTS: There was no significant difference in the HCS scores in both regimens (17.00 ± 3.11 in the SPA group vs 16.21 ± 3.60 in the control group; $p = 0.188$); however, the use of SPA was superior to written instructions in overall successful cleansing (100% vs 90.9%; $p = 0.003$.) (HCS scores A or B), with specifically better cleansing in the right colon ($p = 0.016$) and in the transverse colon ($p = 0.040$), respectively. Patient-reported tolerability and the overall experience with the prescribed bowel preparation was significantly higher for the SPA group than for the control group ($p < 0.001$).
CONCLUSION: Successful cleansing and patient acceptability with the use of SPA were superior to written instructions in outpatients submitted for colonoscopy prepared 2-L PEG solution plus ascorbic acid.
Disclosure of Interest: None declared

P1317 ENDOSCOPIC MUCOSAL RESECTION FOR PARIS TYPE 0-I S AND TYPE 0-II SUPERFICIAL COLORECTAL NEOPLASIA

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INTRODUCTION: Endoscopic mucosal resection (EMR) is an endoscopic technique developed for removal of sessile or flat neoplasms confined to the superficial layers of colorectal mucosa. EMR can provide effective cure for Paris type Is and type II colorectal neoplasia and node-negative early cancer, avoiding the need of surgical resection.
AIMS & METHODS: 186 colorectal neoplasm in 142 patients were removed by EMR between January 2012 and November 2013. All patients previously underwent total colonoscopy by EC590ZW/L («Fujinon», Japan) or CF-160L («Olympus», Japan) endoscopes. Resection included following stages: (1) guided local or total chromoscopy by 0.5% indigo carmine solution, (2) mucosal examination of pit-pattern, (3) submucosal injection of fluid, (4) snare mucosectomy, (5) estimation of results, (6) clip closure of defect when feasible.
RESULTS: EMR were performed in total of 186 colorectal neoplasia: 152 Paris type II and 34 Paris type Is. Neoplasia lesions size ranged from 3-39 mm (mean size 17.8 mm). Mean resection time was 11.8 min (range 1-38 min). Mucosectomies were performed in total of 152 non-polypoid lesions with 91 (59.9%) right colonic, 39 (25.6%) left colonic and 22 (14.5%) identified rectal lesions. Histology confirmed adenoma (tubular, tubulo-villous, villous) in 94, adenoma with LGD in 29, adenoma with HGD in 20, and intramucosal Ca in 9 lesions respectively. The majority of lesions - 90 (59.2%) were lesions of type 0-IIa, 8 (5.3%) type 0-IIb, 2 (1.3%) type 0-IIc, 30 (19.7%) type 0-IIa+c or 0-IIc+a, and 22 (14.5%) - Lateraly Spreading Tumor.
Mucosectomies were performed in 34 polypoid lesions (Is) with 12 (35.3%) right colonic, 14 (41.2%) left colonic and 8 (23.5%) identified rectal lesions. Histology confirmed adenoma (tubular, tubulo-villous, villous) in 25, adenoma with LGD in 5, adenoma with HGD in 2, and intramucosal Ca in 2 lesions respectively. The majority of lesions - 30 (88.3%) were lesions of type 0-Is, 4 (11.7%) type 0-Is+IIc. En-block resection was performed in 172 (92.5%) cases, resection by several fragments – in 14 cases (7.5 %). All removed in parts lesions were over 20 mm in size. Three patients experienced an episode of delayed bleeding. No perforation were seen. In two patients we found relapses of neoplasia (after 1y). 21 cases of dysplasia and 8 cases of adenocarcinoma were revealed in 36 neoplasms with 0-IIc component. With the absence of 0-IIc component (150 neoplasms) dysplasia was observed in 35 cases and adenocarcinoma – in 3 cases.
CONCLUSION: Endoscopic management – EMR is a safe and effective treatment for Paris type Is and type II of colorectal neoplasia and may be an alternative to surgery in selected patients. Presence of 0-IIc focus significantly correlates to the presence of dysplasia or adenocarcinoma.
Disclosure of Interest: None declared

P1318 THE MANAGEMENT OF DIMINUTIVE ADENOMATOUS POLYP USING PIT PATTERN CLASSIFICATION

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INTRODUCTION: It is now available to estimate histological feature of colorectal lesions using magnifying chromo-endoscopy (pit pattern classification). In regard to diminutive (≦5mm) adenomatous polyps (DAP), it has been reported that the prevalence of advanced histological features was low[1)]. However diminutive invasive cancer has been found. We basically permit to left untreat and follow up DAP with type IIIL pit pattern and resect ones with type IIIs, IV or V in routine colonoscopy.
AIMS & METHODS: The aim of this retrospective study was to assess our management DAP using pit pattern classification. Objective was the patients who were performed total colonoscopy between April 2000 and December 2012 in Showa University Northern Yokohama Hospital. Inclusion criteria was defined as follows; 1: all polyps were performed magnifying chromo-endoscopy. 2: all adenomatous polyps of >5mm were removed or no adenomatous polyp was detected at initial colonoscopy. 3: followed up colonoscopy was examined>3 years after initial colonoscopy. Patients who had a history of familial adenomatous polyposis, hereditary non-polyposis, advanced colorectal cancer or inflammatory bowel disease were excluded. They were divided into three groups according to the finding and treatment at initial colonoscopy as follows; Group A: No neoplastic polyp was detected. Group B: All neoplastic polyps including DAP were resected. Group C: DAP with type IIIL pit pattern were left untreated. The groups were compared in cumulative incidence of index lesion (≧10mm, or high grade dysplasia) or invasive cancer at follow-up colonoscopy.
RESULTS: A total of 4550 patients were enrolled in our study. 1565 patients classified into Group A, 2021 in Group B, 964 in Group C. Index lesion was detected in 18 patients (1.2%) in Group A, 145 (7.2%) in Group B, and 64 (6.7%) in Group C, respectively. Invasive cancer was detected in 10 patients (6.3%) in Group A, 10 (4.9%) in Group B, and 4 (4.1%) in Group C, respectively. There were not significant differences in incidence of invasive cancer among three groups. In regard to incidence of index lesion, Group A was significant lower than Group B and Group C. There was no significant difference between Group B and Group C.
CONCLUSION: Removing DAP with type IIIL pit pattern did not decrease an incidence of index lesion and invasive cancer, significantly. DAP with type IIIL pit pattern could be allow to left untreat and follow up.

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Disclosure of Interest: None declared

P1319 EVALUATION OF COLORECTAL TUMOUR HYPOXIA BY AUTOFLUORESCENCE IMAGING WITH A HIGH-PERFORMANCE CMOS IMAGER

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INTRODUCTION: Autofluorescence is the natural emission of light by biological structures such as nicotinamide adenine dinucleotide (NADH) and flavins. NADH is increased in tumour cells because of anaerobic glycolysis. Recent report that the dual-wavelength excitation method is useful technique for the detection of early colonic tumours, reveals that the precise measurement of NADH fluorescence intensity as a method for visualizing colonic tumours with cooling EM-CCD[1)].
AIMS & METHODS: The aim of this study is to evaluate colorectal tumour hypoxia by autofluorescence imaging with a high-performance CMOS imager that needs no cooling.
Study samples were 91 colorectal tumour specimens obtained by endoscopic resection in our department between October 2012 and February 2014 (12 sessile serrated adenoma/polyp (SSA/P), 40 adenoma and 39 mucosal adenocarcinoma (M-ca) specimens). The resected specimens were irradiated with excitation lights of 365 nm and 405 nm, and autofluorescence images were obtained with a high-performance CMOS imager with band pass (475±25nm) and long pass filters (≥450 nm). Ratio images (F365ex/F405ex, band pass filter images (bp images) and long pass filter images (lp images)) were created for evaluation of lesion brightness (High, Iso or Low) compared with the brightness of normal mucosa.
RESULTS: In bp images, to evaluate the brightness of the lesion in all case is that High group is 84.6% (77/91), Iso group is 8.8% (8/91) and Low group is 6.6% (6/91). Histologic SSA/P was depicted on a total of 12 bp images, with 66.7% (n = 8) falling into the High group, 8.33% (n = 1) falling into the Iso group and 25.0% (n = 3) falling into the Low group; adenoma/M-ca was depicted on a total of 79 bp images, with 87.3% (n = 69) falling into the High group, 8.86% (n = 7) falling into the Iso group and 3.80% (n = 3) falling into the Low group.
In lp images, to evaluate the brightness of the lesion in all case is that High group is 70.3% (64/91), Iso group is 19.8% (18/91) and Low group is 9.9% (9/91). Histologic SSA/P was depicted on a total of 12 lp images, with 33.3% (n = 4) falling into the High group, 33.3% (n = 4) falling into the Iso group and 33.3% (n = 4) falling into the Low group; adenoma/M-ca was depicted on a total of 79 lp images, with 75.9% (n = 60) falling into the High group, 17.7% (n = 14) falling into the Iso group and 6.33% (n = 5) falling into the Low group.
CONCLUSION: Our results show that autofluorescence images obtained with a high-performance CMOS imager may be useful for clinical detection and functional diagnosis of colon tumours.
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Disclosure of Interest: None declared

P1320 CLINICAL COURSE AFTER CIRCUMFERENTIAL AND SUB-CIRCUMFERENTIAL RECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LARGE RECTAL NEOPLASMS

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INTRODUCTION: Recently, the techniques of endoscopic submucosal dissection (ESD) have been improved, and rectal circumferential and sub-circumferential ESD has been often performed. In esophageal ESD, several clinical studies reported that resection of more than three-quarter circumference is closely related to esophageal stricture after ESD. However, little is known about clinical course after ESD for wide spreading rectal neoplasms.
AIMS & METHODS: The aim of this study is to clarify clinical course of patients who underwent circumferential and sub-circumferential rectal ESD. Fifty nine rectal neoplasms in 59 patients which required more than three-quarter circumferential resection at our hospital and an affiliated hospital from April 2005 to December 2013 were included in the analysis.
RESULTS: Of 59 lesions in this study, 48 lesions were morphologically classified as lateral spreading tumor (LST) granular type, 2 were LST non-granular type, 2 were 0-IIa, and 7 were 0-I. The median specimen and tumor size were 85 (ranging 43-254) cm and 72 (12-245) cm, respectively. The median procedure time was 139 (33-596) minutes. In terms of the range of submucosal defects that resulted from ESD treatments, 6 lesions required circumferential dissection, 5 lesions required more than 11/12 (eleven-twelfth), and 48 lesions required three-quarter to 11/12 circumferential dissection. Perforation and postoperative bleeding occurred in one case each, however, both could be treated conservatively. To prevent post-operative rectal strictures, steroids were injected into ulcer floor after ESD in 5 cases, steroid suppositories were administered in 3 cases, and oral steroids were administered in one case. There were 9 cases of non-curative resection due to deep invasion or lymphatic/venous invasion, and, 7 cases underwent additional surgery. Fifty two cases, excluding 7 surgical cases, were followed up by colonoscopy to evaluate the rectal strictures after ESD. Four surgical treatment cases were also evaluated for strictures by follow-up colonoscopy and/or by surgical specimens. Of these total 56 cases, strictures occurred in 7 cases (13%). All cases were the lesions which required resection of more than 11/12 circumference, and some cases did not receive steroid treatment. Endoscopic balloon dilation (EBD) was performed to treat the stricture, and it was successfully improved in all cases.
CONCLUSION: Our data shows that less than 11/12 circumferential rectal resection never causes stricture. Only more than 11/12 circumferential rectal resection has a risk of developing stricture after ESD, however, it could be treated by the combination of steroid therapy and EBD, or EBD alone. Because ESD is less invasive and can preserve anal function compared to surgical resection, indication of ESD for large rectal neoplasms which needs more than three-quarter circumferential resection could be effective and beneficial.
Disclosure of Interest: None declared

P1321 EVALUATION FOR THE DIAGNOSTIC PERFORMANCE OF TRADITIONAL SERRATED ADENOMA USING MAGNIFYING CHROMOENDOSCOPY

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INTRODUCTION: Serrated neoplastic pathway has been proposed in recent years as a new oncogenic pathway for development of colorectal carcinoma. Traditional serrated adenoma (TSA) is focused of attention as one type of precursor lesion. We use magnifying chromoendoscopy for diagnosis about colorectal lesions, Type III H pit-pattern (fernlike pit-pattern) and IV H pit-pattern (pinecone pit-pattern) are used for diagnosis of TSA.
AIMS & METHODS: The aim of this investigation was to evaluate the diagnostic performance using magnifying chromoendoscopy (MCE) in identifying TSA. We analyzed a total of 50 histologically proven TSA and a total of 150 non TSA lesions that underwent endoscopic resection at a single tertiary hospital between January 2007 and June 2013. For each lesion images taken by conventional white light endoscopy and magnified indigo carmine spraying were reviewed by five experienced and five non-experienced colonoscopists. A diagnosis of TSA or non-TSA was made on a six-point scale of confidence. Diagnostic performance was evaluated using Receiver Operating Characteristic (ROC) analysis based on calculation of the Area Under the Curve (AUC).
RESULTS: AUC was 0.91 for correctly diagnosis TSA or non TSA with MCE for all reviewers. AUC was 0.95 in experienced group and 0.85 in non-experienced group, respectively ($P < 0.001$). The lesions was diagnosed correctly with high confidence in 89% of the experienced group and in 57% of the non-experienced group ($P < 0.001$). AUC was 0.95 which diagnosed with high confidence versus 0.75 which diagnosed with low confidence in experienced group, and 0.87 versus 0.67 in non-experienced group. In both groups, diagnostic performance was significantly higher when diagnosed with high confidence ($P < 0.001$). Interobserver agreement for diagnosis of TSA was 0.72 (kappa value) in experienced group and 0.42 (kappa value) in non-experienced group.
CONCLUSION: The performance of MCE for diagnosis of TSA was highly accurate when the experienced group diagnosed with high confidence. Interobserver agreement was good results in experienced group. In non-experienced group, the diagnostic performance was still high. With education and experience in recognizing the typical findings of TSA a high diagnostic accuracy can be achieved.
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P1322 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL TUMOR BECAME SAFE AND CURATIVE PROCEDURE AS COMPARED WITH EMR AND PIECEMEAL EMR

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INTRODUCTION: Endoscopic submucosal dissection (ESD) technique has made it possible to perform one-piece resection of colorectal tumors regardless of lesion size and location. However, ESD has been regarded as a procedure with the high risk complication than endoscopic mucosal resection (EMR) and piecemeal EMR. In this study, we compared the safety and curability between these endoscopic treatments.
AIMS & METHODS: ESD was performed for 766 cases of tumor in 760 patients (male: female = 449:311; mean age, 65.7 years) including 8 withdrawal cases. In same periods, we experienced 4.870 EMR cases and 507 cases with piecemeal EMR. We compared the incidence of perforation and residual/local recurrence between ESD, EMR, and piecemeal EMR.

RESULTS: We completed ESD procedure on 758 of 766 colorectal tumors (84 lesions in the caecum, 129 in the ascending colon, 142 in the transverse colon, 33 in the descending colon, 180 in the sigmoid colon and 190 in the rectum), and other 8 cases were abandoned endoscopic treatment due to severe degree fibrosis relating deep SM cancer invasion and screen-like fibrosis. The average lesion size was 34.0mm (range: 5-170 mm), and 11 lesions were larger than 100 mm in diameter. The average operation time was 74.2 minutes (range, 7-480 min).
The incidence of perforation was 0.25% (12/4.870) with EMR, 0.59% (3/507) with EPMR, and 0.13% (1/766) with ESD including 8 withdrawal cases. This result revealed that ESD has become a very safe procedure than the EMR and piecemeal EMR technique. The incidence of residual/local recurrence was 0.49% (24/4.870) with EMR, 5.33% (27/507) with piecemeal EMR, and 0.13% (1/758) with ESD excluding 8 withdrawal cases. Thus, although there is no significant difference in the incidence of perforation between these endoscopic procedures, the rate of residual/local recurrence after piecemeal EMR was significantly higher ($p < 0.001$) than after EMR and ESD. The possibility to completing ESD for colorectal tumor sometime depends on the existence of fibrosis in submucosal layer rather than the size and location. Among 766 ESD cases, 190 cases were accompanied by SM fibrosis. Among 190 cases with SM fibrosis, of which 59 cases were considered related to cancer invasion and 131 cases were unrelated. En bloc resection rate of the tumor without fibrosis was 97.6% (562/576), and the tumor was accompanied with fibrosis in 84.7% (161/190). We experienced only one case of perforation (0.13%), which was accompanied by fibrosis. From the view point of safety and curability, use of the ESD procedure is thought to be limited for this group at high risk of perforation and recurrence. For the above mentioned reasons, we have developed laparoscopy endoscopy cooperative surgery (LECS) in order to perform an one-piece resection of tumor, which was difficult to complete ESD due to firm fibrosis in submucosal layer. And we have achieved one-piece resection for 4 cases by using LECS procedure successfully.
CONCLUSION: ESD for colorectal tumors became safe and curative procedure owing to the progress of endoscopic technique and devices as compared with EMR and piecemeal EMR. And we have established LECS procedure in order to overcome the limitation (high risk of perforation due to wide and firm fibrosis in SM layer) of ESD procedure.
Disclosure of Interest: None declared

P1323 COMPARISON OF EFFICACY BETWEEN COLONIC SELF-EXPANDING METALLIC STENTS AND TRANSANAL TUBE FOR PALLIATION OR AS A BRIDGE TO ELECTIVE OPERATION IN MALIGNANT LARGE BOWEL OBSTRUCTION

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INTRODUCTION: Acute colorectal obstruction often accompanies advanced colorectal cancer and requires urgent surgical treatment. Approximately 30% of patients present with acute obstruction, which represents a surgical emergency associated with mortality and morbidity rates higher than when surgery is performed in elective conditions. To avoid major postoperative complications such as anastomotic leakage with septic multiple organ failure resulting in high morbidity and mortality, most surgeons advocate two-step surgery. However, various methods for performing one-step surgery have been reported including intraoperative colonic lavage, preoperative small bowel and colonic decompression and lavage with a long nasointestinal tube, decompression with self-expandable metal stent (SEMS) and decompression with a transanal drainage tube (TDT). However, each of these methods still presents unsolved problems or difficulties with regard to efficacy, safety and technical aspects. In particular, the efficacy and safety between SEMS and TDT placement as a bridge to elective surgery or definitive palliation is debated. This study aimed to evaluate the outcomes of patients with colorectal obstruction treated using different strategies.
AIMS & METHODS: Fifty eight patients with colorectal obstruction caused by advanced colon cancers were studied between January 2009 and January 2014. Twenty three patients underwent SEMS as a bridge to elective surgery ($n = 11$) or for definitive palliation ($n = 12$). On the other hand 35 patients underwent TDT as a bridge to elective surgery ($n = 33$) or for definitive palliation ($n = 2$). Colonic obstruction was identified as the cause of the mechanical ileus by computed tomography (CT) scan in all patients. The site of the obstruction was the rectum for 27 patients, the sigmoid colon for 25 patients, the descending colon for 5 patients and the transverse colon for 1 patient. The histologic diagnosis was confirmed by endoscopic biopsy at SEMS or TDT placement, or by examination of the operation specimen.
RESULTS: Placement of SEMS was technically successful in 92.3 % and clinically successful in 100 % of the technically successful cases. Placement of TDT was technically successful in 85.7 % and clinically successful in 93.5 % of the technically successful cases. The short-term complication was perforation in 1 patient of SEMS group and 1 patient of TDT group. However, there were no complications such as migration, occlusion, colon bleeding and abdominal pain in both groups. The rates of clinically efficacy and complication were not significantly different between the two groups. The median postoperative hospital stay was 18.8 days in SEMS group versus 38.9 days in TDT group ($P < 0.001$). The in-hospital mortality rates in SEMS group and TDT group were 7.7 % and 11.4%, respectively. The mean procedure time was significantly shorter for SEMS than for TDT (33.9 minutes vs. 46.0 minutes; $P < 0.05$).
CONCLUSION: SEMS achieved a high rate of clinical success and a low rate of complications. In case of colorectal obstruction, SEMS as a bridge to elective operation or definitive palliation should be considered as the treatment for patients given the significant advantages for outcomes compared with TDT.
REFERENCES
Disclosure of Interest: None declared

P1324 PROS AND CONS OF UNSEDATED COLONOSCOPY WITH WATER INFUSION PERFORMED BY EXPERIENCED COLONOSCOPISTS

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INTRODUCTION: Recently, lots of papers has indicated that colonoscopy with water infusion in lieu of air insufflation can relieve unsedated patients' abdominal pain, facilitate colonoscopic performance and increase the rate of successful cecal intubation, et al, especially for trainees. However, non-difficult colonoscopy performed by experienced colonoscopists is still unclear.
AIMS & METHODS: The aim of this study was to identify if the advantages above could be achieved by our endoscopists with great total experience.
Method:This study was conducted at 1st hospital of Harbin medical University from August 2013 through December 2013. A total of 800 patients were randomized to undergo unsedated colonoscopy with either water infusion or air insufflation. Two experienced colonoscopists who had performed at least 10000 standard air insufflation colonoscopies, attained a 95% completion rate and spent no more than 10min in intubating on average conducted these procedures. Cecal intubation times, intent-to-treat (ITT) cecal intubation rates and abdominal pain scores evaluated by visual analogue scale (VAS) were documented in the water infusion group (WIG) compared with the air insufflation group (AIG).
RESULTS: Cecal intubation time in WIG was significantly longer ((273 ±159s) than that in AIG (246s ±146s). ITT cecal intubation rate in WIG was about 97%, significantly higher when compared with AIG(93%). Median pain scores in WIG and AIG were 3 and 5, respectively ($p < 0.01$).
CONCLUSION: Although colonoscopy with water method seemed time-consuming for experts, it could still increase successful cecal intubation rate, improve colonoscopists'performances and effectively relieve patients' abdominal pain at non-difficult colonoscopy. For unsedated colonoscopy conducted by experienced colonoscopists, it was superior to traditional colonoscopy with air insufflation.
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P1325 WATER METHOD FOR DIFFICULT COLONOSCOPY: A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: The femle patients with a lower BMI and abdominal-pelvic surgery history always suffer more abdominal pain during unsedated colonoscopy, even effect cecal intubation rate and insertion time. Recently years, some research revealed the water method could reduce abdominal pain during insertion time. But, without research about water method colonoscopy on femle patients with a lower BMI and abdominal-pelvic surgery history (difficult colonoscopy).
AIMS & METHODS: To perform a randomized, controlled trial comparing water infusion in lieu of air insufflation (study method) and air insufflation (conventional method) in unsedated difficult colonoscopy. One hundred outpatients with difficult colonoscopy that were defined as femle, with a lower BMI and abdominal-pelvic surgery history were randomized divided into a water infusion group (water group) and a traditional air insufflation group (air group). The cecal intubation rate, abdominal pain scores, cecal intubation time and the rate of patients refuse to reapt the unsedated colonoscopy were compared between the water group and the air group.
RESULTS: There was no significant difference in the age and body mass index (BMI) between the water group and the air group. The abdominal pain score of the water group was significantly lower than that of the air group ($P < 0.05$). The rate of patients refuse to repeat the unsedated colonoscopy of water group (8.1%) was significantly lower than that of the air group (29.79%, $P < 0.05$). There was no significant difference in the cecal intubation rate and cecal intubation time between the water group and the air group.
CONCLUSION: Water infusion method instead of air insufflation can reduce the abdominal pain and improve the acceptability of unsedated colonoscopy.
Disclosure of Interest: None declared

P1326 EFFECTIVENESS OF SURGICEL® (FIBRILLAR) IN PATIENTS WITH COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Because the invasive procedure of colorectal endoscopic submucosal dissection (ESD) entails a extensive mucosal defect and submucosal exposure, the procedure may have a substantial risk of complications including delayed bleeding, perforation and bacteremia and/or endotoxemia. Therefore, these complications was increasing the duration of hospital day.
AIMS & METHODS: The aim of our study is to investigate whether Surgicel® would be effective in reducing complications after colorectal ESD.
Between 2011 and 2013, 72 consecutive patients who underwent a colorectal ESD by one skilled endoscopists were enrolled. After the colorectal epithelial neoplasm removed, surgicel® was sprayed onto the submucosal surface using the wet type of application in some cases. We evaluated tumor type, location, size, histology, procedure time, hospital stay and associated complications for both the surgicel® groups (Group A) and non- surgicel® groups (Group B). For assessing inflammatory reaction, white blood cells and body temperature were monitored.
RESULTS: Of the 72 patients, two patients with microperforation were excluded. Of the total 70 patients, 35 cases (50.0%) underwent the surgicel® application. During follow-up period, rebleeding occurred in 0 (0% in Group A) patient and 2 (5.7% in Group B) patients. The fever (>37.7) was 1 (2.9%) and 8 (22.9%) patients, respectively ($p=0.028$) and the leukocytosis (>10.000 cells/μL^3) was 5 (14.3%) and 11 (31.4%) patients, respectively ($p=0.088$). The inflammatory reaction (fever or leukocytosis) was 6 (17.1%) and 13 (37.1%), respectively ($p=0.060$). Blood cultures were obtained in five patients with high fever ($>38^{\circ}C$) and were positive in three of these patients (60%). The isolated microorganism was coagulase-negative *Staphylococcus* in two patients, and *Streptococcus* species in one patient. The mean hospitalization period was 5.14 and 5.97 days, respectively ($p=0.016$). The Group (surgicel Vs non-surgicel, $p=0.034$, odds ratio (OR) = 10.074 (1.186–85.570) was identified as independent predictor for fever by multivariated analysis.
CONCLUSION: Surgicel® application after Colorectal ESD may be effective method to reduce complications and mean hospitalization period. Therefore, Surgicel® application may be considered to be a valuable clinical methods.
Disclosure of Interest: None declared

P1327 RISK OF BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASIAS IN PATIENTS WITH CONTINUED USE OF LOW DOSE ASPIRIN

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INTRODUCTION: Low-dose aspirin (LDA), which prevents platelet aggregation, is prescribed to pharmacologically prevent cardiovascular disease. Japan Gastroenterological Endoscopy Society guideline recommends non-interruption of LDA perioperatively for patients undergoing endoscopic submucosal dissection (ESD) of colorectal neoplasias (CRNs); however, no studies have confirmed the efficacy of this practice.
AIMS & METHODS: To retrospectively confirm the validity of non-interruption of LDA in patients undergoing ESD for CRN. Four hundred and ninety-four patients with 494 CRNs who were resected by ESD at our institution between August 2008 and December 2013 were included in this study. The patients were classified into three groups: Group A, those in whom LDA use was interrupted perioperatively (11 patients treated between August 2008 and November 2010); Group B, those in whom LDA use was continued perioperatively (24 patients treated between December 2010 and December 2013); and Group C, those who did not take any anti-thrombogenic agents (440 patients treated between August 2008 and December 2013). For each group, we investigated the bleeding rate after ESD and compared the rates among the three groups in location, tumor size, and pathological diagnosis. We defined bleeding after ESD as a hemoglobin level decreased by >2.0 g/dL and identified it in those in whom bleeding points were identified by emergency endoscopy for melena after treatment as previously reported. There was no difference in clinicopathological backgrounds among the three groups.
RESULTS: The bleeding rates after ESD were 18% (2/11) in Group A, 21% (5/24) in Group B, and 8% (34/440) in Group C, respectively. There was no significant difference in bleeding rate between Groups A and B; however, that of Group B was significantly higher than that of Group C ($p < 0.01$). Bleeding after ESD occurred in the colon in 13% (1/8), 18% (3/17), and 4% (12/271) of patients and in the rectum in 33% (1/3), 29% (2/7), and 13% (22/169) of patients in Groups A, B, and C, respectively. Bleeding occurred in 0% (0/2), 33% (1/3), and 11% (6/53) of patients with tumor size <20 mm, and in 22% (2/9), 19% (4/21), and 7% (28/387) of patients with tumor size$\geqq$20 mm in Groups A, B, and C, respectively. Bleeding occurred in 0% (0/5), 0% (0/10), and 8% (14/173) of patients with adenoma, in 33% (1/3), 38% (3/8), and 9% (15/173) of patients with Tis carcinoma, and in 33% (1/3), 18% (2/11), and 5% (5/94) of patients with T1 carcinoma in Groups A, B, and C, respectively. There were no differences in these variables among the three groups. No patients suffered from ischemic events during the perioperative period.
CONCLUSION: Our data indicate that the continued use of LDA increased the risk of bleeding after ESD compared to its non-use; however, outcomes did not differ significantly when LDA use was perioperatively interrupted or continued in patients with LDA use.
Disclosure of Interest: None declared

P1328 DIAGNOSIS OF COLORECTAL SERRATED POLYPS USING ENDOCYTOSCOPY

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INTRODUCTION: Recently, serrated polyps have gathered much interests as the precursor lesions to colorectal cancers which follow the "serrated pathway" different from adenoma carcinoma sequence.
Accurate endoscopic criteria to differentiate the family of serrated polyps including hyperplastic polyps (HPs), sessile serrated adenoma/polyps (SSA/Ps), and traditional serrated adenomas (TSAs) are needed.
AIMS & METHODS: The aim was to investigate the endocytoscopic features of serrated polyps focusing on elements of the shape of lumens and nuclei.
A total of 590 colorectal lesions were observed with Endocytoscopy (EC, XCF-Q260EC1, CF-Y0020I, Olympus, Tokyo, Japan), and resected endoscopically or surgically in our Center from May 2005 to October 2013. Of these, 83 serrated lesions were analyzed. 39 lesions were HPs, 24 lesions were SSA/Ps, and 20 lesions were TSAs.
In the EC images, the shapes of lumens were divided into straight, star-like, oval, serrated and villous, while the shapes of nuclei were classified into small round and fusiform.
The study protocol was approved by the ethics committee of Showa University Northern Yokohama Hospital (No.1302-01). Informed consent was obtained from all patients before collection of the specimens. This study was registered in UMIN Clinical Trials Registry (UMIN000007850).
RESULTS: The results are shown in the table below.

	lumen					nuclei	
	straght	star-like	oval	serrated	villous	fusiform	small round
HP (%)	6 (15.4)	31 (79.5)	2 (5.1)	0	0	37 (94.9)	2 (5.1)
SSA/P(%)	0	6 (15)	18 (85)	0	0	21 (87.5)	3 (12.5)
TSA (%)	0	0	0	7 (35)	13 (65)	0	20 (100)

Presence of oval lumens was for diagnosing SSA/Ps ($p < 0.05$), and presence of star-like lumens was for diagnosing HPs ($p < 0.05$). Presence of fusiform nuclei and serrated or villous lumens were significant elements for diagnosing TSA ($p < 0.05$).
CONCLUSION: Endocytoscopic diagnosis focusing on the shape of lumens and nuclei would be useful for the differentiation of serrated polyps.
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Disclosure of Interest: None declared

P1329 QUANTITATIVE IMAGE ANALYSIS OF THE LUMINAL AREA FOR HYPERPLASTIC POLYPS AND SESSILE SERRATED ADENOMA / POLYPS WITH ENDOCYTOSCOPY

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INTRODUCTION: Sessile serrated adenoma/polyps (SSA/Ps) are known to be precursors of CRCs. Kimura et al reported that the Type II open pit pattern (Type II-O) was specific to SSA/Ps. [1] Type II-O were wider and more rounded in shape, reflecting dilatation of the crypts. But there are no reports which measured the actual value of the dilatation. Actually we investigated luminal area by using Endocytoscopy (EC).
AIMS & METHODS: The aim was to determine the threshold of the area that differentiate SSA/Ps from Hyperplastic polyps (HPs) using EC.
A total of 247 lesions were observed with a single CCD integrated type Endocytoscopy (CF-Y0020I, Olympus, TOKYO, Japan), and resected endoscopically or surgically in our Center from August 2010 to December 2012. Of these, 19 HPs and 8 SSA/Ps were included. For each lesion we selected one image which showed the widest lumen, then measured the average area of the contiguous three lumens, using Image J software (NIH, Bethesda, MD). We analyzed the specific threshold of the areas.
RESULTS: The average luminal area of SSA/Ps was $9323.3 \pm 4208.1 \mu m2$, while that of HPs was $2565.1 \pm 1556.9 \mu m2$. As assessed by ROC analysis, the luminal area's threshold of $\geqq 6676.3 \mu m2$ was found with moderate accuracy (sensitivity 87.5% and specificity 94.7%, AUC 0.875).
CONCLUSION: This analysis of the luminal area has been revealed to be useful for SSAP's diagnosis.
Endocytoscopy is a promising diagnostic tool not only for neoplastic lesions but also for serrated lesions.
This approach could be adopted to computer-aided diagnosis.
REFERENCES
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Disclosure of Interest: None declared

P1330 COMPARISON OF BIPOLAR RADIOFREQUENCY CUTTING AND MONO POLAR CUTTING FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN A PORCINE MODEL

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INTRODUCTION: Current endoscopic knives utilise mono-polar energy (transmitted from the device across the bowel wall to the return plate) to incise the mucosa, dissect the submucosa and coagulate bleeding vessels. Monopolar devices have proven efficacy but remain technically challenging to use with the risk of major complications (perforation/bleeding).
AIMS & METHODS: A new bipolar endoscopic device (energy localised to the device tip) "Speedboat-RS2, Creo Medical Ltd, UK" was compared to a standard mono-polar endoscopic device (Flush-knife-BT, Fujifilm, Japan) for endoscopic submucosal dissection (ESD) in the porcine colon. The Speedboat-RS2 blade delivers bipolar radio frequency (RF-400KHz) cutting and microwave coagulation (5.8GHz) for hemostasis, and contains a retractable needle for submucosal injection/tissue irrigation. It also has an insulated hull to prevent thermal injury to the underlying muscle layer. ESD was performed and video recorded on 5 consecutive 60kg pigs. The following parameters were measured: time taken to complete resection, complications encountered and histological assessment. Two animals were recovered for one week and four animals for four weeks.
RESULTS: Ten consecutive resections were performed in the colorectum (2 per animal), 5 with Speedboat-RS2 and 5 with Flushknife-BT. Median time for Speedboat RS2 to complete a resection was 44 min, range (33-58 min) using RF cutting 30W, voltage circa 300Vrms and for Flushknife-BT was 52min, range (28-67min) using monopolar cutting for mucosal incision (80W) and for submucosal dissection, monopolar forced coagulation 30W. Median flap size (longest diameter) for Speedboat RS2 was 36.8mm, range (30-42mm) and for Flushknife was 43mm, range (35-55mm). Microwave coagulation was applied for either minor bleeding or visible vessels on 25 occasions (mean energy 7.5W) with Speedboad-RS2. Monopolar coagulation was applied 14 times with Flushknife, mean energy 30W. The Hemostatic Coagrasper was used 7 times to control arteriolar bleeding during Speedboat RS2 dissection when microwave was not sufficient and only once during Flushknife-RS2 dissection. Endoclips were placed to treat deep muscle injury in the resection base on 10 occasions in the Flushknife resections (15clips placed) and on 3 occasions (3 clips) for the Speedboat-RS2 resections. There was only one study perforation - Flushknife-BT group, where urgent peritoneal decompression was required and the resection was abandoned. Histology (Speedboat-RS2 resections) showed an intact muscle layer in four resection bases and in one there was slight muscle alteration but muscle cell viability was retained. The muscle layer was absent in two Flushknife-BT resection bases and moderately altered in one.
CONCLUSION: Compared to Flush knife-BT ESD colonic resections (monopolar) the Speedboat-RS2 was associated with less muscle injury and need for endoscopic clipping. However Speedboat-RS2 resections produced more intraprocedural bleeding requiring the haemostatic forceps.
Disclosure of Interest: Z. Tsiamoulos Consultancy for: Creo Medical Ltd, P. Sibbons Consultancy for: Creo Medical Ltd, C. Hancock Shareholder of: Creo Medical Ltd, A. Polecina: None declared, B. Saunders Consultancy for: Creo Medical Ltd.

P1331 SINGLE CENTRE PILOT EVALUATING THE USE OF ENDOCUFF-VISION IN SCREENING COLONOSCOPY

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INTRODUCTION: Although colonoscopy is considered the optimal procedure for bowel cancer screening, it remains an imperfect tool for cancer prevention, due to missed adenomas and early cancers. Optimal imaging modalities, innovative scopes and accessories (cap-assisted colonoscopy) have attempted to decrease the adenoma miss rate. Adenoma detection rates (ADR) have been shown to be a key performance indicator of quality colonoscopy.
AIMS & METHODS: Endocuff-vision is a simple accessory mounted at the end of the scope with a proximal row of 6mm length soft plastic, finger-like projections. During scope insertion, these projections invert towards the shaft of the tube and during withdrawal they evert to hold back the colonic folds augmenting the forward endoscopic views. ADRs were recorded for screening colonoscopy procedures before and after introduction of Endocuff-vision.
RESULTS: To date, three screening endoscopists (BPS, STG, AH) have used the Endocuff-vision as part of a clinical evaluation process (at the discretion of each endoscopist) from August 2013 until February 2014. From our local Bowel Cancer Screening Program database, the figures of the caecal intubation rate (CIR) and the ADR in 135 screening colonoscopies during April 2013 to July 2013 (BPS-45, STG-42, AH-48) before Endo-cuff were retrieved:
Pre-Endocuff performance:
BPS: CIR-100%/ADR-62%
STG: CIR-97%/ADR-40%
AH: CIR-97%/ADR- 54%
Prior to the introduction of the Endocuff-vision, the mean CIR was 98% and the mean ADR was calculated to be **52%.**
The total number of procedures where Endocuff-vision has been utilized was in 65 occasions (BPS-21, STG-30, AH-14) with similar CIR rates but increased post-Endocuff ADR.
Post-Endocuff performance:
BPS: CIR-100%/ADR-78%
STG: CIR-98%/ADR-74%
AH: CIR-97%/ADR-77%
The mean ADR with the aid of Endocuff was calculated to be **76%.**
On 8 patients the Endocuff-vision was electively removed from the scope due to insertion difficulties through fixed sigmoid colonic segments secondary to severe diverticular disease. There were no adverse events reported during the trial evaluation period.
CONCLUSION: In this small pilot study, use of the Endocuff-vision appeared to improve the average ADR. There were no complications from the use of the cuff although it was electively removed in 8 cases with severe sigmoid colon diverticulosis. Further randomized evaluation of this simple novel device is warranted.
Disclosure of Interest: None declared

P1332 ENDOSCOPIC SNARE PAPILLECTOMY (ESP) FOR AMPULLARY TUMOURS: SAFETY AND OUTCOMES FROM A SINGLE CENTRE TERTIARY CENTRE

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INTRODUCTION: Tumors of duodenal papillae may be malignant or premalignant. Endoscopic snare papillectomy (ESP) may be a minimally invasive solution to treat these lesions. This retrospective single centre study evaluates the safety and outcome of ESP for ampullary tumors.
AIMS & METHODS: Patients with ampullary tumors treated with ESP during 6-years (Feb 2007 to Jan 2013) identified from ERCP database. All underwent pre-ESP EUS and relevant imaging to confirm localized disease and suitability for procedure.
ESP was performed using a diathermy snare followed by biliary and pancreatic stenting - removed at 4 – 6 weeks with base biopsies for residual tumor. Patients with histology adenocarcinoma were counseled for either close follow-up or surgical resection & with benign histology were followed up. Follow up done at 3, 6, 12, 18, and 24 months, yearly thereafter.
RESULTS: 36 patients underwent ESP, mean age 63 years (33 – 83), males – 23. Mean tumor diameter was 18mm (7 – 37). Complications - 2 bleeds (managed endoascopically), one delayed biliary stenosis (underwent stenting) and one fatal pancreatitis after biopsy.
Histopathology: adenocarcinoma – 20 (56%), adenoma – 15 (41%), NET – 1. Margin positive 7 (19.4%) – adenocarcinoma– 4 (20%), adenoma – 3 (20%). Mean follow up 13.6 months (1 – 58).
4 (11%) lost to follow up – 2 each in carcinoma and adenoma group.
Adenoma group – no recurrence at mean 12-month (3 – 36) – 10 (67%), recurrence – 3 (treated by APC), NET 3-month no recurrence.
CONCLUSION: ESP for ampullary tumors is effective and safe. It can be curative for most ampullary adenomas. ESP for localized adenocarcinoma may be potentially curative in > 50% patients and may obviate need for major surgery. Negative resection margin status may be a predictor of improved ESP outcomes.
Disclosure of Interest: None declared

P1333 SECONDARY BILIARY STONES IN PATIENTS WITH ORTHOTOPIC LIVER TRANSPLANTATION

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INTRODUCTION: Secondary biliary stones have been known as a relevant complication after orthotopic liver transplantation (OLT) and may be associated with liver dysfunction. Endoscopic retrograde cholangiopancreatography (ERCP) represents the reference standard for the therapy of biliary stones. Data on the efficacy of ERCP in the treatment of post-OLT biliary stone are scanty.
AIMS & METHODS: To report the rate of secondary biliary stones after OLT, to investigate the possible triggering factors and to describe treatment in our Academic Centre.
From January 2000 to December 2013, 539 patients underwent OLT for HCV (#209) and non-HCV cirrhosis (#330). Among them, 78 OLT-patients (15%) were evaluated for biliary complications (choledoco-choledocal anastomotic stricture, biliary stones, hepatico-jejuno anastomotic stricture, hilary ischemic stricture, biliary leak, sphincter of Oddi dysfunction) on the basis of symptoms, alterations of liver tests (LTs) and non invasive imaging tests (abdominal ultrasound/magnetic resonance cholangiopancreatography). Presence of biliary stones was confirmed by ERCP. Patients with biliary stones during biliary stent exchange to treat anastomotic stricture or leak were excluded.
Comparison between OLT patients with or without biliary stones was done (using Chi-square test) in the view of etiology of cirrhosis (HCV vs non HCV), age, immunosuppressive therapy, use of ursodeoxycholic acid and associated ABS.
RESULTS: Overall 11 patients (10 male, 42-62 y.o.) on 539 (2%) post-OLT patients with secondary biliary stones were found. They had undergone OLT

for HCV, HCV and ETOH, HBV and Wilson's disease associated cirrhosis (# 5, 2, 3 and one respectively). Median timing from OLT was 31 (3-182) mos. Alteration of LTs and symptoms were present in all patients (jaundice in five, abdominal pain in four or both in other two). Median stone diameter was 10 (5-25) mm. In eight patients (73%) stones were multiple and in nine (82%) found above the anastomosis. De novo ABS was found in four patients and recurrence of ABS was found in five at a median time of 20 mos after the end of endotherapy.
In this series 32 ERCPs (1-7/patient) were performed to treat biliary stones. Three patients required multistenting to progressively dilate a recurrent ABS and to access stones above it. Seven perendoscopic, six extracorporeal shock waves and two percutaneous laser lithotripsies were used in four patients, all of them presenting with multiple and large biliary stones associated with recurrent ABS. One patient underwent hepatico-jejuno anastomosis to treat tight and angulated ABS and biliary stones as well. Overall, successful removal of biliary stones was achieved in 9 patients (82%) and ongoing in the remaining two. The presence of secondary biliary stones was significantly associated with the presence of ABS ($p<0.001$) and not associated to the other factors analyzed.
CONCLUSION: Symptomatic secondary biliary stones have been found in 2% of all OLT patients which represents 14% of biliary complications in our series. Recurrence of ABS could play a role as marker of presence of multiple and large biliary stones. Successful treatment of this condition needs a multidisciplinary approach, including multisession endotherapies.
Disclosure of Interest: None declared

P1334 EFFICACY AND SAFETY OF DEEP BILIARY ACCESS WITH GUIDEWIRE CONTROLLED BY THE ENDOSCOPIST COMPARED TO CONTRAST INJECTION AND GUIDEWIRE MANIPULATION BY THE ASSISTANT: SINGLE VS. TWO-OPERATOR CANNULATION TECHNIQUE

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INTRODUCTION: Cannulation with a sphincterotome is an efficient technique to gain biliary access in endoscopic retrograde cholangiopancreatography (ERCP). Contrast injection and two-operator guidewire cannulation technique requires experience and precise coordination between the operators. The short-wire system allowed the endoscopist to manage the guidewire and the endoscope independently (single-operator technique).
AIMS & METHODS: We compared single-operator cannulation technique with two-operator technique collecting data of all consecutive naïve patients (pts) that underwent ERCP in 3 referral centres (2 used the single-operator technique and 1 the two-operator technique). Data on demographics, final diagnosis, cannulation, non-intentionally pancreatic cannulation, stents placement and complications were evaluated.
RESULTS: 80 pts (male 46 [58%], mean age 69.9±16.4 yrs) were evaluated retrospectively in a 1 to 3 ratio (1 from two-operator group vs. 3 from single-operator group). Indications for ERCP were: choledocholithiasis in 46 pts (57.5%), pancreatic carcinoma in 15 (18.7%), cholangiocarcinoma in 12 (15%), oddi dysfunction in 3 (3.8%), benign strictures in 2 (2.5%), ampulloma in 1 (1.4%), biliary leakage in (1.4%). Successful biliary cannulation was achieved in 69/80 pts (86%) without difference between the two groups (81 vs. 75%, p = ns). Cannulation time was 2.81±1.71 min. (2.72 vs. 3.11, p = ns). In biliary cannulation failure: 9/11 achieved a complete biliary drainage after precut papillotomy and 2/11 after EUS-rendez-vous. Non-intentionally guidewire pancreatic cannulation was 7 vs. 30% in the single and two-operator group respectively (p = 0.006; OR 0.16, 95%CI 0.04-0.67) without difference of post-ERCP pancreatitis. Peri/intradiverticular papilla was reported in 14% of pts without difference in terms of cannulation failure or complications between the two groups. No differences concerning plastic or metallic stents placement were observed. Ten/80 pts (13%) experienced a complication (12% in single and 15% in two-operator group, p = ns): 5 pancreatitis/hyperamylasemia, 4 bleeding, 1 perforation. All complications resolved after medical or endoscopic therapy.
CONCLUSION: Our study shows that the single-operator cannulation technique offers the same efficacy and safety compared to the two-operator technique but with lower risk of non-intentionally pancreatic cannulation.
Disclosure of Interest: None declared

P1335 FACTORS INFLUENCING THE SUCCESS OF ERCP IN TREATMENT OF BILIARY ANASTOMOTIC STRICTURES IN PATIENTS AFTER LIVER TRANSPLANTATION

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INTRODUCTION: Biliary anastomotic stricture (BAS) represents the most frequent biliary complication following liver transplantation (LT).
AIMS & METHODS: The aim of the study was to identify epidemiological, clinical and endoscopic factors influencing appearance and resolution of BAS in patients undergoing ERCP. We included 171 consecutive liver transplanted recipients recruited in University Hospital of Udine, Italy from 2004 to 2010 with at least one year of follow-up. All patients with clinical or radiologic suspicion of obstructive jaundice and cholestasis underwent ERCP. The ERCP treatment implied biliary sphyncterotomy followed by stricture dilation and placement of at least one plastic stent, exchangeable every 3-6 months until the final stricture resolution.
RESULTS: During post-operative follow-up 40 patients developed BAS. They underwent median number of 3 ERCP per patient. The median number of 1 stents was inserted per procedure and median period until stricture resolution was 9 months. Stricture resolution was obtained in 83%. The use of Kehr T tube (12/23 Vs 28/148, $p<0.01$) and use of cyclosporine as immunosuppressive therapy (18/54 Vs 22/117, $p<0.05$) were significantly more frequent among patients who developed BAS. We identified use of Kehr T tube (O. R. 5.46, $p<0.01$) and male gender of donor (O. R. 2.61, $p<0.01$) as an independent predictors of BAS development. The elevated number of repeated ERCP (OR 0.659; 95% CI 0.522-0.832; p = 0.000), combined stenting with dilation (OR 0.197; 95% CI 0.074-0.525; p = 0.001), increasing number of inserted stents per procedure (OR 0.896; 95% CI 0.782-1.026; p = 0.112) and longer period of warm ischemia (OR 0.966; 95% CI 0.938-0.995; p = 0.023) were associated with successful endoscopic treatment. On the contrary, longer period of stent in place (OR 1.034; 95% CI 1.005-1.064; p = 0.021), elevated MELD score (OR 1.104; 95% CI 1.035-1.178; p = 0.003), elevated Child-Pugh score (OR 1.679; 95% CI 1.089-2.591; p = 0.019) and high pre-transplantation bilirubin values (OR 1.104; 95% CI 1.007-1.210; p = 0.035) were associated with endoscopic treatment failure.
CONCLUSION: Detailed clinical assessment and skilled endoscopic team is necessary in order to achieve the successful endoscopic treatment of BAS. Understanding clinical and endoscopic risk factors may help in predicting of more appropriate regimen of treatment of patients undergoing ERCP for BAS post-LT.
Disclosure of Interest: None declared

P1336 MANAGEMENT AND OUTCOMES OF ERCP-RELATED PERFORATIONS: EXPERIENCE OF THE LAST 6 YEARS IN THE SINGLE INSTITUTION

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic papillotomy (EPT), being relatively minimally invasive, nevertheless have their own morbidity, the most feared of which is periduodenal perforation, and mortality. The management of ERCP-related perforations remains controversial: some patients requiring immediate surgery, some endoscopy treatment and others only conservative management.
AIMS & METHODS: The aim of the study was to determine the incidence, predisposing factors, management approaches and clinical outcomes of ERCP-related perforations. Patients were evaluated according to ERCP indication, clinical presentation, diagnostic methods, time to diagnosis and treatment, type of injury, management, length of hospital stay, and clinical outcome.
RESULTS: In our hospital ERCP&EPT have been launched in 1977 and at the moment experience equals 13937 cases. For the last 6 years - from 01.2008 till 04.2014 - a total 2788 ERCPs were performed in our department. Perforations were diagnosed in 13 (0.48%) patients. There were 3 males and 10 females. The age ranged from 55 to 83, mean age 62.7±10.3 years. Perforation developed after EPT in 11 pts.; after catheterization with a guide wire in 1; after insertion of an endoscope in 1 pt. Perforation was confirmed immediately during endoscopy in 7 pts.; per ERCP – in 3 pts.; using plain abdominal X-ray or upper abdominal CT scan in 3 pts. Conservative management was employed in 3 (23%) pts., which was successful in all of them. Surgical treatment was carried out in 4 (31%) pts.; 3 of them received surgery within 2 to 5 hours after perforation, the rest one was operated at 8 days after perforation. Two pts. from surgical group died from intra-abdominal abscess and multiple organ failure (mortality rate 50%). Six pts. were managed by endoscopic interventions: by endoclipping - 3, by endoclipping and plastic biliary stenting - 2, by inserting full-covered metal stent and endoclipping - 1. Five pts. recovered without additional complications and their post-operative period was uneventful. One pt. died (16.6%) from abdominal sepsis and multiple organ failure after salvage surgery due to failed endoscopic treatment (biliary stenting with plastic prosthesis and clipping of the perforation). The lengths of hospital stay in conservative, endoscopic and surgical groups were 12.2; 12.3 and 31.6 days, respectively. The overall mortality rate after ERCP-related perforations was 23.1% (3 of 13 pts.).
CONCLUSION: Although rare, ERCP-related perforations are serious complications that may end fatally. Early recognition and appropriate intervention is the only way to avert a fatal outcome. Early diagnosis can be established by prompt intraoperative identification using endoscopic visualization, ERCP, abdominal X-ray and postoperative CT scan. The choice of the management approach should be individualized, depending on endoscopic and radiological findings, the features of perforation type and the clinical picture. Endoscopic clips and biliary stenting should be considered aside from surgical intervention. Based on our experience delay in intervention, surgery treatment and salvage surgery after failed endoscopic management contributed to a longer hospital stay and bad outcomes.
Disclosure of Interest: None declared

P1337 COMPLICATIONS ARISING AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPY PLASTIC STENT INSERTION

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INTRODUCTION: This is a retrospective study looking at possible complications arising after plastic biliary stenting at Endoscopic Retrograde Cholangiopancreatograpy (ERCP). Biliary stenting is performed to relieve biliary obstruction in patients with benign or malignant biliary strictures and in patients with choledocholithiasis if complete common bile duct (CBD) stone clearance is not achieved at ERCP. More than 90% of stents used were 12 cm 10 Fr plastic stents. Patients with cholelithiasis and benign strictures usually undergo elective stent change at 3-4 months while patients stented for malignancy undergo re-stenting after onset of complications.
For the purposes of the study, biliary sepsis was defined as: fever, right upper quadrant pain and jaundice requiring intravenous antibiotics and hospitalization. Stent failure was defined as recurrent obstructive jaundice with biliary hypertension confirmed on CT scan or MRCP but without signs of sepsis.
AIMS & METHODS: All patients who underwent an ERCP between 2009 and 2012 at our hospital were included in this study. Patients were then followed up until 2013 to determine complication rates.
RESULTS: 552 ERCPs were carried out in 420 patients as 96 patients (22.9%) underwent an ERCP more than once. Of these 229 (n = 552 41.4%) patients had a stent inserted, and another 63 (n = 552 11.4%) patients underwent a change of stent. 148 patients (n = 292; 50.7%) underwent stent insertion due to a malignant stricture. 24 of these patients underwent a change of stent. Stents were inserted in 35 patients (n = 292; 12.0%) with underlying benign strictures. 109 patients (n = 292; 37.3%) had a stent inserted due to incomplete CBD stone clearance.
On follow up 62 patients (n = 292; 21.2%) required hospitalization after undergoing their first stent insertion or a change of stent due to biliary sepsis or stent failure. The average time span between stent insertion and readmission due to complications was 232 days. Complications related to sepsis and stent failure were commonest beyond 6 months across all groups. None of the patients experienced problems related to stent migration. Complication rates were similar in all 3 groups.

Reason for stent insertion	Number of months after stent insertion						
	1	2	3	4	5	6	>6
Benign stricture	0	2 (5.71%)	0	2 (5.71%)	0	2 (5.71%)	3 (8.57%)
Choledocholithiasis	4 (3.66%)	4 (3.66%)	3 (2.75%)	0	2 (1.83%)	1 (0.92%)	9 (8.26%)
Malignant stricture	6 (4.06%)	3 (2.03%)	2 (1.35%)	3 (2.03%)	6 (4.06%)	0	10 (6.76%)

Table 1: Number of patients admitted with complications within months from ERCP stenting.
CONCLUSION: Leaving a plastic stent for 6 months appears to be safe and does not seem to result in a disproportionate increase in the rate of biliary sepsis or stent failure.
Disclosure of Interest: None declared

P1338 SERUM LIPASE LEVEL THRESHOLD < 10N AT H4 PREDICTS THE ABSENCE OF POST-ERCP PANCREATITIS OCCURRENCE AND ALLOWS EARLY ORAL REFEEDING

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INTRODUCTION: Acute pancreatitis is a common complication of endoscopic retrograde cholangio-pancréatography (ERCP), varying from 2 to 20 % in the literature. Although several predictors of post-ERCP pancreatitis (PEP) have been described, there is to date no reliable method for predicting its occurrence with a good accuracy. Besides, post-ERCP early refeeding remains discussed among physician endoscopists.
AIMS & METHODS: The aim of the study was to test whether the serum lipase level at H4 after ERCP would: 1) predict the occurrence of PEP; 2) allow an early refeeding.
Patients and Methods. All patients who underwent ERCP between January 2013 and January 2014 were included in this prospective study, with the exception of patients who had acute pancreatitis before ERCP. Serum lipase level was routinely controlled after the endoscopic procedure at H4, to define patients at low risk of pancreatitis (< 10N), and patients at high risk of pancreatitis (> 10N). Threshold of lipasemia upper 10N at H4 was chosen in order to determine the prediction of post- ERCP pancreatitis. This threshold was strongly suggested to be relevant for the prediction of PEP in a previous prospective study of 272 patients (1). When lipase was < 10N and in the absence of abdominal pain, the patients received an oral feeding on the evening of the same day with a calory intake of less than 800 Cal. Patients with lipase > 10N with or without abdominal pain remained fasting overnight. The sensitivity (Se), specificity (Sp) and positive (PPV) and negative predictive values (NPV) of the lipase for predicting a PEP at H4 were calculated. The occurrence of abdominal pain occurring after early refeefing was noted.
RESULTS: Among the 175 consecutive patients, five patients were excluded because they had pancreatitis before ERCP. Data from 170 patients were analyzed. The average age of patients was 70 years, 92 women and 78 men. ERCP was performed for gallstones in the common bile duct (n = 103) or a tumor compressing the CBD (n = 67). The rate of PEP was 10.6%. There was a significant correlation between the value of the serum lipase level at H4 and the occurrence of PEP ($p < 0.0001$, Fisher's exact test). PEP were mild on CT scan (Balthazar stages A to C) except from one severe acute pancreatitis (Balthazar D, 0.6%). The Se, Sp, PPV and NPV of serum lipase level at for predicting PEP were respectively 100 %, 95%, 77% and 100 %. No patient who underwent early post-ERCP oral refeeding showed any pain nor complications. The mortality was 0%. Patients who benefited from early oral refeeding did not show any sign of pancreatitis in postprandial peroid.
CONCLUSION: The dosage of serum lipase level at H4 is a simple, fast and effective method for predicting the occurrence of PEP and identifying patients who may benefit from early oral refeeding after ERCP and early discharge after procedure. None of the patients with a serum lipae level < 10N at H4 developed PEP. Early oral refeeding in patients with serum lipase level < 10 N at H4 did not induce PEP.
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Disclosure of Interest: R. Alhameedi: no conflict, A. Di Fiore: no conflict, M. Antonietti: no conflict, I. Iwanicki-Caron: no conflict, A. Gangloff: no conflict, P. Michel: no conflict, P. Ducrotté: no conflict, S. Lecleire: no conflict.

P1339 MULTICENTER STUDY ON THE OUTCOMES OF ERCP USING A CAP-FITTED FORWARD-VIEWING ENDOSCOPE IN PATIENTS WITH BILLROTH II GASTRECTOMY

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INTRODUCTION: In patients with Billroth II gastrectomy, ERCP has often been performed using a cap-fitted forward-viewing endoscope because of technical difficulty and risk of adverse events in the use of duodenoscope. This study was aimed to investigate the outcomes and the risk factors of adverse events of ERCP using a cap-fitted forward-viewing endoscope in patients with Billroth II gastrectomy as a multicenter study.
AIMS & METHODS: Between August 2008 and May 2013, we retrospectively reviewed the data on the ERCP using a cap-fitted forward-viewing endoscope in patients who had undergone Billroth II gastrectomy. During the study periods, 123 patients were enrolled at five tertiary referral centers in South Korea.
RESULTS: The indications of ERCP were common bile duct (CBD) stone in 80.5% (99/123), CBD stricture in 9.8% (12/123), CBD cancer in 1.6% (2/123) and others in 8.1% (10/123). Successful ERCP could be achieved in 82.1% (101/123). The reasons of failed ERCP were failure of entry to ampulla in 13 patients, failure of cannulation in five patients and the others in four patients. Mean size and number of CBD stones was 10.8±3.9mm and 1.78±1.1, respectively. For the complete removal of CBD stones, mechanical lithotripsy was required in 17.8% (15/84) of patients. Endoscopic papillary balloon dilatation was performed in 68.2 % (84/123) of patients. In these patients, the mean CBD diameter was 15.2±3.9mm and the mean balloon size and mean ballooning time was 10.1±1.4mm and 63.4±27.4sec. Adverse events occurred in 24.3% (30/123), including asymptomatic hyperamylasemia in 15.4% (19/123), post-ERCP pancreatitis in 7.3% (9/123), bowel perforation in 1.6% (2/123). The large stone more than 20mm was the significant risk factors for adverse events (odds ratio 15.5).
CONCLUSION: In patients with Billroth II gastrectomy, the ERCP using a cap-fitted forward-viewing endoscope may be a useful method. Nevertheless, the significant rate of adverse events cannot be ignored, suggesting the need for taking precautions.
Disclosure of Interest: None declared

P1340 EFFICACY AND SAFETY OF ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION FOR DIFFICULT STONES IN HIGH ELDERLY PATIENTS

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INTRODUCTION: Minimally invasive interventions for choledocholithiasis are preferable in elderly patients because they tend to have multiple underlying disorders or a decreased activity of daily living. Endoscopic sphincterotomy and endoscopic papillary balloon dilation have been recognized as first-line treatments for choledocholithiasis excluding difficult cases such as large stones or multiple stones. Recently, the safety and efficacy of endoscopic papillary large balloon dilation (EPLBD) for difficult choledocholithiasis cases have been reported. However, there was a few reports for elderly patients.
AIMS & METHODS: To investigate whether EPLBD can be safety and effectively performed in high elderly patients. The medical records of 204 patients who

underwent EPLBD from November 2006 to August 2013 were analyzed retrospectively. The patients were divided into 2 groups: Group A (≥85 years); Group B (<85 years). The criteria of EPLBD was the patients with large or multiple CBD stones; 13 mm or more in the shortest dimension (i.e., the shortest dimension of the largest stone) or multiple (≥3) bile duct stones with the smallest stone >10 mm in the shortest dimension.
RESULTS: Number of patients are 57 and 147 in Group A and B. The average age are 89.9 (85-102) and 73.2 (31-84) years old in Group A and B, respectively. The patients in Group A had more prevalence of periampullary diverticulum than those in Group B (54.4% vs 36.7 %, p = 0.02). However, there was no significant difference in the success rates in the first session (96.5 vs 95.3 %, p = 0.99) and in the final success rates (100 % in both groups) between Group A and Group B. The adverse event rates (3.5 vs 3.4 %, p = 0.70) and recurrence rates of choledocholithiasis (12.3 vs 10.2 %, p = 0.67) were not significantly different. Post-EPLBD pancreatitis (moderate) was observed in 1 patient in Group A. Perforation developed in 1 patient in Group A and none in Group B. In Group B, mild hemorrhage without a transfusion developed in 4 patient, and acute cholangitis in 1 patients.
CONCLUSION: This study suggested that EPLBD procedure for high elderly patients was safe and effective for difficult stones.
Disclosure of Interest: None declared

P1341 PROGNOSTIC FACTORS OF RESPONSE TO ENDOSCOPIC TREATMENT IN PAINFUL CHRONIC PANCREATITIS - RETROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: Patients with chronic pancreatitis often present with severe abdominal pain, resistant to common analgesics. There is no etiological therapy for chronic pancreatitis. The goal of the endoscopic treatment of painful chronic pancreatitis is to drain the pancreatic duct, reduce the frequency and severity of pain and resolve local complications of the disease. Few data are available on the long term efficacy of endoscopic treatement.
AIMS & METHODS: The aim: to evaluate the endoscopic treatment efficacy and the prognostic factors of long-term response treatment in patients with painful chronic pancreatitis. All the patients with painful chronic pancreatitis who underwent ERCP or endoscopic treatment in the last 5 years at a single tertiary referral endoscopy center were retrospectively identified from the hospital database. The inclusion criteria were: the pancreatic pain and dilated pancreatic duct. Demographics data regarding the clinical history, the endoscopic procedures and the patients follow-up were collected from the medical charts and analyzed. All the patients were called to obtain updated clinical informations.
RESULTS: We included 132 patients (109M,23F, mean age 52, predominant etiology ethanolic). At enrollment, the pancreatography showed:minimal changes of the pancreatic ducts in 10 patients, pancreatic duct stones in 30 patients, pancreatic pseudocyst in 24 patients and 29 patients had chronic pancreatitis related biliary strictures. A total of 375 procedure were performed (mean3/patient). In 25 patients the sphincterotomy was the only procedure required. 2 patients needed ESWL. Pancreatic stone extractions were performed in 39 patients. Pancreatic plastic stenting were performed in 49 patients among which 34 patients required many long term stenting. The pseudocyst have been drained transpapillary (11 patients), transmural (9 patients) and EUS (4 patients). During the follow-up, a part of patients (10 patients) developed a biliary stricture. The biliary decompression was performed by CBD plastic stenting (22 patients), multiple plastic stents (8 patients), SEMS (2 patients). In 90.16% cases the procedures was successful, in 9.8% failed and the patients underwent surgical drainage. Mean follow up after treatment is 24 months. About 90% of patients had substantial improvement of symptoms after endoscopical treatment, including frequency and severity of pain attack. Pain disappeared completely in 56% patients during follow-up. The pseudocysts was successfully drained and did not reappeared during follow-up in 95% cases. The hospitalization admission rate in patients with severe chronic pancreatitis was higher (mean5/patient) compared to those patients with minimal pancreatic changes (mean3.6/patient). No differences were found regarding the number of hospital admission between the patients with pancreatic stones and the patients without pancreatic duct stones. Success of endotherapy in chronic pancreatitis with minimal changes was 94.12% vs. 89.8% in patients with pancreatic duct strictures. None of the patients younger than 40 years required surgical drainage and the success rate in patients older than 40 years was 87%.
CONCLUSION: We consider that in painful chronic pancreatitis the minimal endoscopic treatment is sufficient. Due to the increased risk of complications and higher costs, additional endoscopic treatment and surgical intervention should be reserved for cases with no response to the minimal endoscopic treatment.
Disclosure of Interest: None declared

P1342 ASSESSING ENDOSCOPIC SKILLS DURING ERCP TRAINING – A ROMANIAN TERTIARY CENTER EXPERIENCE

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INTRODUCTION: The current Romanian endoscopy teaching system confronts with several problems including lack of targeted courses for practical skills development. Also, clear criteria for assessing ERCP procedures and the ability to develop and carry out patient management plans are not defined.
AIMS & METHODS: Our aim was to analyze the ERCP learning curve and to assess the development of endoscopic competence.
From January 2011 - May 2013, 4 trainees in our center entered the ERCP training program. The training consisted of modules of 100 cases each. The CBD cannulation in patients with non-altered anatomy and the rate of complications were prospectively recorded for every trainee after every module fulfillment. Trainee success rates were compared to those of the trainer.
RESULTS: Trainees performed 1041 examinations. Each did an average of 251 examinations (range, 109 to 396). The CBD median cannulation rate improved significantly from first module (100 procedures - 54.57%) to 2nd module (200 procedure) (79.33%, P < .048). The 3rd module was completed only by 2 trainees who reached a 82.5 CBD cannulation rate. The rate of complications decreased form 14.67% (first 100 ERCPs) to 8.72% (200 ERCPs) and 6.01% (300 ERCPs), respectively.
CONCLUSION: The success rate for deep biliary cannulation should be assessed in every ERCP trainee. A success rate of at least 80% for deep biliary cannulation should become a threshold for ERCP competence programs.
Disclosure of Interest: None declared

P1343 RISK FACTORS FOR BLEEDING AFTER ENDOSCOPIC SPHINCTEROTOMY IN COMPARISON WITH ENDOSCOPIC PAPILLARY BALLOON DILATION FOR THE PATIENTS WITH ANTIPLATELET THERAPY

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INTRODUCTION: In Japan, endoscopic papillary balloon dilation (EPBD) is classified as low risk procedure of bleeding, and considered endoscopic sphincterotomy (EST) as high risk. EPBD can be performed for the patient with antiplatelet therapy. But Japan Gastroenterological Endoscopy Soaciety Guideline do not recommend to perform EST for the patient with antiplatelet therapy, except for the patient with aspirin monotherapy. This study aimed to evaluate risk factors of bleeding after such endoscopic procedures for the patient with antiplatelet therapy.
AIMS & METHODS: Consecutive patients received EST or EPBD with antiplatelet therapy were retrospectively studied. A total of 118 patients (EST 85, EPBD 33) who were received such endoscopic procedure (Jan 2009 to Dec.2013) were enrolled. Univariate and multivariate analyses to identify risk factors for bleeding were performed using a proportional hazards model.
RESULTS: In EST group (25 female, 60 male, mean age 77.0), the number of patients taking with aspirin, ticlopidine, clopidogrel, other antiplatelet agent, dual agents were 70, 9, 16, 12, 21, respectively. In EPBD group (7 female, 26 male, mean age 76.8), the number of patients were 25, 3, 4, 5, 4, respectively. Perforation did not occur in both groups. Pancreatitis was significantly frequent in EPBD group (EST 2/85 2.4% vs EPBD 4/33 12.1%, p = 0.042). Bleeding occurred with 3 patients in EST group (3.5%), but did not occurred in EPBD group. There was not significant change. The details of patients with bleeding were 2 patients taking with aspirin and ticlopidine, 1 patient with clopidgrel monotherapy. All patient with bleeding took thienopyridine compound. Univariate analysis revealed that ticlopidine therapy (2/9 p = 0.0163), tienopyridine compound therapy (3/25 p = 0.0058), and dual antiplatelet therapy (2/21 p = 0.0031) were risk factors of bleeding after EST for patient with antiplatelet therapy. But by multivariate analysis, none of them were significant.
CONCLUSION: In this study, taking tienopyridine compound and taking ticlopidine, dual antiplatelet therapy were proved to be not statistically significant risk factors for bleeding after EST, but showed increase trend. EPBD may be considered alternative procedure to EST instead of the high incidence of pancreatitis associated with EPBD.
Disclosure of Interest: None declared

P1344 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN BILLROTH II PATIENTS – A SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) in patients submitted to a previously gastrectomy with a Billroth II reconstruction is technically challenging, with success rates ranging from 50 to 90 %.
AIMS & METHODS: In this study we aimed to analyse ERCPs performed in Billroth II patients, addressing techniques and accessories used, difficulties found, success rate and complications.
Medical and endoscopic records of Billroth II patients submitted to ERCP between January 2011 and December 2013 at our institution were retrospectively reviewed.
RESULTS: A total of 15 ERCPs performed in 12 patients (9 male and 3 female, mean age 71 years, range 51-88 years) were included in the analysis.
A duodenoscope was used in 12 procedures (3 of which with a guidewire previously placed in the afferent loop), a paediatric colonoscope in 2 and an endoscope in 1 procedure.
Afferent loop intubation was achieved in all patients. In one patient, papilla was not reached due to duodenal stenosis. Precut was used for biliary cannulation in 9 ERCPs (60%). Of these, 3 were performed in a previously placed Wirsung stent, and 2 were followed by dilation without sphincterotomy.

ERCP was successful at first attempt in 9 procedures. Inability to perform selective cannulation in 5 cases and the presence of a duodenal stenosis in 1 prevented the completion of ERCP in the remaining cases. A second ERCP was performed in 3 patients, successful in all of them. The overall success rate was 80%.
One ERCP was interrupted due to patient hemodynamic instability and in another patient there was a self-limited papilla bleeding after dilation. No perforation was recorded.
CONCLUSION: ERCP is effective and safe in Billroth II patients. The choice of the most appropriate technique in each case seems to be the best way to increase the success rate in these patients and to avoid complications.
Disclosure of Interest: None declared

P1345 PROSPECTIVE EVALUATION OF ERCP PERFORMANCE – RESULTS OF A NATIONWIDE QUALITY REGISTRY

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INTRODUCTION: Despite significant interest by health authorities, patient organizations and insurance companies, data on procedural outcome and quality of ERCP in general and academic practice are sparse. The aim of this study was to assess procedural outcome of ERCP within a large prospective registry in the Netherlands and to evaluate associations between endoscopist-related factors and procedural outcome.
AIMS & METHODS: All endoscopists performing ERCP in the Netherlands were invited to register their ERCPs over a one-year period using the Rotterdam Assessment Form for ERCP (RAF-E). Primary outcome measure was procedural success. A priori difficulty level of the procedure was classified according to Schutz. Baseline characteristics of the endoscopist, e.g. previous experience, were recorded at study entry. Regression analysis was performed to identify predictors of procedural outcome.
RESULTS: A total of 8575 ERCPs was registered by 171 endoscopists from 61 centers. This entails about 50% of all ERCPs performed in that period nationwide. Overall procedural success was 85.8%. An intact papillary anatomy was present in 5106 patients (59.5%): procedural success in this subset of patients was 83.4% versus 89.4% after sphincterotomy ($p < 0.001$). Regression analysis through Generalized Estimating Equations identified "degree of difficulty" ($p < 0.001$), "intact papillary anatomy" ($p < 0.001$), and "previous ERCP failure" ($p < 0.001$) to be independently associated with procedural failure. "Yearly volume of ERCPs" ($p < 0.01$) and "trainee involvement" ($p < 0.05$) were independently associated with success.
CONCLUSION: Our nationwide prospective RAF-E registry proved to be a valuable tool to gain insight in procedural outcome of ERCPs. The overall procedural success rate for ERCP was 85.8%. Factors predictive of outcome include Schutz classification (degree of difficulty), papillary anatomy, previous ERCP failure, ERCP volume, and trainee involvement.
Disclosure of Interest: None declared

P1346 HIGH RATE OF DEEP SEDATION WITH A COMBINATION OF MIDAZOLAM AND FENTANIL IN A CONSECUTIVE SERIES OF PATIENTS UNDERGOING UPPER EUS

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INTRODUCTION: A good level of sedation increases outcomes and safety in interventional endoscopic procedures. With benzodiazepines and morphinic based protocols a high frequency of deep sedation has been reported. This is our experience with a midazolam/fentanil based protocol of sedation in patients undergoing upper digestive endoscopic ultrasonography (EUS) with particular attention to the level of sedation.
AIMS & METHODS: We retrospectively analyzed data on sedation in all patients undergoing EUS, collected prospectively from March to October 2013. Demographic data, indication, type of procedure, data on technique, ASA score, dosage of drugs, outcomes and complications were collected. Patients were sedated with a combination of 1-2 mcg/Kg of fentanil and 0.05 mg/Kg of midazolam as initial bolus. Repeated boluses of 1 mg of midazolam every 5 minutes were then administered based on patient's response. Sp02, blood pressure, heart rate and respiratory movements were continuously monitorized during the procedure. OASS score was calculated every 5 minutes. Patients were discharged when the score was > 5. We evaluated patients and endoscopist satisfation on a scale from 0 to 10 after the procedure.
RESULTS: During the observation period, 320 upper EUS procedures were performed. 178 patients were males, mean age was 65 (range 25-89), 280 outpatients (88%). There were 22 ASA IV patients (7%), 98 ASA III patients (31%) and 200 ASA I and II patients (62%). In 96 cases a FNA was performed (30%). The mean duration of procedures was 25 minutes (range 5-45). The mean dose of midazolam was 8.5 mg (range 2-15) and the mean dose of fentanil was 95 mcg (range 0-200). In 125 procedures (39%) the mean OASS was < 2 (deep sedation), in 149 (46%) was between 2 and 4 (moderate sedation), in 46 (15%) > 4 (mild sedation). We reported 20 minor desaturation events (Sp02 $<90\%$ but $> 85\%$ for more than 10 seconds) that responded promptly to increase in oxygen flux. One patient required bag-mask ventilation for 2 minutes. In this case the procedure was completed after rescue maneuvers. The mean recovery time was 65 minutes (range 45 to 90). The patients and endoscopist mean statisfation was 8.5 (range 6-10) and 7.3 (range 6-9).
CONCLUSION: In our series, midazolam and fentanil based sedation allowed the execution of all upper EUS with a good safety profile. The doses needed to obtain a good compliance resulted in a consistent rate of deep sedation in our experience.
Disclosure of Interest: None declared

P1347 HIGHER CA 19-9 LEVELS ARE RELATED WITH HIGHER DIAGNOSTIC YIELD OF EUS-FNA IN PANCREATIC ADENOCARCINOMA

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INTRODUCTION: Endoscopic ultrasonography guided fine needle aspiration (EUS-FNA) sensitivity and accuracy described in literature is 60-90% and 60-95%, respectively. Size and type of needle, multiple passes and on-site cytopathology assessment increases diagnostic accuracy. Serologic CA 19-9 correlates with pancreatic adenocarcinoma stage.
AIMS & METHODS: To assess the relationship between CA 19-9 and diagnostic yield of EUS-FNA. Retrospective analysis of 293 patients with pancreatic mass diagnosed between January 2009 and May 2013. A total of 87 patients underwenting first EUS-FNA were included. Two groups were analyzed: cytology diagnostic of adenocarcinoma (group 1) and inconclusive cytology (group 2). Median expression of CA 19-9 was compared and CA19-9 was analyzed as dichotomous variable (≥ 1000 or < 1000 U/L). Mann-Whitney and Qui-square tests were used for groups comparison.
RESULTS: FNA was suggestive of adenocarcinoma in 69 patients (mean age 70 years, 49% male) and inconclusive in 18 patients (mean age 67 years, 56% male). EUS-FNA sensitivity for adenocarcinoma diagnosis was 73%. The median CA 19-9 in group 1 was 1000 U/L (range 0-48462 U/L) and in group 2 was 196 U/L (range 0-7685 U/L), $p = 0.04$. In the subgroup with CA 19-9 ≥ 1000 U/L, 7.9% of all EUS-FNA were inconclusive vs. 30.6% when CA 19-9 < 1000 U/L ($p = 0.009$).
CONCLUSION: To the best of our knowledge this is the first study assessing the relationship between CA 19-9 levels and EUS-FNA diagnostic yield. Patients with first EUS-FNA diagnostic for adenocarcinoma have higher levels of CA 19-9. When using a cut- off ≥ 1000 U/L cytology is less often inconclusive.
Disclosure of Interest: None declared

P1348 A PROSPECTIVE COMPARISON OF 22-GAUGE FLEXIBLE NEEDLE AND SIDE PORT NEEDLE IN EUS-FNA FOR PANCREATIC MASSES

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INTRODUCTION: Two different needles; a cobalt chromium needle with an end port alone to enhance flexibility (Expect™: flexible needle, Boston Scientific) and a stainless steel needle with both side and end ports (EzShot2: side port needle, Olympus Medical Systems), have been developed to improve the diagnostic yield of EUS-FNA.
AIMS & METHODS: The aim of this study was to compare the performance of the 22-gauge flexible needle and side port needle in EUS-FNA for pancreatic masses. Fifty-two consecutive patients who underwent EUS-FNA for pancreatic masses were prospectively enrolled in this study from January 2013. EUS-FNA was performed for each mass using both with randomization of puncture sequence. Then, differences of diagnostic accuracy was evaluated, as well as, the score of adequateness of obtained specimens for cytological evaluation, needle visibility and ease of puncture (0: poor, 1: good, 2: excellent) 1).
RESULTS: A total of 86 punctures (43 with the flexible needle and 43 with the side port needle) were analyzed in 42 patients with pancreatic masses. The final diagnosis based on results of EUS-FNA, surgery and clinical course were pancreatic carcinoma in 32 patients, chronic pancreatitis in 6 and autoimmune pancreatitis in 5. The pancreatic mass was located in the head of pancreas in 25 patients, the body in 11, and the tail in 7. Sensitivity, specificity and accuracy with the overall, flexible needle and side port needle for detecting pancreatic carcinoma were 93.5/100/95.2%, 83.9/100/88.1%, and 77.4/100/83.3%, respectively (N. S). Although the score of visibility of both needles was similar (1.9 vs. 1.86, $p = 0.4$), the score of adequateness of specimens of flexible needle was significantly higher than that of side port needle (1.88 vs. 1.69, $p = 0.039$). In addition, there was no significant difference in the score of adequateness of specimens obtained from masses of the pancreatic head and body/tail with the flexible needle (1.87 vs. 1.89), while the score of adequateness for specimens obtained from pancreatic head masses with the side port needle was significantly lower than that for pancreatic body/tail masses (1.57 vs. 1.83, $p = 0.02$). The score of ease of puncture of flexible needle was significantly higher than that of side port needle (1.88 vs. 1.38, $p < 0.001$).
CONCLUSION: The flexible and side port needles have similar overall diagnostic yield, when EUS-FNA is performed for pancreatic masses. However, the flexible needle was superior in the adequateness of obtained specimens, especially from pancreatic head lesions, because puncture is significantly easier. Therefore,

the exploitation of new needle should probably be focused on enhancement of puncture performance.

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Disclosure of Interest: None declared

P1349 REVIEW OF 114 ENDOSCOPIC ULTRASOUND-GUIDED CYSTGASTROTOMIES FOR PANCREATIC PSEUDOCYST IN TWO LONDON TEACHING HOSPITALS

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INTRODUCTION: With the advancement of interventional endoscopic ultrasound (EUS), EUS-guided cystgastrostomy is now regarded as a good alternative to surgical or percutaneous drainage in the management of pancreatic fluid collections. This procedure was performed in University College London Hospital (UCLH) since 1998 and was started in Royal Free Hospital (RFH), London from 2009 when the two services were combined.

AIMS & METHODS: This is a retrospective review of all EUS-guided cystgastrostomies performed in UCLH from 1998 to 2013 (16-year period) and RFH from 2009 to 2013 (5-year period). Case details including demographics, indications, procedure method and outcome were retreived from patient record database and endoscopy reporting tool, which were then reviewed and analyzed.

RESULTS: A total of 114 EUS-guided cystgastrostomies were identified, with 80 performed at UCLH and 34 at RFH. The male-to-female ratio was 1.5:1 and the median age was 55 years (range 23-85). The median onset of pancreatitis before drainage was 6 months (range 1-120). The most common causes of pancreatitis were gallstones (44.7%), idiopathic (23.7%), alcohol (20.2%), and post-ERCP (3.5%). The pseudocyst was usually located over the pancreatic body (45.6%) or head (14.9%). Indications for drainage included abdominal pain (40.4%), increasing pseudocyst size (35.1%), both pain and increasing size (3.51%), infected pseudocyst (14%) or luminal or biliary obstruction (5.3%). 87.7% of patients had only one pseudocyst. The median maximum diameter of the pseudocyst was 97.5mm (range 42-200). Nine patients had received previous percutaneous drainage while one patient had previous surgical drainage.

Bulge sign was reported in 28 cases (24.6%). The routes of puncture were via body (64%), antrum (13.2%), fundus (7.9%) and duodenum (6.1%). A cystotome was used in 71.1% of cases. The median length of follow-up was 13 months (range 1-138). The procedure was technically successful in 86% (98/114); drainage failed in fourteen cases (12.3%) and in two cases the pseudocyst was aspirated to dryness without stent insertion. Among those technically successful cases, a pseudocyst recurred in 13.3% (13/98) cases and one pseudocyst persisted despite drainage. Those with recurrence were managed conservatively (7/13), by repeat EUS-guided cystgastrostomy (3/13), by surgical drainage (2/13) or percutaneous drainage (1/13). Complications occured in 8.8% (10/114) including three cases of pneumoperitoneum which required laparotomy, one oesophageal perforation, four gastrointestinal bleeding (two required blood transfusion), one pneumothorax and one aspiration pneumonia. The median length of hospital stay was 7 days (range 0-174). The 30-day mortality was zero.

CONCLUSION: EUS-guided cystgastrostomy is increasingly employed in the management of pancreatic fluid collections. This large series demonstrated comparable rates of technical success, recurrence and reintervention to those reported by other groups. In comparison to surgical cystgastrostomy, rates of technical success appear to be similar but with lower complication rates and shorter hospital stays. Further studies are needed to define clear pathways for use of interventional EUS in the management of pancreatic fluid collections.

Disclosure of Interest: None declared

P1350 A NEW NEEDLE PLATFORM FOR EUS-GUIDED FNA: A PROSPECTIVE RANDOMIZED CLINICAL TRIAL COMPARING THE 22G NEEDLE AND THE 25G NEEDLE

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INTRODUCTION: EUS-FNA is safe and effective in obtaining samples from the GI masses and lymphnodes. Available needles include 25G, 22G and 19G. A recently developed needle platform allows for interchangeability of all needle sizes through a universal delivery system (BNX system, Beacon Endoscopic, Newton, MA).

AIMS & METHODS: The primary endpoint of this prospective, randomized, trial was to compare the performance of 25G and 22G needle by evaluating the adequacy of the aspirated obtained from solid lesions. Secondary aims were the ease of needle pass, needle malfunctions, n° of passes, n° of crossovers to the other needle size, major complications.

Consecutive patients referred for EUS-FNA for solid masses were randomized to the 25G or to the 22G needle arm. Inclusion criteria: EUS appearance of a solid lesions, age >18 yrs, informed consent. Crossover to the other size of needle was allowed when the endoscopist experienced difficulties in puncturing the mass, or when the material was not adequate after 3 passes.

RESULTS: Eighty-two patients were enrolled from Aug 2013 to Apr 2014 (50 M, 32F), mean age 67 years (range 29-87). Sixty pancreatic masses, 17 lymphnodes and 5 parietal lesions were biopsied. Forty-one patients were randomized to the 25G needle arm: in 8 cases (19.5%) a crossover to the 22G was asked by the pathologist in order to obtain more material for immunohistochemistry (neuroendocrine tumors or lymph-nodes). Forty patients were randomized to the 22G needle arm: in 9 cases (22%) a crossover to the 25G was done because of the hardness of the tumor. The mean of needle passes was 2.2 (±1.08 SD) per lesion. In 37 cases the aspirate was both smeared for cytological examination and put into formalin for histology. Final diagnosis was confirmed by surgical resection or radiological follow up. Overall adequacy was 86%. In 11 cases the aspirated was inadequate: 1 adenocarcinoma, 3 lymphnodes (1 sarcoidosis, 2 colliquative nodes), 1 GIST, 1 pseudosolid pancreatic mass, 1 suspected groove pancreatitis, 1 IPMN, 1 tumor involving the hepatic hylum, 2 hypervascularized pancreatic lesions. In patients with adequate specimen the sensitivity and accuracy were 95% and 91% for the 22G needle and 97% and 97% for the 25G needle, respectively. In 5 cases a resistance to 22G needle advance was felt by the endosonographer. No major complications were observed.

CONCLUSION: The BNX-platform is accurate for the diagnosis of solid masses, with results comparable to those of the literature and with no significant difference between the performance of the 22G and 25G needle. Nearly one fourth of all procedures may require crossover with a higher adequacy rate.

Disclosure of Interest: None declared

P1351 CHARACTERIZATION OF FLUID COLLECTIONS USING QUANTIFICATION OF SOLID DEBRIS IN ACUTE PANCREATITIS - A COMPARATIVE STUDY OF EUS VS. CT FOR PREDICTION OF INTERVENTION

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INTRODUCTION: Computed tomography (CT) is the commonest imaging modality used to detect fluid collections in acute pancreatitis. However CT poorly differentiates solid necrotic debris from liquid component, which plays an important role in planning intervention and predicting outcome.

AIMS & METHODS: To evaluate the role of CT and EUS in defining the morphological characteristics of pancreatic fluid collections along with quantification of the solid debris and evaluate their predictability for intervention and outcome.

Consecutive patients of acute pancreatitis with fluid collections detected on CECT, between January-October, 2013 were evaluated further by EUS using Pentax and Olympus linear echoendoscopes. Morphological characteristics of fluid collections (based on revised Atlanta) i.e. nature of collection, location, size and the amount of solid debris, were correlated for need of intervention and final outcome using CT and EUS. The amount of solid debris was graded as minimal (<10%), moderate (10-50%) and profound (>50%) and compared between various types of collections. CECT images were analysed by 2 experienced radiologists and EUS images were analysed by 2 independent endosonologists.

RESULTS: 50 patients (mean age-41.84±11.7 years, 44% males) of acute pancreatitis with fluid collections were analysed. 61 fluid collections were detected in these 50 patients, 11 of which were distant collections and could be demonstrable only on CT and remaining 50 were pancreatic/peri-pancreatic collections which could be analysed using both on CT & EUS. 18 (36%) had acute necrotic collections (ANC), 29 (58%) had walled off necrosis (WON) and 3 (6%) had pseudocysts. The mean size of fluid collections on CT was significantly more than on EUS (9.3 vs. 7.7 cm, $p<0.001$). Solid debris was detected in 46 (92%) patients using EUS while only 16 (32%) patients could be identified with CT ($p<0.001$). On EUS, minimal solid debris was noted in 11 (22%), moderate solid debris in 23 (46%) and profound solid debris in 16 (32%). 72% of ANC's labelled on CT had profound solid debris and 30% of pseudocysts labelled on CT had moderate solid debris, all of whom were managed conservatively. Amongst WON's labelled on CT, 8 (27.5%) had minimal solid debris who could be managed conservatively; 18 (62%) had moderate solid debris, 7 (38%) of whom required intervention (4-percutaneous; 3-endoscopic drainage) and 3 (10.3%) had profound solid debris, all (100%) of whom required intervention (2-endoscopic necrosectomy; 1-percutaneous drainage) ($p<0.001$).

CONCLUSION: EUS is a better modality than CT in detecting solid debris in pancreatic fluid collections. As the fluid collections evolve from ANC into WON the solid debris decreases making EUS the preferred modality for follow up of fluid collections. EUS quantification of solid debris can be used as a guide for selecting the treatment modality.

Disclosure of Interest: None declared

P1352 EFFICACY OF ENDOSCOPIC ULTRASONOGRAPHY FOR TREATMENT OF EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic ultrasonograpy (EUS) is thought to be the most reliable preoperative method for evaluation of depth of invasion. Findings on endoscopy can also predict the depth of tumor invasion.

AIMS & METHODS: The aim of this study was to evaluate the accuracy of EUS for depth of invasion and to compare the accuracy of EUS with that of conventional endoscopy (CE) to predict suitable candidates for endoscopic submucosal dissection (ESD) according to standard and expanded indication.

Between May 2009 and May 2013, 300 patients were underwent EUS and curative treatment for early gastric cancer (EGC). We reviewed the medical and compared preoperative CE and EUS staging with the pathological staging results.
RESULTS: The overall accuracy of CE and EUS to evaluate the invasion depth of EGC were 73.3% versus 76.5% ($p=0.209$). Large size, submucosal invasion, radial EUS were associated with accuracy of EUS. The accuracy of CE and EUS to identify proper candidate of ESD were 98.8%, 89.9 ($p=0.568$) in standard indication and 60.0%, 71.8% in EUS ($p=0.0064$). Undifferentiated histology (100% and 66.7%, $p=0.007$) or invasion depth confined to the mucosa (80.3% and 63.6%, $p=0.033$) were associated with higher accuracy of EUS to select the proper candidates according to expanded ESD indication compared with CE.
CONCLUSION: EUS staging could be helpful to decide the optimal treatment according to expanded indication. Especially, lesion with undifferentiated histology should be carefully considered prior to ESD by pretreatment EUS staging.
Disclosure of Interest: None declared

P1353 USEFULNESS AND SAFETY OF ENDOSCOPIC ULTRASONOGRAPHY-GUIDED DRAINAGE FOR POSTOPERATIVE PANCREATIC FISTULAS

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INTRODUCTION: Endoscopic ultrasonography (EUS)-guided drainage has recently been shown to be useful for treating walled-off pancreatic necrosis (WOPN), a late complication of necrotizing pancreatitis that consists of loculated fluid collections with necrotic material. With this development in mind, we became interested in determining if EUS-guided drainage is also useful for treating postoperative pancreatic fistula (POPF). Hence, the objective of this study was to examine the usefulness and safety of EUS-guided drainage for POPF.
AIMS & METHODS: A total of 37 patients who had undergone EUS-guided drainage for treatment of POPF or WOPN between December 2002 and March 2013 were enrolled in this retrospective study. We reviewed the success rates of the procedures, rates of lesion size reduction, treatment success rates, and complication rates associated with EUS-guided drainage. By comparing the resultant data for EUS-guided drainage of the two conditions (POPF and WOPN), we were able to determine the usefulness and safety of EUS-guided drainage for POPF.
RESULTS: EUS-guided drainage was performed in 14 patients with POPF and in 23 patients with WOPN. There were no significant differences in the clinical characteristics—including sex, age, and lesion size—of the patients in the POPF and WOPN groups who underwent EUS-guided drainage. The procedures required for EUS-guided drainage included aspiration in three cases, an external fistula in one case, internal fistulas in four cases, and external and internal fistulas in six cases in the POPF group, but no endoscopic necrosectomy. The corresponding numbers for the WOPN group were aspiration in five cases, external fistulas in three cases, internal fistulas in three cases, external and internal fistulas in seven cases, and endoscopic necrosectomy in three cases. The successful procedures, reduced lesion size, and successful treatment rates were 100 %, 100 %, and 93 %, respectively, in the POPF group and 91.3 %, 78.2 %, and 71.4 %, respectively, in the WOPN group. The reduced lesion size and treatment success rates were significantly higher in the POPF group than in the WOPN group. No complications occurred in the POPF group, whereas four patients in the WOPN group suffered such complications as perforative peritonitis and procedure-related bleeding. In all, 26 (13 POPF, 13 WOPN) of 37 patients were followed up for a mean of 22 ± 4.2 months. There were no recurrences in the POPF group, whereas three patients in the WOPN group did have a recurrence.
CONCLUSION: EUS-guided drainage is a useful treatment not only for WOPN but also for POPF. Comparing the usefulness and safety of EUS-guided drainage in patients with POPF using the same parameters as those used to assess its use in those with WOPN indicated that EUS-guided transmural drainage can be a good option for treating POPF.
Disclosure of Interest: None declared

P1354 CLINICAL IMPACT OF LIQUID-BASED OR CELL BLOCK PREPARATION OF RESIDUAL MATERIAL AFTER ANALYSIS OF CYTOLOGICAL SMEARS IN ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION

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INTRODUCTION: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is an accurate technique to biopsy lymph nodes and masses for cytological analysis. Residual material, being residue aspirate or an extra aspiration after preparation of cytological smears or residual tissue, can be used for liquid-based or cell block preparation, which may be useful when smears are inadequate and/or immunohistochemistry is required. For liquid-based preparation, residual material is placed in hemolytic solution and then placed on a slide, resulting in a thin layer of cells. For cell block preparation, residual material is clustered, embedded in a fixative and then cut, enabling analysis of tissue particles that are too thick to be analysed with cytological smears. The diagnostic value of these additional tests is unclear. We hypothesised that analysis of residual material is a valuable addition to EUS-FNA.
AIMS & METHODS: The aim of this study was to evaluate the additional diagnostic yield of liquid-based or cell block prepared residual material after routine cytological smear analysis in EUS-FNA procedures. EUS-FNA procedures between 2002 and 2013 were identified using a single center endoscopy database. Diagnostic yield and accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of cytological smears and smears combined with residual material were calculated and compared using one-sided testing. Diagnostic yield was defined as the proportion in which the pathologist could make a diagnosis. Diagnostic accuracy was defined as the proportion in which the diagnosis of the pathologist was in line with the final diagnosis based on a histologal biopsy, surgical resection or clinical outcome.
RESULTS: In total, 510 cases were identified. EUS-FNA was successful in 482 cases (95%), on-site evaluation was available in 448 (93%). A total of 580 sites were targeted, a lymph node was targeted 444 times (77%) and a mass 136 times (23%). The most frequently aspirated sites were the subcarina ($n=264$, 46%), pancreas ($n=64$, 11%) and aortopulmonary window ($n=64$, 11%). Residual material was available in 216 cases (45%), which directly benefited the diagnosis in 30 cases (14%). In 11 cases (37%), it led to the diagnosis, in 4 cases (13%) it enabled differentiation in origin of the tumour and in 15 cases (50%) immunohistochemistry was useful to determine the origin of the tumour. In cases with residual material available and using the cytological smears only for analysis vs. combining this with analysis of residual material, the diagnostic yield was 88% vs. 88% ($p=0.5$), diagnostic accuracy 82% vs. 92% ($p=0.01$), sensitivity 79% vs. 90% ($p=0.01$), specificity 97% vs. 97% ($p=0.5$), PPV 99% vs. 99% (0.44) and NPV 55% vs. 72% ($p=0.03$). Number needed to test with regard to residual material was 7.2.
CONCLUSION: Additional analysis of liquid-based or cell block prepared residual material after analysis of cytological smears benefits diagnostic accuracy, sensitivity and NPV in EUS-FNA procedures. Future studies are warranted to establish whether adding the analysis of residual material is indeed cost-effective.
Disclosure of Interest: None declared

P1355 ROLE OF ENDOSONOGRAPHY IN DETECTING GASTRIC MALIGNANCIES

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INTRODUCTION: Assessing the role of endoscopic ultrasound (EUS) examination in the diagnosis of non-typical or malignancy suspected stomach lesions found in conventional upper endoscopy.
AIMS & METHODS: Twenty eight patients (64.3% male, 35.7% female) at mean age 55±18 years with endoscopy findings of stomach ulcers (25%), polyps (21.4%), polypoid mucosal changes (35.7%) or enlarged folds (17.9%) were evaluated by linear EUS in our centre following conventional forceps biopsies. According to the endosonographic features of the lesions: homogeneity, thickening or loss of wall stratification, lesion margins, presence of necrotic areas and lymph nodes, they were classified as EUS benign and EUS malignant. Biopsy results were also subdivided into two groups – benign (gastritis, adenoma, hyperplastic and fundic gland polyp) or malignant (carcinoma, lymphoma) and compared to EUS groups. All lesions signed as malignant were further evaluated by computer tomography, second look biopsies and/or laparoscopy/laparotomy.
RESULTS: Patients' evaluation resulted in the following groups: EUS benign – 42.9%, EUS malignant – 57.1%; biopsy benign 67.9%, biopsy malignant 32.1%. When comparing EUS and biopsy groups we found that EUS features of malignancy were present in 7 cases (43.8%) with benign histology results, while all EUS benign lesions corresponded to benign histology ($p=0.002$). The mismatch cases were further evaluated resulting in change of diagnosis in all patients of this group from benign to malignant. In the malignant EUS groups, the predominant EUS features were: presence of lymph nodes (87.5% vs. 12.5%, $p=0.005$), loss of wall stratification (93.8% vs. 6.3%, $p<0.001$) and lesion heterogeneity (87.5% vs. 12.5%, $p<0.001$).
CONCLUSION: Endosonography of stomach lesions is a reliable method for neoplasm detection. Even in patients with negative conventional biopsy histology result certain EUS features are indicative for malignancy and can lead to the final diagnosis.
Disclosure of Interest: None declared

P1356 CONTRAST-ENHANCED ENDOSCOPIC ULTRASONOGRAPHY CAN PREDICT A HIGHER MALIGNANT POTENTIAL OF GASTROINTESTINAL STROMAL TUMORS BY VISUALIZING LARGE NEWLY FORMED VESSELS

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INTRODUCTION: Contrast-enhanced endoscopic ultrasonography (CE-EUS) is a new imaging modality for detecting intratumoral vessels in real time.
AIMS & METHODS: The aim of this study was to elucidate the histological and clinical implications of detection on CE-EUS of intratumoral vessels in gastrointestinal stromal tumors (GISTs). A total of 13 patients, each having a GIST, and all of whom were referred for surgery, underwent presurgical CE-EUS. Final diagnoses were made by pathologic examination of resected specimens. The GIST malignancy potential, assessed according to the modified Fletcher risk classification system, and the histological degree of angiogenesis were compared to the presence or absence of intratumoral vessels on CE-EUS.

RESULTS: Intratumoral vessels were observed on CE-EUS in 6 patients, but not in the remaining 7. Of the 6 tumors with intratumoral vessels, 5 (83%) were intermediate- or high-risk GISTs, and all negative cases were categorized as very low risk or low risk. Presence of intratumoral vessels on CE-EUS was significantly correlated with a higher-risk classification (according to the modified Fletcher classification system) ($P = 0.005$). All GISTs with the visualized vessels with CE-EUS incorporated vessels more than 500 μm in histology. The large intratumoral vessels of the 5 intermediate- or high-risk GISTs lacked elastic fibers, suggesting that they were neovascular in nature. These higher-risk tumors were also found, by immunohistochemical analysis, to have high expression of vascular endothelial growth factor.
CONCLUSION: Intratumoral vessels observed in GISTs on CE-EUS are large vessels, by histological examination, and are correlated with higher malignant potential.
Disclosure of Interest: None declared

P1357 THE ACCURACY OF ENDOSCOPIC ULTRASONOGRAPHY IN DIFFERENTIATING OF T1M AND T1SM ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: According to TNM classification of esophageal cancer, the T1 stage is subdivided into mucosa (T1m) and submucosa (T1sm). Endoscopic submucosal dissection (ESD) is a newly developed skill to complete resection gastrointestinal (GI) tract early cancer. The limitation of ESD is cancer invasion to submucosal layer and increasing the risk of lymph node metastasis (20-28%), therefore, the accurate T1 stage subdivision of esophageal cancer prior to ESD is essential.
Endoscopic ultrasound (EUS) is a useful examination for detecting the T stage of GI tract cancer, the reported accuracy of different T stage are around 70-90%, however, there are few published data on the detail discrimination of EUS among each subdivision T1m or T1sm of esophageal cancer. The aim of this study is to evaluate the accuracy of T1 stage subdivision of esophageal cancer by higher frequency EUS probe.
AIMS & METHODS: From April 2009 to March 2014, there are 1125 patients diagnosed with esophageal cancer, further stage with EUS, computered tomography and PET-CT. The EUS examination is performed with miniprobe (UM-2R, 12 MHz, UM-3R, 20 MHz; Olympus Optical Co. Ltd., Tokyo, Japan) and water immersion method.
The enrolled criteria of this study: 1. esophageal squamous cell carcinoma was proved by biopsy result. 2. T1m or T1sm stage diagnosed by EUS. 3. Further treatment with ESD or radical surgery. All EUS-T stage results were correlated with final pathological T stage.
RESULTS: There were 134 patients with T1 stage of esophageal squamous cell carcinoma by EUS, and 73 patients received further ESD (33) or surgical esophagectomy (40). All lesions were confirmed as T1 on pathology, EUS stage of T1m in 55 patients and 45 (82%) were confirmed as T1m on pathology; of the 18 T1sm on EUS and12 (67%) were confirmed as T1sm. Positive predictive value of EUS for T1m was 82%, negative predictive value was 67%, sensitivity 88%, specificity 55%.
CONCLUSION: EUS demonstrated median degree of accuracy for distinguishing between stages T1m and T1sm of esophageal squamous cell carcinoma. Even with high frequency miniprobe, peritumoral inflammation or submucosal fibrosis causes some difficulties in differentiating mucosal from submucosal lesions, and develops more advanced EUS device is needed. EUS remains a valuable tool when endoscopic treatment is considered.
Disclosure of Interest: None declared

P1358 EUS GUIDED CARDIAC APRROACH-EUS GUIDED TRANSESOPHAGEAL PERICARDIOCENTESIS

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INTRODUCTION: EUS-guided intervention has been established for diagnostic and therapeutic procedures in gastroenterology. Echocardiographic-guided pericardiocentesis is the preferred initial procedure for the diagnosis and treatment of pericardial effusion. Pericardial effusion is rarely located in the posterior side of pericardial sac, which makes it difficult for cardiologist to perform Echocardiographic-guided pericardiocentesis through the subxiphoid route. Cardiac intervention using EUS- guided transesophageal approach might be anatomically practical but has still been experimental.
AIMS & METHODS: AIM: These clinical cases are to show our experience of EUS guided-transesophageal pericardiocentesis successfully and safely. METHODS: Three patients who failed echo-cardiography guided diagnostic pericardiocentesis were offered EUS-guided approach. Informed consent was obtained. Diagnostic EUS-pericardiocentesis was performed with sedation of meperidine and midazolam. EUS guided transesophageal puncture using 22G needle was performed into the pericardial effusion. The fluid was fully aspirated for evaluation of tumor makers, cytology and culture. Patients were carefully monitored during and after the procedure and given third generation cephalosporins.
RESULTS: EUS-guided pericardiocentesis performed in 3 patients in hemodynamic stable condition (Male = 2, Average 69 year old). The puncture was via lower portion of the esophagus. The average procedure time is 10minutes. The median fluid amount was 15ml. EUS guided aspiration confirmed non-diagnostic in 2 patients and tubeculosis in 1 patients. No early or late complications: no infection, arrythmia, heart failure and/or bleeding.
CONCLUSION: EUS guided transesophageal approach to pericardiocentesis was successful in the limited cases. The cases must be applied to the procedure only if echocardiographic pericardiocentesis fails.
Disclosure of Interest: None declared

P1359 GUIDE-WIRE ASSISTED INSERTION OF AN ULTRATHIN ENDOSCOPE INTO THE PROXIMAL JEJUNUM: A NOVEL TECHNIQUE

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INTRODUCTION: Insertion into the proximal jejunum with conventional esophagogastroduodenoscopy (EGD) by push technique is difficult. The reasons for difficulty are that an endoscope bends in the stomach and the distal end of an endoscope has less flexibility for advancement. Although the flexible ultrathin endoscope (UTE) has the drawback of easily bending in the stomach, when inserting the stiff guide-wire through the biopsy channel, the bending of the UTE in the stomach is avoided. Using these characteristics of the UTE, we made it possible to insert the UTE assisting with a balloon and a super stiff guide-wire into the common bile duct (Endoscopy 2012; 44). Recently, we have developed a novel technique which inserts the UTE assisting with only a super stiff guide-wire into the proximal jejunum. We report here the method and the feasibility of this technique.
AIMS & METHODS: 20 consecutive patients were evaluated in a preliminary prospective feasibility study. 16 patients were suspected of the distal duodenal and proximal jejunum diseases (7 strictures, 4 obscure gastrointestinal bleedings, 2 tumors and 3 others) and 4 patients needed injection of enteral feeding from the distal duodenal and proximal jejunum. All unsedated patients underwent this procedure via transnasal route. After observing the upper gastrointestinal tract with the UTE (EG580NW, FujiFilm, Tokyo, Japan), we inserted a guide wire (Amplatz superstiff 0.035) using the biopsy channel of the UTE until about 20 cm distal end of the UTE to maintain the stiffness of the UTE to avoid the bending in the stomach. This facilitated insertion of the UTE into the proximal jejunum and made it possible to perform not only EGD but also jejunoscopy at the same time (ultrathin esophagogastroduodenojejunoscopy: UT-EGDJ). We assessed the success rate, procedure time and usefulness in diagnosis. Successful UT-EGDJ was defined as the fluoroscopically-confirmed advancement of the UTE beyond the duodeno-jejunal angle.
RESULTS: UT-EGDJ was performed successfully in 19/20 patients (95%). We failed to complete UT-EGDJ in only one patient who had a huge abdominal aortic aneurysma placed the stent graft in. The median (interquartile range) time to reach the proximal jejunum was 300 (240-327) seconds. This procedure revealed 3 SMA syndromes, one small intestinal adenoma with bleeding and one lupus enteritis. No significant clinical complications related to UT-EGDJ.
CONCLUSION: UT-EGDJ appears to be sufficiently feasible and may be available for a screening of the deep duodenum and proximal jejunum as a bridge to balloon small intestinal endoscopy.
Disclosure of Interest: None declared

P1360 EFFECTIVENESS OF ENDOSCOPIC ULTRASONOGRAPHY DURING DOUBLE BALLOON ENTEROSCOPY FOR SUSPECTED SMALL BOWEL TUMORS

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INTRODUCTION: Endoscopic Ultrasonography (EUS) performed during Double Balloon Enteroscopy (DBE) was firstly reported in 2006. The combination of these two techniques allows the endoscopists to evaluate extraluminal small bowel (SB) lesions previously considered inaccessible. Despite appearing a promising diagnostic technique, his employment is still limited and his usefulness is not widely assessed.
AIMS & METHODS: The aim of this retrospective study was to evaluate the diagnostic rate of EUS during DBE for suspected small bowel tumors (SBT) and its usefulness for characterization of sub mucosal tumors (SMT) in a large cohort of patients. The secondary endpoint was to compare, for the first time, DBE and EUS with computerised tomography (CT) and small bowel capsule endoscopy (SBCE).
Patients with a suspected SBT, who underwent EUS-DBE in our Institution between 2007 and December 2013, were retrospectively reviewed. Demographic datas, clinical, endoscopic and radiological findings, therapeutical management, final diagnosis and follow-up were considered. DBE, EUS, SBCE and CT diagnostic rate and concordance among the 4 procedures analysed.
RESULTS: Sixty-one patients with suspected SBT were included in the study (38 male, 54 years old). DBE and EUS were performed in all patients, CE in 29 and CT in 56. SBT were diagnosed in 46 patients, 30 were SMT while the remnant 16 SBT involved the mucosa. DBE and EUS diagnosed SBT in 44 (96%) and 43 (93%) patients respectively. In particular a correct characterization of SMT was obtained by DBE and EUS in 8 (27%) and 20 (67%) patients respectively ($p = 0.0014$). GIST (8), carcinoid (1), metastasis (3), haemangioma (3) were successfully diagnosed in all case by EUS while the characterization of SB pancreatic

rest (3/8), lymphangioma (1/4) and lipoma (0/2) was limited. In addition CE detected 10 SB tumors out of 19 (53%) and CT 34 out of 44 (77%). SBT diagnosis concordance rates among the procedures were the following: DBE-EUS 91% (42/46), DBE-CE 53% (10/19), DBE-CT 73% (32/44), EUS-CE 47% (9/19) EUS-CT 68% (30/44), CE-CT 42% (8/19).
CONCLUSION: Our results suggest that EUS performed during DBE is a useful technique for SBT diagnosis and in particular for SMT characterization. Therefore we recommend integrating EUS to DBE practice to establish a certain diagnosis, in order to provide the most appropriate medical management.
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P1361 GAY INDEX IN ROUTE SELECTION FOR SINGLE-BALLOON ENTEROSCOPY AFTER POSITIVE FINDINGS IN CAPSULE ENDOSCOPY

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INTRODUCTION: After positive findings in capsule enteroscopy, device-assisted enteroscopy route is not always evident. Gay *et al*[1] developed an index to predict the correct route for device-assisted enteroscopy after a positive capsule enteroscopy (if transit time until the finding > 0.75 of orocecal time – anal route). Recently, Li *et al.*[2] proposed another índex (if transit time between pylorus and the finding >0.6 of small bowel transit – anal route).
AIMS & METHODS: To evaluate Gay index ability to predict the correct route for single balloon enteroscopy after positive findings in capsule enteroscopy. To compare Gay index with Li index.
A single-center retrospective study evaluated patients with positive findings on capsule enteroscopy that were subsequently submitted to a single balloon enteroscopy. Considered the period between January 2010 and September 2013. Single balloon enteroscopy route selected accordingly to Gay index. Comparison with Li index.
RESULTS: 49 patients (female gender 57.1%; mean age 66.7 years) were evaluated. Angioectasias (n:20) and bleeding without an identified source (n:17) were the most important capsule enteroscopy positive findings. Accordingly to Gay index, oral route was selected in 69.4% (n:34) of the cases. The single-ballon enteroscopy goal was not fulfilled in 12.2% (n:6). Nevertheless, in 5 cases the goal was not achieved for reasons not related to the distance (fixed angulation: 3; technical issues 1; stenotic ileo-colic anastomosis: 1). In one case it was attempted the alternative route, without success. Gay index and Li index were concordant in 98% (n:48) of the cases.
CONCLUSION: In our study 1) the single-balloon enteroscopy goal was achieved in most of the patients; 2) Gay index revealed a good ability to predict the single-balloon enteroscopy route; 3) Li index and Gay index revealed a similar ability to predict the correct insertion route.
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Disclosure of Interest: None declared

P1362 CELIAC DISEASE AND DOUBLE-BALLOON ENTEROSCOPY: WHAT CAN WE ACHIEVE? THE EXPERIENCE OF TWO EUROPEAN TERTIARY REFERRAL CENTERS

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INTRODUCTION: The indications for and efficacy of device-assisted enteroscopy is not standardised in celiac disease (CD).
AIMS & METHODS: We present the largest study to date to evaluate the clinical role of double-balloon enteroscopy (DBE) in complicated CD. DBE findings in CD patients with suspected small bowel complications were retrospectively evaluated in two tertiary referral centers (Milan and Sheffield). Demographic data of the studied cohort were compared with a database of 1000 non complicated CD patients.
RESULTS: Findings from 14 oral and seven anal DBE in 19 CD cases (11 males p = 0.003 vs control database) were reviewed. Mean age at CD diagnosis (39±19 vs 27±18) and at small bowel evaluation (49±15 vs 38±13) was significantly higher in the DBE group compared to controls (p < 0.001). Indications for DBE were the follow up of known refractory coeliac disease (RCD) (#7), suspicion of small bowel complications due to gastrointestinal symptoms (#4), severe iron deficiency anemia (#6) and long standing poor dietary adherence (#2). All DBE were performed after small bowel capsule endoscopy, except for one case. Three patients from the known RCD group had evidence of TCR gamma monoclonality on biopsy (type 2 RCD). One of these patients had jejunal ulceration whilst the other 2 cases had areas with small white raised patches. A further RCD case had evidence of jejunal ulceration however biopsies didn't show any evidence of TCR gamma monoclonality. Patchy small bowel atrophy was observed in all the non adherent patients and in 2 patients with persistent gastrointestinal symptoms who had only been on a gluten free diet for a short time. Two jejunal adenocarcinomas and an ileal neuroendocrine tumour were detected. All 3 of these patients presented with iron deficiency anaemia. A therapeutical approach was planned in 30% of patients after DBE. No events were detected at follow up (18 months; 5-55).
CONCLUSION: This is the largest international DBE outcomes study in CD patients. DBE could be useful in selected CD cases to exclude/confirm malignant or premalignant conditions, possibly associated even with minor mucosal lesions. Evaluation of non-responsive/refractory symptoms by DBE was associated with older patients and a higher proportion of males than an uncomplicated CD population. Studies are needed to understand the clinical relevance of the small bowel endoscopic features and to optimise DBE indications.
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Disclosure of Interest: None declared

P1363 THE SIGNIFICANCE AND BENEFIT OF THE COMPLEX ENTEROSCOPY IN PATIENTS WITH SMALL BOWEL NEOPLASIA

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INTRODUCTION: Diagnosis of small bowel tumor can be a very challenging. Videocapsule endoscopy (VCE) and balloon-assisted enteroscopy (BAE) have their own specific limitations.
AIMS & METHODS: To estimate the benefits of combined use of VCE and BAE in diagnosis and treatment of small bowel tumors. From II. 2007 until IV.2014 VCE followed by BAE were performed in 43 pts. (m-18, f-25, mean age 45±13.9 yrs., range 18-73) with strongly suspected small bowel neoplasia. Small bowel tumors have been detected in 31 (72.0%) pts. (m-14, f -17, mean age 42±14.5 yrs., range 18-70). Obscure GI bleeding was an indication for VCE in 19 (61.3%) of them. The insertion route for BAE was determined according to the site of the suspected lesions detected by VCE. For precise diagnosis and tumor evaluation we performed sonde-EUS through the enteroscope in 13 (41.9%) pts. with intestinal neoplasia.
RESULTS: According to VCE data tumor was suspected in 30 (96.7%) pts. while BAE detected the neoplastic lesions in 29 (93.5%) pts. (plus in 2 pts. with negative BAE we've performed laparoscopy and revealed tumors with extra-organic growth). BAE-EUS in 13 pts. provided detailed and useful information about the echogenicity, its echo-structure and the layer of origin of the tumor that helped to determine the treatment policy and method of tumor removal. Histologically the tumors were defined as neuroendocrine tumors in 6 (19.3%) pts., GIST in 4 (12.9%) pts., adenocarcinoma in 2 (6.4%) pts., lymphoma in 1 (3.2%) pt., Peutz-Jeghers hamartomas in 8 (25.8%) pts., hyperplastic polyps in 4 (12.9%) pts., tubular adenoma in 2 (6.4%) pts., cavernous haemangioma in 2 (6.4%), angiofibrolipoma in 1 (3.2%), lymphangioma in 1 (3.2%) pt. Intestinal tumors mainly localized in jejunum in 16 (51.6%) pts. and in ileum 8 (25.8%) pts. and in 7 (22.6%) pts. with Peutz-Jeghers syndrome (5) and neuroendocrine tumors (2) the lesions extended segmental in jejunum and ileum. Conservative specific treatment was applied in 1 (3.2%) patient with B-cell lymphoma as well as endoscopic haemostasis by APC during BAE because of tumor bleeding. Endoscopic treatment (polyp removal) was performed in 11 (35.5%) pts.: EMR (1) and polypectomy (10). Surgery was performed in 18 (58.1%) pts.

Diagnostic accuracy	VCE	BAE	VCE+BAE
Sensitivity	**96.6%**	**93.3%**	**100%**
Specificity	**77.0%**	**92.3%**	**92.3%**

CONCLUSION: Complex enteroscopy (VCE+BAE) provides all the benefits of gradual, proper and accurate diagnosis of small bowel tumors as well as possibilities of conservative/endoscopic treatment through the endoscope in 38.7% patients. Combination of VCE and BAE demonstrates a higher effectiveness in the diagnosis of small bowel neoplasia than its separate usage.
Disclosure of Interest: None declared

P1364 A PROSPECTIVE COHORT STUDY EVALUATING NAVIAID AB - A NOVEL PLATFORM FOR DEEP SMALL BOWEL ENTEROSCOPY

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INTRODUCTION: Endoscopic visualization of the small-bowel is facilitated by device-assisted enteroscopy. Deep small-bowel intubation mostly requires a significant amount of time, involved a prolonged learning curve, and coopers often two assistance. Notable, it has been shown that more than 75% of lesions within the small bowel are located in the proximal jejunum.

AIMS & METHODS: To evaluate the feasibility, usability, and safety of a novel platform for deep small bowel enteroscopy featuring the very recently introduced NaviAid AB device. This was a prospective, single-center pilot and feasibility study. Patients underwent deep small bowel enteroscopy featuring the newly introduced NaviAid AB device for evaluation of obscure gastrointestinal bleeding, suspicious small-bowel Crohn's disease, celiac disease, familial adenomatous polyposis or abdominal pain. Study end points included successful deep small bowel enteroscopy, time to evaluate the small bowel, success of therapeutic interventions, adverse events, and endoscopists' subjective evaluation of NaviAid AB.
RESULTS: Overall, 23 patients, aged 19 - 77 years were prospectively included. Enteroscopy was feasible in all cases. Mean time to prepare the system was 2 minutes (Range 2-5 minutes). The estimated small bowel intubation depth was 200 cm (Range 90-280 cm) past the ligament of Treitz. Average time of the procedure was measured as 14 minutes (Range 13-18 minutes). Findings included small bowel Crohn's disease, small bowel diverticulosis, NSAID enteropathy, celiac disease, small bowel polyps and angiovascular malformations. No procedure related complications occurred.
CONCLUSION: The newly introduced NaviAid AB device allows safe and fast on demand deep enteroscopy. Approaching the deep jejunum could be achieved within only 14 minutes. The device allows stable positioning of the scope for therapeutic interventions. Therefore, the new NaviAid AB device could become an additional device to explore the small bowel. Future studies should now focus on the learning curve and if even total enteroscopy is feasible.
Disclosure of Interest: None declared

P1365 UTILITY OF DOUBLE BALLOON ENTEROSCOPY IN PATIENTS WITH SURGICALLY ALTERED BOWEL ANATOMY AFTER OBESITY SURGERY

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INTRODUCTION: Endoscopic investigation of the gastrointestinal (GI) luminal and pancreatobiliary tracts in patients with surgically-altered GI anatomy after bariatric surgery is challenging and often impossible. The advent of balloon-assisted enteroscopy (BAE) has increased our ability to navigate through the surgically altered bowel. Despite the existence of BAE since more than a decade there is few data available on it potential utility for evaluation post-obesity-surgery patients.
AIMS & METHODS: To evaluate the diagnostic yield, success and complications rates of double-balloon enteroscopy (DBE) in consecutive patients with GI problems necessitating endoscopic evaluation.
Materials and Methods: Single-center, observational, cohort study of consecutive patients with post-obesity-surgery undergoing DBE during a 12-months period. Patients' demographics, procedure indications, findings, endoscopic interventions, and post-procedural recovery data were recorded.
RESULTS: A total of 265 DBE were performed at our institution during the 12-months study period. Thirty-three patients (12.1%) with post-obesity surgery were evaluated using DBE. The most common indication for DBE was obscure GI bleeding (OGIB) (n = 12), followed by DBE-ERCP (n = 11), and evaluation of and abdominal pain (n = 10). The excluded stomach could be reached in 90% of patients. The overall diagnostic yield of DBE-ERCP was 65% (stones, n = 4, sphincter stenosis, n = 3, bile leak, n = 2, bile duct stricture, n = 1). The yield of DBE for abdominal pain was 20% (n = 2: gastric erosions, gastro-gastric fistula) and DBE for OGIB 75%. Of the 12 patients with OGIB, 9 had active bleeding at the time of DBE. In all but one case, the bleeding was occurring at the site of the anastomosis, whether that be hepaticojejunal, jejunojejunal, or gastrojejunal. Of these patients 5 patients had arteriovenous malformations at the anastomotic site, 5 had ulcers or erosions, and 2 were bleeding secondary to Dieulafoy's lesions. A total of one complication (3%) was observed (small bowel perforation after application of argon plasma coagulation to the jejunojejunal anastomosis).
CONCLUSION: DBE is a feasible and relatively safe technique to evaluate the small intestines, stomach and biliary tract and associated with reasonably high diagnostic yield in patients with surgically altered bowel anatomy in the setting of bariatric surgery.
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P1366 LABORATORY PREDICTORS OF HYPERAMYLASEMIA AND HYPERLIPASEMIA AFTER DOUBLE BALLOON ENTEROSCOPY

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INTRODUCTION: The causal mechanism of acute pancreatitis after oral double balloon enteroscopy (DBE) is still uncertain. The most probable cause seems to be a mechanical straining of the endoscope with an over-tube on the pancreas. Hyperamylasemia and hyperlipasemia after DBE are frequent and usually asymptomatic. They do not represent the immediate risk factor of acute pancreatitis. The aim of this prospective study was to investigate several laboratory markers to predict patients in a higher risk of hyperamylasemia and hyperlipasemia and/or possible DBE-associated acute pancreatitis.
AIMS & METHODS: A total 38 patients (18 men and 20 women, mean age 51 years) with 44 DBEs and 30 matched healthy controls with no endoscopy entered the study. Following laboratory markers were investigated before, 4 hours and 24 hours after DBE and once in controls: serum hs-CRP, prokalcitonin, total S100 protein, cathepsin B, SPINK1, lactoferrin, E-selectin, alfa-1-antitrypsin, malondialdehyde, amylase and lipase. The mean time of DBE was 80 min. (range 20 – 210 min.), the mean number of push-and-pull cycles was 14 (range 1 – 41). We have not recorded any DBE-associated acute pancreatitis in this series.
RESULTS: Serum amylase and lipase rose significantly with the maximum 4 hours after DBE, with increased abnormal values in 31/44 (70%) of serum amylase and 29/44 (66%) of serum lipase ($p < 0.001$ and $p < 0.001$). Serum cathepsin and procalcitonin decreased significantly 4 hours after DBE compared to healthy controls and patients' values before DBE ($p = 0.018$ and $p = 0.031$). There was a statistically significant, but clinically irrelevant, difference in malondialdehyde between males and females 4 hours after DBE (0.33±0.20 vs. 0.20±0.13 μmol/L; $p = 0.012$). No other gender-associated difference was recorded. There was a trend for an association between number of push-and-pull cycles in DBE and procalcitonin ($r = -0.384$; $p = 0.011$) and urine amylase ($r = 0.313$; $p = 0.043$) 4 hours after DBE; between procalcitonin and alfa-1-antitrypsin ($r = 0.358$; $p = 0.021$), cathepsin ($r = 0.362$; $p = 0.020$) and hs-CRP ($r = 0.358$; $p = 0.021$); and between E-selectin and malondialdehyde ($r = 0.364$; $p = 0.019$) 4 hours after DBE. Either serum amylase or lipase 4 hours after DBE did not correlate with any markers before DBE.
CONCLUSION: Our current results support our previous hypothesis that endoscope-induced mechanical straining during DBE is the most important factor responsible for the increase of amylase and lipase or even for progression to acute pancreatitis. We found no laboratory predictive markers that would identify in advance those patients in a higher risk.
Disclosure of Interest: None declared

P1367 EFFICACY OF SINGLE-BALLOON ENTEROSCOPY FOR TREATMENT OF THE STENOSIS IN SMALL INTESTINE

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INTRODUCTION: Before the progress of balloon-assisted enteroscopy (BAE) and wireless capsule endoscopy, the stenoses of the small intestine were detected by CT or radiological enteroclysis. They were often difficult to diagnose, and surgery was selected for diagnostic therapy. BAE has enabled to make diagnosis and treat small intestinal lesions. We evaluated the efficacy of single-balloon enteroscopy (SBE) for treatment of small intestinal stenosis.
AIMS & METHODS: A total of 632 cases of SBE were performed between September 2005 and December 2013 at our center, and 62 stenotic cases of the small intestine detected by SBE were enrolled in the study. Stenosis was defined as difficulty in penetrating the enteroscope or sliding tube. Endoscopic balloon dilation (EBD) was performed to the suitable cases of benign stenosis. The indications of EBD were as follows: ①benign stenoses with the length being less than or equal to 5cm, ②strictures without deep ulcers, fistulas, or abscesses, and ③stenoses without sharp angle. Adopted cases were divided into two groups: 'CD' group with stenoses caused by Crohn's disease, and 'non CD' group with benign stenoses caused by other factors. We assessed the first EBD success rate, restenotic rate, duration until restenosis, cumulative surgical free rate and occurrence of complications.
RESULTS: The causes of the stenosis cases included 23 Crohn's disease (CD, 37.1%), 4 postoperative stenosis (6.5%), 4 ischemic enteritis (6.5%), 6 adenocarcinoma (9.7%), 4 cases of invasion of small intestine from other carcinoma (6.5%), 6 malignant lymphoma (9.7%), 5 other cases (8.1%), and 10 cases of unknown etiology (16.1%). Of the 62 cases, 24 were suitable for EBD therapy, and 15 cases were included in the 'CD' group while 9 cases (2 ischemic enteritis, 2 postsurgical stenoses, and 5 others) were in the 'non CD' group. The first EBD successful rate was 100% for each. Eight of the 15 CD cases had restenosis, while restenosis occurred in one of nine non CD cases. The two groups had a significantly different restenotic rate ($P < 0.05$). Duration until occurrence of restenosis was 10.9±1.9 months on average. The cumulative surgical free rate after EBD was 87.5% (21/24), and the observation period was almost 4 years. One case had a post-EBD bleeding, but perforation or other complications did not occur.
CONCLUSION: EBD was performed safely in most cases. The result suggests it is necessary to consider periodical SBE for stenotic lesions in the small intestine, especially in CD cases. There is a possibility that surgery can be avoided by doing EBD in cases of small intestinal stenoses.
Disclosure of Interest: None declared

P1368 USEFULNESS OF CAPSULE ENDOSCOPY IN THE DIAGNOSIS OF OVERT OBSCURE GASTROINTESTINAL BLEEDING COMPARED WITH BALLOON-ASSISTED ENTEROSCOPY

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INTRODUCTION: Although overt obscure gastrointestinal bleeding (OGIB) is difficult to diagnose, capsule endoscopy (CE) and balloon-assisted enteroscopy (BAE) are very effective approaches that are essential to the control of small intestinal bleeding. CE in particular is a very simple and convenient technique for overt OGIB. Despite great progress, few cases could not be detected using CE. Here we checked the detection and lack of detection rates of CE and BAE.
AIMS & METHODS: Between April 2005 and June 2013, a total of 364 patients had both CE and BAE (239 men, 125 women; mean age, 60 years) in our institute; of these, 155 had overt OGIB. When the diagnosis of overt OGIB using CE (Pillcam SB2; Given Imaging) was first made, BAE (single-balloon enteroscopy; Olympus Medical Systems) was checked for the diagnosis and treatment. If lesions were suspected in the small intestine by another modality, BAE was used despite negative CE findings. CE was checked independently by at least two doctors. BAE was performed using an oral or anal approach according to the CE results. Prior to checking small intestinal lesions with CE and BAE, esophagogastroduodenoscopy and total colonoscopy were both performed to confirm a lack of gastrointestinal bleeding except in the small intestine.
RESULTS: CE findings of 155 overt OGIB cases included: angiectasia, 30%; erosion/ulcer, 28%; carcinoma, 7%; and Crohn's disease, 1%. Active bleeding was observed in 47 of 155 patients (30%) using CE, and all cases were confirmed using BAE. A total of 39 (83%) of 47 cases were diagnosed by BAE, and some cases such as angiectasia were simultaneously treated with BAE. However, 17 (17%) of the 47 cases could not be diagnosed using BAE. Of the 155 cases of overt OGIB, 108 (70%) could not be detected by bleeding points using CE, but five (3.2%) cases were diagnosed using another modality such as scintigraphy or BAE. They were three cases of Meckel's diverticulum, one case of jejunal sarcoma, and one case of angiectasia of the ileum. CE images of these patients were not consistent with lesions, so the diagnoses could not be made by CE only.
CONCLUSION: CE is very useful for the detection and diagnosis of overt OGIB. However, some cases could not be detected in the present study. Therefore, even if bleeding points cannot be detected by CE and bleeding occurs repeatedly, another modality such as BAE should be applied.
Disclosure of Interest: None declared

P1369 FACTORS INFLUENCING CECAL INTUBATION TIME DURING RETROGRADE SINGLE-BALLOON ENTEROSCOPY: IS IT THE SAME AS THAT DURING COLONOSCOPY?

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INTRODUCTION: The retrograde technique for single-balloon enteroscopy (SBE) seems to be more difficult than the antegrade technique because of the need to pass through the colon. The predisposing factors for prolonged cecal intubation time (CIT) during colonoscopy have been well identified. However, the factors influencing CIT during retrograde SBE have not been addressed.
AIMS & METHODS: The aim of this study was to determine the factors influencing CIT during retrograde SBE. We investigated patients who underwent retrograde SBE at a medical center from January 2011 to March 2014. The medical charts and SBE reports were reviewed. The patients' characteristics and procedure-associated data were recorded: age, sex, body mass index (BMI), indication, history of surgery, bowel preparation, CIT, total procedure time, endoscopic findings, and endoscopic interventions. These data were analyzed with univariate analysis as well as multivariate logistic regression analysis to identify the possible predisposing factors.
RESULTS: The median CIT was 17.4 minutes. With univariate analysis, there was no statistical difference in age, sex, BMI, or history of abdominal surgery, except for bowel preparation ($P = 0.022$). Multivariate logistic regression analysis showed that bowel preparation (odds ratio 7.80, 95% confidence interval 2.76–22.02; $P < 0.001$) and previous history of pelvic surgery (odds ratio 0.26, 95% confidence interval 0.70–0.97; $P = 0.045$) were the independent predisposing factors for prolonged CIT during retrograde SBE.
CONCLUSION: Bowel preparation and previous history of pelvic surgery were the independent predisposing factors for prolonged CIT during retrograde SBE.
Disclosure of Interest: None declared

P1370 SMALL BOWEL AND COLONIC MUCOSAL HEALING IN CROHN'S DISEASE - A PILOT STUDY WITH PILLCAM COLON 2 FOR ENTIRE GASTROINTESTINAL CAPSULE ENDOSCOPY

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INTRODUCTION: In Crohn's Disease (CD), both small bowel and colonic mucosa are affected in almost half the patients. PillCam COLON2 Capsule (PCC2) allows for the non-invasive evaluation of the entire gastrointestinal tract.
AIMS & METHODS: Our aim was to evaluate mucosal healing in patients with both small bowel and colon distribution of CD using PCC2.
We included patients with non-stricturing non-penetrating small bowel *plus* colonic CD in corticosteroid-free remission (Harvey-Bradshaw Index < 5); patients had been submitted to ileocolonoscopy (identifying active CD lesions such as ulcers, erosions and spontaneous bleeding) and small bowel capsule endoscopy (with Lewis Score assessment) at diagnosis.
After $\geq$ 1 year of follow-up, patients underwent entire gastrointestinal tract evaluation with PCC2, which was reviewed by an independent researcher, blinded to both the initial endoscopic results and current CD therapy. Primary endpoint: to assess mucosal healing in small bowel and colon mucosa, defined as a Lewis Score (LS) < 135 and no active CD lesions in the colon.
RESULTS: Twelve patients were included, 7 male; mean age was 32 (18-50) years, mean follow-up was 38 (12-62) months. At diagnosis, most patients ($n = 8$, 66.7%) presented with segmental CD lesions in ileocolonoscopy; moderate to severe activity (LS$\geq$790) was observed during SBCE in 7 patients (58.3%), while 5 (41.7%) presented with mild activity (LS 135-790). Two patients were treated with combination immunossupression therapy (anti-TNFα and azathioprine), 8 with azathioprine in monotherapy and 2 with messalazine. We are currently recalling patients for PCC2.
Six patients already completed the procedure: the entire gastrointestinal tract was observed in all of them. Small bowel mucosal healing (LS$<$135) occurred in 3 patients (50%) patients - 2 of them, with a LS$\geq$790 at diagnosis, treated with azathioprine in monotherapy, and the other one, with previous LS 135-790, was treated with messalazine. Two patients maintained moderate to severe activity in the small bowel despite treatment with azathioprine, and another one, also under azathioprine monotherapy, was shown to have intensified inflammatory activity (mild activity at diagnosis and moderate to severe activity in the small bowel observed with PCC2).
Mucosal healing of the colonic mucosa was observed in 3 patients (50%), two of them treated with azathioprine, and the remainder with messalazine; 2 patients maintained a segmental pattern of colon CD, and in one patient, treated with azathioprine, CD lesions throughout the entire colonic mucosa persisted during follow-up.
CONCLUSION: With this pilot study, in a population of patients with both small bowel and colonic Crohn's Disease, we have shown that endoscopy of the entire gastrointestinal tract with PCC2 is feasible and safe, allowing for mucosal inflammatory activity assessment in patients in clinical remission, evaluating mucosal healing as a surrogate of treatment efficacy.
Disclosure of Interest: None declared

P1371 VIRTUAL CHROMOENDOSCOPY IMPROVES THE DIAGNOSTIC YIELD OF SMALL BOWEL CAPSULE ENDOSCOPY IN OBSCURE GASTROINTESTINAL BLEEDING

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) represents the initial form of investigation for obscure gastrointestinal bleeding (OGIB). FICE mode is a virtual chromoendoscopy technique designed to enhance focal lesions during endoscopic procedures.
AIMS & METHODS: Our objective was to compare and analyze the differences in diagnostic yield using both FICE 1 and conventional SBCE imaging.
Included 60 consecutive patients referred to SBCE for OGIB. Every SBCE exam was independently reviewed by four researchers using conventional imaging and FICE 1, and afterwards compared by an independent researcher for consensus report.
Diagnostic yield was defined as the presence of at least one small bowel lesion with high bleeding potential (P2), such as angioectasia, ulcer or tumor, after the exclusion of false positive results.
Statistical analysis of the data was performed with SPSS v21.0, using the McNemar test for categorical variables and paired-samples T-test for continuous variables.
RESULTS: SBCE diagnostic yield using FICE 1 was significantly higher than conventional imaging (58.3 vs 41.7 %, $p = 0.021$). Using FICE 1 we additionally found a superior number of P2 lesions (74 vs 44, $p = 0.003$), particularly angioectasias (54 vs 26, $p = 0.002$). No differences were observed regarding the number of ulcers (17 vs 15, $p = 0.568$) or tumors (3 vs 3, $p = 1.000$) when comparing FICE 1 with conventional imaging.
CONCLUSION: FICE 1 viewing during small bowel capsule endoscopy for obscure gastrointestinal bleeding was significantly superior to conventional imaging, resulting in a 16% improvement in diagnostic yield. Potentially bleeding lesions were more often observed when using FICE 1, in particular angioectasias. Our results support the generalization of this technique while reviewing small bowel capsule endoscopy for obscure gastrointestinal bleeding.
Disclosure of Interest: None declared

P1372 ACTIVE SMALL BOWEL BLEEDING: EARLIER DETECTION, EARLIER REACTION

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INTRODUCTION: Obscure gastrointestinal bleeding (OGIB) is the leading indication for small bowel capsule endoscopy (SBCE). Despite being present in only a minority of patients undergoing SBCE, early detection of active bleeding allows for treatment adjustments and prognostic improvement.
AIMS & METHODS: We aimed to ascertain whether some clinical and analytical patient characteristics would correlate with active bleeding in the small bowel observed during capsule endoscopy.
Unicentric retrospective study comprising all patients submitted to SBCE for OGIB over 6 years. The following variables were analyzed: age, gender, comorbidities (hypertension, chronic kidney disease, diabetes mellitus, ischemic heart disease), antiplatelet and anticoagulant drug use, and the need for hospital admission. Both active bleeding and potentially bleeding lesions in the small bowel were assessed during SBCE. Statistical analysis was performed with SPSS 21.0, and a p value < 0.05 was considered significant.
RESULTS: Among the 244 patient included, potentially bleeding lesions were found in 65 (26.6%), while active bleeding on SBCE was observed in 21 patients (8.6%). Small bowel hemorrhage was significantly more frequent among patients presenting with visible gastrointestinal bleeding (19 *versus* 7%, $p = 0.008$). Elder patients (72 *versus* 60 years $p = 0.003$), hospitalized patients (17 *versus* 7%, $p = 0.034$) and those with ischemic heart disease (16 *versus* 5%, $p = 0.007$) displayed significantly more often small bowel active bleeding. Only 1% of the patients with no comorbidities was found to have active bleeding during SBCE, compared to 14% among patients with 2 or more comorbidities ($p = 0.007$). Antithrombotic drugs were not associated with an increased risk for small bowel active bleeding.
CONCLUSION: Small bowel active bleeding was significantly more frequent in patients presenting with visible OGIB. Advanced age, the need for hospital admission and comorbidities, particularly ischemic heart disease, were associated with an increased prevalence of active bleeding during SBCE. In such patients, carrying out small bowel capsule endoscopy early on is of prime importance as to swiftly detect and treat the observed lesions.
Disclosure of Interest: None declared

P1373 DELIVERING A CAPSULE ENDOSCOPY SERVICE TO A WIDE GEOGRAPHICAL AREA – THE SOUTH TYNESIDE EXPERIENCE

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INTRODUCTION: Video capsule endoscopy (VCE) is an increasingly utilised small bowel investigation. Not all hospital sites offer it; patients may need to travel to have the procedure performed. It involves several appointments; assessment prior to the procedure, patency capsule (PC) procedure, follow up radiology, & the VCE procedure itself.
In the Northern region of England, 2 centres offer an established VCE service, with a 3rd service recently commissioned. Despite efforts to develop services in the most appropriate localities, the referral area to these centres is large with potential journey times of over 2 hours.
South Tyneside District Hospital (STDH) started performing VCE in 2006, and began a telephone assessment service in 2010. Referrals are received from across the Northern region, frequently extending as far as Cumbria, North Yorkshire and South Teeside, and occasionally from further afield (Scotland, the Midlands). Prior to the telephone service, patients were admitted for assessment, PC (if appropriate, based on clinical information and patient informed choice), bowel prep, and VCE procedure – equating on average 1-3 nights in hospital.
AIMS & METHODS: We describe the patient pathways before and after the telephone service began, and evaluate the service up to January 2014. Average patient stay was calculated, bed days saved and cost differences described using NHS costings for elective stays in hospital.
RESULTS: The telephone service started in August 2010. Two 30-minute slots are allocated each week to the service, and are reserved for patients from outside the local area.
A nurse consultant conducts the telephone consultation. Those requiring PC are sent the device to their home to take unsupervised, or may attend their local hospital to be observed. They attend STDH the following day for a scan +/- AXR/localised CT abdomen. They either stay locally overnight for VCE the following day, or return home with a future plan for VCE. Alternatively, they are admitted to STDH, and VCE administered the following day. If not requiring PC, bowel preparation, consent forms and instructions are sent to the patient, with the patient attending STDH for VCE to be delivered. Patients can be admitted to STDH for inpatient preparation if required.
1164 VCE procedures have been performed at STDH. From 525 referrals from outside STDH, 205 telephone assessment appointments have been utilised.
The highest number of telephone assessments have come from hospitals in Cumbria: 77 referrals from Carlisle, and 52 from Whitehaven; 73 and 111 miles from STDH respectively. Saving each patient one return journey by using the telephone service has reduced patient journeys by almost 23,000 miles. An elective inpatient bed costs £225 per night. A telephone service appointment is charged at £23.69. PC device and VCE device costs are the same in both pathways. Therefore, making a conservative estimate of cost savings (assuming all telephone service patients have reduced their inpatient stay by one night), £38,000 has been saved by this service in 4 years.
CONCLUSION: A telephone assessment clinic for patients distant to the VCE centre has been well utilised at STDH. This has reduced the inpatient stay required for VCE investigation, reducing costs, the impact on the gastroenterology inpatient service, and travel burden on patients.
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P1374 CAPSULE ENDOSCOPY: DIAGNOSTIC ACCURACY OF LEWIS SCORE IN PATIENTS WITH SUSPECTED CROHN'S DISEASE

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) has assumed an increasing importance in the diagnosis of Crohn's Disease (CD). The Lewis Score (LS) aims to standardize the quantification of inflammatory activity detected in the small bowel mucosa.
AIMS & METHODS: The aim of this study was to evaluate the diagnostic accuracy of the LS in patients undergoing SBCE for suspected CD. We performed a retrospective single-center study including 95 patients who underwent SBCE for suspected CD between September 2006 and February 2013, with at least 12 months of follow-up after the capsule. Patients were divided in 2 groups according to the criteria of the *International Conference on Capsule Endoscopy* (ICCE) for the definition of suspected CD. Group 1: 37 patients not fulfilling ICCE criteria; Group 2: 58 patients with ≥ 2 ICCE criteria. Inflammatory activity on SBCE was objectively assessed by determining the LS. The diagnosis of CD during follow-up was based on a combination of clinical, analytical, endoscopic, histological and imaging elements.
RESULTS: SBCE detected significant inflammatory activity (LS $\geq$ 135) in 46 patients (48.4%), 7 patients from group 1 (18.9%) and 39 patients from group 2 (67.2%) ($p < 0.001$).
The diagnosis of CD was established in 38 patients (40%): 8 patients (21.6%) from Group 1, 30 patients from Group 2 (51.7%) ($p = 0.003$), 34 patients with LS $\geq$ 135 (73.9%) and 4 patients with LS $<$ 135 (8.2%) ($p < 0.001$). The LS $\geq$ 135 had an overall diagnostic accuracy of 83.2 %. The LS Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value for the diagnosis of CD were 89.5%, 78.9%, 73.9% and 91.8%, respectively.
CONCLUSION: The application of LS $\geq$ 135 as the cut-off value for the presence of significant inflammatory activity in patients undergoing SBCE for suspected CD may be useful to establish the diagnosis. In patients with LS $<$ 135, the probability of having CD confirmed on follow-up is low.
Disclosure of Interest: None declared

P1375 IS IT WORTH REPEATING PREVIOUSLY UNREMARKABLE SB2 CAPSULES WITH THE NEW SB3?

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) has become a valuable tool for investigating the small bowel and technology is rapidly advancing. One of the most recent devices available for capsule endoscopy (Pillcam® SB3, Given Imaging) has improved image resolution and a variable frame rate. The aim of this work is to address whether these innovations lead to increased mucosal visualisation and diagnostic yield in clinical practice and therefore whether a repeat SB3 capsule should be considered in those patients with an equivocal SB2 result.
AIMS & METHODS: A review was undertaken of the last 100 Pillcam® SB2 capsules and the first 100 Pillcam® SB3 capsules to be performed at South Tyneside District Hospital (14/01/13 - 13/03/14). Visualisation of the ampulla was used as a surrogate marker of mucosal visualisation and diagnostic yield was assessed by reviewing the reports. Statistical significance was calculated using Fisher's exact test.
RESULTS: Results are summarised in the table below. The ampulla was visualised in 14% of SB2 capsules and 14% of SB3 capsules ($p > 0.05$). 44% of SB2 capsules were abnormal and SB3 capsules were abnormal in 60% of cases ($p < 0.05$)

Capsule type	Number	Ampulla seen (%)	Pathology found (%)
SB2	100	14 (14%)	44 (44%)
SB3	100	14 (14%)	60 (60%)
p value		1.0000	0.0335

CONCLUSION: It is recognised that the views obtained by SBCE can be compromised in the duodenum due to "rapid transit" and variable frame rates hope to address this by capturing more images when the capsule is moving quicker. We showed no statistically significant difference in ampullary visualisation between the SB2 and SB3 capsules. However the overall yield of pathology from SB3 capsules was significantly higher than that in SB2 capsules. Given the overall

increased yield of pathology it may be beneficial to repeat an SB3 capsule in someone with a previously equivocal SB2 result.

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P1376 IS THERE A ROLE FOR URGENT SMALL BOWEL VIDEO CAPSULE ENDOSCOPY?

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INTRODUCTION: Capsule endoscopy has become a valuable modality for imaging the small bowel and has been suggested as a useful diagnostic tool in the emergency diagnosis of overt occult GI bleeding when used in the appropriate context[1]. Diagnostic yield (DY) is known to be greatest if the study is performed as soon as possible after the bleeding episode[2]. This is not possible in centres without a capsule endoscopy service who therefore refer for urgent studies. Presently the DY of urgent small bowel video capsule endoscopy (SBCVE) is unclear. This work aims to assess the DY of urgent SBVCE in a district general hospital acting as a tertiary referral centre for SBVCE.

AIMS & METHODS: All referral letters since 2008 were reviewed. Referrals were classified as urgent if the referrer had indicated a degree of urgency or if the team at South Tyneside felt the SBVCE should be done urgently. DY was assessed by reviewing the capsule endoscopy reports and then relating the findings to the indication. Considered as positive findings were active bleeding, angiodysplasias, ulcers, strictures, tumours, villous atrophy and polyps.

RESULTS: 127 studies were identified from reviewing the referral letters (1164). Of these 60 were requested as urgent, 24 were expedited and 43 were changed to urgent by the capsule endoscopy team. 57 of the 127 capsules had a significant finding (45%). The table below summarises the results. Active bleeding was defined as patients having melaena or ongoing transfusion requirements. Abnormal imaging was defined as a CT or MRI showing potentially abnormal small bowel. Diarrhoea only and weight loss only were indications where the referrer was not querying the possibility of Crohn's disease.

Indication	Number	%	Significant?	%
?Active bleeding	47	37.01%	25	53.19%
?Crohn's disease	12	9.45%	3	25.00%
Abnormal imaging	14	11.02%	5	35.71%
Anaemia	27	21.26%	16	59.26%
Crohn's assessment	5	3.94%	2	40.00%
Diarrhoea only	3	2.36%	1	33.33%
Weight loss only	11	8.66%	3	27.27%
Other	8	6.30%	2	25.00%
Total	**127**	**100.00%**	**57**	

CONCLUSION: The most common indication for an urgent capsule was the suspicion of active bleeding and more than half of these SBVCEs showed a bleeding point. Urgent investigations for anaemia also had a high yield of positive findings. Other indications with more than 10 urgent studies performed did not show an appreciable yield. Our data adds weight to the argument that capsule endoscopy may be a useful test in active occult GI bleeding while also suggesting it may play a role in the assessment of severe anaemia in the absence of overt GI bleeding. Such patients should be referred for urgent assessment to maximise diagnostic yield.

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P1377 MAJOR PREDICTORS OF PORTAL HYPERTENSIVE ENTEROPATHY IN PATIENTS WITH LIVER CIRRHOSIS

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INTRODUCTION: Since portal hypertensive enteropathy (PHE) has been acknowledged as a source of bleeding, predicting its presence has become more important. However, few previously published reports discuss factors that predict its presence in the context of portosystemic shunts (PSs).

AIMS & METHODS: We aimed to assess PHE in patients with liver cirrhosis (LC) using capsule endoscopy (CE) and investigated factors that may predict its presence, including PSs.

One hundred and thirty-four consecutive patients with LC (78 males and 56 females), with a mean age of 66.7 years (range: 27–88 years) who underwent CE at our hospital between February 2009 and September 2013, comprised the study population. All had undergone dynamic computed tomography (CT) and esophagogastroduodenoscopy before CE examination. The frequencies and types of PHE lesions were investigated. The distribution of the lesions was also determined. Moreover, the relationships between PHE and the patients' clinical characteristics, which included age, sex, liver function, etiology of cirrhosis, PSs, ascites, hepatocellular carcinoma, splenomegaly, portal thrombosis, esophageal varices (EVs), gastric varices, and portal hypertensive gastropathy (PHG), were examined. PSs were evaluated using dynamic CT during the portal venous phase and coronal CT imagery. Left gastric veins, short gastric veins, posterior gastric veins, paraesophageal veins, splenorenal shunts, and paraumbilical veins with diameters greater than 3 mm were defined as PSs. Comparisons were performed using Student's t-test for quantitative data and the chi-square test for categorical data. All tests were 2-sided, and a P value < 0.05 was considered statistically significant. The impacts of the clinical variables on PHE were estimated by calculating the odds ratios (OR) and the 95% confidence intervals (95% CI) using logistic regression analyses.

RESULTS: PHE was found in 91 (68%) patients, and 70 (52%) patients had erythema, 25 (19%) had erosions, 24 (18%) had angioectasia, 18 (13%) had villous edema, and 10 (7%) had varices. Most lesions were located in the jejunum. The clinical characteristics associated with the presence of PHE were a Child-Pugh grade of B or C ($P = 0.0058$), and the presence of PSs ($P < 0.0001$), ascites ($P = 0.0017$), portal thrombosis ($P = 0.016$), EVs ($P = 0.0017$), and PHG ($P = 0.0029$). The other factors had no significant relation with the presence of PHE. Subsequent multivariate analysis determined that the presence of PSs was an independent predictor of PHE (OR: 3.15; 95% CI: 1.27–7.95). The shunt types significantly associated with PHE on univariate analysis were the left gastric vein ($P = 0.00068$), the paraesophageal vein ($P = 0.029$), and splenorenal shunts ($P = 0.03$). Subsequent multivariate analysis determined that left gastric vein (OR: 5.31; 95% CI: 1.97–17.0) and splenorenal shunts (OR: 4.26; 95% CI: 1.29–19.4) were independent predictors of PHE.

CONCLUSION: PSs appear to reliably predict the presence of PHE. Furthermore, CE should be considered in patients with LC accompanied by PSs, especially left gastric vein and splenorenal shunts.

Disclosure of Interest: None declared

P1378 THE FACTOR OF IMPROVEMENT THE DIAGNOSTIC YIELD OF THE CAPSULE ENDOSCOPE IN OBSCURE GASTROINTESTINAL BLEEDING WITH NEGATIVE SMALL BOWEL COMPUTED TOMOGRAPHY

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INTRODUCTION: Capsule endoscopy (CE) is currently recommended as first-line study in the evaluation of obscure gastrointestinal bleeding (OGIB), some consider small bowel computed tomography (SBCT) as a complementary test to CE

AIMS & METHODS: AIMS: This study evaluated the factors of improvement the diagnostic yield of CE in patients with OGIB and negative SBCT.

METHODS: We reviewed the medical records related to forty one patients with OGIB who was performed SBCT and CE from July 2007 to February 2013, focusing our attention with negative SBCT. SBCT is defined including enteral phase with or without neutral enteric contrast material. We evaluated forty one patients with negative SBCT and analyzed the detection rate of CE obscure bleeding focus. Cases were divided into two groups; first group who had diagnostic finding of CE ($n = 26$) and second group who had non-diagnostic finding of CE ($n = 15$). The two groups were compared retrospectively.

RESULTS: Twenty six of 41 (63.4%) CE studies had diagnostic results. Mucosal lesions (75.6%) were the most common findings, followed by nonspecific findings (17.1%) and tumorous lesions (2.4%). In comparison between patients with and without diagnostic CE finding, mucosal lesion (Odds 21.660, CI 2.269-206.755; $p = 0.008$) and using of neutral enteric contrast material before SBCT (Odds 15.828, CI 1.005-249.350; $p = 0.050$) were significant factor for diagnostic CE finding.

CONCLUSION: In the patients with OGIB and negative SBCT, using of neutral enteric contrast material before SBCT is possible to improve the diagnostic yield of the CE

Disclosure of Interest: None declared

P1379 SELF-EXPANDABLE METAL STENTS IN THE MANAGEMENT OF BENIGN ESOPHAGEAL DISEASES

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INTRODUCTION: The use of self-expandable metal stents in the esophagus for the management of benign disease has grown immensely over the last decade. Fully covered self-expandable metal stents (FCSEMS) are considered a viable alternative to serial bougienage and endoscopic dilation in the management of

refractory benign esophageal strictures. The use of SEMS, particulary partially covered (PCSEMS), in the treatment of anastomotic esophageal leaks or fistulas is a valid and efficacious resource in order to restore the gastrointestinal function, resume oral nutrition and avoiding a, potencially costly, surgical re-intervention.
AIMS & METHODS: The primary aim of this retrospective study was to determine the efficacy and safety, in our institution (Jan 2008 - Feb 2013), of FCSEMS for refractory benign esophageal strictures and SEMS (mainly PCSEMS) in the management of anastomotic esophageal leaks/fistulas.
RESULTS: A total of 14 patients underwent SEMS placement for benign esophageal conditions. 8 patients for refractory esophageal stricture and 6 for post-surgery leak/fistula. In the stricture group, 19 FCSEMS were used (patient/stent ratio: 2.4) and in the post-surgery group, 13 SEMS were needed (patient/stent ratio: 2.0). Regarding the etiology, stricture group: post-surgery (n = 3), radiation-induced (n = 2), caustic (n = 1) and peptic (n = 1). In the anastomotic esophageal leak/fistula group, the most common procedure was a laparoscopic gastric sleeve (n = 4) and gastric bypass (n = 2). In 50% of the cases, 2 stents were deployed in the same session. In the stricture group, the preferred stents were the Wallflex@ Boston Scientific (n = 11) and the Hanarostent@ M. I. Tech (n = 5). The stent body diameter ranged from 18 and 23mm. In the post-surgery group, the preferred stent was the partially covered Ultraflex@ Boston Scientific (n = 5), Wallflex@ Boston Scientific (n = 4) and Evolution@ Cook Medical (n = 3). In this group, the use of PCSEMS dominated (n = 10; 77%). The mean stent body diameter was 25mm and length 125mm. The technical immediate success rate was 79% (15/19) and 100% (6/6) for the stricture and post-surgery groups, respectively. Global stent migration rate, for the stricture group, was 63% (12/19). No migration events were reported in the post-surgery group. Stent occlusion by tissue hyperplasia occurred more in the stricture group (3 events vs 1 event). All the stents were removed successfully, including those who migrated, and no procedure nor stent-related complications were reported. Clinically, at the end of the study, in the stricture group, 3 out of 8 patients (38%) remain symptom-free and their stricture was deemed solved, another 3 out of 8 patients (38%) had a temporary clinical benefit but remain dependent of endoscopic dilation and 2 cases (25%) demanded an invasive procedure. In the leak/fistula group, complete resolution was achieved in 83% (5/6).
CONCLUSION: Althought far from being the perfect solution for refractory benign esophageal strictures, FCSEMS appear to be a valid and safe option in their management. Their clinical success is moderate (38%) but migration rates seem to remain a frequent issue (63%). On the other hand, the use of PCSEMS in the management of anastomotic esophageal leaks or fistulas seems to hold a high clinical success rate (83%) without complications or migration events.
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P1380 GASTRIC OUTLET OBSTRUCTION TREATMENT WITH ENDOSCOPIC PLACEMENT OF SELF-EXPANDING METAL STENT: DATA FROM A LARGE SERIES OF PATIENTS TREATED IN A TERTIARY REFERRAL HOSPITAL FOR PALLIATIVE CARE

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INTRODUCTION: Gastric outlet obstruction (GOO) can occur in several different GI malignant conditions (intrinsic or extrinsic) that can be treated with endoscopic placement of self-expanding metal stents (SEMS). In non operable patients SEMS placement ensure a prompt oral intake with less morbidity and shorter hospital stay compared to surgical jejunostomy. Clinical success rate is similar between surgical and endoscopic treatment (around 90%).
AIMS & METHODS: The aims of this study are to evaluate the efficacy and safety of SEMS placement in a large consecutive series of patients with malignant inoperable gastroduodenal obstruction. From March 2007 to March 2014 we collected data on all consecutive patients treated with SEMS placement (Wallflex Enteral by Boston Scientific) due to malignant GOO. Baseline gastric outlet obstruction scoring system (GOOSS) score was recorded (0 = no oral intake; 1 = liquid diet; 2 = soft solid diet; 3 = low residue or normal diet). Stents were deployed under fluoroscopic and endoscopic guidance after traversing the stricture with a catheter/guidewire. If needed, balloon dilation was performed before stent placement. Technical and clinical success, and adverse events were recorded.
RESULTS: 63 patients (42 male [67%]), with a mean age of 69.6±12.7 year, were treated: 34 had pancreatic head cancer (54%), 13 antro-bulbar cancer (21%), 7 gallbladder cancer/cholangiocarcinoma (11%), 4 retroperitoneal sarcoma (6%), 3 peritoneal carcinomatosis (5%), 2 duodenal obstruction due to colon cancer (3%). Thirty-one of these patients had biliary involvement too (49%) treated with biliary SEMS placement. Baseline GOOS score was: 0 in 27 patients (43%), 1 in 23 (36%), 2 in 10 (16%), 3 in 3 (5%). Technical success was achieved in all patients with a satisfactory oral feeding after 24-42 hours. Median lenght of SEMS was 9 cm (range 6-12). At 1 month the median GOOSS score improved from 1 [range 0 -3] to 2 [range 2-3]. In patients with both biliary and duodenal obstruction the double stenting allowed significant improvement in oral feeding and bilirubin levels reduction (at least 50% of the baseline value). None complications related to the SEMS placement were recorded. Stent occlusion due to ingrowth occurred in 3 patients (5%). The median hospital stay was 4 days (range 3-8) with a median survival time of 7 months (range 3-9). All deaths were due to the natural course of underlying malignancy.
CONCLUSION: Endoscopic management of gastroduodenal obstruction with SEMS placement is the treatment of choice in advanced unresectable gastroenteric neoplasm. It is a safe procedure and it enhances patients quality of life. In advanced diseases or in frail patients palliative surgery should be considered only in case of endoscopic failure.
Disclosure of Interest: None declared

P1381 EFFICACY OF THE 'OVER-THE-SCOPE CLIP' (OTSC) IN THE MANAGEMENT OF IATROGENIC GASTROINTESTINAL PERFORATIONS

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INTRODUCTION: Perforation is a rare but serious complication of endoscopic procedures. The over-the-scope clip (OTSC, Ovesco®, Tuebingen, Germany) is a novel endoscopic tool used in the non surgical management of gastrointestinal perforations. However, data from clinical use are still limited.
AIMS & METHODS: The aim of this study is to evaluate the efficacy and safety of this clip in closure of iatrogenic perforations occurring during diagnostic and therapeutic endoscopies. We conducted a monocentric retrospective study. From June 2011 to September 2013, eight consecutive patients (mean age: 72 years [43-93], 7 women) had an acute iatrogenic perforation treated with an OTSC.
RESULTS: The perforation was located in the sigmoid in five patients, the duodenum in two patients and the cardia in one patient. The mean size of the perforation was 11.8 mm [10-20]. Endoscopic repair was performed by using a single OTSC. The twin grasper was used in 50% of the cases to approximate the edges of perforation. Complete sealing of the perforation was achieved with OTSC in all patients. An exsufflation of the pneumoperitoneum using an 18-gauge needle was performed in two patients. An abdominal CT scanner was done in the following 48 hours in five patients and showed a pneumoperitoneum without leakage. The overall clinical success rate was 75% (6/8 patients). One patient required surgical intervention although the clip had completely sealed the perforation because of the presence of a localized peritonitis with fever and abdominal pain. An adverse event occurred in one patient in whom the OTSC placement in the sigmoid was complicated by right ureteral obstruction; this patient had to undergo surgery in order to perform a ureteral resection and anastomosis and remove the clip.
CONCLUSION: OTSC is effective for endoluminal closure of iatrogenic gastrointestinal perforations, with a complete sealing of the perforation in 100% of cases. Complications can occur but are exceptional.
Disclosure of Interest: None declared

P1382 USE OF BARIATRIC SELF-EXPANDABLE METAL STENTS FOR THE TREATMENT OF STAPLE LINE LEAKAGE FOLLOWING LAPAROSCOPIC SLEEVE GASTRECTOMY- CASE SERIES

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INTRODUCTION: Laparoscopic sleeve gastrectomy is gaining popularity as a treatment for obesity. This procedure is prone to some complications, including staple line leak, sleeve stricture and bleeding. Several therapeutic approaches have been suggested for leaks but limited data is available regarding the safety and efficacy of each technique.
AIMS & METHODS: Describe a single tertiary center experience using bariatric designed, self-expandable metallic stents (BSEMS) for the treatment of post-operative leaks.
We reviewed the medical records and imaging studies of consecutive patients diagnosed with staple line leakage between June 2012 and December 2013 and treated with BSEMS.
Either the Hanaro stent (MI-Tech, Seoul, Korea) with a length of 18-24cm or the Niti-S stent (Teawoong, Seoul, Korea) with a length of 18 or 23 cm were used.
RESULTS: Twenty six patients were referred to our clinic and treated with BSEMS. The average treatment duration was 28 days. Success, defined as avoiding further surgical intervention, removal of external drain tubes, weaning off TPN and resuming oral diet was achieved in 65%. A higher rate of 81% was reached when excluding 5 patients in which the stent was removed less than 2 weeks after insertion.
In 8 patients endoscopic fistule closure was achieved and in 7 patients reposition was needed due to migration.
Severe adverse event were noted in 5 patients that mandated early removal: 4 patients with severe intolerance and 1 patient with severe upper gastrointestinal bleeding. Minor AE were universal, including discomfort and ulceration.
CONCLUSION: BSEMS is a safe and effective treatment for staple line leak following LSG.
Disclosure of Interest: None declared

P1383 EFFICACY OF A WALLFLEX ENTERAL STENT FOR MALIGNANT GASTRIC OUTLET OBSTRUCTION DURING CHEMOTHERAPY

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INTRODUCTION: Gastric outlet obstruction (GOO) occurs due to different gastroenteral malignancy. It causes nausea, deficient oral intake, resulting in a low quality of life. The newly available enteral WallFlex stent (Boston Scentific) has been reported to be useful to improvement of these troublesome symptoms. It might benefit survival, improving not only nutrition but also the compliance to

the chemotherapy of the patients. To date, this matter has not been fully evaluated.
AIMS & METHODS: The aim of this study is to investigate the efficacy of enteral WallFlex stent for malignant gastric outlet obstruction (GOO) during chemotherapy of unresectable gastroenteral malignancy. Twenty-one consecutive patients with symptomatic malignant GOO who were treated with a WallFlex stent between September 2011 and January 2014 at our hospital were analyzed retrospectively. All the patients gave the written informed consent. We evaluated the following clinical outcomes: the improvement of oral intake, the timing of stent insertion during the cancer treatment progress, and the survival after stent insertion. A four-point GOO scoring system (0-3) was used to estimate oral intake. We also analyzed the complications. The statistical analysis was performed by Kaplan-Meier method in April 2014.
RESULTS: Among 21 patients, median age was 69 years (43-77), and 15 were male. Sixteen patients had pyloric stenosis, 3 had stenosis of bulbs, and 2 had stenosis of more anal side of duodenum. Seventeen patients had stenosis due to primary tumor, and others due to extraductal compression by the pancreatic or biliary cancer. Sixteen patients had gastric cancer, 1 had duodenal cancer, and 4 had pancreatic or biliary cancer. Almost all patients had the GOO score of 0 before insertion. Of them, improved score of more than 2 points was achieved in 16 patients (76%). The improvement was achieved within 2 days after treatment on average. Seven patients were released from the total parenteral nutrition. Median survival time after the stent insertion was 96 days (95%CI, 96-155). Seven patients underwent the treatment as the initial step of clinical course, and 14 as the sequential course among the chemotherapy. Fifteen patients could continue the chemotherapy after the insertion (71%). The survival time was not significantly different with or without the therapy before the insertion [initial insertion vs after chemotherapy: 82 days (95%CI, 46-117) vs. 96 days (95%CI, 22-169), $p = 0.85$]. However, the survival time of the patients who could continue the chemotherapy after stent insertion was significantly longer compared with the other group [150 days (95%CI, 59-240) vs 40 days (12-67),$p = 0.0022$]. Although there was no statistical significance, the patients who could continue the chemotherapy showed the trend wherein GOO score after the treatment was improved. Five patients experienced tumor in-growth and were successfully treated by stent in stent. In these cases, median time to tumor in-growth was 116 days (95%CI, 96-135). No life-threatening complication or treatment-related death occurred within 30 days.
CONCLUSION: Placement of enteral WallFlex stent for malignant GOO could benefit survival other than improvement of oral intake, supporting the compliance of chemotherapy. Further research should be continued.
Disclosure of Interest: None declared

P1384 COMPLICATIONS OF ENDOSCOPIC DILATATION FOR ESOPHAGEAL STENOSIS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL CANCER

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INTRODUCTION: Esophageal stenosis is a major problem after performing endoscopic submucosal dissection (ESD) for large superficial esophageal cancer. Endoscopic dilatation (ED) is useful for benign strictures caused by reflux esophagitis or anastomotic stenosis after esophagectomy. However, little is known about the incidence of complications of ED for stenosis caused by esophageal ESD.
AIMS & METHODS: Between September 2002 and December 2012, a total of 111 patients underwent ED for stenosis after esophageal ESD. Among these patients, we retrospectively assessed the following factors; age, sex, use of antithrombotics, location of lesion, circumferential extent of mucosal defect after ESD, diameter of the specimen resected by ESD, number of ED sessions, period from ESD to starting ED, treatment duration of ED, and complications. Since ED is considered as a high-risk procedure for bleeding in the Japanese guideline [1], antithrombotics were generally discontinued a minimum days before ED.
RESULTS: The patient population included 90 men and 21 women. The median age was 69 years old. Among them, 19 patients (17%) had daily usage of antithrombotics. The major location of the lesions was the middle or lower thoracic esophagus (81/111, 73%). The mucosal defect was larger than 3/4 circumferential extent in 75 patients (68%), and the median diameter of the resected specimen was 50 mm (range 23-106mm). A total of 1250 ED sessions were performed, and the median number of ED sessions per patient was 17 (range 1-70). The first ED session was performed a median of 13 days (range 1-154 days) after ESD, and the median treatment duration was 86 days (range 1-1079 days).
The incidence of bleeding was 0.9% (1/111) per patient, 0.1% (1/1250) per session. The only case of bleeding occurred in the middle thoracic esophagus with a mucosal defect less than 1/2 of circumference. This patient did not take daily antithrombotics. Bleeding occurred at the first time of ED session which was performed 23 days after ESD. The bleeding was stopped endoscopically without the need of blood transfusion. The incidence of perforation was 4.5% (5/111) per patient, 0.4% (5/1250) per procedure.
The location of the lesion among these five patients was upper/middle/lower/abdominal esophagus 1/2/1/1, respectively. The mucosal defect was 1/2-3/4 / 3/4-semicircular / whole circumference 1/2/2, respectively. Perforation occurred at a median of second time of ED session (range 2-9), and a median of 18 days (range 8-29) after ESD The median treatment duration of ED among these five patients was 190 days which was longer compared to that of the whole population. Four patients recovered by conservative treatment but there was one fatal case that developed pyogenic spondylitis after 26 times of ED.
CONCLUSION: The incidence of bleeding caused by ED for esophageal stenosis after ESD was small. Relevant risk of perforation should be considered for patients requiring multiple sessions of ED.
REFERENCES
[1] Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. *Dig Endosc* 2014; 26: 1-14.
Disclosure of Interest: None declared

P1385 INCIDENCE OF BLEEDING AND PERFORATION CAUSED BY ENDOSCOPIC DILATATION FOR GASTRIC STENOSIS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Gastric stenosis is a major problem after performing endoscopic submucosal dissection (ESD) for large superficial gastric cancer. Endoscopic dilatation (ED) is a safe and useful treatment for benign strictures caused by postoperative anastomotic stenosis or peptic ulcer disease. However, little is known about the incidence of bleeding and perforation caused by ED for gastric stenosis after ESD.
AIMS & METHODS: Between September 2002 and December 2012, a total of 64 patients underwent ED using a wire-guided balloon dilator for stenosis after gastric ESD. Among these patients, we retrospectively assessed the following factors; age, sex, use of antithrombotics, location of the lesion, circumferential extent of mucosal defect after ESD, diameter of the specimen resected by ESD, number of ED sessions, period from ESD to starting ED, treatment duration of ED, and complications of bleeding and perforation. Since ED is considered as a high-risk procedure for bleeding in the Japanese guideline [1], antithrombotics were generally discontinued a minimum days before ED.
RESULTS: The patient population included 48 men and 18 women. The median age was 75 years old. Among them, 19 patients (30%) had daily usage of antithrombotics. Lesions were located in the upper part of the stomach in 38% (24/64), lower part in 58% (37/64). The mucosal defect was larger than 3/4 circumferential extent in 46 patients (72%), the median diameter of the resected specimen was 66 mm (range 27-147 mm). A total of 341 ED sessions were performed, and the median number of ED sessions per patient was four (range 1-25). The first ED session was performed a median of 28 days (range 9-90) after ESD, and the median treatment duration was 30 days [1-282].
The incidence of bleeding was 3% (2/64) per patient, 0.6% (2/341) per session. One patient who continued taking antithrombotics because of concomitant disease required blood transfusion. The incidence of perforation was 8% (5/64) per patient, 1.5% (5/341) per procedure. All five cases of perforation occured in the lower stomach, and the mucosal defects were larger than 3/4 circumference. Among them, two patients underwent surgery.
There was no significant increase in the incidence of complication among patients taking antithrombotics when they were discontinued before ED.
CONCLUSION: The incidence of bleeding and perforation caused by ED for gastric stenosis after ESD was small.
REFERENCES
[1] Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. *Dig Endosc* 2014; 26: 1-14.
Disclosure of Interest: None declared

P1386 COMPARISON OF ENDOSCOPIC COLORECTAL STENT AS A BRIDGE TO SURGERY AND CURATIVE SURGERY ONLY IN THE MANAGEMENT OF ACUTE MALIGNANT OBSTRUCTION

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INTRODUCTION: Recently, the use of endoscopic colorectal stenting for palliation or as a bridge to surgery in acute malignant colorectal obstruction has increased. However, there are many questions whether endoscopic colorectal stenting as a brige to surgery is really useful for obstructive colorectal cancer, according to the results of recently pulblished studies.
AIMS & METHODS: The aim of this study was to compare the outcomes between operation after colorectal stenting and surgery only for curative purpose in patients with colorectal obstruction.
100 patients who were treated for obstructive colorectal cancer between May 2009 and May 2013 were enrolled. We reviewed the medical records retrospectively. 37 patients underwent endoscopic colorectal stent as a bridge to curative surgery (stent group). 40 patients underwent a curative operation without colorectal stent (surgery only group). Primary outcomes included the stoma rate and the length of hospital stay after surgery, postoperative complication including in-hospital mortality and the emergency and open surgery rate. Secondary outcomes included the technical success rate of stent insertion and symptom improvement rate after stenting, complication during procedure.
RESULTS: The stoma rate was 27.0% (10/37) in stent group versus 45.0% (18/40) in surgery only group ($p = 0.10$). The median postoperative hospital stay was 12.3±5.8 versus 12.2±7.4 days ($p = 0.92$). The postoperative complication rate was 8.1% (3/37) versus 10.0% (4/40) ($p = 1.00$). In-hospital death happened two case (5.4%, 2/37) in stent group and one case in surgery only group ($p = 0.60$). 7

patients (18.9%) in stent group and 11 patient (27.5%) in surgery group underwent emergency surgery ($p = 0.37$). Open surgery rate was 32.4% (12/37) versus 40.0% (16/40), respectively ($p = 0.49$). Subgroup analysis showed that emergency surgery rate of stent group who had successful stent insertion was significantly lower compared to surgery only group (6.7%, $p < 0.01$). The overall success rate of colorectal stent insertion for malignant colorectal obstruction was 88.7% (77/86). The success rate of stent as a bridge to curative surgery was 81.1% (30/37). Failure of the guidewire passage through lesions occurred in 5 patients (13.5%). Perforation during procedure occurred in 2 patients (5.4%). All patients who were performed stent insertion successfully, achieved symptom improvement.
CONCLUSION: The role of endoscopic colorectal stenting for bridging procedure before surgery is limited in the management of acute malignant obstruction. When the patients have high risks of complications of emergency surgery, stent can be considered as alternative approach to emergency surgery.
Disclosure of Interest: None declared

P1387 OUTCOMES OF STENT-IN-STENT TECHNIQUE FOR PRIMARY-FAILURE AND RECURRENCE OF SYMPTOMS IN MALIGNANT COLORECTAL OBSTRUCTION CASES WITH SELF-EXPANDABLE METALLIC STENTS

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INTRODUCTION: Self-expandable metallic stents (SEMS) placement was widely accepted procedure for malignant colorectal obstruction (MCRO), however, we sometimes encounter the primary failure or recurrence of colorectal obstruction (RCRO) after SEMS placement. In these cases, additional SEMS insertion through the previous SEMS, so-called stent-in-stent (SIS) technique, was effective, but was not well reported.
AIMS & METHODS: To estimate the safety and efficacy of SIS technique for MCRO, we retrospectively reviewed the clinical records. Between Mar. 2006 to Apr. 2014, 104 patients underwent endoscopic SEMS placement for MCRO. Primary SEMS failure was defined as un-resolved symptom of MCRO and RCRO as the recurrence of colorectal obstructive symptoms after SEMS placement. Technical success was defined as deployment of the stent across the entire length of the stricture on the first attempt. Clinical success was defined as a resolution of symptoms and radiological relief of the obstruction within 24 h, confirmed by radiographic observation. To pass the stricture in the previous SEMS, a hydrophilic biliary guidewire was promoted in a J-turn shaped by way of prevention for passing through the SEMS's mesh. We excluded the obstruction at the different locations.
RESULTS: Primary stent failure and RCRO occurred in 2 and 21 patients, retrospectively. The causes of primary stent failure were insufficient expansion (0) and remaining stricture with too-short SEMS because of underestimation of stricture length (2). Those of RCRO were kinking at the stent edge (8), tumor in/overgrowth (10) and stool impaction (3). Four patients underwent surgical intervention (bypass operation = 1, colostomy = 3), stent-in-stent placements were performed for 15 patients. We used covered (5) and uncovered (10) stents. The obstructions were located at rectum (5), sigmoid colon (4), splenic flexure (3), descending colon (1), and transverse colon (1) and cecum (1). Six patients had colorectal cancer. The remaining 9 patients had extra-colonic obstruction by following malignancies; pancreatic cancer (4), stomach cancer (2), ovarian cancer (2) and gallbladder cancer (1). Technical success was 100%, and clinical success was 86.7% (13/15). The median duration of secondary stent patency and survival was 161 (1-234) days and 122 (24-487) days, respectively. There was no severe adverse event. Long-term clinical failure occurred in 9 of 15 patients, attributed to re-occlusion of SEMS. Of these patients, tertiary SEMS placements were attempted for 4 patients, technical success was 100%, and clinical success was 50% (2/4). One patient underwent colostomy because of immediate perforation at 1 day after last stent insertion. Of the remaining 6 patients without tertiary stent insertion, four patients received palliative surgery and 2 patients were managed with total parenteral nutrition through a central venous catheter.
CONCLUSION: Stent-in-stent placement for primary failure and RCRO showed high technical and clinical success rate without any serious complications for both colonic and extra-colonic obstruction. We should carefully assess effectiveness of tertiary SEMS placement.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
SURGERY III – POSTER EXHIBITION – HALL XL

P1388 THE USEFULNESS OF A CLOSURE OF ULCER FOR THE PREVENTION OF DELAYED PERFORATION AND BLEEDING AFTER DUODENAL ESD

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INTRODUCTION: Duodenal ESD is difficult, because of narrow cavity, thin wall and poor maneuverability. And complication rate such as delayed bleeding and perforation is higher than that of gastric ESD. We tried the closure of ESD ulcer by clip for the prevention of delayed perforation and bleeding.
AIMS & METHODS: The aim of this study is to investigate the usefulness of a closure of ESD ulcer by clip for the prevention of delayed perforation and bleeding after duodenal ESD.
68 patients who had duodenal tubular adenoma or adenocarcinoma treated by ESD from May 2001 to December 2013 were enrolled into this retrospective study. The patients were divided into 2 groups, one was followed up without closure (non-closure group), the other was closure group. EZ clip made by Olympus (HX-610-090L) was used for the closure. Second look endoscopy was performed on 2 to 5 days after ESD to check delayed bleeding and perforation. Characteristics of the lesions were as follows. Bulbs / 2nd portion / 3rd portion was 1/3/0 in non-closure group and 0/57/7 in closure group. The median diameter of resected specimen was 25 (23 - 30) mm and 17 (10 - 44) mm, respectively (P: 0.0239). The median diameter of lesion was 17 (13 - 22) mm and 9 (2 - 34) mm, respectively (P: 0.018). The oral intake of anticoagulant drug and under artificial dialysis were 0, 5 and 0, 2, respectively.
RESULTS: 1. The delayed bleeding rate was 50% (2/4) in non-closure group and 5% (3/64) in closure group. There was significant difference (P :0.0248). Three patients who had the delayed bleeding in closure group had risk of bleeding such as oral intake of anticoagulant drug, hemodialysis and diabetes mellitus.
2. The delayed perforation rate was 25% (1/4) in non-closure group and 0% (0/64) in closure group (P: 0.06).
3. The successful rate of the closure was 98% (63/64). The mean number of clips was 8.7 (range 4 to 17). The ESD ulcer of only one patient could not be closed by clips. Therefore, ENPD and ENBD was performed to prevent complications. And, the patient was fine without any complications such as delayed perforation and bleeding.
CONCLUSION: The incidence of delayed bleeding or perforation after duodenal ESD is high. However, the closure of ESD ulcer by clip is useful for the prevention of delayed perforation and bleeding after duodenal ESD.
Disclosure of Interest: None declared

P1389 TRANSORAL DIVERTICULO-ESOPHAGOSTOMY AS TREATMENT OF ZENKER DIVERTICULUM

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INTRODUCTION: Transoral diverticulo-esophagostomy (TDE) is a modern treatment for Zenker diverticula (ZD) with low morbidity rate and high rate of symptom improvement. Residual or recurrent symptoms may impair patient's QoL and may request retreatment. Aim of this study is to analyze mode of presentation, diagnosis and treatment details of patients (pts) submitted to TDE who needed retreatment.
AIMS & METHODS: From March 1998 to September 2013, 96 out of 101 candidates, pts were submitted to TDE. TDE was performed with linear stapler with modified anvil (Endo GIA 30, 3.5) in all patients and, since 2009 (44 cases), with placement of two stay sutures on the septum to increase the length of section. All patients underwent FU at 1 month with barium swallow, whenever symptoms occurred by endoscopy and manometry, and at the time of this analysis.
RESULTS: Oropharyngeal dysphagia occurred in 83/96 pts; regurgitation, inhalation, throat lump were also recorded. Complications were: 4 dental lesions, 2 perforation treated conservatively, 1 bleeding. Two bleeding from the stapled line required endoscopic hemostasis. Twenty pts complained persistent symptoms due to residual spur or recurrent diverticulum: in 3/20 stay sutures were used; 15/20 pts (with a residual spur < 2 cm) were treated with flexible endoscopy with further treatment required in 2 cases; in 5/20 pts with a spur longer than 2 cm second TDE (4 pts) or open diverticulectomy (1 pt) were performed. Mean interval between TDE and retreatment was 7 months. After retreatment 4/20 patients complained mild symptoms. At a median FU of 42 months symptoms disappeared globally in 94% of patients.
CONCLUSION: Transoral treatment of ZD shows good results in terms of symptom reduction and patients' satisfaction. In few cases results were optimized by complementary treatment. The use of stay sutures allows to obtain better results.
Disclosure of Interest: None declared

P1390 TUMOR STROMA RATIO (TSR) IN ESOPHAGEAL ADENOCARCINOMA BIOPSIES IN THE PREDICTION OF RESPONSE TO NEOADJUVANT THERAPY AND OVERALL SURVIVAL

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INTRODUCTION: The incidence of esophageal carcinoma has been rising over the past decades. Surgical resection remains an important part of curative treatment. Several studies have demonstrated a survival benefit for patients receiving neoadjuvant therapy compared to patients that underwent surgical resection alone. Identification of non responders at an early stage could prevent patients from the toxicity of neoadjuvant therapy and avoid a possible fatal delay in the performance of potentially curative surgery. Tumor stroma ratio (TSR) in primary tumor biopsies taken before neoadjuvant therapy and surgery proved to be a prognostic factor for patient's survival. The aim of this study was to evaluate the prognostic value of the TSR in biopsies of esophageal adenocarcinomas taken before neoadjuvant therapy and surgery, in correlation to the response to neoadjuvant therapy prior to esophagectomy. In addition the correlation of the tumor stroma ratio with overall survival was evaluated.

AIMS & METHODS: In a retrospective study, we selected 141 patients with esophageal adenocarcinoma who underwent neoadjuvant chemoradiotherapy prior to esophageal resection between 2004 and 2011. The haematoxylin-eosin (H&E) stained sections of the tumor biopsies were reanalysed. TSR was scored as TSR low (< 50% carcinoma) or TSR high (> 50% carcinoma). Response to neoadjuvant therapy was determined in the resected specimen based on the tumor regression grade (TRG). The chi-square and Fisher's exact tests were used to evaluate the correlation of TSR with TRG. Survival was calculated from the date of surgery using the Kaplan–Meier method.
RESULTS: 141 patients were analysed. 55 (39%) patients were defined as responders (TRG 1 and 2) and 86 (61%) as non-responders (TRG 3 and 4). Estimation of the TSR was performed successfully in all the tumors (100%). 104 (74%) patients were classified as TSR high and 37 (26%) patients as TSR low. The correlation of TSR with TRG was not significant ($p = 0.537$). The correlation of TSR with overall survival was not significant ($p = 0.793$).
CONCLUSION: Our results suggest that the TSR in biopsies of esophageal adenocarcinomas does not have a prognostic value in correlation to the response to neoadjuvant therapy prior to esophagectomy. Moreover, according to our results TSR is not a prognostic characteristic for overall survival.
Disclosure of Interest: None declared

P1391 OCCUPATIONAL STATUS AFTER ESOPHAGECTOMY FOR CANCER

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INTRODUCTION: In the last decade, work participation of cancer survivors has received growing attention worldwide and cancer survivors are at risk for job loss, unemployment and social and work disability. Cancer survivors who are unable to resume a former job face the risk of a financial loss.
AIMS & METHODS: The purpose of the current study was to evaluate the impact of esophagectomy for cancer on patients' occupation. We also evaluated the association between the job condition and perceived quality of life at one year after esophagectomy.
We retrospectively evaluated all consecutive patients referring to our department between 2009 and 2012 for esophageal cancer. Inclusion criteria was esophagectomy for cancer. Patients not suitable for work (due to psychiatric disease or tetraplegia) and patients with missing information about their job were excluded. Working condition at diagnosis, at one month before surgery and at one year after surgery was collected. Patient's and tumor characteristics – along with therapeutic strategies – were also collected. Quality of life was evaluated at diagnosis and at one year after surgery using Financial Difficulties (FI), Social Functioning (SF), Role Functioning (RF) and Global health status (QL2) scores of EORTC QLQ-C30 questionnaire.
RESULTS: Fifty-one active workers and 29 retirees underwent surgical resection for esophageal cancer.
At diagnosis, retirees had slightly lower FI score than active workers (9.0±15.1 vs. 18.9±27.8, $p = 0.07$), whereas self-employed subjects had slightly higher RF (93.6±12.8 vs. 78.5±31.3, $p = 0.05$) and QL2 (80.1±17.2 vs. 65.6±23.6, $p = 0.06$) than employees.
At one year after surgery, 64% active workers were still in labor force whereas 36% quit their job; SF score (92.9±13.1 vs. 86.7±17.3, $p = 0.34$), FI score (14.3±26.2 vs. 22.7±26.7, $p = 0.47$), RF score (71.4±28.4 vs. 86.7±22.6, $p = 0.15$) and QL2 score (67.9±18.3 vs. 73.0±22.1, $p = 0.58$) were similar between the two groups.
CONCLUSION: Retirees reported less financial concerns than active workers at cancer diagnosis. A considerable number of patients quit their job after esophagectomy for cancer. Adequate welfare strategy should be implemented for esophageal cancer survivors.
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Disclosure of Interest: None declared

P1392 OMENTECTOMY IN GASTRIC CANCER SURGERY: A PROSPECTIVE COHORT STUDY IN 100 PATIENTS

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INTRODUCTION: There is no evidence for a complete omentectomy as part of a radical gastrectomy with a modified D2 lymphadenectomy in potentially curative gastric cancer. In this study we prospectively evaluated the presence of metastases in the greater omentum in potentially curative radical gastrectomy for gastric cancer patients.
AIMS & METHODS: In this multicenter prospective cohort trial 100 consecutive patients with gastric cancer underwent a (sub) total gastrectomy with complete en-bloc omentectomy and a modified D2 lymphadenectomy. After resection of the specimen, the omentum was separated from the stomach distal to the gastro-epiploic vessels and separately sent for pathological examination. The primary endpoint was the presence of metastases in the greater omentum.
RESULTS: In 5 of 100 patients (5.0%) metastases were detected in the greater omentum (2 patients with omental lymph node metastases, 3 patients with omental tumor deposits). These patients had pT4N1M1, pT4N1M0, ypT4N1M0, ypT3N0M1, ypT3N3M0 disease. In all 5 patients with omental metastases, the resection was irradical (R1) at the proximal ($n = 3$) or distal ($n = 2$) resection margin. Two patients were operated for linitis plastica and 3 had a proximal gastric tumor. In 3 patients the tumor expanded in the esophagus, in 2 in the duodenum.
CONCLUSION: Metastases in the greater omentum are infrequent. It seems that there are factors demonstrable that coincide with the presence of metastases in the greater omentum. In all patients with omental metastases an irradical resection was performed. This study suggests that omentectomy could possibly be omitted in some gastrectomy for gastric cancer patients. However, identification of these patients, safety and true benefit of omentum preservation needs further investigation in a randomized controlled trial.
Disclosure of Interest: None declared

P1394 PREDICTIVE FACTORS FOR CHOOSING MINIMALLY INVASIVE SURGERY IN PATIENTS WITH ADVANCED GASTRIC CANCER

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INTRODUCTION: The most important part of advanced gastric cancer surgical treatment consists of either open surgery or minimally invasive surgical procedures, both techniques being under current evaluation for the clinical impact and prognosis of each patient. According to various parameters which can be revealed by pre-procedure imaging and endoscopy, the minimally invasive surgery is generally preferred. However, there are certain cases in the evolution of advanced gastric cancer when the results indicate the necessity to switch to open surgery due to safety and better outcome reasons.
AIMS & METHODS: We retrospectively evaluated 187 patients known with advanced gastric cancer, whom were operated on between 2008 and 2014 in the Surgery Department of Clinical Institute Fundeni. The patients were divided into 2 groups according to the type of surgery performed: either open or minimally invasive surgery. We analysed the following parameters obtained by upper endoscopy: location of cancer, aspect, extension, involvement of pylorus and cardia, presence of haemorrhage; and tomographic imaging: metastasis, peritoneal carcinomatosis, lymph node involvement, surpassing the gastric wall, invasion of cardia, pylorus, duodenum and great vessels, presence of ascites. The obtained data were processed in Prism5 programme for statistical analysis using chi-square test.
RESULTS: Following statistical analysis we retain that 66% were male patients; 73% were operated by open surgery. A statistical significant p value (< 0.05) was obtained for Bormann classification type 2 relevant for a clear indication of open surgery ($p = 0.0091$), while type 3 could be managed by minimally invasive techniques ($p = 0.0003$). Non-involvement of cardia and pylorus was an indicator for the minimally invasive surgery with a p-value of 0.0037 and 0.00259, respectively (endoscopic parameters). Regarding the results from computer-tomography, minimally invasive surgery was used in the absence of the following parameters: great intra-abdominal vessel involvement ($p = 0.0177$), cardia invasion ($p = 0.0067$), surpassing of gastric wall ($p = 0.019$) and the presence of metastasis ($p = 0.05$).
CONCLUSION: The minimally invasive surgery of gastric cancer has gained increased interest among surgeons. It should be considered in the majority of cases, except when there is a sum of indicators such as local invasion (cardia, pylorus, great vessels, gastric wall), metastatic disease, lymph nodes involvement and Borrmann 2 lesions in which open surgery is rather recommended. Type 1 and 4 Borrmann lesions and active haemorrhage did not show a precise correlation.
Disclosure of Interest: None declared

P1395 CARDIOPULMONARY COMPLICATIONS AFTER ESOPHAGECTOMY FOR CANCER: PREOPERATIVE PREDICTION OF RISK FACTORS

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INTRODUCTION: The esophagectomy for cancer is still burdened by many complications. Simple, easy-to-use clinical predictors of cardiopulmonary complications may help in preventing and managing these events.

AIMS & METHODS: This study aimed at identify predictive factors of cardiac and pulmonary post-operative complications before patients undergo surgery in order to improve the outcome and shorten the hospital stay. Every patients underwent a cardiologic evaluation with echocardiography, ECG with further stress-test when required and pulmonary evaluation with function tests. The cardiologic parameters considered were the QT corrected interval, the E/A ratio, the diastolic volume of the left ventricle, the presence of mitral and/or tricuspid valves insufficiency, the ejection fraction and the evidence of myocardial asynergy at the cardiac US. The pulmonary function tests considered the observed/theoretical ratio in vital capacity (VC), forced expiratory volume in one second (FEV1), total lung capacity (TLC), transfer coefficient for carbon monoxide (KCO), FEV1/VC, RV/TLC. Logistic regression analysis was used.
RESULTS: In our center, 212 patients underwent esophagectomy for cancer from 2008 to 2013. Cardiologic complications were reported in 14 patients (6.6%): 7 arrhythmias with no hemodynamic instability (3.3%), 1 cardiac tamponade (0.5%), 4 myocardial infarctions (1.9%). Pulmonary complications were observed in 20 patients (9.4%): 19 pleural effusion (9%) and one acute respiratory distress syndrome (0.5%). Overall cardiac complications were predicted only by the presence of myocardial asynergy at cardiac US [OR 6.41 (95% CI = 1.84-22.36), p = 0.003] that also predicted cardiac arrhythmias [OR 6.08 (95% CI = 1.07-34.32), p = 0.041]. Pulmonary complications were predicted by the presence of myocardial asynergy at the cardiac US (p = 0.018), male sex (p = 0.046), reduced observed/theoretical ratio in: TLC (p = 0.019), KCO (p = 0.039) RV/TLC (p = 0.007), VC (p = 0.008). At the multivariate analysis the reduced observed/theoretical ratio in KCO resulted to be the only independent predictor of pulmonary complication [OR 0.94 (95% CI = 0.91-0.98), p = 0.009].
CONCLUSION: Cardiac and pulmonary complications after esophagectomy can be predicted by simple, repeatable and low cost tests. Therefore, studying every patient with cardiac US and pulmonary function tests should become part of the path to esophagectomy in order to adopt preventive medical therapy before and/or after surgery, to improve the outcome and to reduce the hospital stay with a cost-effectiveness benefit.
Disclosure of Interest: None declared

P1396 DINAMICS OF ENDOSCOPIC AND HISTOPATHOLOGICAL CHANGES OF THE MUCOUS AND SMOOTH ESOPHAGEAL MUSCLE AFTER SURGICAL TREATMENT ACHALASIA

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INTRODUCTION: Achalasia is associated with functional esophageal obstruction. Food stasis can predispose for esophagitis. For surgical treatment of achalasia there is important to study and compare in the dynamics in the long term of the endoscopic data with structural and morphological changes of the mucous membrane and smooth muscle of the esophagus and the incidence of esophagitis.
AIMS & METHODS: To investigate the correlation between endoscopic data and morphological changes of the mucous, incidence and severity of esophagitis in achalasia patients after surgical treatment with Heller-Dor or Heller-Toupet procedures. Before surgery on endoscopy biopsy specimens of mucous were sampled just above and at the zone of gastro-esophageal junction and the pieces of smooth esophageal muscle were taken above esophageal incision and at the zone of gastro-esophageal junction after myotomy. We performed routine histological sections and electron-microscopic studies of muscle biopsies. The macroscopic esophagitis graded according the Los Angeles classification (grades A–D) and histology was graded into grade 1-3. In the long term after surgery patients were seen in 1, 2, 4, 7, 10 and 17 years with upper GI endoscopy and inspection of the presence macroscopic esophagitis, three to four biopsy specimens were sampled just above and at the zone of gastro-esophageal junction for investigation.
RESULTS: Before surgical treatment 51 patients with achalasia had according radiological examination stage I - 3, stage II -5, stage III – 32 and stage IV – 11 pts. Endoscopic sings of esophagitis A – 22 (43, 2%), B – 15 (29, 4%), C – 9 (17, 6%), D – 5 (9, 8%) and histology grade I –27 (52, 9%), II – 18 (35, 3%) and III - 6 (11, 8%). The association between endoscopic food stasis and histological inflammation was significant. The ultrastructural alterations in the smooth muscle of all patients included muscle filament disarray, mottling of the fibre density in myocytes, thick and long cytoplasmic dense bodies, long dense plaques, and relatively few nexus junctions. In achalasia, the smooth muscle cells exhibited nuclear and cytoplasmic inclusions. The changes are most commonly seen between the narrowed and dilated segment of the esophagus but at the narrowed area of gastro-esophageal junction there was a striking loss of small nerve fibres and reduced numbers of granules in the remaining fibres. All patients were followed for mean values of 9.4 years (range: 1–22). The average number of endoscopies with biopsy sample sets per patient was 5 (range: 1–17). 19 (37, 3%) patients had no histological signs of esophagitis throughout follow-up, 32 (62, 7%) had esophagitis grade I – 29 (90, 6%) and grade II – 3 (9, 4%). Specialized intestinal metaplasia was found in 5 patients. The association between endoscopic food stasis and histological inflammation was significant. The association between the severity of clinical signs evaluated by a modified symptom score as the sum of the scores for dysphagia, regurgitation and chest pain with endoscopic signs of esophagitis and histological inflammation was poor.
CONCLUSION: Results of our studies evidence that in the long term after surgical treatment of esophageal achalasia with antiflux fundoplication is a considerable improvement of clinical symptoms, endoscopic sings and histological evidence of esophagitis. The dynamics of improvement depends on the duration and disease stage.
Disclosure of Interest: P. Fomin Financial support for research from: no, Lecture fee(s) from: no, Consultancy for: no, Shareholder of: no, Directorship (s) for: no, Other: no,: no, A. Kurbanov: None declared

P1397 THE IMPACT OF LYMPH NODE METASTASIS NEAR THE CELIAC TRUNK IN PATIENTS WITH CANCER OF THE DISTAL ESOPHAGUS OR GASTRO-ESOPHAGEAL JUNCTION

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INTRODUCTION: The present TNM staging system (7th edition, 2010) does not take into account the location of truncal nodes metastasis after neoadjuvant therapy. Therefore the aim of the present study is to identify the incidence and prognostic significance of celiac trunk metastasis in patients who underwent neoadjuvant chemo (radiation) therapy followed by an esophagectomy.
AIMS & METHODS: Between March 1994 and September 2013 a total of 462 consecutive patients with cancer of the mid-to-distal esophagus or gastroesophageal junction (GEJ) who underwent potentially curative esophageal resection after neoadjuvant chemotherapy (N = 88, 19%) or chemoradiotherapy (N = 374 (81%) were included.
RESULTS: 71 (15.4%) patients had positive truncal nodes in the resection specimen. Metastases to these nodes occurred more frequent in male patients with adenocarcinoma and in GEJ tumors. Pretreatment staging was significantly more advanced. While the number of resected nodes was comparable, a worse Mandard score, a higher yT and yN stage and a worse grade of differentiation were significantly related to truncal node metastases. Patients with positive truncal nodes had a worse median disease free survival (11months vs 65 months). In multivariate analysis, yN stage as well as positive truncal nodes were independently associated with a worse survival. Only 22 (31%) of 71 patients with positive truncal nodes were identified preoperatively with EUS or CT. 37 patients had suspicious truncal nodes on EUS or CT, but metastases in the pathology specimen were absent.
CONCLUSION: In the present study, it is demonstrated that positive truncal nodes are associated with advanced tumor stages and are an independent factor for worse survival. It seems that celiac nodal involvement is a "marker" for widespread microscopic disease that may later become evident, since patients with positive truncal nodes in the resection specimen have a dismal prognosis. Future studies need to investigate to what extent truncal node status should influence surgical decision making.
Disclosure of Interest: None declared

P1398 RELATIONSHIP BETWEEN RIGHT GASTROEPIPLOIC ARTERY LYMPH NODE DISSECTION AND PYLORUS-PRESERVING GASTRECTOMY BASED ON THE SENTINEL LYMPH NODE BASIN THEORY

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INTRODUCTION: Pylorus preservation decreases weight, prevents the dumping syndrome, and prevents bile reflux and gallstone formation.
Postoperative quality of life (QOL) is often the most important concern for patients with early gastric cancer; therefore, pylorus-preserving surgery has an important clinical significance.
In the present study, we identified the involvement of certain lymph nodes as sentinel nodes (SNs) using the Sentinel Lymph Node Basin theory to ensure appropriate lymph node dissection during pylorus-preserving gastrectomy (PPG) in patients with middle-third early gastric cancer.
AIMS & METHODS: Totally, 283 patients with middle-third gastric cancer who underwent PPG from 2002 to 2013 were included. The inclusion criteria were as follows: no previous treatment, tumor size < 4 cm, single tumor, cT1N0 disease. Informed consent was obtained from all patients.
We evaluated the lymphatic flow in all patients to identify the involvement of lymph nodes 4d and 6 as sentinel nodes (SNs). PPG was then performed on the basis of this detection.
RESULTS: Lymph node 6 was identified as an SN in 27 of the 283 patients, with a detection rate of 7.1%, 5.9%, 22%, and 7.1% in the lesser curvature, greater curvature, anterior wall, and posterior wall, respectively, while the detection rate for lymph nodes 6 and 4d as SNs was 16%, 84%, 72%, and 44%, respectively, in these regions.
Our findings showed that lymph nodes 6 and 4d were less frequently involved as SNs in patients with lesser curvature lesions, with lymph node 6 being directly involved without the involvement of lymph node 4d.
On the other hand, the frequency of detection of lymph node 6 as an SN was high in patients with greater curvature lesions; furthermore, it was always associated with the involvement of lymph node 4d.
Anterior wall lesions exhibited the highest frequency of lymph node 6 involvement as an SN.
CONCLUSION: The probability of lymph node 6 involvement as an SN was 9.5% in patients with middle-third early gastric cancer. Therefore, lymph node 6 dissection should be mandatory during PPG in these patients.
Disclosure of Interest: None declared

P1399 THE USEFULNESS OF SEDATION USING A COMBINATION OF PROPOFOL AND DEXMEDETOMIDINE HYDROCHLORIDE UNDER THE CONTINUOUS AIRWAY TONE MONITORING WITH A PROPRIETARY MICROPHONE IN THE ESOPHAGEAL ESD

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INTRODUCTION: The esophageal endoscopic submucosal dissection (ESD) is known to be technically more difficult and riskier about intraoperative complication than gastric ESD due to the narrow space and the thin wall of the esophagus. Although proper sedation is essential for successful esophageal ESD, it is sometimes difficult to achieve stable sedation with midazolam or other benzodiazepines alone. Recently, introduction of new sedatives such as propofol and dexmedetomidine hydrochloride on ESD are expected to be useful agents. There are few reports investigating the effects of such sedatives on ESD performance and complications.
AIMS & METHODS: Objective: We started new sedation using a combination of propofol and dexmetomidine under the continuous airway tone monitoring with a proprietary microphone in the esophageal ESD since August 2013. The study was conducted to investigate the safety and efficacy of our new sedation. Subjects: The present study included consecutive 35 patients undergone esophageal ESD before and after introducing the new sedation on August 2013, in which 20 patients were sedated either with midazolam or other benzodiazepines alone (Conventional group) just before introducing the new sedation between July 2012 and August 2013, and 15 patients were sedated with a combination of propofol and dexmetomidine (New group) between August 2013 and April 2014. Outcome Measurements: The clinical characteristics (age, sex, body mass index, alcohol consumption and underlying disease) was collected. Minimum value of systolic blood pressure (sBP), minimum value of blood oxygen saturation (SpO_2), and the degree of body movement leading to the interruption of maneuver during ESD were compared between the groups. The clinical characteristics (age, gender, body mass index, alcohol consumption and underlying disease) was collected. We consequently compared the following outcome of ESD between the groups: procedural time, en block resection rate, resected lesion size and incidence of complications (massive bleeding or perforation).
RESULTS: There was no significant difference between the two groups in the clinical characteristics. Minimum value of sBP (mmHg) in the New group was lower than in the Conventional group (82.27 ± 16.77 vs 102.10 ± 19.30, $p = 0.002$). Minimum value of SpO_2 (%) in the New group was higher than in the Conventional group (97.13 ± 2.07 vs 94.15 ± 2.41, $p = 0.001$). Regarding ESD performance, there was no statistically significant difference in en block resection rate, maximum diameter of specimen and incidence of complications during ESD between the two groups. However, the mean procedural time (min) in the New group was significantly shorter than in the Conventional group (105.13 ± 43.48 vs 134.95 ± 45.58, $p = 0.013$).
CONCLUSION: The continuous airway tone monitoring with a proprietary microphone may provide the prevention of respiratory suppression by earlier detection of apnea, glossoptosis and laryngeal spasm. Sedation using a combination of propofol and dexmedetomidine hydrochloride under the continuous airway tone monitoring with a proprietary microphone can improve procedural time without respiratory suppression in the esophageal ESD.
Disclosure of Interest: None declared

P1400 NEW METHOD OF LAPAROSCOPY ASSISTED ENDOSCOPIC FULL-THICKNESS RESECTION WITH SILICON AND POLYGLYCOLIC ACID SHEETS IN PORCINE MODEL

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INTRODUCTION: It is reported that the sentinel node concept is valid in cases of early gastric cancer using lymphatic basin dissection method. It means that dissection of the lymph nodes outside the basins may be avoided when the sentinel nodes were negative for metastasis. We have previously shown the safety and benefits of endoscopic full-thickness resection (EFTR) in *in vivo* porcine models. Furthermore, we initiated a clinical study of EFTR in patients with submucosal invasive gastric cancer who were diagnosed as negative for lymph node metastasis by laparoscopic sentinel lymph node biopsy. With this technique, the lesion can be resected with an appropriate surgical margin, since the resection is performed while confirming the lesion. On the other hand, it has some disadvantages, such as loss of endoscopic view caused by collapse of the stomach and intra-peritoneal infection by outflow of gastric juice. Thus, we tried new method of covering the serosa of stomach with silicon sheet and polyglycolic acid felt to prevent collapse of the stomach and outflow of gastric juice.
AIMS & METHODS: Three domestic pigs were used for LA-EFTR. Under general anesthesia, virtual lesions measuring 2 to 3 cm in diameter were set in various positions of the stomach. Silicon sheet and polyglycolic acid (PGA) felt (Neoveil ®) were put on the serosa of the virtual lesion and pasted with fibrinogen, thrombin solution. Then, full-thickness incision was performed by IT knife.
RESULTS: By covering the serosa with PGA felt, endoscopic view was kept during EFTR without collapse of the stomach. The felt was detached from the stomach by laparoscopic forceps after EFTR and removed through oral cavity.
CONCLUSION: This method prevents the collapse of the stomach and enables endoscopic resection with stable endoscopic view. EFTR may be a useful surgical treatment as the extent of resection is limited to the minimum necessary and the remnant gastric volume is preserved.
Disclosure of Interest: None declared

P1401 MODIFIED INTRODUCER METHOD FOR PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) DOES NOT NEED ADMINISTRATION OF SYSTEMIC PROPHYLACTIC ANTIBIOTICS - A PROSPECTIVE, RANDOMISED, DOUBLE-BLIND STUDY

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) is the most common method of enteral nutrition in patients who require long-term tube feeding. According meta-analysis, administration of systemic prophylactic antibiotics for PEG tube placement reduces peristomal infection. However, several recent developments of its procedure and instruments, the risk of infection having been reduced. We want to assess necessity of systemic antibiotic prophylaxis for a new modified introducer method PEG.
AIMS & METHODS: A prospective, randomised, double-blind trial. A total of 278 patients undergoing PEG were assessed for inclusion. Ninety-one patients with an indication for PEG who gave informed consent to participate were randomized. Forty-six patients received prophylactic ampicillin (sulbactam sodium/ampicillin sodium) and 45 patients received a placebo. Introducer method for PEG using Kangaroo-II Seldinger PEG kit was performed. Primary outcome was the occurrence of clinically evident wound infection within 3 and 7 days after insertion of the PEG catheter. Secondary outcomes were fever and any infection within 3 and 7 days after PEG.
RESULTS: There were not significant difference between 2 groups in all parameters, including wound infection within 3 and 7 days, any fever within 3 and 7 days, any infection witin 3 and 7 days, and successive rate of finising antibiotics.
CONCLUSION: The new modified introducer method PEG might not needed for systemic antibiotic prophylaxis.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
IBD III – POSTER EXHIBITION – HALL XL

P1402 A MICROFLUIDIC BASED CHIP MODEL FOR THE STUDY OF INTESTINAL MUCOSA BIOPSIES

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INTRODUCTION: Biopsy tissue has advantages over animal- and single cell models as both the original disease mechanisms and the cell-matrix interactions are maintained. Several authors have developed chip-based model for tissue culture (1,2),
AIMS & METHODS: The chip was produced in-house of glass and PDMS with a $2mm^3$ biopsy chamber. Microfluidic channels ($200\mu m$) flushed the biopsy with DMEM in separate flows to the epithelial and the basolateral surface. A syringe pump established the flow ($120\mu lmin\text{-}1$) and the effluents from both sides were collected for analyses. The use of microfluidic channels ensured spatial and temporal regulation of solute concentration essential for the control of biomimetic processes To ensure that the epithelial and the basolateral flow did not mix, phenol red was added to the fluid on the epithelial side and the effluents examined with a photometer.
With proper consent from the ethics boards (UK) and after written patients consent, biopsies were taken from patient with IBD. To investigate tissue survival, the tissue was processed for histology (HE) at start, at 24, 48 and 72 hours. Furthermore, the biopsies were treated with Triton-X 100 at the same time-points and the release of LDH was measured. The acute phase protein SA-100 was measured in the effluent from tissue with macroscopic, inflammatory changes and compared to normal looking tissue.
RESULTS: Photometry of the effluents demonstrated that the media did not mix. Histology (HE) demonstrated that the epithelial layer was intact after 72 hours. Application of the Triton-X buffer sharply increased the LDH in the effluent on both sides. S-100A was significantly higher in IBD than in effluents from the non-IBD biopsies. This relationship was maintained up to 50 hours. Staining with Ki-67 demonstrated proliferating cells in the crypts even at 50hours.
CONCLUSION: We have established a dual channel, chip method for tissue culture that ensure tissue viability and maintain inflammatory characteristics for more than 50 hours.
Three-dimensional culture models with intact cell-cell and cell-matrix connections have several advantages over single cell models. Our goal is to develop this model to study individual disease mechanisms and therapy responses in IBD. Our dual flow model may enable us to study the influence of luminal metabolites on the colonic mucosa.
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Disclosure of Interest: None declared

P1403 THE EFFECT OF THE ANTI-TNFA ADALIMUMAB ON THE LEVELS OF ANGIOGENIC FACTORS IN MUCOSAL CULTURES FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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INTRODUCTION: Effectiveness of adalimumab (ADA) treatment could be related to the modification of different angiogenic proteins, including VEGF, Ang1, Ang2 and their receptor Tie2.
AIMS & METHODS: The aim of this study was to compare the concentrations of several angiogenic factors in colonic mucosa culture supernatant (MCS) in patients with IBD and matched controls and to analyze their modifications with the *in vitro* ADA addition to the culture.
Prospective study in patients with IBD and non-IBD controls that underwent endoscopy. Duplicates of colonic mucosa samples from affected and non-affected mucosa from each IBD patient were obtained for comparison. Both were washed and then cultured at 37°C in 5% CO_2 medium under shaking for 24hours. In one duplicate, ADA was added up to a final concentration of 10μg/mL prior to culture. MCS levels in AP were determined by ELISA. Endoscopic ulcerative colitis (UC) and Crohn's disease (CD) activity was ascertained by Mayo subscore and SES-CD indexes, respectively.
RESULTS: 28 patients with IBD (16 UC, 12 CD) and 21 controls were included. Mean age was 41±16 years, and 61% were women. The mean disease duration was 7±7 years. According to endoscopic activity, 36% of patient had quiescent, 32% mild, 28% moderate, and 4% severe activity. All angiogenic factors mean levels in MCS were higher in affected than in non-affected MCS; VEGFA (19.1±18.7 vs. 8.7±10.5 pg/mL/mg) and Ang2 (21.3±15.7 vs 11.8±8.9 pg/mL/mg) ($p<0.05$). There were no differences in MCS depending on endoscopic activity. Levels of VEGFA, Ang1 and Ang2 from the affected, and VEGFA and Tie2 from the non-affected mucosa, were lower when cultured with ADA than without it (table 1). In UC patients, VEGFA and Ang1, and all angiogenic factors MCS mean levels were lower in the affected-mucosa and non-affected mucosa, and in the non-affected mucosa when cultured with ADA, respectively. In contrast, in CD patients, there were no differences in MCS angiogenic factors levels and the addition of ADA to the culture.
Table 1. Levels of angiogenic factors in MCS from IBD patients after culture.

	Affected mucosa	Affected mucosa + ADA	p-value
VEGFA	19.1±18.7	14.6±14.5	0.003
Ang1	15.7±8.8	12.2±6.2	0.021
Ang2	21.3±15.7	19.4±13.1	0.021
Tie2	12.0±5.5	12.4±16.1	0.911

Concentrations are expressed in pg/mL per mg of tissue.
CONCLUSION: ADA might downregulate the production of angiogenic factors in MCS. ADA addition to mucosal cultures affects angiogenic factors levels in samples from patients with UC differently than in patients from CD.
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P1404 EFFECT OF CHONDROITIN SULPHATE ON PRO-INFLAMMATORY MEDIATORS AND DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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INTRODUCTION: Chondroitin sulphate, a glycosaminoglycan that modulates NF-κB, might modulate several pro-inflammatory proteins involved in the pathogenesis of IBD.
AIMS & METHODS: The aim of our study was to evaluate the incidence rate of relapse in patients with IBD under chondroitin sulphate treatment and its effect on the concentrations of diverse pro-inflammatory mediators in serum and urine. Prospective observational 12-month (m) follow-up study in patients with IBD in remission for at least 6 m, starting chondroitin sulphate treatment (Condrosan®, CS Bio-Active™, Bioibérica S. A., Barcelona, Spain) for osteoarthritis (OA) (dose: 800 mg o.d.). Visits were as follows: Baseline, 3rd, 6th, 9th and 12th m. CDAI and modified Truelove-Witts clinical indexes were calculated for Crohn's disease (CD) and ulcerative colitis (UC) respectively. C-reactive protein (CRP), orosomucoid, and erythrocyte sedimentation rate (ESR) were also determined. Levels of VEGFA, VEGFC, FGF2, HGF, Ang1, Ang2, TGFβ, TNFα, IL1β, -6, -12, -17, -23, ICAM1, VCAM1, MMP3 and PGE2 were quantified by ELISA. OA joint pain was evaluated by a visual analogue scale (VAS).
RESULTS: 37 patients with IBD (19 UC, 18 CD) were included. Mean age was 59.8 years, and 70% were women. The mean disease duration was 12.7 years. 62% of patients were under mesalazine, 5% with sulfasalazine, 22% with thiopurines, and 3% with methotrexate. There was only one patient (with UC) that had a flare during follow-up (6th m visit). The incidence rate of relapse was 3.4% per patient-year of follow-up. That figure is lower than the relapse rate previously reported for IBD patients. 12 UC and 11 CD patients completed the 12 m follow-up. In all patients with IBD, mean serum VEGFA levels were higher after 12 months of CS treatment (799 pg/mL) as compared to baseline (492 pg/mL) ($P<0.05$). Further differences regarding the other studied pro-inflammatory markers were not found. At 12th m, the OA joint pain had improved in all but four patients (from 5.9 to 3.0) ($P<0.01$). 43% of patients suffered adverse events, but only 5% were related to the drug.
CONCLUSION: The incidence of IBD relapse in patients under chondroitin sulphate treatment was lower than the generally reported. This treatment might modulate VEGFA serum levels, but it is not associated with modifications in the concentrations of the other studied pro-inflammatory mediators. Chondroitin sulphate decreases pain related to OA in patients with IBD.
Disclosure of Interest: P. M. Linares: None declared, M. Chaparro Other: Dra. M Chaparro has served as a speaker and has received research funding from MSD and Abbvie., A. Algaba: None declared, M. Román: None declared, I. Moreno Arza: None declared, F. Abad Santos: None declared, D. Ochoa: None declared, I. Guerra: None declared, F. Bermejo: None declared, J. P. Gisbert Other: Dr. P. Gisbert has served as a speaker, a consultant and advisory member for, and has received research funding from MSD and Abbvie.

P1405 INTERLEUKIN-17A HOMODIMER REDUCES PRO-INFLAMMATORY CYTOKINE PRODUCTION BY INFLAMMATORY BOWEL DISEASE MUCOSA CULTURED EX VIVO

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INTRODUCTION: Interleukin (IL)-17A, which is up-regulated in inflammatory bowel disease (IBD) mucosal lesions, and IL-17F are normally present as IL-17AA and IL-17FF homodimers and may occasionally form IL-17A/F heterodimers. The role of each IL-17 dimer in IBD is currently unknown.
AIMS & METHODS: Here we studied the effects of IL-17AA, IL-17FF and IL-17-A/F in ulcerative colitis (UC) and Crohn's disease (CD) mucosa. Inflamed colonic biopsies from 17 IBD patients (6 UC and 11 CD) were cultured *ex vivo* for 24 hours with IL-17AA, IL-17FF or IL-17A/F (1 ng/ml). Mucosal myofibroblasts isolated from the inflamed colon of 4 CD and 4 UC patients were cultured for 24 hours with tumor necrosis factor (TNF)-alpha 20 ng/ml or with increasing concentrations (1-100 ng/ml) of IL-17AA, IL-17FF or IL-17A/F. IL-6 and IL-8 were measured in culture supernatants by ELISA.
RESULTS: IL-17AA, but not IL-17FF, significantly reduced both IL-6 and IL-8 production by inflamed IBD biopsies cultured *ex vivo*, whereas IL-17A/F decreased IL-8 release by IBD mucosa. No difference was observed between CD and UC. Neither IL-17AA, nor IL-17FF, nor IL-17A/F exerted any effect on IL-6 and IL-8 production by IBD myofibroblasts. As expected, TNF-alpha stimulation significantly increased IL-6 and IL-8 production by both CD and UC myofibroblasts *in vitro*. No difference was observed between CD and UC myofibroblasts.
CONCLUSION: IL-17AA exerts an anti-inflammatory action on inflamed IBD biopsies cultured *ex vivo*. The action of IL-17AA is not mediated by myofibroblasts, therefore further studies are underway to ascertain which cell type is the main target of IL-17AA in IBD mucosa.
Disclosure of Interest: None declared

P1406 THE ROLE OF NADPH OXIDASE IN THE PATHOGENESIS OF COLON INFLAMMATION IN MICE

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INTRODUCTION: Reactive oxygen species (ROS) induced oxidative stress is one of most important etiological factor involved in the inflammation [1-2]. The key producers of ROS in the cells are NADPH oxidase enzymes. Several studies have shown that epithelial NADPH oxidase might be responsible for normal immune response to antigens in the gut [1,3]. On the other hand, little is known about the molecular pathways controlling ROS production via NADPH oxidase enzymes in the primary intestinal epithelial cells during inflammation.
AIMS & METHODS: AIM: To investigate the role of NADPH oxidase in colon epithelial cells in pathogenesis of acute and chronic colon inflammation using mice dextran sulphate sodium (DSS) colitis model.
METHODS: BALB/c mice were divided into three groups: 8 mice with acute DSS colitis (3.5% DSS solution; 7 days), 8 mice with chronic DSS colitis (3.5 % DSS solution for 5 days + water for 6 days; 4 cycles; total: 44 days) and 12 mice without DSS supplementation as control group. The primary colonic epithelial cells were isolated using chelation method. The cells were cultivated in the presence of mediators (lipopolysaccharide (LPS), apocynin or diphenyleneiodonium). Viability of cells was assessed by fluorescent microscopy. Production of reactive oxygen species (ROS) by the cells was measured fluorimetrically using

Amplex Red. Production of tumour necrosis factor- *alpha* (TNF- α) by the colonic epithelial cells was analysed by ELISA. *Nox1* gene expression was assessed by real-time (RT) PCR.
RESULTS: Our study showed that TNF-α level was increased in unstimulated primary colonic cells both in the acute and chronic DSS colitis groups, whereas decreased viability, increased ROS production, and expression of *Nox1* was characteristic only for chronic DSS colitis mice when compared to the controls. The stimulation by LPS increased ROS generation via NADPH oxidase and decreased cell viability in mice with acute DSS colitis. Treatment with NADPH oxidase inhibitors increased cell viability decreased the levels of ROS and TNF- α in the LPS-treated cells isolated from mice of both acute and chronic DSS colitis groups.
CONCLUSION: Our study revealed the importance of NADPH oxidase in pathogenesis of acute and chronic colon inflammation. Moreover, the treatment with NADPH oxidase inhibitors had a protective effect against pro-inflammatory action of LPS in mice colonic epithelium cells during DSS colitis.
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P1407 ROLE OF ADENOSINE A2B RECEPTORS IN THE CONTROL OF INFLAMMATION, FIBROSIS AND MOTILITY IN EXPERIMENTAL COLITIS

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INTRODUCTION: The adenosine system is emerging as a pathway involved in the regulation of balance between tissue repair and fibrosis. However, the role of adenosine in the pathophysiology of gut fibrotic remodelling has been scarcely investigated.
AIMS & METHODS: This study evaluated the role of adenosine A2B receptors on inflammation, pro-fibrotic TGF-beta/SMAD signalling and motility in experimental colitis. Colitis was induced in rats by intrarectal 2,4-dinitrobenzenesulfonic acid (DNBS). After 6 days, systemic [body and spleen weight] and tissue inflammatory parameters [macroscopic and microscopic damage, myeloperoxidase (MPO)] were assessed. Three days before colitis assessment, animals were treated daily with BAY606583 (BAY, A2B agonist, 2 mg/kg) or MRS1754 (MRS, A2B antagonist, 1 mg/kg) by i.p. route. At sacrifice, molecular factors involved in fibrosis (collagen I and III, fibronectin, TGF-beta, phosphorylated SMAD2) were analyzed by western blot. Collagen fibers (Sirius red) and elastic fibers (orcein) were examined by histochemistry. Colonic longitudinal muscle strips were suspended in organ baths (Krebs solution with NK 1, 2 and 3 receptor antagonists, guanethidine, L-NAME) to record atropine-sensitive cholinergic motor activity. Contractions were evoked either by electrical stimulation or by carbachol in the presence of tetrodotoxin.
RESULTS: DNBS-induced inflammation was associated with a decrease in body weight and increase in spleen weight, tissue MPO as well as macroscopic and microscopic alterations. Western blot revealed an increased expression of collagen I and III, fibronectin, TGF-beta and pSMAD2, as compared with controls. Histochemistry confirmed an increment of collagen deposition and a loss of elastic fibers. In functional assays, both electrically-evoked and carbachol-induced contractions were reduced, as compared with controls. In the setting of colitis, treatment with MRS counteracted the inflammatory indexes, while not affecting the molecular parameters related with fibrotic remodelling. By contrast, the administration of BAY failed to modify both systemic and tissue inflammatory indexes. However, BAY increased the expression of collagen I and fibronectin, while downregulating the TGF-beta/pSMAD2 pathway. With regard for motility, the altered motor patterns associated with colitis were not affected by BAY, while they were partly normalized by MRS.
CONCLUSION: DNBS-induced colitis is associated with colonic fibrotic remodelling and altered excitatory motility. In this setting, the pharmacological activation of A2B receptors did not modify the inflammatory indexes and abnormal patterns of cholinergic motility, while it increased the fibrotic remodelling through molecular pathways independent of TGF-beta signalling. By contrast, the pharmacological blockade of A2B receptors counteracted bowel inflammation and improved colonic dysmotility, without affecting fibrotic remodelling. Overall, these findings suggest a marginal role of endogenously activated A2B adenosine receptors in the pathogenesis of fibrosis associated with bowel inflammation.
Disclosure of Interest: None declared

P1408 HUMAN ALPHA-DEFENSIN 6 REGULATED BY BOTH ATOH1 AND BETA-CATENIN MIGHT BE THE PATHOGENESIS OF CROHN'S DISEASE

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INTRODUCTION: Antimicrobial mucosal barrier dysfunction, including the reduction of Human alpha-Defensin (HD) 5, is one of the most crucial pathogenesis of Crohn's disease (CD). Human Paneth cells produce two α-defensin peptides, which called HD5 and HD6. Recently, it has been reported that HD6 promotes mucosal innate immunity through self-assembled peptide ''nanonets'' whereas HD5 has the antimicrobial activity. The transcriptional regulation of HD6 has not been elucidated. Moreover the association of HD6 expression with CD also remains unknown.
AIMS & METHODS: We therefore aimed to elucidate the transcriptional regulation of HD6 and the pathogenesis of CD by HD6 expression.
For the analysis of the transcriptional regulation of HD6, We transgened Atoh1 into colon cancer cell line; SW480 by lentivirus infection. The expression of HD6 was assessed by quantitative RT-PCR and immunofluorescence. The transcriptional activity of HD6 promoter was assessed by the luciferase reporter assay. For the analysis of the HD6 expression in CD, non-inflamed jejunum biopsy specimens of 8 CD patients and 9 healthy controls using double balloon enteroscopy (DBE) were assessed.
RESULTS: HD6 was significantly increased by Atoh1 expression in SW480 whereas other antimicrobial peptides such as HD5, Lysozyme and phospholipase A2 were not changed. Atoh1 also enhanced the transcriptional activity of HD6 promoter. We found that HD6 promoter within 200-bp from ATG contains a transcription factor (TCF) binding site and four E-box binding site. The deletion of each binding sites revealed that not only TCF4/β-catenin protein complex but also Atoh1 is indispensable for HD6 expression. Moreover, ChIP assay showed that Atoh1 directly binds to the promoter region of HD6.
Finally, we assessed the pathogenesis of CD by HD6 expression. The microarray using mapping biopsy of whole small intestine in CD patient showed that almost inflammatory related genes were not shown in jejunum, suggesting that the pathogenesis before the onset of CD might remain in jejunum. The expression of Atoh1 and secretory cell markers (HD5, HD6, MUC2 and CgA) in jejunum of CD patients were significantly lower than that of healthy controls. Moreover, HD6 positive Paneth cells of CD patients were significantly lower than that of healthy controls.
CONCLUSION: Both TCF4/β-catenin protein and Atoh1 are essential to express HD6 in different from HD5. The decrease of HD6 in small intestine might cause mucosal barrier dysfunction suggesting that HD6 might be one of the pathogenesis of CD.
Disclosure of Interest: None declared

P1409 DIVERSITY OF ADHERED MICROBIAL COMMUNITIES IN COLON MUCOSAL BIOPSIES OF CROHN PATIENTS BY 16S RRNA GENE PYROSEQUENCING, EVIDENCES FOR TWO MAIN DISTINCT GROUPS

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INTRODUCTION: The human gut microbiota participates actively in the host homeostasis and plays an important role in Crohn's disease (CD) pathogenesis. Microbial diversity measures based on environmental 16S rRNA genes had permitted the recognition of the vast diversity of yet uncultured microorganisms in environmental samples. Next Generation Sequencing (NSG) techniques produce thousands of sequences, and had been thoroughly used to reveal diversity in environmental samples with identifications based on clustering sequences into Operational Phylogenetic Units (OPUs).
AIMS & METHODS: We aimed to study the microbiota adhered in the gut mucosa of CD patients and compare with healthy controls by means of a high-throughput NGS approach. Mucosal biopsies of 13 CD and 7 healthy controls submitted to colonoscopy for medical indications were recruited between Augost 2011 and March 2012. Demographics and clinical characteristics (disease localization, inflammatory activity, behavior, medication and surgical history) were also collected. Biopsies were immediately placed in sterile tubes and stored at -80°C for DNA/RNA extraction. The mucosal adhered microbiota was studied by high quality deep-sequencing of 16S rRNA gene amplicons. High quality sequences (mean 500 nuc) were applied to OPUs identification approach based on clustering sequences. The Balearic Islands' Ethical committee approved the study.
RESULTS: CD samples showed a mean of 83 ($\pm$16) OPUs, whereas HC samples showed a mean of 101 ($\pm$19). Two major groups of CD patients with different mirobiomes could be discriminated. Both groups presented a common trend mainly exhibited as depletion in members of the class *Clostridia*. In addition, CD1 showed enhanced presence of co-colonizing *Bacteroidetes* as a result of the disappearance of *Firmicutes*; whereas CD2 seemed to exhibit an opportunistic colonization of the mucosa by members of *Proteobacteria*.
CONCLUSION: CD patients exhibited consistently lower microbiota diversity than controls. CD may include different pathological disorders resulting in different adhered microbial profiles with a similar inflammatory end process. Simple amplification tests checking the presence or absence of *F. prausnitzii*

and the relative abundances of *Firmicutes*, *Bacteroidetes* and *Proteobacteria* could serve as diagnosis of both major CD groups found here and may help in the recognition of the genetic or metabolic disorders that conduct to the CD phenotypes.

Disclosure of Interest: None declared

P1410 THE ROLE FOR THE CYTOKINES INTERLEUKIN-22 AND INTERLEUKIN-17A AND PATHOGEN-ASSOCIATED MOLECULAR PATTERNS DURING THE PATHOGENESIS OF CROHN'S DISEASE ASSOCIATED PERIANAL FISTULAS

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INTRODUCTION: Intestinal and perianal fistulas represent an important complication of Crohn's disease (CD). Therapeutic outcome using conventional drugs such as antibiotics, immunosuppressive agents and biologics is poor and surgical intervention is often required. Chronic inflammation, failure of the intestinal barrier function and a bacterial imbalance may contribute to the induction of epithelial-mesenchymal transition (EMT) and the consequent formation of fistula tracts. Tumor necrosis factor alpha (TNF-α), transforming growth factor beta (TGF-β) and interleukin (IL)-13 synergistically contribute to the migration and invasiveness of intestinal epithelial cells (IECs). The underlying extracellular matrix is broken down to enable IECs to invade.

AIMS & METHODS: Human perianal fistula tissue was investigated for the IL-22 receptor subtype RA1 and IL-17A using immunohistochemical procedures. Multicellular three-dimensional HT-29 IEC constructs were exposed to MDP (100 ng/ml) or IL-22 (50 ng/ml) for one, five and seven days and assessed microscopically as well as on a molecular level. Monolayer IECs were challenged to IL-22, IL-17A (100 ng/ml), TGF-β (100 ng/ml) or a combination of IL-22 plus TGF-β or IL-17A plus TGF-β.

Here, we investigated the impact of the Th17 and/or innate lymphoid cell derived cytokines interleukin (IL)-22 and IL-17A and pathogen-associated molecular patters (PAMPs) such as muramyldipeptide (MDP) on the induction of EMT.

RESULTS: After exposure to MDP for seven days, the spheroids lost the well-defined globular shape and the epithelial cells separated indicating the onset of EMT. This was not seen in untreated control spheroids. In accordance with these microscopic findings, MDP treated spheroids up-regulated mRNA levels of EMT-related genes, including *SNAIL1* ($p < 0.05$), *TGF-β* ($p < 0.05$) and *IL-13* ($p < 0.05$) after treatment for seven days. In contrast to MDP, IL-22 did not induce EMT in spheroids. When IECs were co-treated with IL-22 and TGF-β, the effects of TGF-β were abrogated, but a further enhanced mRNA expression of *β6-Integrin* ($p < 0.001$) was observed. A similar pattern was found for the co-treatment with IL-17A and TGF-β; TGF-β induced up-regulation of *SNAIL1* ($p < 0.05$) and *IL-13* ($p < 0.01$) *was* abolished and the reduced *E-Cadherin* ($p < 0.05$) levels were restored. Interestingly, we observed a strong staining signal for IL-22RA1 and IL-17A in fistula tissue of non-smoking CD patients whereas smokers revealed almost no expression of the indicated proteins.

CONCLUSION: Here, we demonstrate that PAMPs might contribute to the onset of EMT and therefore to the development of CD fistulas. The observed effects for the cytokines are indicative for an antagonistic effect of IL-22 and IL-17A on TGF-b. We therefore hypothesize that IL-22 and IL-17A might exert protective effects in the pathogenesis of CD-associated fistulas. There are some tremendous differences in the protein expression between smokers and non-smokers, indicating an altered immune response during fistula pathogenesis. In summary, our data suggest that bacterial pathogens likely impact the pathogenesis of CD-associated fistulas and the nicotine status might impact the response to fistula development.

Disclosure of Interest: None declared

P1411 ACTIVE CROHN DISEASE IS ASSOCIATED WITH TRYPTOPHAN DEFICIENCY

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INTRODUCTION: Malnutrition leads to intestinal inflammation and diarrhoea. In recent studies we have identified ACE2 as a key regulator of dietary amino acid homeostasis, innate immunity, gut microbial ecology, and transmissible susceptibility to colitis which can be directly regulated by the dietary amino acid tryptophan (TRP) (1). Moreover, B0AT1, the colonic TRP transporter, is downregulated in IBD mucosa (1). In an ongoing study we have investigated the role of TRP in a consecutive series of patients with IBD (n = 445, UC.n = 165, CD:n = 280) and controls (healthy controls and disease specificity controls = 125). More than 200 patients were seen twice and are not included in the basic statistics.

AIMS & METHODS: Patients with IBD were recruited consecutively from an outpatient setting, controls comprise healthy blood donors and disease specificity controls (patients with suspected IBD, in whom the diagnosis of IBD was not confirmed). A serum sample was prospectively obtained during a three months, ongoing sampling campaign to assess TRP levels. Patients were clinically characterized and TRP levels were related in an exploratory analysis to clinically characteristics, age, severity of disease, gender, BMI, smoking status CRP and duration of disease. A forward and backward logistic regression was performed.

RESULTS: TRP levels in patients with IBD were significantly lower ($P < 0.00001$) than in controls (UC: $p = 0.028$, CD: $p < 10E\text{-}8$) (Fig.1). Levels were lower in CD patients lower than in UC ($P < 0.0001$). In a first analysis of 258 patients a clear relationship of low TRP levels was seen with high disease activity ($p = 0.0077$ for UC and $p = 0.0070$ in CD). Female individuals had lower TRP levels than male individuals, both in controls ($p = 0.0097$) and patients ($p = 0.0006$). TRP levels were correlated with BMI ($p = 0.015$ in controls and $P < 0.0001$ in patients). The examination of TRP and smoking status was heavily confounded by the uneven distribution of smokers (n = 8 (10.3%) in UC, n = 67 (36-5%) in CD, $P < 0.0001$). No correlation of TRP levels and age or duration of disease could be found.

CONCLUSION: Tryptophane deficiency appears to be an important, novel mechanism in IBD. It appears likely that low TRP levels in serum reflect a reduced availability of TRP metabolites on the mucosal surface or an increased local consumption through the inflammatory process. In analogy to murine models TRP deficiency could cause the microbial changes seen in IBD and promote the rise of a colitogenic flora. While it high TRP exposure is poorly tolerated in the GI tract, a controlled delivery formulation of TRP derivatives with low toxicity is under clinical development for the use in IBD.

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P1412 THE EXPRESSION OF MYOSIN LIGHT CHAIN KINASE INDUCED BY NK-KB ACTIVATION IS INVOLVED IN THE DEVELOPMENT OF COLITIS-ASSOCIATED CANCER

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INTRODUCTION: It has been suggested that prolonged inflammatory bowel disease may promote carcinogenesis in the epithelia. Myosin light chain kinase (MLCK) has been reported to be essential to the permeability of epithelial barrier in the context of colitis, however its role in the development of colitis-associated cancer (CAC) is still unknown.

AIMS & METHODS: The aim of this study was to examine the effects of NF-kB activation and MLCK expression in the setting of CAC. Wild type C57BL/6 mice were pre-treated with azoxymethane and then three times with dextran sodium sulfate to induce a model of CAC.

RESULTS: Semi-quantitative polymerase chain reaction (qPCR) revealed that inflammatory cytokines such as IL-1b, IL-6 and MIP-2, which are known to be associated with tumor growth, were up-regulated in the inflamed colonic lamina propria. Western blotting (WB) showed slight up-regulation of MLCK in the colonic epithelia in association with the phosphorylation of IkBa and p65. NF-kB and MLCK were further up-regulated in the tumor tissues compared to the non-tumor areas, as well as up-regulation of the specific receptor for tumor necrosis factor (TNF) assessed by qPCR and WB. Immunohistochemistry (IHC) and transmission electron microscopy (TEM) showed that MLCK inhibitor, ML-7, treatment prevented the disruption of epithelial tight junctions. IHC and TEM also showed that anti-TNF mAb, MP6-XT22, treatment restored the disrupted tight junctions and suppressed tumor development.

CONCLUSION: Our studies suggest that permeability of epithelial layer in the inflamed tissues is associated with MLCK up-regulation and susceptibility to inflammatory cytokines that potentially promote CAC growth.

Disclosure of Interest: None declared

P1413 SERUM REG3ALPHA LEVELS IN CROHN'S DISEASE PATIENTS UNDERGOING IMMUNOABLATION AND AUTOLOGOUS HEMOPOETIC STEM CELL TRANSPLANTATION IN THE ASTIC TRIAL

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INTRODUCTION: Regenerating islet-derived 3-alpha (REG3α) has been shown to be a promising biomarker with remarkable specificity for lower gastrointestinal Graft versus Host Disease (GvHD) after allogeneic stem cell transplantation, allowing better risk stratification of patients and the prediction of non-relapse mortality (1). GvHD shares many similarities (histological features and genetic risk factors) with Crohn's disease (CD). We aimed to investigate the role of serum REG3α as a diagnostic and prognostic biomarker in CD patients undergoing autologous hemopoetic stem cell transplantation (HSCT) in the multicenter ASTIC trial.

AIMS & METHODS: Stored serum samples from the ASTIC trial were analyzed using a commercially available ELISA-kit to measure serum REG3α levels (Ab-

Match Assembly Human PAP1 kit, MBL International Cooperation, Catalog Number 5323). Clinical, laboratory and endoscopic data was available from the ASTIC trial. Serum REG3α levels were correlated with clinical (Crohn's disease activity index (CDAI), harvey bradshaw index (HBI)) and endoscopic disease activity (CDEIS) as well as overall outcome 1 year after HSCT, which was assessed by changes in CDAI and CDEIS, and by clinical (CDAI≤150) or endoscopic remission (CDEIS < 4), respectively.
RESULTS: As of January 2014, 132 serum samples were available from 37 of the 45 ASTIC trial participants. Mean concentration of serum REG3α was 101.8 ng/ml (95% CI 22.6-258.3). No significant elevation of serum REG3α levels was found among patients with moderate or severe symptoms compared to patients in clinical remission (106.3 vs. 91.4, p = 0.289) and no correlation of REG3α to CDAI was identified within the group of symptomatic patients. Nonetheless, patients with moderate to severe endoscopic disease activity (CDEIS > 9) showed slightly although not significantly elevated REG3α levels compared to patients in endoscopic remission (95.4 vs. 52.4, p = 0.052). Baseline REG3α of patients without clinical or endoscopic remission 1 year after HSCT was not elevated compared to patients in remission after HSCT (63.1 vs. 66.9, p = 0.947, and 68.4 vs. 59.2, p = 0.796, respectively). Changes in CDAI or CDEIS after HSCT did not show any correlation with REG3α levels at study enrolment.
CONCLUSION: We did not observe a correlation of serum REG3α levels with Crohn's disease activity except for a trend regarding endoscopic disease activity scores. In contrast to the findings in GvHD after allogeneic HSCT baseline REG3alpha did not have any prognostic value for clinical and endoscopic outcome 1 year after HSCT. Given the divergent findings compared to GvHD (1), we conclude that REG3α is not a promising diagnostic and predictive biomarker in CD patients undergoing autologous HSCT.
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Disclosure of Interest: None declared

P1414 THE IMPORTANCE OF INTESTINAL EOTAXIN-1 - EOSINOPHIL AXIS IN INFLAMMATORY BOWEL DISEASE, RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: Eotaxin-1 is a potent eosinophil chemoatractant which is considered a major contributor to tissue eosinophilia. Elevated tissue Eotaxin-1 has been previously reported in Ulcerative colitis (UC) patients. Simultaneous serum and tissue sampling from intestinal biopsies can be used to demonstrate the effect of tissue vs. serum Eotaxin-1 levels on tissue eosinophila in patients with UC or Crohn's disease (CD).
AIMS & METHODS: To evaluate serum and tissue levels of Eotaxin-1 in patients with Crohn's disease (CD) and Ulcerative colitis (UC) compared with healthy controls.
METHODS: Serum samples and intestinal biopsies were obtained from consenting patients with known CD or UC or healthy individuals undergoing screening colonoscopy. Biopsies were used for quantitative assessment of tissue Eotaxin-1 levels and for histological evaluation of tissue eosinophlia as measured by average eosinophil count per high power field (HPF), by a blinded pathologist. These parameters were than compared between the patients, which were sub-grouped according to diagnosis and disease activity.
RESULTS: Intestinal biopsies were obtained from 60 patients (10 controls, 15 active UC, 10 UC in remission, 16 CD active and 9 CD in remission). Mean tissue Eotaxin-1 levels were 34.02 pg/mg protein in control group compared to159.79 and 219.62 pg/mg protein in active UC and active CD respectively (p < 0.001 for both) and compared to 106.13 and 97.78 pg/mg protein in UC and CD in remission (p = 0.06 and 0.07 respectively). Tissue Eotaxin-1 levels in active CD were significantly elevated compared with non active CD patients (p < 0.05).
No significant difference was noted in serum Eotaxin-1 levels in neither CD nor UC patients, regardless of disease activity.
In healthy control, a strong correlation was found between tissue and serum eotaxin-1 levels (r = 0.75, p = 0.01). A weak correlation was found in CD and UC patients.
Tissue but not serum eotaxin-1 levels correlated tissue eosinophilia in active UC patients only (r = 0.63, p = 0.01).
CONCLUSION: This study demonstrates elevated tissue Eotaxin-1 levels as a hallmark of both UC and CD, especially in active disease. The increase in tissue but not in serum eotaxin-1 levels suggests its importance as a local mediator of mucosal inflammation.
The correlation between tissue eotaxin-1 and tissue eosinophila in active disease, marks its central role in mediating local inflammation, and also suggests that its role in the pathogenesis of CD is not restricted to eosinophils recruitment.
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P1415 COMPARATIVE BEHAVIOUR OF MACROPHAGES ISOLATED FROM PATIENTS WITH CROHN'S DISEASE OR ULCERATIVE COLITIS AND CONTROLS IN RESPONSE TO ADHERENT-INVASIVE OR NON-PATHOGENIC E. COLI INFECTION

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INTRODUCTION: Ileal lesions of 36.4% of Crohn's disease (CD) patients are colonized by pathogenic adherent-invasive *Escherichia coli* (AIEC), able to highly replicate in mature phagolysosomes within cultured macrophages. The aim of this study was to assess whether macrophages from CD patients showed impaired ability to control intracellular bacteria replication and pro-inflammatory cytokine expression in response to pathogenic AIEC or non-pathogenic *E. coli* infection.
AIMS & METHODS: Human peripheral blood monocyte-derived macrophages were obtained from CD patients, ulcerative colitis (UC) patients and controls. All patients and controls were genotyped for the main coding mutations in *NOD2* and for *ATG16L1*. Following in vitro infection with AIEC reference strain LF82 or non-pathogenic *E. coli* K-12 levels of intracellular bacteria at 1h and 10 h post-infection was assessed by using gentamicin protection assay. IL-6, IL-8, and tumour necrosis factor alpha (TNF-α) cytokine levels were evaluated at 10h post-infection by ELISA. The effect of neutralization of TNF-α on the number of intracellular AIEC LF82 bacteria were analysed in CD macrophages untreated or not with Infliximab at 1 μg/ml.
RESULTS: A higher number of AIEC bacteria than non-pathogenic *E. coli* is internalized within macrophages whatever cell origin. The intracellular AIEC replicate rate was the highest in macrophages from CD patients. This was not observed when macrophages were infected with non-pathogenic *E. coli*. In our cohort of CD patients, only macrophages heterozygous for a NOD2 polymorphism were found and they did not show significant difference in their ability to control AIEC intracellular replication. Concerning ATG16L1 polymorphism, high levels of intracellular AIEC bacteria were observed in AIEC-infected macrophages homozygous for ATG16L1 (T300A). AIEC infection of macrophages induced the secretion of IL-6, IL-8 and TNF-α at levels higher than infection with the non-pathogenic *E. coli* whatever cell origin. The levels of IL-6 cytokine secreted were higher with AIEC-infected macrophages from CD patients. A positive correlation was observed between the number of intracellular AIEC bacteria at 10 h post-infection and the level of TNF-α secreted by infected CD macrophages. In contrast no significant difference in TNF-α or IL-6 secretion was observed between non-pathogenic *E. coli*-infected macrophages from CD and UC patients or from controls. Infliximab have not effect on the control of intracellular bacterial replication within macrophages.
CONCLUSION: Human peripheral blood monocyte-derived macrophages from CD patients compared to those of UC patients or controls showed specific characteristics in response to AIEC infection but not to non-pathogenic *E. coli* challenge including load of intracellular bacteria and secretion of pro-inflammatory TNF-α and IL-6 cytokines.
Disclosure of Interest: None declared

P1416 A PROSPECTIVE STUDY OF CIGARETTE SMOKING AND THE RISK OF CROHNS DISEASE

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INTRODUCTION: Prospective studies on smoking and the risk of Crohn's disease (CD) in the general population are limited.
AIMS & METHODS: We aimed to conduct a cohort study of both men and women investigating smoking and the development of CD in the " EPIC-IBD Study". In total 401,326 participants, aged 30-74 years, were recruited from 12 regions in 8 countries in Europe between 1991 and 1998. Baseline questionnaires recorded data on smoking status and the number of cigarettes. The cohort was monitored until at least June 2004 to identify participants who developed CD. Each case was matched with four controls (age at recruitment, gender, centre and recruitment date) and odds ratios (ORs) calculated using conditional logistic regression.
RESULTS: In total, 110 participants developed incident CD (73% women, mean age at diagnosis = 55.7, SD = 11.1 years) after a median follow-up of 5.4 years (range 1.5-14.3 years). Current smoking at recruitment was associated with an increased odds of CD (OR = 1.95, 95% CI = 1.14-3.34) compared to non-smoking, but not former smoking (1.23, 95% CI = 0.71-2.12). There was some evidence of a dose-response with an increasing number of cigarettes (P trend = 1.28, 95% CI = 0.96-1.63, p = 0.05), with for those smoking >20/day reporting an OR = 2.34 (95% CI = 0.90-6.12, p = 0.08). Similarly also for a duration effect with an association with current smoking at the time of recruitment for those diagnoses more than 5 years after recruitment (OR = 2.13, 95% CI = 1.09-4.17), but none for those diagnosed within 5 years of recruitment. Ileal disease only was associated with smoking (OR = 3.02 95% CI = 1.11-8.20), but not colonic involvement only (OR = 1.02, 95% CI = 0.35-2.98).
CONCLUSION: The positive associations with smoking help to confer a causal link with CD due to the prospective collection of data and some evidence of a dose response. Further work should elucidate the biological mechanisms for these associations.
Disclosure of Interest: V. Andersen Consultancy for: Janssen & Merck.

P1417 DISTURBED PARACELLULAR MOVEMENT OF PHOSPHATIDYLCHOLINE TO INTESTINAL MUCUS PREDISPOSES THE DEVELOPMENT OF ULCERATIVE COLITIS

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INTRODUCTION: Phosphatidylcholine (PC) in intestinal mucus establishes a hydrophobic barrier against the colonic microbiota. In ulcerative colitis (UC) intrinsic low mucus PC concentration may result from disturbed PC translocation into mucus.
AIMS & METHODS: Elucidation of the mechanism of PC translocation across the mucosa and its disturbance in UC. Apical PC translocation was examined in CaCo2 cells plated on transwell tissue culture dishes under various conditions. Mucus PC recovery was also evaluated in genetic UC mice models with intestinal deletion of kindlin1 and 2 as well as in mucosa specimens of patients with UC, Crohn's disease and controls.
RESULTS: In intestinal mucosa derived CaCo2 cells we demonstrate that out of various phospholipids only PC translocates via paracellular movement across lateral tight junctions (TJ) to the apical (mucus) compartment driven by stepwise negative charge generation from TJ to mucins. Driving force is CFTR mediated HCO_3 secretion and binding to membrane localized mucin3. The efficacy of apical PC movement increases from 4.7 ± 0.6 % to 8.0 ± 0.9 % in presence of mucin1 or 2. PC is basally presented as complex with apolipoprotein which itself is not apically translocated. In in vivo mouse models with disrupted TJ (intestinally deleted kindlin1 and 2), apical PC secretion into the ileal lumen is by >70 % reduced with consequent low mucus PC concentration. It preceded the development of ulcerative colitis. This was prevented by therapeutic supplementation of orally applied PC. Finally, mucosa specimens of patients with ulcerative colitis revealed disturbed TJ with suppression of paracellular luminal PC movement determined by immunofluorescence microscopy.
CONCLUSION: Disturbance of the TJ barrier results in impaired apical PC secretion and, thus, loss of hydrophobic protection which is of pathogenetic relevance for development of ulcerative colitis.
Disclosure of Interest: None declared

P1418 MULTIGENE ANALYSIS UNVEILS HELPER T CELL-RELATED GENES EXPRESSION IN INTESTINAL MUCOSA THAT CORRELATES WITH ENDOSCOPIC SEVERITY IN ULCERATIVE COLITIS

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INTRODUCTION: Helper T cells (Th) and their related cytokines have validated roles in mediating gut inflammation in inflammatory bowel diseases such as ulcerative colitis (UC). Although anti-TNF therapy has been shown highly effective in a subset of patients with UC, specific anti-cytokine therapy according to tissue cytokine expression may still be warranted. Efforts to date to examine the relation between mucosal expression of immune mediators and disease severity in UC have yielded inconsistent and inconclusive results, possibly partly due to the common practice of single-marker analyses that are insensitive to the interaction of different molecules and are susceptible to large between-sample variation. We hypothesized that joint expression of important immune molecules, which is unidentifiable by univariate analysis, may significantly correlate with disease severity, as we have previously reported a similar method for differentiating UC from Crohn's disease (reference 1).
AIMS & METHODS: 47 patients with UC underwent colonoscopy and were assessed with Rachmilewitz endoscopic index (REI), which quantifies mucosal damage. Biopsy samples were obtained from inflamed (REI = 3-12, n = 40) and noninflamed (REI < 3, n = 47) colonic mucosae and examined for mRNA expression of cytokines and transcription factors related to Th1 (IFN-γ, IL-12p35, IL-12p40, T-bet, and TNF-α), Th2 (IL-4, IL-13, IL-33, and GATA3), Th17 (IL-17A, IL-17F, IL-23p19, IL-21, IL-22, IL-6, and RORC) and regulatory T cells (TGF-β and Foxp3) by quantitative PCR. Univariate and multivariate analyses were performed to identify expression pattern that paralleled the endoscopic severity.
RESULTS: Although 16 of 18 targets were upregulated in inflamed mucosae compared with noninflamed mucosae, none of the targets examined was univariately correlated with REI in the inflamed mucosae, which showed large expression variation between samples. Multiple regression analysis with stepwise selection, however, identified a significant expression pattern predictive of REI ($p = 0.0009$, $RSq = 0.443$, $RMSE = 2.0104$), consisting of IL-17A, IL-17F, IL-21, IL-22 and Foxp3. In this model IL-17A (positive, $p = 0.0002$) and IL-17F (negative, $P < 0.0001$) were the most influential parameters in predicting REI, where IL-21 (negative, $p = 0.0139$) and IL-22 (positive, $p = 0.0105$) were also significant parameters. A simplified version of this model, IL17A/IL-17F ratio, substantially correlated with REI ($\rho = 0.5186$, $p = 0.0006$). Markers such as IL-13, IFN-γ, TNF-α and etc. did not serve as significant parameters in any useful REI-predictive model.
CONCLUSION: IL-17A/IL-17F expression ratio in inflamed mucosae significantly paralleled the endoscopic severity in UC. Our findings indicate that IL-17A and IL-17F might have different roles in mucosal inflammation and that they might be of equal or even higher importance to other key inflammatory mediators in exacerbation of UC.
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Disclosure of Interest: None declared

P1419 IS HOSPITALIZATION PREDICTING THE DISEASE COURSE IN CROHN'S DISEASE? PREVALENCE AND PREDICTORS OF HOSPITALIZATION AND RE-HOSPITALIZATION IN CROHN'S DISEASE IN A POPULATION BASED INCEPTION COHORT BETWEEN 2000-2012

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INTRODUCTION: Limited data are available on the hospitalization rates in population-based studies.
AIMS & METHODS: Since this is a very important outcome measure, the aim of this study was to analyze prospectively if early hospitalization is associated with the later disease course as well as to determine the prevalence and predictors of hospitalization and re-hospitalization in a population based inception cohort in the Veszprem province database between 2000 and 2012. Data of 304 incident CD patients diagnosed between January 1, 2000 and December 31, 2010 were analyzed (mean age at diagnosis: 32.2; SD: 15.4 years). Both in- and outpatient records were collected and comprehensively reviewed.
RESULTS: Probabilities of first hospitalization and first re-hospitalization were 54.9%, 72% 76% and 22.8%, 34%, 52.3% after 1, 2 and 5 years of follow-up in Kaplan-Meier analysis. Main reasons for hospitalization in the first year were diagnostic procedures (48.5%), IBD related surgery (29.9%) and disease activity (14.3%). Non-inflammatory disease behavior at diagnosis (HR: 1.41, 95%CI: 1.41-1.89, $p = 0.02$) was the only factor significantly associated with time to hospitalization while both non-inflammatory disease behavior at diagnosis (HR: 1.92, 95%CI: 1.35-2.74, $p < 0.001$) and disease behavior change (HR: 1.89, 95%CI: 1.27-2.81, $p = 0.002$) were associated with time to first re-hospitalization in multiple Cox-regression analysis. Early hospitalization (within the year of diagnosis) was associated with age at onset ($p = 0.002$), non-inflammatory disease behavior at diagnosis (OR: 2.67, $p < 0.001$), internal fistulizing disease (OR: 2.02, $p = 0.04$) and it was predictive for need for immunosuppressives (OR: 1.74, $p = 0.018$) and need for surgery/multiple surgeries (OR: 2.63, $p = 0.018$ and OR: 2.54, $p = 0.005$) during the disease course.
CONCLUSION: Early hospitalization was associated with clinically significant outcomes (need for immunosuppressives and surgery). Hospitalization and re-hospitalization rates are still high in this population-based cohort. Non-inflammatory disease behavior at diagnosis was identified as the pivotal predictive factors for both hospitalization and re-hospitalization.
Disclosure of Interest: None declared

P1420 HOSPITALIZATION RATE BEFORE AND AFTER ANTI-TNF THERAPY: HOSPITALIZATION RATES ARE ASSOCIATED WITH TIME TO ANTI-TNF THERAPY

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INTRODUCTION: Hospitalization is an important outcome measure and a major driver of costs in patients with IBD.
AIMS & METHODS: Our aim was to analyze prospectively the prevalence and predictors of hospitalization and re-hospitalization before and after anti-TNF therapy. Data of 194 consecutive IBD (152 CD, 42 UC) patients were analyzed (male/female: 88/106, median age at diagnosis: 24.0, IQR: 19-30 years, duration: 8, IQR: 8-12.5 years) in whom anti-TNF therapy was started after January 1, 2009. Total follow-up was 1874 patient-years and 474 patient-years with anti-TNF exposure. Both in- and outpatient records were collected and comprehensively reviewed.
RESULTS: The hospitalization rate in the 2 years preceding anti-TNF therapy was significantly higher compared to the hospitalization rate during anti-TNF therapy (61.6/100 patient-years vs. 43.2/100 anti-TNF exposed patient-years, OR: 0.64, 95%CI 0.43-0.95, $p = 0.03$). The risk for hospitalization decreased only in CD (OR: 0.57, 95%CI 0.36-0.90, $p = 0.02$), but not UC In addition, there was an association with disease duration, the risk of hospitalization decreased in CD patients with early (within 3-years from diagnosis, $p < 0.001$), but late anti-TNFs exposure. In a logistic regression analysis complicated disease behavior ($p = 0.03$) concomitant AZA ($p = 0.02$) use but not anti-TNF type, gender, perianal disease or previous surgeries were associated with the risk of hospitalization during anti-TNF therapy.
CONCLUSION: Hospitalization rate decreased significantly in this referral CD but not UC cohort after the introduction of anti-TNF therapy and it was

associated to time to anti-TNF therapy. Complicated disease phenotype and concomitant AZA use were additional factors defining the risk of hospitalization.
Disclosure of Interest: None declared

P1421 PREVALENCE OF DYSLIPIDEMIA IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The risk of venous thromboembolic events in inflammatory bowel disease (IBD) is increased (relative risk 2.5). However, the incidence of cardiovascular and cerebrovascular events is only modestly elevated (relative risk 1.19). In this subgroup, a disorder of lipid metabolism mediated by pro-inflammatory cytokines may trigger an accelerated atherogenic process.
AIMS & METHODS: To determine the prevalence of dyslipidemia in IBD. We retrospectively analysed patients with Crohn's disease (CD) and Ulcerative Colitis (UC) and determined the lipid profile [total cholesterol (TC), triglycerides (Tg), LDL-cholesterol (LDL) and HDL cholesterol (HDL)], endoscopic activity and comorbidities [chronic kidney disease (CKD) and alteration of glucose metabolism (AGM)]. Dyslipidemia was defined by TC > 190 mg/dl, Tg > 160 mg/dl, LDL > 115 mg/dL and HDL < 40/45 mg/dl (men/women) and CKD and AGM by 2 consecutive values of creatinine > 1.0 mg/dl and/or glucose > 100 mg/dl. We used samples from several portuguese Dyslipidemia prevalence studies (VALSIM, BECEL and ALTO-MAR - 34522 individuals) as a control group.
RESULTS: We evaluated 478 patients, 282 women (59 %), mean age 44.0 years±16.2 years with CD (67.6 %) and UC (32.4 %). The prevalence of CKD and AGM was 23.4% and 23.7%. We assessed mean levels of TC (176.4 ± 41.8 mg/dl), Tg (111.1 ± 58.0 mg/dl), LDL (97.9 ± 35.3 mg/dL) and HDL (54.6 ± 18.3 mg/dl). In UC, TC and LDL were higher and Tg were lower compared to CD ($p < 0.02$). The overall prevalence of dyslipidemia among patients was 58.6% (61.9% in UC and 57.0% in CD). Endoscopic activity was associated with higher Tg and lower LDL levels. Only HDL levels were significantly lower compared to the control group (27.3 % versus 12.8%).
CONCLUSION: In our series, despite a high prevalence of dyslipidemia, levels did not reach the high values reported in the control group. However, the prevalence of HDL-dyslipidaemia was significantly higher. In IBD the pro-inflammatory state is associated with increased phospholipase A2 and decreased lipoprotein lipase activity, both implicated in decreased levels of HDL. Given the recognized anti-inflammatory and anti-atherogenic role of HDL, their compromise may have na influence on the progression of IBD.
Disclosure of Interest: None declared

P1422 INCREASE OF INFLAMMATORY BOWEL DISEASE INCIDENCE IN TEENAGERS IN A PROSPECTIVE POPULATION-BASED STUDY DURING A 21-YEAR PERIOD (1988-2008)

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INTRODUCTION: Few data are available on recent temporal trends in the incidence of paediatric-onset inflammatory bowel disease (IBD) in industrialized countries.
AIMS & METHODS: The aim of this study was to assess the change in incidence and location at diagnosis of paediatric-onset IBD during a 21-year period.
Patients & Methods: Paediatric-onset IBD was defined by an age at diagnosis ≤ 17 years. Data at diagnosis were extracted from the population-based IBD study in Northern France (Epimad Registry) between 1988 and 2008. Age groups and digestive location at IBD diagnosis were defined according to the Paris (1) classification with age: <10 yrs or ≥ 10 yrs and location as follows: 1) for CD: pure small bowel involvement (L1); pure colonic involvement (L2) or ileocolonic involvement (L3); 2) for UC: proctitis (E1); left sided colitis (E2); extensive colitis (E3); pancolitis (E4).
RESULTS: During this 21-year period, 1147 incident paediatric-onset IBD cases were recorded (8% of all IBD) including 846 CD, 271 UC and 30 IBD unclassified (IBDU) cases. Median age at diagnosis was not significantly different in CD (14.5 years [Q1 = 11.9-Q3 = 16.1]) and UC (14.1 years [11.0-16.0]) and did not change over time. There was significantly more males in CD than in UC (53.4% *vs* 45.0%; $p = 0.02$). Median time between onset of symptoms and IBD diagnosis was stable over time at 3 months [1-6]. Mean incidence was $4.0/10^5$ for IBD as a whole (3.0 for CD, 0.9 for UC and 0.1 for IBDU). During this 21-year period a dramatic increase of both CD and UC incidences was observed in teenagers [10-16 years]: for CD from 4.3 in 1988-90 to $9.6/10^5$ in 2006-2008 (+123%; $p < 10^{-3}$) and for UC, from 1.6 to $2.9/10^5$ (+81%; $p < 10^{-3}$) in both genders. Digestive location did not change over time in both CD and UC; for CD L1 = 12.2%, L2 = 14.5% and L3 = 73.3% and for UC E1 = 31.1%, E2 = 25.4%, E3 = 10.5% and E4 = 33%.
CONCLUSION: In this large population-based study the incidence of both CD and UC dramatically increased in teenagers during a 21-year period without modification of neither age, location at diagnosis nor time between onset of symptoms and diagnosis. This suggests that a strong environmental factor predisposing to IBD is at work in this population.
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P1423 OBESITY INFLUENCES THE COURSE OF CROHN'S DISEASE-SINGLE CENTRE RETROSPECTIVE ANALYSIS

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INTRODUCTION: Despite the widespread perception of Crohn's disease (CD) as a wasting disorder there is a well-recognised sub-population of obese patients with the disease (1). Notwithstanding the possibility of a pathogenic link, obesity may influence the severity and phenotype of CD.
AIMS & METHODS: We conducted a retrospective analysis of our Institution's electronic patient record to stratify and compare CD patients by body mass index (BMI) at diagnosis, with regard to their disease characteristics, medication use and outcomes. Smoking status recorded on the hospital database was validated by survey with general practitioners. All statistical analysis was conducted using GraphPad Prism 6.0. Mann-Whitney U test and Kruskal-Wallis with Dunn post-test were used when the data was not normally distributed. Fisher-exact test was used for contigency tables, one way ANOVA and t-test if the data was normally distributed.
RESULTS: Reliable data was available for 282 patients with CD (130 female, age 43.6 ± 14.3y). At diagnosis, BMI ≥35 was recorded in n = 20 (7.09%), ≥30 in 43 (15.2%), 25-29.9 in 68 (24.1%), 24.9-18 in 144 (51.06%) and <18 in 7 (2.4%). The proportion of smokers did not differ significantly in each group. Patients with BMI > 30 were older ($p < 0.0001$) compared to the other groups. Rates of operative intervention per patient year were slightly higher in BMI≥30 group compared to the normal BMI group (0.08 vs 0.04, $p = 0.007$). The median time to surgery was significantly shorter in BMI≥35 (11.5 months) and BMI ≥30 (18months) compared to the other groups ($p = 0.053$). The median time to anti- TNF therapy in the morbidly obese group and the obese groups were 11.5 and 14 months respectively compared to 48 months in BMI 29.9-25.36 months in the normal BMI, and 12 months in BMI < 18 group respectively ($p = 0.008$). Other comparators are shown in the table below.
Table: Disease characteristics across different BMI groups.

Disease Characteristics	BMI≥ 35	BMI≥30	BMI 29.9-25	Normal BMI 24.9-18	BMI <18	P value
Average age	49.2±12.1	51.4±13.1	47.6±13.1	39.7±13.1	42.2±21.1	<0.0001
Female: Male	14:6	23:20	35:33	82:62	5:2	0.001
Ileal disease	8/20	10/63	28/66	37/128	2/7	0.08
Colonic disease	3/20	32/63	16/66	29/128	2/7	
Ileo colonic disease	9/20	21/63	23/66	62/128	3/7	
B1 inflammatory	11/18	7/60	40/68	72/128	3/6	0.61
B2 stricturing	6/18	32/60	18/68	33/128	3/6	
B3 fistulizing	1/18	21/60	10/68	23/128	0/6	

CONCLUSION: Obesity is a common phenomenon in this representative cohort of patients with CD with 22.3% having BMI > 30 – nearing the national average of 26%. Obesity is associated with slightly increased operative intervention per patient year. Our data also imply a more aggressive inflammatory phenotype in terms of requiring surgery and biologic therapy significantly earlier in the natural history of disease.
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Disclosure of Interest: None declared

P1424 VITAMIN D INFLUENCES HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Several lines of evidence indicate that vitamin D (VD) plays an important role in the pathogenesis of inflammatory bowel diseases (IBD).
AIMS & METHODS: We investigated the effect of VD concentrations and VD supplementation on health related quality of life in Crohn's disease (CD) and ulcerative colitis (UC) patients. A cohort of 220 IBD patients (141 CD and 79 UC) was followed-up at a tertiary IBD centre. A subgroup of the cohort (n = 26)

took VD supplements for >3 months. Health related quality of life was assessed using the short IBD questionnaire (sIBDQ). VD serum concentration and sIBDQ score were assessed during summer/autumn period and winter/spring period.
RESULTS: During summer/autumn and winter/spring period, 28% and 42% of IBD patients were VD-deficient (<20 ng/ml), respectively. In winter/spring period, there was a significant correlation between sIBDQ score and VD serum concentration in UC patients ($r = 0.35$, $p = 0.02$), with a trend towards significance in CD patients ($r = 0.17$, $p = 0.06$). In winter/spring period, VD-insufficient patients (<30 ng/ml) had a significantly lower mean sIBDQ score than VD-sufficient patients; this was true of both UC (48.3±2.3 vs. 56.7±3.4, $p = 0.04$) and CD (55.7±1.25 vs. 60.8±2.14, $p = 0.04$) patients. In all analysed scenarios (UC/CD, summer/autumn period and winter/spring period), health related quality of life was the highest in patients with VD serum concentrations of 50–59 ng/ml. Supplementation with a median of 800 IU/day VD day did not influence VD serum concentration nor the sIBDQ score.
CONCLUSION: VD serum concentration correlated with health related quality of life in UC and CD patients during winter/spring period. Supplementation with currently recommended doses of VD did not influence health related quality of life.
Disclosure of Interest: None declared

P1425 SMOKING AND USE OF ANTIBIOTICS DURING PREGNANCY ARE RISK FACTORS FOR INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The pathogenesis of inflammatory bowel disease (IBD) is unclear. Environmental factors in combination with genetic predisposition may play a role. The aim of this study was to analyse prenatal risk factors for IBD in a well described birth cohort from Northern Finland.
AIMS & METHODS: The prospectively collected Northern Finland Birth Cohort 1966 (NFBC 1966) is a longitudinal research program to promote health and well-being of the population (http://www.oulu.fi/nfbc/). The population is comprised of mothers living in the two northernmost provinces of Finland, Oulu and Lapland with expected dates of delivery between Jan 1st - Dec 31st, 1966 (12 068 mothers, 12 231 children, 96.3% of all births during 1966 in that area). Information about family history, social relationships, environment, mother's health habits and clinical parameters were collected from antenatal clinics, hospital registers and by postal questionnaires. Between years 2012 and 2014, at the age of 46 years, a large health examination was performed including both questionnaires and clinical examination, including questions about physician's diagnosis of IBD. 6852 subjects (66%) answered for the postal questionnaires. Data were analyzed by chi square test, Fishers exact test and counting relative risks (RR).
RESULTS: Data were available from 6685 individuals, of whom 175 (2.6%) reported physician's diagnosis of IBD, 88/2957 male and 87/3553 women. Maternal age, gestation age, gestation weight, maternal comorbidities, parity, number of siblings, household farm animals or pets, living in an urban area and social class were not associated with IBD of children until 46 years of age. However, consumption of antibiotics during pregnancy [(23/549 vs. 140/5375) RR 1.6 (1.0-2.4), $p = 0.041$], smoking during pregnancy [continued, 37/892 RR 1.7 (1.2-2.5) vs. stopped, 8/406 RR 0.7 (0.4-1.5) vs. never smoked 128/5247 RR 0.7 (0.5-1.0), $p = 0.0033$] and living in the most northern part of Finland [above the Arctic Circle 19/419 RR 1.7 (1.1-2.8) vs. southern Lapland 45/1943 RR 0.8 (0.6-1.1) vs. Oulu district 111/4148 RR 1.0 (0.7-1.3), $p = 0.0188$] were associated with IBD.
CONCLUSION: Smoking and consumption of antibiotics during pregnancy and mothers' living above the Arctic Circle were risk factors for IBD until the age of 46.
Disclosure of Interest: None declared

P1426 CLINICAL AND ENDOSCOPIC FEATURES OF RESPONDERS AND NON-RESPONDERS TO THERAPEUTIC DEPLETION OF MYELOID LINEAGE LEUCOCYTES IN PATIENTS WITH ULCERATIVE COLITIS: WHY THIS NON-PHARMACOLOGICAL TREATMENT OPTION IS FAVOURED BY PATIENTS?

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INTRODUCTION: Patients with active inflammatory bowel disease have elevated and activated myeloid lineage leucocytes, notably the CD14 (+)CD16 (+) monocyte phenotype, which is a major source of tumour necrosis factor-α (Belge KU, et al. J Immunol 2002). Hence selective depletion of these leucocytes by granulocyte/monocyte adsorption (GMA) with an Adacolumn is expected to alleviate inflammation and promote remission or at least enhance drug efficacy. However, studies in ulcerative colitis (UC) reported contrasting efficacy outcomes, from an 85% (Cohen RD. Gastroenterology 2005) to a statistically insignificant level (Sands, et al. Gastroenterology 2008). Patients' demographic variables in the aforementioned studies were very different.
AIMS & METHODS: In 143 consecutive UC patients, we were interested to identify clinical and endoscopic features, which could mark a patient as a responder or otherwise as a non-responder to GMA. Seventy-three patients were steroid naive, and 70 were steroid dependent. Patients received up to an 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated according to Rachmilewitz, allowing each patient to serve as her or his own control. Clinical activity index (CAI) ≤4 at week 12 was defined as response to GMA. Additionally, biopsies from colonoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.
RESULTS: At entry the average CAI was 12.8, range 10-17. Ninety-two of the 143 patients (64.3%) responded to GMA, 52 of 73 steroid naïve patients (71.2%) and 40 of 70 steroid dependent patients (57.1%). On average remission was sustained for 8.6 months in steroid naïve patients and for 10.4 months in steroid dependent cohort. Upon relapse, the majority of patients responded well to a second course of GMA. Over 1200 biopsies were processed. Infiltrating leucocytes were overwhelmingly neutrophils and monocytes/macrophages. GMA was associated with a marked reduction of infiltrating leucocytes. Patients who had extensive deep UC lesions together with near total loss of the mucosal tissue at the affected sites were identified as non-responders. Patients with the first UC episode were identified as the best responders (100%) followed by steroid naive patients. Additionally, a short duration of active UC prior to GMA marked a patient as a likely responder. No GMA related serious adverse event was observed.
CONCLUSION: Depleting elevated myeloid lineage leucocytes by GMA should have significant efficacy in patients with UC, but before the disease has become very severe with deep ulcers and extensive loss of the mucosal tissue, and when the disease does not respond well to pharmacological interventions. Most notably, first episode and steroid naïve cases respond well to GMA and attain a favourable future clinical course by avoiding medications like corticosteroids from the start. Likewise, GMA should be applied immediately after a relapse. Generally, GMA is very much favoured by patients for its safety profile and for being a non-drug therapeutic intervention. Accordingly, patient compliance is always good.
Disclosure of Interest: None declared

P1427 THE RISK OF SKIN CANCER IN PATIENTS TREATED FOR INFLAMMATORY BOWEL DISEASES IN THE PROVINCE OF QUEBEC

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INTRODUCTION: Treatment of inflammatory bowel disease (IBD) with immunosuppressive medications has been associated with an increased risk of developing melanoma and non-melanoma skin cancer.
AIMS & METHODS: The aim of this study was to evaluate the risk of melanoma and non-melanoma skin cancer (NMSC) associated with immunomodulator and anti-TNF-α medications in IBD patients. Using provincial health insurance databases (RAMQ/MedECHO), a nested-case control analysis was conducted within a cohort of patients diagnosed with IBD (Crohn's disease [CD] or ulcerative colitis [UC]) between 1996 and 2009. Cohort entry was defined as the date when patients met a strict IBD definition (i.e. at least one hospitalization with a primary diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) or four physician claims with the CD or UC diagnosis within a two-year period). Patients were excluded if they had a diagnosis of any cancer prior to cohort entry or within the first year from the inclusion, and if they had less than 1 year of prescription coverage prior to inclusion in the cohort. Cases were patients newly-diagnosed with melanoma and NMSC during follow-up. For each case, up to 10 controls were randomly selected and matched on age, sex, and duration of disease. Conditional logistic regression was used to estimate odds ratios (ORs) with 95% confidence intervals (CIs) of melanoma and NMSC associated with ever use of immunomodulators and anti-TNF-alpha-α medications. Secondary analyses considered duration of exposure and stratification by IBD type (CD vs UC). The models were adjusted for history of IBD-related hospitalizations.
RESULTS: A total of 41,176 IBD patients were identified in the RAMQ/MedECHO database; 19582 patients were eligible for inclusion in the study. The mean age at inclusion was 42.5 ± 19.3 years and 45.4% of the patients were male. The mean duration of follow-up was 5.6±3.3 years and CD was the primary diagnosis in 60.2% of the cases. Immunomodulators were utilized in 25.4%, and anti-TNF-α medications in 2% of the patients. A total of 102 cases of melanoma were identified in the cohort. Neither immunomodulators (OR: 1.38, 95% CI- 0.82-2.31), nor anti-TNF- α medications (OR: 6.28, 95% CI-0.59-60.79) were associated with an increased risk of melanoma. A total of 474 cases of NSMC were identified. Treatment with immunomodulators for ≥ 3 years was associated with a significantly increased risk of NSMC (OR: 1.78, 95% CI- 1.25-2.54) and this increased risk was seen in both CD and UC patients. No cases of NMSC occurred in patients exclusively exposed to anti-TNF-α medications.
CONCLUSION: In a large provincial IBD cohort, treatment with immunomodulators for ≥3 years was associated with an increased risk of non-melanoma skin cancer. No association was demonstrated between the risk of melanoma and immunomodulator medications. Although no association between melanoma and NMSC with anti-TNF-α medications was identified, no firm conclusions can be made given the small number of patients on these medications in the cohort.
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P1428 INCIDENCE AND INITIAL DISEASE COURSE OF INFLAMMATORY BOWEL DISEASES IN 2011 IN EUROPE AND AUSTRALIA: RESULTS OF THE 2011 ECCO-EPICOM INCEPTION COHORT

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INTRODUCTION: The aim of the present study was to validate the IBD (inflammatory bowel diseases) incidence reported in the 2010 ECCO-EpiCom (European Crohn's and Colitis Organization - Epidemiological Committee) inception cohort[1] by including a second independent inception cohort from participating centers in 2011 and an Australian centre to investigate whether there is a difference in the incidence of IBD between Eastern and Western European countries and Australia.

AIMS & METHODS: Fourteen centers from 5 Eastern and 9 Western European countries and one center from Australia participated in the ECCO-EpiCom 2011 inception cohort. Patients' data regarding disease type, socio-demographic factors, extraintestinal manifestations and therapy were entered into the web-based EpiCom database, www.ecco-epicom.eu.

RESULTS: A total of 711 adult patients were diagnosed during the inclusion year 2011, 178 (25%) from Eastern, 461 (65%) from Western Europe and 72 (10%) from Australia; 259 (37%) patients were diagnosed with Crohn's disease, 380 (53%) with ulcerative colitis and 72 (10%) with IBD unclassified. The mean annual incidence rate for IBD was 11.3/100,000 in Eastern Europe, 14.0/100,000 in Western Europe and 30.3/100,000 in Australia. Significantly more patients were diagnosed with complicated disease at diagnosis in Eastern Europe compared to Western Europe (51% vs. 37%, $p = 0.03$).

CONCLUSION: Incidence rates, disease phenotype and initial treatment characteristics in the 2011 ECCO-EpiCom cohort were not significantly different from that reported in the 2010 cohort.

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Disclosure of Interest: None declared

P1429 EVALUATION OF ELECTROCARDIOGRAPHIC ABNORMALITIES AND HEART RATE VARIABILITY IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH HOLTER ECG

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INTRODUCTION: Electrocardiographic (ECG) abnormalities have been described in inflammatory bowel disease (IBD) patients. Underlying chronic inflammation, medicines used, nutritional deficiencies can cause many rhythm disorders. Most commonly encountered rhythm disorders are atrial fibrillation than less commonly supraventricular tachycardia, ventricular tachycardia and atrioventricular block. Previous studies mostly used 12 lead normal surface ECG and many rhythm disorders that can be detected only by holter ECG were probably missed. This may caused underestimation of the prevalence of arrhythmia in inflammatory disease patients.

AIMS & METHODS: 67 IBD patients aging between 18-65 years referring to gastroenterology clinic between October 2013-March 2014 were included in this study. Patients with previous history of coronary heart disease, patients with heart failure or cardiac valve disease were excluded. Patients with thyroid hormone abnormalities were also excluded from the study. Physical examination and baseline echocardiography were performed to search for evidence of organic heart disease in cardiology clinic. Patients who do not have evidence of organic heart disease were monitored by Holter ECG for 24 hours and results were analyzed by using special computer software programs.

RESULTS: Of 67 patients 64.2 % were male. Mean age was 42.67 ±12.8 years; mean body mass index was 25.1±4.39 kg /m2. 14 patients (20.9%) had Crohn's disease. 53 patients suffered from ulcerative colitis. Mean time from disease diagnosis was 3.57±3.43 years. Only 12% of the patients had hypertension while 17.9 % had diabetes. 35.8 % of the patients had active bowel disease at the time of evaluation. Mean heart rate of the patients were 75.8±9.3beats/ min. Arrhythmia was detected in 55.1 % of the patients. Mean number of supraventricular extrasystoles were 47.4±217 and mean number of ventricular extrasystoles was 17.4±47.6. Patients with active IBD had higher minimum heart rate ($p = 0.03$) and significantly lower SD5, AVG, SDTF and SDVLF values. These values are parameters used to calculate heart rate variability by the help of special computer software programs. (p values: 0.01, 0.02, 0.03, 0.03 respectively). Comparison of holter parameters between ulcerative colitis and Crohn's disease patients were also performed. SDANN5 (standard deviation of 5 min mean values of RR) was found significantly lower in ulcerative colitis patients (120.3 ±38.4 vs 145.3 ±41.3, p:0.04)

CONCLUSION: Heart rate variability (HRV) was found to be significantly decreased and minimum heart rate was found to be significantly increased in active inflammatory bowel disease patients. Furthermore HRV was found to be significantly lower in ulcerative colitis patients than in Crohn's disease patients. Decreases in HRV have been reported in many cardiologic and noncardiologic diseases. In this study active IBD patients and patients with UC were found to have autonomic dysfunction which is known to be associated with increased cardiac morbidity and mortality. Various symptomatic and asymptomatic rhythm disorders were detected by 24-hour holter suggesting that physicians should be cautious about rhythm abnormalities in follow-up of these patients.

Disclosure of Interest: None declared

P1430 MULTI-COUNTRY, CROSS-SECTIONAL STUDY TO DETERMINE PATIENT-SPECIFIC AND GENERAL BELIEFS TOWARDS MEDICATION AND THEIR TREATMENT ADHERENCE TO SELECTED SYSTEMIC THERAPIES IN 6 CHRONIC IMMUNE-MEDIATED INFLAMMATORY DISEASES (ALIGN)

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INTRODUCTION: Adherence to therapy is critical to achieve and sustain optimal outcomes in patients (pts) with immune-mediated inflammatory disease (IMID). Pts' beliefs about the necessity of treatment and potential adverse effects could strongly influence adherence.

AIMS & METHODS: ALIGN was a multi-country cross-sectional study exploring pts' beliefs, concerns, attitudes and adherence toward TNF inhibitors (TNFi) and conventional therapies used alone or in combination across multiple IMIDs. Adults age ≥18 y with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), Crohn's disease (CD), ulcerative colitis (UC) or psoriasis (PsO), receiving conventional therapy and/or disease-modifying antirheumatic drugs (including TNFi), were recruited. Pts completed validated questionnaires, e.g., the Beliefs about Medicines Questionnaire (BMQ) and short Morisky Medication Adherence Scale (MMAS-4). BMQ scores, MMAS-4 scores and pts' attitudes toward their medications are presented.

RESULTS: 7197 pts in 33 countries met eligibility criteria. Pts had RA (27.5%), AS (11.3%), PsA (8.9%), CD (17.3%), UC (8.8%) or PsO (26.2%). Mean age was 47.5 y (range, CD = 38.0; RA = 54.8). Mean disease duration was 11.7 y (range, UC = 8.1; PsO = 18.7). The largest proportion of pts received conventional therapies (40.3%), followed by TNFi mono- (32.0%) and combination therapy (27.7%). An attitudinal analysis of BMQ necessity and concern scores revealed that most pts were either "accepting" (high necessity/low concern) or "ambivalent" (high necessity/high concern) toward their medication irrespective of disease or treatment. Adherence across diseases was generally higher in pts receiving TNFi with or without conventional therapy (range of mean MMAS-4 scores, 3.4–3.7; 0–1 = low, 2–3 = medium, 4 = high adherence), vs pts receiving conventional mono- (2.6–3.3) or combination therapy (2.8–3.4). Across treatments, high adherence according to MMAS-4 was consistently lower for "ambivalent" pts (46.1%–69.0%) vs "accepting" pts (55.8%–77.6%) according to combined BMQ scores **(Table)**.

Table. N (%) of Patients Accepting and Ambivalent Toward Their Medications Who Were Adherent.

Monotherapy, n (%)				TNFi + Conventional Combination Therapy, n (%)			
Conventional		TNFi		Conventional		TNFi	
Accepting (n = 1347)	*Ambivalent* (n = 1151)	*Accepting* (n = 1251)	*Ambivalent* (n = 834)	*Accepting* (n = 900)	*Ambivalent* (n = 739)	*Accepting* (n = 1031)	*Ambivalent* (n = 786)
751 (55.8)	531 (46.1)	919 (73.5)	504 (60.4)	550 (61.1)	374 (50.6)	800 (77.6)	542 (69.0)
P < 0.0001		*P < 0.0001*		*P < 0.0001*		*P < 0.0001*	

CONCLUSION: Compared with "accepting" pts, "ambivalent" pts appeared to be less often highly adherent (MMAS-4 score = 4), which could negatively affect treatment efficacy. The high percentage of "ambivalent" pts reveals the need to better explore concerns about medication and address erroneous beliefs regarding benefit-risk of treatments.

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P1431 THE EFFECT OF INCREASING BODY MASS INDEX ON CLINICAL OUTCOMES IN PATIENTS WITH CROHN'S DISEASE TREATED WITH INFLIXIMAB

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INTRODUCTION: The incidence of obesity is increasing worldwide and there is growing evidence that obesity is associated with low-grade 'background' intestinal inflammation. The role of obesity in progressive inflammatory conditions needs to be assessed and there is very little known about the effect of obesity on outcomes in severe Crohn's disease. Recent data seems to suggest that obesity is associated with diminished responsiveness to biological agents in patients with IBD (ref).
AIMS & METHODS: We aimed to examine the influence of obesity as measured by BMI on the response to Infliximab in CD. A retrospective analysis was performed on all patients identified from our CD registry, receiving Infliximab for severe Crohn's disease. The main variable of interest was BMI, assessed using categorical and continuous scales. The outcomes of interest were 1) IBD related flare (defined as increase in dose or steroid use or need for IBD related hospitalization or surgery), 2. Any IBD related surgery and 3) IBD related resectional surgery. Kaplan Meier (KM) curves were used to compare survival curves for each outcome of interest stratified according to the BMI strata (WHO criteria). Additionally variables of interest were entered into a stepwise multivariate logistic regression analysis for each outcome of interest.
RESULTS: Overall, 388 (87.8%) patients met our predefined inclusion criteria, with mean BMI of 24.1kg/m^2 (+/- 5.1). 22.2 % were classed overweight (BMI 25-29.9) and 11.9% as obese (BMI >30). 232 (60.6%) patients had an IBD related flare during mean follow-up of 33.5months (+/-30.9). Of these 82 (21.4%) required CD-related surgery, of which 39 (10.2%) required CD-related bowel resection surgery. Being categorised as overweight (BMI: 25.0-29.9kg/m^2) increased the risk of a clinical flare (adjusted HR: 1.7, $p=0.045$) compared to normal BMI (18.5-24.9kg/m^2). However the risk of surgery (both all IBD-related and resection surgery alone) decreased per unit increase of BMI on a continuous scale (adjusted HR: 0.924, $P< 0.001$). Female sex increased the likelihood of CD-related bowel resection surgery (adjusted HR: 3.5, $p=0.001$) as did disease phenotype (adjusted HR structuring or penetrating versus non-stricturing and non-penetrating: 4.0, $P<0.001$). KM curves did not show any differences in rates of any of the outcomes of interest for the different BMI strata (based on the WHO criteria), (log rank test $p<0.05$).
CONCLUSION: In patients with severe CD on Infliximab, being classed as overweight increased the risk of having an IBD related flare. This may however reflect the variability in definition of an IBD related flare as this outcome occurred in 60% of patients. Increasing BMI was associated with a decreased risk of IBD related resectional surgery. The reasons for this could include better nutritional reserve in these patients and physician reluctance to operate on patients with higher BMI. The role of obesity in outcomes in CD needs further validation in large prospective studies.
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Disclosure of Interest: None declared

P1432 PSYCHOMETRIC EVALUATION OF THE SIGNS AND SYMPTOMS MODULES OF THE ULCERATIVE COLITIS PATIENT-REPORTED OUTCOMES MEASURE (UC-PRO/SS)

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INTRODUCTION: The Ulcerative Colitis Patient-Reported Outcomes Signs and Symptoms (UC-PRO/SS) measure was recently developed to evaluate symptom outcomes in clinical trials of ulcerative colitis (UC).
AIMS & METHODS: To examine the structure, reliability and validity of the UC-PRO/SS. An observational study was conducted in adults with UC and included three clinic visits: Day 1 (Visit 1), Day 7 (Visit 2), and Day 28 (Visit 3). Subjects completed the UC-PRO/SS on a daily basis using an electronic device. Descriptive statistics, factor analysis, and Rasch analysis were conducted to determine final structure. Test-retest reliability was assessed among stable subjects, defined as those with "no change" on patient-rated global rating of change in UC severity from Visit 2 to Visit 3, using paired *t*-test and intraclass correlation coefficients (ICCs). Cronbach's coefficient alpha was used to assess internal consistency. Construct validity was examined based on correlations with the Inflammatory Bowel Disease Questionnaire (IBDQ), Partial Mayo Score, and other ancillary measures. Known-groups validity was evaluated by comparing UC-PRO/SS domain scores by groups defined by the Partial Mayo Score, Patient Global Rating of Disease Severity, and Clinician Global Rating of Disease Severity using ANCOVA models adjusted for age and gender.
RESULTS: Of the 200 participants, 117 (59%) were female; mean (SD) age was 46 (14.6) years. The 14-item UC-PRO/SS includes three domains: Bowel Movement (BM) Signs and Symptoms, Abdominal Symptoms, and Systemic Symptoms. Alpha coefficients ranged from 0.66 to 0.80. No significant differences were observed in UC-PRO/SS domain scores between visits for stable subjects, with ICC values of 0.71-0.81. The BM Signs and Symptoms scale was strongly correlated to the Partial Mayo Score (0.79) and moderately to strongly correlated with the IBDQ (0.51 to 0.73). Moderate correlations (0.45-0.65) were observed between Abdominal Symptoms and Partial Mayo Score, IBDQ, and BPI – Worst Pain. Similar correlations were observed for Systemic Symptoms. Findings indicate that UC-PRO/SS domain scores were significantly different ($p<0.0001$) by known groups.
CONCLUSION: Findings from this study support the UC-PRO/SS as a reliable and valid measure for the evaluation of signs and symptoms in UC clinical trials. Future studies conducted within the context of a clinical trial will examine relationships with clinical measures to assess treatment response.
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P1433 PSYCHOMETRIC EVALUATION OF THE COPING, DAILY LIFE IMPACT, AND EMOTIONAL IMPACT MODULES OF THE ULCERATIVE COLITIS PATIENT-REPORTED OUTCOMES (UC-PRO) MEASURE

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INTRODUCTION: The Ulcerative Colitis Patient-Reported Outcomes (UC-PRO) measure includes five modules that assess the signs, symptoms, and impact of UC. Modules 1 and 2 comprise the UC-PRO Signs and Symptoms measures, while Modules 3-5 assess Coping, Daily Life Impact, and Emotional Impact.
AIMS & METHODS: To examine the structure, reliability and validity of UC-PRO Modules 3-5. An observational study was conducted in adults with UC and included three clinic visits: Day 1 (Visit 1), Day 7 (Visit 2), and Day 28 (Visit 3). Subjects completed Module 3 (Coping) on a daily basis using an electronic device, while Modules 4 and 5 (Daily Life Impact and Emotional Impact) were completed at clinical visits. Descriptive statistics, factor analysis, and Rasch analysis were conducted to determine final structure. Test-retest reliability was assessed among stable subjects, defined as those with "no change" on patient-rated global rating of change in UC severity, using paired *t*-test and intraclass correlation coefficients (ICCs). Internal consistency reliability was assessed using Cronbach's coefficient alpha and the Kruder-Richardson Formula-20 (KR-20). Construct validity was examined based on correlations with the Inflammatory Bowel Disease Questionnaire, Partial Mayo Score, and other ancillary measures. Known-groups validity was evaluated by comparing module scores by groups defined by the Partial Mayo Score, Patient Global Rating of Disease Severity, and the Clinician Global Rating of Disease Severity using ANCOVA models adjusted for age and gender.
RESULTS: Of the 200 participants, 117 (59%) were female; mean (SD) age was 46 (14.6) years. The final UC-PRO Modules 3-5 include Coping (7 items), Daily Life Impact (9 items), and Emotional Impact (8 items). Cronbach's alphas were 0.94 and 0.91 for Daily Life Impact and Emotional Impact, respectively; the KR-20 coefficient was 0.71 for Coping. No significant differences were observed in Daily Life Impact and Emotional Impact between visits for stable subjects, with ICC values of 0.93 and 0.85, respectively. There was a significant difference in scores observed for Coping (p value 0.001), but the ICC value was 0.84, providing support of test-retest reliability. All three modules were moderately to strongly correlated to ancillary measures. Module scores were significantly different ($p<0.0001$) by known-groups.
CONCLUSION: Findings from this study support the reliability and validity of UC-PRO Modules 3-5 to assess the impact of UC on coping strategies, daily life impact, and emotional impact.
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P1434 COMPARISON OF BREATH AND URINE VOLATILE ORGANIC MARKERS IN INFLAMMATORY BOWEL DISEASE (IBD)

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INTRODUCTION: Early diagnosis of inflammatory bowel disease (IBD) remains a challenge. Latterly the role of volatile organic compounds (VOCs) have come to the fore showing distinct patterns in those with Crohn's disease as well as Ulcerative colitis compared with controls. VOC detection reflects the altered gut fermentome which is perturbed in IBD. Moreover its sampling is non-invasive with various compounds being identified from faecal, breath and urine. We and other have previously reported that urine can be used to diagnose IBD and the same can be achieved with breath and stool.
AIMS & METHODS: Aim: The aim of our study was to compare urine and breath VOC sampling using FAIMS (Field asymmetric ion mobility spectroscopy) in patients with IBD.
Methods: 133 subjects were recruited 86 patients with established IBD (formed from both Crohns and Ulcerative Colitis patients) and 46 volunteers for controls. Urine samples were collected and sampled using the FAIMS system. Urine was heated to 40°C and headspace analysed for VOC patterns using an Owlstone Lonestar FAIMS instrument, fitted with an ATLAS sampling system. For breath analysis, a subset of the subjects (11 controls and 20 with established IBD) were tested. End expiratory breath was captured using a Warwick device and captured in a 3L tedlar bag prior to analysis. Linear discriminatory analysis (LDA) was employed in all cases to determine differences between the two sample modalities, with a "leave on out", combined with a K-nearest neighbour reclassification algorithm to calculate sensitivity and specificity.
RESULTS: VOC signature patterns were clearly separable in IBD patients compared with controls using both urine and breath. We achieved a sensitivity of 86% and specificity of 76% with the FAIMS, However, the analysis of the breath samples achieved a sensitivity of 95% and a specificity of 90%.
CONCLUSION: In this pilot study, we have applied FAIMS technology to the analysis of patients with IBD. Here breath samples tested by FAIMS appear to show superior results than urine samples analysed by the same method. Further statistical work is currently being undertaken to distinguish between Crohns disease and Ulcerative Colitis for both urine and breath samples, whilst a larger patient group is being recruited for further breath sample analysis.
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Disclosure of Interest: None declared

P1435 CAN CT ENTEROGRAPHY PREDICT LACK OF MEDICAL RESPONSE REQUIRING COLECTOMY IN SEVERE ULCERATIVE COLITIS? A PILOT STUDY

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INTRODUCTION: Magnetic resonance imaging (MRI) and Multiple Slice Computed Tomography (CT) have improved the diagnosis and monitoring of patients with inflammatory bowel disease (IBD), particularly in Crohn's disease (CD). In ulcerative colitis (UC) the usefulness of CT enterography (CTE) has been limited to rule out CD during the diagnostic process. No studies to date have evaluated the prognostic value of CTE findings in patients with severe active UC.
AIMS & METHODS: Our main objetive was to evaluate CTE findings associated with poor response to treatment in patients with severe relapse of UC requiring colectomy. We prospectively included adults hospitalized with a severe relapse of UC according to Truelove–Witts criteria in the gastroenterology unit of a university hospital from April 2010 to October 2013. CTE findings, response to treatment and the need of colectomy were evaluated, as well as endoscopic, biochemical and clinical findings. Variables were compared in order to determine factors associated with poor outcome and colectomy using the SPSS 17.0 statistical system.
RESULTS: Seventeen patients hospitalized with severe UC were included, 9 were women, with a median age of 38.4 years (19-81). The mean time since UC diagnosis was 3.9 years (0-19). Of the 17 patients included, 5 had progression of the affected colon extension at the time of the flare. All patients underwent CTE in a mean time of 3.4 days from the hospitalization. Regarding the response to steroid treatment, 10 patients were refractory, 6 dependent and 1 responder. Eight patients received rescue treatment with Infliximab without primary response. When we compared CTE findings of patients requiring colectomy ($n=11$) versus those who did not ($n=6$), free fluid in the abdominal cavity was observed in 64% vs. 0% ($p=0.043$): haustra loss: 100% vs. 50% ($p=0.029$): megacolon (transverse colon diameter greater than 5 cm) 27 % vs. 0 % (NS): extensive involvement: 72% vs. 50% (NS), wall thickening (>5mm): 100% vs. 66% (NS): and ulcers and/or pseudopolyps: 100% vs 66% (NS). None of the patients had clinical or laboratory evidence of complications related to the CTE.
CONCLUSION: In this pilot study, it seems that in patients with severe relapse of UC, CTE is useful to determine the risk of colectomy while allows us to rule out extra-intestinal complications. Although in IBD MRI is usually preferred due to its lack of radiation, in this particular setting of severe UC, CTE is a reasonable option, widely available and fast to implement in the emergency. Prospective studies with large number of patients are required to assess independent factors that would allow us to choose treatment and predict response.
Disclosure of Interest: None declared

P1436 PROSPECTIVE COMPARISON OF MAGNETIC RESONANCE IMAGING, RECTAL AND TRANSPERINEAL ULTRASOUND AND THE SURGICAL FINDINGS OF COMPLICATED PERIANAL CROHN'S DISEASE: A NEW KID ON THE BLOCK

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INTRODUCTION: Magnetic resonance imaging (MRI) and rectal ultrasound (RUS) are the two accepted imaging modalities for the evaluation of perianal fistulas and abscesses. Transperineal ultrasound (TPUS) is a new technique, witch easy to learn and can be performed at any time.
AIMS & METHODS: To prospectively compare the diagnostic accuracy of MRI, RUS and TPUS with the surgical findings of CD patients with perianal fistulas and abscesses. All patients underwent MRI, RUS and PUS within a few days before perianal surgery. Fistulas were classified as simple (43.8%) or complex (52.2%). Perianal Disease Activity Index (PDAI) was estimated in every patient.
RESULTS: Twenty-three patients with active perianal CD (12 women, 11 men, mean age: 36.7 years; current therapy: antibiotics in 69.6%, azathioprine in 56.5%, biologicals in 73.9%; frequency of previous surgery 26.1%; proportion of smokers 39.1%) were included in this prospective study. The mean PDAI was 8.43 (4-15). The validity of MRI, RUS and PUS in the diagnosis of perianal fistulas were 82.6%, 82.6% and 100%, respectively. PUS was significantly more sensitive in the diagnosis of the perianal abscesses than MRI and RUS (100%, 58.8% and 92.8%).
CONCLUSION: PUS is a very accurate and easy to perform diagnostic method with an outstanding sensitivity compared to MRI and RUS in the evaluation of complicated perianal CD. Due to its simplicity and low cost, PUS is recommended be the first diagnostic modality in case of complicated CD.
Disclosure of Interest: None declared

P1437 NONINVASIVE URINARY METABONOMIC DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE USING GAS CHROMATOGRAPHY/MASS SPECTROMETRY

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INTRODUCTION: Accurate diagnosis of inflammatory bowel disease (IBD) and classification of its clinical subtypes, namely Crohn's disease (CD) and ulcerative colitis (UC), are of increasing importance in its management and prognosis. However, diagnosis of IBD based on conventional radiological, endoscopic, and histopathological techniques is often inconclusive and invasive. Urinary metabonomics represents an emerging systems biology approach for the identification of noninvasive metabolic biomarkers of IBD. While previous studies have focused on the use of NMR spectroscopy for urinary metabotyping of IBD patients, complementary analytical tools that may broaden the metabolic coverage for biomarker discovery have been underexplored.
AIMS & METHODS: In this study, the role of gas chromatography/mass spectrometry (GC/MS)-guided urinary metabonomics in the noninvasive characterisation of IBD was investigated for the first time. Marker metabolites characterizing specific subtypes of IBD were further elucidated. Urine samples from 9 IBD patients (5 UC and 4 CD patients) with active disease (CDAI $>$ 150 or Truelove & Witt Activity $>$mild activity, without biological immune-modifiers) and 10 matched healthy controls were metabotyped using gas chromatography/time-of-flight mass spectrometry (GC/TOFMS). The acquired data were subjected to multivariate partial least squares discriminant analysis (PLSDA). The PLSDA model was validated using response permutation testing and subjected to receiver operating characteristic (ROC) analysis.
RESULTS: IBD patients were clearly distinguished from healthy controls based on their urinary metabonomic profiles [validated PLSDA, $R^2X=0.264$, $R^2Y=0.669$, Q^2 (cumulative)$=0.519$]. The robustness of the PLSDA model was demonstrated by an area of 0.978 under the ROC curve and a sensitivity of 100% and specificity of 90% in detecting IBD. Marker metabolites that were dysregulated similarly in UC and CD (e.g. elevated xylose), as well as unique metabolites that characterized each subtype (e.g. increased fucose and decreased

nicotinic acid, picolinic acid and valine in UC; reduced hippuric acid in CD) were further revealed ($p<0.05$).
CONCLUSION: While this diagnostic technique requires further evaluation, our work established surprisingly robust proof-of-principle for the ability of a non-invasive GC/TOFMS-based urinary metabonomic approach to identify patients with IBD and uncovered valuable marker metabolites that may aid in the diagnostic distinction between CD and UC.
Disclosure of Interest: None declared

P1438 RISK FACTORS FOR INTRAEPITHELIAL NEOPLASIA IN ULCERATIVE COLITIS - A CROSS-SECTIONAL STUDY

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INTRODUCTION: Ulcerative colitis (UC) is associated with an increased risk of colorectal cancer (CRC). Identification of risk factors for CRC is important to enhance surveillance. Risk factors identified so far resulted mainly from retrospective studies carried out in referral centers and involving high-risk patients.
AIMS & METHODS: Aim: To identify risk factors for intraepithelial neoplasia (IN) in patients with longstanding UC and without primary sclerosing cholangitis (PSC) and/or history of IN.
Methods: 150 patients with longstanding (≥8 years) distal/extensive UC and without PSC and/or history of IN, were prospectively screened by colonoscopy with chromoendoscopy-guided endomicroscopy (n = 73) or convencional colonoscopy with random biopsies (n = 77). In the chromoendoscopy group aberrant crypt foci (ACF) were sought at the lower rectum.
RESULTS: IN was detected in 10 patients (6.7%). Patients with IN have a significantly higher number of ACF than patients without IN (4.83±3.13 vs 2.17±2.78, p = 0.029). ACF prevalence was 100% in patients with IN and 56.7% in patients without IN (p = 0.056). Although not reaching statistical significance, there was a trend for association between the risk of IN with older ages (57.90±13.52 vs 49.51±14.26 years, p = 0.070) and longer disease duration (22.40±10.26 vs 16.37±7.73 years, p = 0.059). There is also a trend towards lower prevalence of treatment with oral mesalazine in patients with IN (70% vs 90%, p = 0.054). Age at diagnosis, extent of disease, presence of pseudopolyps, smoking status, family history of CRC and body mass index revealed no significant association with the risk of IN.
CONCLUSION: In longstanding UC patients without PSC and/or history of IN, the following are risk factors for IN: prevalence/number of ACF, older age, longer disease duration and lack of medication with oral mesalazine.
Disclosure of Interest: None declared

P1439 RISK FACTORS FOR ABERRANT CRYPT FOCI IN ULCERATIVE COLITIS

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INTRODUCTION: Aberrant crypt foci (ACF) were identified as biomarkers of sporadic colorectal cancer (CRC) and, more recently, of dysplasia/CCR associated with ulcerative colitis (UC). Therefore, it is important to identify risk factors for ACF, which were previously only explored outside the scope of inflammatory bowel disease.
AIMS & METHODS: Aim: To identify risk factors for ACF in UC.
Methods: Seventy six patients with longstanding (≥8 years) distal/extensive UC and without primary sclerosing cholangitis (PSC) and/or history of intraepithelial neoplasia (IN) were prospectively included in the study. ACF were sought at the lower rectum after chromoendoscopy with methylene blue. Demographic and clinical data were obtained with a standardized questionnaire filled out by reviewing the medical charts and a patient interview at the time of enrolment. Associations of various factors with the prevalence and the number of ACF were sought by univariate and multivariate analysis.
RESULTS: ACF were detected in 46 patients (60.5%) with a per patient average number of 2.4±2.8. ACF prevalence was significantly higher in patients with a family history of CRC (100% vs 56.5%, p = 0.038) and it was also found a trend for a positive association with body mass index (BMI) (p = 0.055). The number of ACF was significantly higher in patients aged >40 years (2.8±3.0 vs 1.4±2.0; p = 0.032), family history of CRC (4.1±3.6 vs 2.2±2.7; p = 0.044) and higher BMI (0, 1.9±2.6, 2.6±3.1, 3.7±2.5 for BMI <18.5, 18.5-24.9, 25-29.9 and ≥30 respectively, p = 0.028). In multivariate analysis only the association with BMI remained statistically significant (p = 0.030).
CONCLUSION: In patients with longstanding UC and without PSC and/or history of IN, having family history of CRC or high BMI are risk factors for ACF.
Disclosure of Interest: None declared

P1440 ANTI-TNF THERAPY AND DISEASE PHENOTYPE: DETERMINANTS OF RISK OF RADIATION EXPOSURE IN CROHN'S DISEASE

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INTRODUCTION: Patients with Crohn's Disease (CD) require repetitive imaging of the gastrointestinal tract for diagnosis, assessment of activity and response to therapy. Epidemiological data suggest that a protracted exposure of a dose of 50–100 millisieverts (mSv) is associated with increased risk of cancer.
AIMS & METHODS: Calculate the cumulative dose of radiation (CDR) in patients diagnosed with CD and its correlation with different variables. Cohort of 630 patients diagnosed with CD between January 1990 and December 2013 treated at an Inflammatory Bowel Disease outpatient clinic. The total dose of effective radiation was estimated for each patient collecting the number and type of radiographic imaging studies since the onset of the symptoms. The CDR was determined for each patient according to the value set in the reference table in units of mSv.
RESULTS: 630 patients were included (49.8% male) with CD phenotype according to the Montreal classification: B1 n = 263, B2 n = 54, B3 n = 313. The CDR mean value was 41.45 mSv (0 - 642.49). There was a correlation between the number of abdominal computed tomography exams performed and the CDR. However, the increased duration of the disease was not associated with a higher CDR. Eighty-six patients (13.7 %) were exposed to a CDR > 50 mSv. There was a relationship between higher CDR and CD phenotype: B1: 27.54 mSv; B2: 34.47 mSv; B3: 40.66 mSv. A CDR > 50 mSv was related to the penetrating phenotype (40.66 vs 27.54, p < 0.001), anti-TNF therapy (52.38 vs 33.04, p = 0.003), surgical treatment (49.86 vs 33.87, p = 0.005) and continuous or intermittent course of the disease vs chronic illness with minimum activity after diagnosis (45.56 vs 29.9, p = 0.004). Azathioprine therapy was not associated with greater CDR.
CONCLUSION: Anti-TNF therapy, surgical treatment, penetrating phenotype and continuous or intermittent course of the disease were factors associated with greater amount of CDR.
Disclosure of Interest: None declared

P1441 CALPROTECTIN PREDICTS RELAPSE OF IBD EVEN IN THE PRESENCE OF A 'NORMAL' COLONOSCOPY

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INTRODUCTION: Faecal calprotectin (FCALP) is a sensitive and reliable marker of mucosal inflammation and mucosal healing in IBD. It has always been compared against endoscopic appearance as the presumed gold standard for assessment of disease activity. Several strands of evidence – using magnifying[1] or image-enhanced endoscopy as well as confocal laser endomicroscopy[2] – highlight abnormalities in colonic mucosa reported as 'normal' by standard white light colonoscopy (WLC). This may be compounded by the difficulties in bowel preparation in IBD[3] and the non-widespread use of high definition technology (although the latter has not been specifically studied in relation to IBD). We wished to determine whether an elevated FCALP could predict relapse even in the presence of an ostensibly normal WLC.
AIMS & METHODS: As part of a larger study correlating FCALP to histologic assessment of disease activity, retrospective data was collected for consecutive patients with IBD on stable therapy undergoing colonoscopy for disease assessment. FCALP (Bühlmann ELISA) was collected as close as possible (prior) to the colonoscopy. When the colonoscopic appearances were reported as normal (Mayo endoscopic subscore 0 for ulcerative colitis, UC, and ulceration score equating to SES-CD = 0 for Crohn's disease, CD), patients were followed to determine if they relapsed, with time to relapse (or last recorded follow-up) taken from the date of colonoscopy. For the purposes of this study, relapse was defined generally as "continuous or worsening intestinal symptoms requiring an escalation in therapy". Switching between 5ASA classes was not included in this definition unless the specifically stated to be in response to uncontrolled symptoms.
RESULTS: 46 patients with UC and 37 with CD were identified with the above criteria. Median time between FCALP measurement and colonoscopy was 0.70 (max 2.89) and 0.90 (max 1.5) months respectively. Normal FCALP was detected in 16 patients with UC and 12 with CD.
Median calprotectin in the 'high' group was 377 (229-794) in UC and 192 (118-247) in CD. At 12 months, relapse-free survival proportions were 86% with UC and normal FCALP compared to 34% in those with high FCALP (p < 0.01 in Kaplan-Meier analysis). In CD, these proportions were 50% and 12% respectively (p = 0.02).
CONCLUSION: Elevated levels of FCALP predict relapse even in the presence of a macroscopically normal colonoscopy. This finding is in general agreement with studies of state-of-the-art endoscopic techniques that detect mucosal abnormalities predictive of relapse, when WLC is reported as 'normal'. FCALP may provide a cheaper and acceptable alternative to routine monitoring endoscopy in IBD.
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Disclosure of Interest: None declared

P1442 THERAPEUTIC DRUG MONITORING OF INFLIXIMAB IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Tumour necrosis factor (TNF)–antagonists are effective treatments for inflammatory bowel disease (IBD), but secondary loss of response (LOR) occurs in 10-15% patients/year. Therapeutic drug monitoring (TDM) has emerged to facilitate decision-making around secondary LOR. In Addenbrooke's Hospital 107 and 41 IBD patients are on infliximab and adalimumab respectively.
AIMS & METHODS: Assess serum infliximab and antibodies to infliximab (ATI) in IBD patients and determine usefulness of TDM in clinical decision-making. Prospective cohort study of IBD patients on infliximab between Aug 2013-Jan 2014. Demographic and clinical data collected. Disease activity assessed using Harvey-Bradshaw index (HBI) for Crohn's disease (CD) and Simple Clinical Colitis Activity Index (SCCAI) for Ulcerative colitis (UC). C-reactive protein and faecal calprotectin were measured. Bloods assayed for trough level of infliximab (TLI)+/-ATI using LISA-TRACKER Premium ELISA kits (Theradiag). ATI only if intermediate or subtherapeutic TLI and positive evidence of inflammatory activity. TLI interpretations:Therapeutic level > 2μg/mL, Intermediate level 1.0–2.0μg/mL and Subtherapeutic level < 1.0μg/mL. ATI analytical range: 10–200ng/mL.
RESULTS: 107 patients (55males,52females) recruited. Mean age 35.9 years (range,18-74 years). Mean disease duration 9.6 years (range,7months-39 years). Mean disease duration before starting infliximab 6.8 years (range,1month-39 years). Diagnoses of CD, UC and IBD-Unspecified were 104, 2 and 1 respectively. Majority 70 (66%) were on 8-weekly regime. Mean duration of infliximab 3.3 years. For TLI results,73 (68.2%),12 (11.2%) and 22 (20.6%) were in the therapeutic, intermediate and subtherapeutic range respectively. For subtherapeutic TLI group,14 (63%) had undetectable ATI,3 (14%) had ATI of 42ng/mL,31ng/mL and 50ng/mL; and 5 (23%) did not have ATI done as they had no evidence of inflammatory activity. For intermediate TLI group,8 (67%) had undetectable ATI,1 (8%) had ATI of 160ng/mL and 3 (25%) did not have ATI done as they had no evidence of inflammatory activity. For therapeutic TLI group,24 (33%) had evidence of inflammatory activity.39 (36%) were not on immunomodulators (IM). Among 68 patients who were on IM,62 (91%) were on thiopurines and 6 (9%) on methotrexate. In thiopurines group,34 (55%) had thiopurine metabolites (6-TGN) done, of which 25 (74%) were within therapeutic range. Among 68 patients who were on IM,51 (75%) achieved therapeutic TLI and 2 (3%) had detectable ATI versus among 39 patients who were not on IM,24 (61%) achieved therapeutic TLI and 2 (5%) had detectable ATI ($p = 0.143$). There was no significant correlation between 6-TGN and TLI levels ($p = 0.324$).
CONCLUSION: 73 (68.2%) achieved therapeutic TLI. With TDM,58 (54.2%) patients may benefit from interventions:a) Potential infliximab discontinuation (Subtherapeutic TLI + remission)8 (7.5%),b) Potential dose intensification to recapture response (Subtherapeutic TLI with no ATI but clinical/biochemical activity)22 (20.6%) and (Subtherapeutic TLI with low ATI)3 (2.8%),c) Potential switch to other anti-TNF agent (Subtherapeutic TLI with high ATI)1 (0.9%) and d) Potential switch to non-anti TNF agent (Therapeutic TLI + activity) 24 (22.4%). 26/58 (44.8%) patients needed ATI for decision making. To save cost, initial test should be TLI with addition of ATI if needed. Concomitant infliximab and IM seemed to be associated with higher rate of therapeutic TLI. However, there was no significant correlation between 6TGN and TLI levels.
Disclosure of Interest: None declared

P1443 THIOPURINES AND ANTI-TNFS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND A POSITIVE HISTORY OF NEOPLASIA

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INTRODUCTION: The possible role of immunomodulators (IMM) in the development and/or outcome of neoplasia in Inflammatory Bowel Disease IBD) is still debated. Whether IBD patients with a previous diagnosis of neoplasia may be treated with IMM, including anti-TNFs is undefined.
AIMS & METHODS: In a retrospective cohort study, the outcome of IBD patients treated with IMM and/or anti-TNFs after a diagnosis of neoplasia was evaluated. Clinical characteristics of all IBD patients under regular follow up at our tertiary IBD center from 2000 to 2013, with a proven diagnosis of neoplasia were reviewed. Among this subgroup of IBD patients with a history of neoplasia, only patients treated with IMM and/or anti-TNFs after the diagnosis of neoplasia were included. Parameters considered: 1. IBD type (Crohn's Disease, CD vs Ulcerative Colitis, UC); 2. Gender; 3. Age at diagnosis of IBD; 4. Age at diagnosis of neoplasia (yr); 5. IMM (Azathioprine, AZA;6-mercapopurine,6MP) or anti-TNF (Infliximab, IFX, Adalimumab, AD); 6. IBD duration at time of diagnosis of neoplasia; 7. Time interval between diagnosis of neoplasia and IMM use; 8. Follow up duration after the diagnosis of neoplasia; 9. Characteristics of neoplasia. Data were expressed as median (range)
RESULTS: In the 13 yrs follow up, a history of neoplasia was observed in 82 IBD pts. Among these 82 IBD pts, 15 (18.2%) were treated with IMM for IBD after the diagnosis of neoplasia. This group included 12 CD and 3 UC pts. (8M,5F; age at diagnosis of neoplasia 41, range 21-69; age at diagnosis of IBD 27, range 12-66, IBD duration at diagnosis of neoplasia 10, range 1-38). IMM after the diagnosis of cancer included thiopurines in 12 (AZA n = 8; 6MP n = 4), anti-TNFs in 3 (ADA n = .2; IFX n = 1). Among the 15 IBD pts treated with IMM after the diagnosis of neoplasia, neoplasia included: thyroid (n = 4), skin (NMSC n = 2; 1 basal cell carcinoma, 1 spinal cell carcinoma); breast (n = 2), colon (n = 2), prostatic cancer (n = 2) lymphoma (HL n = 1), seminoma (n = 1), carcinoid of the appendix (n = 1). Time interval between the diagnosis of neoplasia and IMM use: 6 yrs (range 1-26). After a 10 yrs follow up from the diagnosis of neoplasia (range 3-30), none of the 15 IBD pts treated with IMM after the diagnosis of neoplasia showed recurrence or new onset of neoplasia. No cancer-related deaths were observed, as only 1/15 pts. had a cirrhosis-related death..
CONCLUSION: In a retrospective study, the use of thiopurines and anti-TNFs did not appear to worsen the outcome of IBD pts with a positive history of neoplasia. Larger prospective longitudinal studies are needed to further address this relevant issue in IBD
Disclosure of Interest: None declared

P1444 PROSTAGLANDIN E-MAJOR URINARY METABOLITE AS A RELIABLE SURROGATE MARKER FOR MUCOSAL INFLAMMATION IN ULCERATIVE COLITIS

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INTRODUCTION: A simple, non-invasive biomarker of ulcerative colitis (UC) activity is required. Because prostaglandin-E2 (PGE2) production is associated with colonic inflammation, we evaluated whether prostaglandin E-major urinary metabolite (PGE-MUM) can be used as a biomarker of UC activity by comparing the PGE-MUM levels of volunteers with those of UC patients. PGE is known to be involved in the development of colon cancer as well as inflammation of the large intestine.
AIMS & METHODS: Urine samples were obtained from 408 non-smoking (172 male and 236 female) volunteers who visited the Health Check Department of the Japanese Red Cross Medical Center for general health checkups and from 79 UC (53 male and 26 female) patients at Jikei University Hospital. UC activity was evaluated using the simple clinical colitis activity index (SCCAI), Mayo endoscopic scoring system, and Matts' grading system (histological activity scoring). PGE-MUM levels were measured by using a radioimmunoassay kit.
RESULTS: PGE-MUM levels were associated with UC activity ($P < 0.01$). The PGE-MUM levels in the active phase were significantly higher in UC patients than in healthy volunteers. The main advantage of PGE-MUM appears to be the differentiation of colonoscopic or histologic remission from active disease in UC patients. In remission, PGE-MUM levels of UC patients were close to those of healthy volunteers.
CONCLUSION: Because PGE-MUM can be estimated using a simple, quick, and non-invasive method and is associated with UC activity, it appears to be a useful biomarker of UC activity. PGE-MUM levels are low in remission in UC patients owing to successful treatment. PGE production in the colon is a risk factor for colon cancer along with cyclooxygenase-2. By keeping PGE-MUM levels low in the long term, it is possible to reduce UC recurrence and the incidence of colorectal cancer.
Disclosure of Interest: None declared

P1445 POOR RECOGNITION AND MANAGEMENT OF IRON DEFICIENCY ANAEMIA IN INFLAMMATORY BOWEL DISEASE: A MISSED OPPORTUNITY

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INTRODUCTION: Iron deficiency anaemia (IDA) is a common complication of inflammatory bowel disease (IBD) that has an impact on the patient's quality of life. IDA is caused by inadequate dietary intake, malabsorption of iron and iron loss through intestinal bleeding. Current guidelines recommend that all patients with IBD should be assessed for IDA and that iron supplementation be given as indicated.[1]
AIMS & METHODS: The aim of this study was to ascertain the prevalence of IDA in our IBD cohort, to look at whether iron replacement therapy (and in what form) was given and to assess treatment response.
A single centre, retrospective analysis of IBD patients from a large district general NHS trust in North London was performed. The database of patients was collated by the IBD Clinical Nurse Specialist. Electronic patient records (blood results and outpatient clinic letters) were used to collect data on patient demographics, diagnosis, screening parameters for IDA (Hb, Ferritin/transferrin saturation, CRP) and iron replacement therapy. The WHO definitions of anaemia were used (Hb < 13g/dL in men and Hb < 12g/dL in non pregnant women). Iron deficiency was diagnosed if ferritin < 30 ug/L in quiescent IBD or < 100ug/L in active IBD (CRP elevated) or transferrin saturation < 16%.

RESULTS: 333 IBD patients were identified in the database. 3 patients were excluded because of insufficient data as their care was transferred. 293/330 (88.8%) were checked for IDA using the screening parameters. 146/293 (49.8%) of this group were found to be anaemic. 101/146 (69.2%) had evidence of iron deficiency. 61/101 (60.4%) were treated using oral and/or intravenous (IV) iron preparations or blood transfusions. Most patients (50/61) received oral iron while 10 patients had IV iron (4 had failed oral therapy) and 6 had a transfusion. The recurrence rate of IDA was 21/50 with oral iron, 4/10 with IV iron and 4/6 with transfusions. We also noted that there were 39/184 patients (21.2%) with iron deficiency in the absence of anaemia. Only 3 of these patients were treated for iron deficiency.
CONCLUSION: The prevalence of IDA in our IBD group was close to 50%. Current practice in our trust does not comply with guidelines as only 60.4% of IDA patients were treated. Iron replacement therapy was mostly administered in the oral form. Recurrence of IDA was similar (about 40%) with both oral and IV iron therapy. There is little guidance on management of iron deficiency in the absence of anaemia and supplementation was not widespread in this group. Barriers to appropriate recognition of IDA including lack of routine monitoring and knowledge on iron data interpretation will need to be addressed to improve practice.
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Disclosure of Interest: None declared

P1446 A NOVEL SIMPLE SCORE FOR THE DIAGNOSIS OF CROHN'S DISEASE

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INTRODUCTION: Rapid and accurate diagnosis of Crohn's disease (CD) is essential for early intervention, however, a gold standard is not available. Lennard-Jones et al. defined widely adopted macroscopic and histological criteria for CD diagnosis, but these await validation.
AIMS & METHODS: To develop an alternative diagnostic model for CD based on the criteria by Lennard-Jones.
Included were patients from 3 tertiary centres (Nancy, Barcelona and Vienna) with long-standing CD whose records from up to 6 months after initial diagnosis were reviewed. Cases were then re-classified according to Lennard-Jones criteria (LJC). CD was rated as "established" (granuloma + one minor criterion or 3 minor criteria, which include macroscopic discontinuity, transmural inflammation, fibrosis, lymphoid aggregates or discontinuous inflammation on histology), "probable" (2 minor criteria without granulomas) or "non CD". Sensitivity, specificity and balanced accuracy were calculated for the overall sample and for each center separately including patients with ulcerative colitis (UC) as controls. The prognostic value of the 6 variables was modelled by logistic regression. Variables which proved highly significant ($p<0.0001$) in the first model were included in the final model. One hundred 10-fold cross-validations were conducted. ROC-curves were calculated and the value with the best Youden-Index was taken as the optimal cut-off for the diagnosis of CD.
RESULTS: Overall, 328 patients with CD and 170 patients with UC were assessed. At time of diagnosis nearly half of all patients were diagnosed as "non CD" (see Table 1).
Table 1 Diagnosis of CD according to LJC:

	Established CD, n (%)	Sensi/ Speci*	Probable CD, n (%)	Sensi/ Speci**	Non CD, n (%)
Barcelona	49/101 (48%)	0.49/1.00	18/101 (18%)	0.66/0.98	34/101 (34%)
Nancy	19/94 (20%)	0.20/1.00	21/94 (22%)	0.43/0.90	54/94 (58%)
Vienna	44/133 (33%)	0.33/0.99	15/133 (11%)	0.44/0.97	74/133 (56%)

Logistic regression of all 6 variables showed high significance by the 4 factors, granuloma, fibrosis, transmural inflammation, and macroscopic discontinuity with parameter estimates of 4.6, 4.4, 2.3 and 2.3, respectively. A cut-off score value of $\geq$2.28 was associated with highest balanced accuracy (0.82), a sensitivity of 0.8 and a specificity of 0.85 and reflecting a diagnosis of "probable CD". A cut-off value of $\geq$4.4 for "established CD" would be associated with a specificity of 1, but a sensitivity of 0.45.
CONCLUSION: In nearly half of patients managed as long-standing CD at 3 referral centres the LJC would not provide the diagnosis of CD from initial examinations. We elaborated an alternative simple score for the diagnosis of CD resulting in higher sensitivity and specificity by subjecting the criteria by Lennard-Jones to logistic regression modelling.
Disclosure of Interest: None declared

P1447 CHEMERIN, VISFATIN AND VASPIN SERUM LEVELS IN RELATION TO FAT MASS AND BONE MINERAL DENSITY IN IBD

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INTRODUCTION: It has been suggested that the bone and fat interface is implicated in the pathogenesis of osteoporosis. Several studies have shown a strong correlation between fat mass (FM) and bone mineral density (BMD) in patients with IBD, but data including the action of adipokines on this association are limited. The aim of this study was to investigate the role of the adipokines chemerin, visfatin and vaspin in patients with ulcerative colitis (UC) and Crohn Disease (CD) in relation to FM and BMD
AIMS & METHODS: 115 patients with IBD (67 CD, 48 UC) and 98 matched healthy controls (HC) were enrolled in this study. All patients underwent bone densitometry by dual energy x-ray absorptiometry at the femoral neck and lumbar spine, and evaluation of body mass composition with GE-Lunar Prodigy along with host software Encore. Chemerin, visfatin and vaspin serum levels were measured in IBD patients and HC using commercially available enzyme linked immunosorbent assays (ELISA)
RESULTS: Osteopenia was observed in 75 patients with IBD (65.2%, 59 CD and 26 UC) and osteoporosis in 23 patients (20%,19 CD,4 UC). Osteoporotic patients had a significant lower total fat mass (19501.3±8085.2gr) than osteopenic patients (23089.2±9939.9 gr) and the patients with normal BMD (28410±10692 gr)($p=0.01$). Mean (±standard deviation) serum chemerin levels were 14.1±6.6ng/ml in CD patients, 13.5±3.3ng/ml in UC patients and 7.8±2.7ng/ml in HC ($P<0.0001$). No differences between males and females or between UC and CD were observed. Subgroup analysis of correlation of chemerin levels with clinical characteristics showed significant association only with indices of osteoporosis. Chemerin serum levels were found significantly correlated with T score both at the femoral neck and lumbar spine ($r=0.25$ $p=0.007$ and $r=0.19$, $p=0.03$ respectively). There was no significant correlation of chemerin levels with BMI, CRP and fat distribution. No significant correlations between visfatin or vaspin and any of the examined parameters (including disease type or characteristics, FM and BMD) were observed.
CONCLUSION: Fat mass seems to play an important role in the development of osteoporosis in IBD patients. Serum chemerin levels are significantly increased in patients with IBD compared to HC and significantly correlated with the development of osteoporosis.
Disclosure of Interest: None declared

P1448 MAGNIFYING COLONOSCOPY OF THE RECTUM IS IMPORTANT IN PATIENTS WITH QUIESCENT ULCERATIVE COLITIS: RESULTS OF 15-YEAR FOLLOW-UP

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INTRODUCTION: Histologic healing has been shown to be associated with favorable outcomes in patients with ulcerative colitis (UC). Although mucosal healing (MH) is reported to be an important goal, MH is not always an accurate indicator of histologic healing because microscopic evidence of inflammation is common even in patients with clinically and colonoscopically quiescent colitis.
AIMS & METHODS: We prospectively investigated the usefulness of a high-resolution video-magnifying colonoscope with chromoscopy for UC patients diagnosed with MH by routine colonoscopy to predict exacerbations over a long period (15 years). Magnifying colonoscopy was performed in 25 UC patients in remission who had been found to have MH by routine colonoscopy. Pit patterns in the rectal mucosa were classified into three magnifying-colonoscopy (MCS) grades on the basis of size, shape, and arrangement. Mucosal macrophage inflammatory protein (MIP)-1a activity in biopsy specimens of rectal mucosa was measured and the specimens were microscopically graded according to the system of Riley. The patients were followed until relapse or for 15 years. Multivariate survival analysis was performed to determine independent predictors of clinical relapse.
RESULTS: Of the 25 patients, 4 were MCS grade 1, 10 were grade 2, and 11 were grade 3. A positive correlation was identified among MCS grade, histological grade and mucosal MIP-1a activity. Follow-up for 15 years after the start of the study was possible in all patients. During the study 8 patients (grade 1: 0%, grade 2: 0%, grade 3: 73%), 20 patients (grade 1: 50%, grade 2: 80%, grade 3: 91%), 21 patients (grade 1: 50%, grade 2: 90%, grade 3: 91%), and 22 patients (grade 1: 75%, grade 2: 90%, grade 3: 91%) relapsed within 1, 5, 10, and 15 years, respectively. After magnifying colonoscopy, patients with MCS grade 1 relapsed later than 2 years and those with MCS grade 3 relapsed within 2 years. Multivariate proportional hazards model analysis showed that MCS grade was a significant predictor of relapse. Kaplan-Meier estimates of relapse during the 15-year follow-up increased with increasing MCS grade ($P=0.01$).
CONCLUSION: MCS grading is associated with the degree of histological inflammation and mucosal MIP-1a activity in quiescent UC patients, and may predict the probability of subsequent disease relapse in UC patients in remission over a long period.
Disclosure of Interest: None declared

P1449 PREGNANCY DOES NOT AFFECT FECAL CALPROTECTIN CONCENTRATIONS IN HEALTHY PREGNANT WOMEN

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INTRODUCTION: Fecal calprotectin (CP) is a promising activity marker in the differentiation of inflammatory bowel diseases (IBD) vs. functional gastrointestinal diseases. Non-invasive activity markers are extremely important in conditions, like pregnancy, when endoscopy is not recommended to be performed. No data is available on the alteration of fecal CP concentration during pregnancy.
AIMS & METHODS: The **aim** of this study was to determine fecal CP concentrations in healthy non-pregnant and pregnant women and in patients with IBD. Healthy women planning pregnancy (waiting for in vitro fertilisation (IVF) treatment), pregnant women and patients with active and inactive IBD were prospectively enrolled in the study. Demographic and clinical parameters, clinical disease activity scores in case of patients with IBD were recorded. Blood and stool samples were obtained from every patient to determine C-reactive protein (CRP) and fecal CP levels. Fecal CP concentration was quantified by use of enzyme-linked immunosorbent assay.
RESULTS: One hundred and three subjects were enrolled in the study (19 women planning pregnancy, 21 healthy pregnant females, 40 patients with active and 23 patients with inactive IBD). Mean fecal CP and CRP levels were 32.4 μg/g and 6.5 mg/l in pregnant women. Fecal CP concentration was significantly higher in both active and inactive IBD compared to pregnant women ($p<0.001$, $p=0.001$) and also to those waiting for IVF ($p<0.001$, $p=0.001$). No significant difference was detected in CRP levels between the groups. No difference could be detected in the fecal CP concentrations between pregnant and non-pregnant healthy women.
CONCLUSION: Since fecal CP levels did not change during pregnancy, it seems to be useful noninvasive diagnostic tool in pregnancy and maybe beneficial in the future for monitoring disease activity in pregnant patients suffering from IBD. Further studies are necessary to confirm these results.
Disclosure of Interest: None declared

P1450 HEALTH CARE RESOURCE UTILIZATION AMONG MODERATE TO SEVERE ULCERATIVE COLITIS PATIENTS TREATED WITH CONVENTIONAL THERAPIES IN EUROPE: THE UC CARES (ULCERATIVE COLITIS CONDITION, ATTITUDE, RESOURCES AND EDUCATIONAL STUDY)

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INTRODUCTION: Ulcerative colitis (UC) is a chronic inflammatory disorder of the gastrointestinal tract and can interfere with patient's ability to have full personal and professional lives. Thiopurine immunomodulators are recommended for moderate to severe UC patients. Little data exists on health care resource utilization among UC patients treated with conventional therapies.
AIMS & METHODS: This study is to describe the health care resource utilization among moderate to severe UC patients who were biologics naïve and treated with conventional therapies (5-ASA, steroids and/or thiopurines).
Biologic naïve patients with moderate to severe UC (Mayo score $\geq$6), $\geq$18 years who received conventional therapies during the previous year were recruited in Belgium, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. Patients who underwent colectomy or ileo-anal J-pouch reconstruction were excluded. Medical charts for the 12 months prior to enrollment were reviewed to collect clinical data. Health resource utilization included the tests (imaging, diagnostics, and laboratory) and health care professional visits such as ambulatory hospitalization, emergency room visits and inpatient hospitalization. Descriptive analyses of the health resource utilization during the 12 months prior to enrollment were conducted in this post-hoc analysis.
RESULTS: A total of 250 patients were included in the analysis. Patients' mean (SD) age was 46.6 years (16.3) and 59% were male. The median duration of UC was 6.9 years (IQR 2.3-14.4). Extent of UC included 21.6% proctitis, 28.4% left-sided, and 49.6% extensive colitis. At the enrollment date, the percentages of patients receiving thiopurines, aminosalicylates, corticosteroids and other types of immunosuppressants were 63.2%, 75.2%, 23.6% and 3.6%, respectively.
During the 12 months prior to the enrollment date, only 19 (7.6%) patients had an abdominal X-Ray. In terms of diagnostic tests the most frequently reported tests were colonoscopy (18.4% of patients), flexible sigmoidoscopy (9.2%), and abdominal ultrasound (6.0%). Laboratory tests were performed on half the patients with 51.2% reporting at least one blood chemistry test and 52% at least one hematology test. Most imaging and diagnostic tests were performed once on each patient. The abdominal ultrasound and colorectal biopsy which were performed a mean (SD) of 2.27 (1.92) and 2.40 (1.15) times on each patient. Only 2.4% of patients included in the study had at least one ambulatory hospitalization, 5.6% reported at least one emergency room visit, and 4.4% at least one inpatient hospitalization. The median number of inpatient hospitalization days was 7 days (IQR 4-9).
CONCLUSION: Overall, during 12 months prior to the enrollment date, less than 20% of the patients had imaging or diagnostic tests and half of the patients had laboratory tests. Only 2-5% of the patients had at least one health resource utilization including ambulatory hospitalization, emergency room visit and inpatient hospitalization.
Disclosure of Interest: G. Van Assche Consultancy for: Merck & Co., Inc, L. Peyrin-Biroulet Consultancy for: Merck & Co., Inc, T. Fan Other: Employee of Merck & Co., Inc, Q. Ding: None declared, N. Lara Consultancy for: Merck & Co., Inc, M. Lynam Consultancy for: Merck & Co., Inc, S. Rojas-Farreras Consultancy for: Merck & Co., Inc.

P1451 PHOTODYNAMIC DIAGNOSIS OF COLITIS-ASSOCIATED CANCER/DYSPLASIA BY VISUALIZATION FOLLOWING ORAL 5-AMINOLEVULINIC ACID SENSITIZATION IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Colitis-associated cancer or dysplasia (CC/D) is a very important complication that is encountered during clinical management of patients with long-standing ulcerative colitis (UC). However, it is very difficult to detect CC/D with conventional colonoscopy (CE) and image-enhanced endoscopy (IEE). The use of many endoscopic procedures such as chromoendoscopy and target biopsy has been suggested for more efficient detection of CC/D lesions, but the reliability of endoscopic detection methods remains uncertain. Recently, photodynamic diagnosis (PDD) has been utilized clinically to detect the extent of the neoplasms, especially in neurosurgical and urologic procedures. The 5-aminolevulinic acid (5-ALA) is converted intracellularly into the sensitizer protoporphyrin IX (PpIX), which accumulates selectively in neoplastic tissue, allowing the detection of its signal. As there are very few reports regarding this use of 5-ALA for UC surveillance, its effectiveness is unclear and controversial.
AIMS & METHODS: This pilot study aimed to evaluate the efficacy of PDD for endoscopic detection of dysplasia in patients with UC by visualization, using autofluorescent endoscopy (AFE), following orally administered 5-ALA sensitization. Eleven patients with a >10-year history of pancolitis were enrolled at the Jikei University Hospital from October 2010 to September 2012. Prior to this study, we confirmed that the 5-ALA metabolite PpIX was detected *in vitro* as strong fluorescence signals, using AFE (CF-FH260AZI, Olympus Medical Systems, Tokyo, Japan). The 5-ALA (20 mg/kg BW; SBI-Pharma, Tokyo, Japan) was administered orally, and conventional colon lavage was undertaken. Endoscopic examination was performed 5 h after oral 5-ALA administration. Each segment of the large intestine was first examined by CE including chromoendoscopy and then reexamined by AFE.
RESULTS: No adverse side effects of 5-ALA were observed. On examination with CE, 81 lesions were suspected and biopsied, and 18 of these were pathologically diagnosed as CC/D. During subsequent AFE, 22 lesions with strong fluorescence signals of a characteristic shape were detected and biopsied, and 14 lesions were diagnosed as CC/D on pathological examination. Positive (PPV) and negative predictive values (NPV) of CE were 22% and 71%, respectively. On the other hand, those of AFE were 68% and 91%, respectively. Among the LGD lesions, CE detected 13 of 81, and AFE detected 10 of 22 suspected lesions. The PPV and NPV of CE were 16% and 71%, and those of AFE were 45% and 92%, respectively. Although the number of HGD/cancer lesions was limited, the accuracy of CE was 13.6% and that of AFE was 78.4%.
CONCLUSION: AFE after 5-ALA sensitization offers the possibility of detecting CC/D lesions by their characteristic shape and color enhancement. Although the number of patients enrolled in this study was small, our experience indicates that AFE is a promising method for detecting CC/D lesions during UC surveillance.
Disclosure of Interest: None declared

P1452 MARKERS OF SUBCLINICAL ATHEROSCLEROSIS IN A POPULATION OF PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Patients with ulcerative colitis (UC) have an excess risk of cardiovascular (CVD) morbidity due to accelerated atherosclerosis. Markers identifying individuals with subclinical atherosclerosis as measured by carotid intima-medial thickness (IMT) and ankle-brachial index (ABI) may allow for attenuation of CVD risk [1]. The aim of the study was to find the possible correlations between inflammation and subclinical atherosclerosis; also, another purpose was the one to establish possible correlations between ulcerative colitis disease activity index (UCDAI), inflammation and atherosclerosis.
AIMS & METHODS: The study included 108 patients with UC (female: male 52:56, mean age 38.3 $\pm$ 12.8 years, mean disease duration 10.97 $\pm$ 1.04 years). The control group consisted of 112 healthy controls (female: male 54:58 mean age 35.4 $\pm$ 11.6). In order to detect subclinical atherosclerosis, we measured carotid IMT and ABI. The results were correlated with markers of lipid spectrum (total cholesterol, HDL, VLDL, triglycerides, and calculated LDL (using the Friedewald equation), hs CRP, homocysteine, IL-6 and fibrinogen. Clinical disease activity was evaluated by UCDAI score. Lifestyle and other important factors were examined per protocol and by questionnaire.
RESULTS: A significant difference of carotid IMT (0.843 ± 0.11 mm vs 0.625 ± 0.09 mm, $p \leq 0.01$) and ABI (0.97 ± 0.12 vs 1.1 ± 0.16, $p \leq 0.04$) were found

between the UC patients and sex-age adjusted healthy controls. A significant correlation between carotid IMT, ABI and disease duration, age, UCDAI, use of corticosteroids were found. Conventional lipids, systolic blood pressure, fibrinogen and smoking were not significantly correlated to carotid IMT and ABI. However, the correlation between carotid IMT and hsCRP was different regarding the cardiovascular risk: there was a significant positive correlation in patients with hsCRP > 3mg/l (r = 0.58; CI 95% 0.513 – 0.644) and a inverse correlation in patients with values between 1 and 3mg/l (r = – 0.27; CI 95% –0.205–0.321; p = 0.14), correlated with IL – 6 (r = 0.36; CI 95% 0.108 – 0.559), statistically significant (p = 0.03) and with homocysteine (r = 0.19; CI 95% 0.103 – 0.287 p < 0.05). A stepwise logistic regression analysis was conducted with ABI as the dependent variable and lipid spectrum, hs CRP, homocysteine, IL-6 and treatment with statins as independent variables. Following adjustment for age and gender, only the hs CRP and IL-6 remained significantly associated with ABI.
CONCLUSION: Carotid IMT and ABI measurements could be used as a clinical predictor of risk of accelerated atherosclerosis in UC patients. The association of arterial stiffening with circulating levels of hsCRP and IL-6 implicates chronic inflammation as important mediator of this process.
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Disclosure of Interest: None declared

P1454 DIAGNOSIS OF IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE BY TRANSFERRIN RECEPTOR-FERRITIN INDEX

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INTRODUCTION: Iron deficiency (ID) is common in patients with inflammatory bowel disease (IBD) but can be difficult to diagnose in the presence of inflammation. Serum ferritin level < 30 ng/mL is a diagnostic criterion of ID. Guidelines in IBD [1] consider ferritin level between 30-100 ng/mL associated with inflammation as criteria for ID diagnostic. The sTransferrin receptor-ferritin index (TfR-F) has a high sensitivity for ID diagnosis in chronic diseases [2]. The aim of the study was to assess the added value of TfR-F index to diagnosis of ID in a prospective cohort of IBD patients.
AIMS & METHODS: All consecutive IBD patients seen in our hospital from February 2013 to March 2014 were asked to participate in the study. Exclusion criteria were iron supplementation in the 3 previous months or lack of patient consent. IBD activity was assessed on symptoms and markers of inflammation (CRP, endoscopy, calprotectin). All patients had serum dosages of hemoglobin, hsCRP (N < 2.5 mg/L), ferritin (F), transferrin saturation, vitamin B9 and B12, LDH, haptoglobin. Soluble transferrin receptor (sTfR) was measured by Roche Tina-quant®. TfR-F index was calculated as the ratio sTfR / log10 F. ID was defined by F < 30 ng/mL or TfR-F index > 2 in the presence of inflammation; TfR-F index < 1 excluded ID.
RESULTS: 150 patients aged 38 (16-78) years, 69 males, 105 Crohn's disease (CD), 43 ulcerative colitis (UC) and 2 indeterminate colitis were included. 68 patients (45.3%) had active disease. 42 patients (28%) had anemia (WHO criteria), including 28 CD and 14 UC. 9 patients (6%) had vitamin B12 deficiency and 9 (6%) vitamin B9 deficiency. No one had hemolysis. Mean F level was 80 (9-359) ng/mL and sTfR, 3.7 (1.5-12.8) mg/L. 36 patients (24%) had F < 30 ng/mL, 69 (46%) F between 30-100 ng/mL and 45 (30%) F > 100 ng/mL. 30 patients (20%) had F between 30-100 ng/mL and CRP > 2.5 mg/L: 1 had vitamin B12 deficiency excluding TfR-F analysis, 12/29 patients (41.4%) had TfR-F > 2 and 1 patient (3.5%) TfR-F < 1. Three patients (6.6%) with F > 100 ng/mL had TfR-F > 2. Overall, ID was diagnosed in 48/150 patients (32%), in which 24% on the basis of F < 30 ng/mL and 8% with TfR-F index > 2 in the presence of inflammation.
CONCLUSION: This prospective study in IBD shows that TfR-F index in addition to serum ferritin < 30 ng/mL criterion, increases by 8 % diagnosis rates of ID. Only 41.4% of the patients with ferritin between 30-100 ng/mL and inflammation have ID, suggesting that guidelines [1] overestimate ID in IBD. TfR-F index seems useful to the diagnosis of ID in IBD and prevents from overtreating by iron supplementation.
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Disclosure of Interest: None declared

P1456 SIALIC-ACID-BINDING IG-LIKE LECTINS, POTENTIAL PERIPHERAL MARKERS FOR MUCOSAL DAMAGE OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are characterized by relapsing/remitting nature of the inflammatory process. While some cases with IBD are controllable by means of medical treatment, we encounter many cases with recurrent deterioration of disease which necessitates intensive treatment like high dose of steroid therapy, immunosuppressant or even surgery. In damaged intestinal mucosa of IBD, the mucus layer, which covers intestinal epithelial cell surface with heavily glycosylated mucin, is deteriorated and abnormally glycosylated. Recently, we reported that colonic immune cells express sialic acid-binding Ig-like lectins, siglecs, which recognize cell surface glycans preferentially expressed in normal colonic epithelium. We have speculated that the interaction of siglecs with these glycans might be involved in immune tolerance in the mucosal tissue. However, differential expression of siglecs and its regulation in the peripheral immune cells, as well as the function of siglecs in these cells, has been largely unknown.
AIMS & METHODS: The aim of this study was to investigate whether the siglecs expression of peripheral blood mononuclear cells (PBMCs) may reflect the condition of damaged/unhealed mucosa with abnormal glycosylation, and moreover, predict exacerbation of the disease. IBD patients and disease control (intestinal tuberculosis, Behcet disease (BD), and rheumatoid arthritis (RA)), and healthy volunteers were analyzed. PBMCs were isolated and the expression pattern of siglec-7/-9 was analyzed by flowcytometry.
RESULTS: Flow cytometric analysis revealed that $CD33^+$ macrophage/dendritic cells of healthy PBMCs expressed siglec-9 but not Siglec-7, while $CD33^+$ cells isolated from IBD blood frequently expressed Siglec-7. The frequency of siglec-7^+siglec-9^+ cells in $CD33^+$PBMCs of IBD patients was significantly higher than that of normal control, however; there was no difference between UC and CD. High frequency of siglec-7^+siglec-9^+ $CD33^+$ cells was not observed in intestinal tuberculosis, BD, nor RA blood, even at active stage. In IBD cases, the incidence of siglec-7^+siglec-9^+ cells in $CD33^+$PBMCs correlated with abdominal pain and ESR but not CRP, ALB, Hb, the number of WBC, neutrophils, and platelets, suggesting that inflammation is not essentially parallel to the expression of siglec-7. In fact, some UC patients in clinical remission with high frequency of siglec-7^+siglec-9^+ cells, resulted in aggravated disease several months later.
CONCLUSION: The frequency of siglec-7^+siglec-9^+ cells in $CD33^+$PBMCs of IBD patients, especially at active stage, was significantly higher than those of normal control and patients with non-IBD inflammatory disease, such as intestinal tuberculosis, BD, nor RA. These results suggest that the emergence of siglec-7^+siglec-9^+ cells in the peripheral $CD33^+$PBMCs reflects presence of the mucosal damage in an IBD-specific manner, which may be clinically cryptic without apparent sign of inflammation. Thus, it may predict exacerbation or relapse in IBD patients.
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J Immunol 2012; 188: 4690-700.
Disclosure of Interest: None declared

P1457 SAFETY AND EFFICACY OF LOW DOSE AZATHIOPRINE AND ALLOPURINOL CO-THERAPY: A LARGE SINGLE CENTRE EXPERIENCE

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INTRODUCTION: The effectiveness of full dose azathioprine (FDA) for inflammatory bowel disease (IBD) has been questioned in recent scientific literature. A popular strategy to improve its outcomes recommends the use of low dose azathioprine with allopurinol co-therapy (LDAA) for patients profiled as "hypermethylators" (30% of non-responders).
AIMS & METHODS: Aims: The aim of this study was to determine the safety and efficacy of LDAA without using thiopurine metabolite (TM) profiling.
Methods: Records of IBD patients treated with LDAA were retrospectively analysed. Patients who had poor response and/or side-effects to FDA were offered LDAA by all consultants whilst a single IBD physician also offered LDAA to thiopurine-naïve patients. Azathioprine dose was reduced to 25% of the thiopurine methyl transferase (TPMT) adjusted dose (0.5mg/kg for wild type and 0.25mg/kg for heterozygotes) followed by conventional haematological monitoring. Non-adherence was assessed by TM measurements. Full response (FR) was defined as steroid free remission (Harvey Bradshaw index ≤3, Truelove-Witts normal) for greater than 3 months after a 3 month induction period for LDAA.
RESULTS: Of 300 LDAA patients, adequate data was available for 295 cases. Group 1 (G1) were treated 1st line (n,105) and Group 2 (G2) were switched from FDA to LDAA (n,190). Overall, for both groups, there were 207 (70%) full responders (FR), 20 partial responders (PR) and 68 non-responders (NR). Full response rate was 78% in G1 and 66% in G2. The commonest indication for switching to LDAA was non-response to FDA (n,118).

	Clinical Response (n)				
Indications for LDAA	**FR**	**PR**	**NR**	**TOTAL**	**Percentage FR**
AZA Naïve					
(LDAA without FDA exposure)	**82**	**7**	**16**	**105**	**78%**
Switched from FDA to LDAA	**125**	**13**	**52**	**190**	**66%**
Reason for switch to LDAA and outcomes					
Poor response	**81**	**10**	**27**	**118**	**69%**
GI intolerance	**16**	**0**	**11**	**27**	**60%**
Hepatotoxicity	**7**	**1**	**3**	**11**	**64%**
Myelotoxicity	**13**	**2**	**1**	**16**	**81%**
"Flu-like" symptoms	**3**	**0**	**1**	**4**	**75%**
Other	**5**	**0**	**9**	**14**	**36%**
Total	**207**	**20**	**68**	**295**	**70%**

Analysis of haematological indices revealed significant changes ($p<0.05$) in erythrocyte sedimentation rate, white cell count and platelet count after therapy induction.
Myelotoxicity occurred in 5 patients (all NR, WCC >2 and <3.5) and 12 patients had asymptomatic hepatotoxicity (ALT range: 100-700) which resolved by increasing allopurinol to 200 mg in 9 patients (all FR).
Time on treatment: 208 patients took LDAA for more than twelve months with a median length of therapy of 24 months.
CONCLUSION: Appropriately dosed LDAA therapy delivers a therapeutically effective dose of azathioprine without the need for dose escalation. It appears to be more effective, better tolerated and safer (less haematological disturbance) than FDA. These results will serve to allay the fear of toxicity of LDAA and question the need for thiopurine metabolite level profiling prior to using this apparently superior therapeutic approach.
Disclosure of Interest: None declared

P1458 ENDOSCOPIC BALLON DILATATION IN CROHN'S DISEASE: REAL IMPACT ON CLINICAL EVOLUTION OF THE DISEASE

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INTRODUCTION: Endoscopic recurrence after surgery for Crohn's disease (CD) is high; 50% of patients require additional surgery. Endoscopic balloon dilation (EBD) is an alternative to surgery, but data on safety and efficacy, as well as factors associated with the need for dilatation are limited.
AIMS & METHODS: The aim of this study was to determine the efficacy and safety of EBD in patients with CD with anastomotic strictures and to evaluate the factors associated with the need for dilatation.
Cross-sectional study of patients with CD who underwent ileocolectomy (stenosis/abscess) proposed for re-evaluation and endoscopic dilation between March/2010 and February/2014. Success of EBD was defined as passage of the scope into the ileum after dilatation.
RESULTS: Endoscopic evaluation of 100 patients (52% female) with a mean age of 44 ± 13 years; median follow-up was 12 months. Thirty-eight percent of patients had anastomotic stricture, of which 34 were dilated (success rate - 89.5%). There were no complications. Thirty-two patients had Rutgeerts score≥2. Twenty patients required a second dilatation, which was performed in median 11 months after the first procedure. The success of dilation avoided the need for surgery after dilatation (3.2% *vs* 50%, $p=0.014$, OR 0.094 [95% CI 0020-0447]). Patients with perianal disease, occlusive symptoms and active smokers required dilatation earlier after the first surgery ($p=0.042$, $p=0.003$ and $p=0.019$, respectively). Patients under treatment with immunomodulators had less dilatations (23.4% *vs* 52.8%, $p=0.003$) and underwent dilatation later (7161 ± 3158 *vs* 4030 ± 648, $p<0.001$).
CONCLUSION: EBD is a safe and effective procedure and avoids the need for surgery in most patients. Perianal disease, active smoking, occlusive symptoms and no therapy with immunomodulators are associated with the need for early dilatation.
Disclosure of Interest: None declared

P1459 INFLIXIMAB TROUGH LEVELS AND ANTIBODIES: ACADEMIC INTEREST OR USEFULNESS IN CLINICAL PRACTICE?

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INTRODUCTION: Infliximab (IFX) has demonstrated effectiveness in inducing and maintaining remission in Crohn's Disease (CD) and Ulcerative Colitis (UC). However, not all patients respond to the therapy and some lose response over time. Low trough levels and high antibodies titers have been associated with loss of response.
AIMS & METHODS: To evaluate the usefulness of trough levels and antibodies against IFX in the clinical management of patients with CD and UC we analyzed this group of patients followed in our IBD department. IFX trough levels and antibodies were performed in patients with clinical activity despite optimal therapy. Tests were performed using ELISA (Theranostic, Lisa-Tracker®).
RESULTS: A total of 109 patients were treated with IFX. 45 patients were included (27 females; mean age 44 + 13.2 years). 39 had CD and 6 UC. Average time of IFX therapy was 48 months. 27 (60%) patients were under combined therapy with azathioprine and 10 had a previous abdominal surgery. Low IFX levels (0.01-1.5 μg/mL) were detected in 15 (33.3%) patients. 11 (24.4%) patients had detectable antibodies against IFX (5-240 UA).
Of the 11 patients with antibodies against IFX: 72.7% were on combined therapy with azathioprine, 7 (64%) had antinuclear antibodies (ANA) and 5 (45%) had anti-dsDNA. All patients presenting with anti-dsDNA (n = 5) had simultaneously antibodies against IFX.
Endoscopic evaluation around the laboratory date was performed in 17 patients and, despite normal IFX level and absence of antibodies, 5 patients didn't show endoscopic remission.
This data led to stopping IFX in 7 (15.5%) patients, dose adjustment in 12 (26.7%) and introduction of methotrexate in 2 (4.4%). Of the 7 who stopped IFX, 6 were started on Adalimumab and one on methotrexate monotheraphy.
CONCLUSION: In our study, infliximab trough levels and antibodies provided important information, leading to optimization of therapy in 47% of patients. It may demonstrate a useful tool in the management of IBD patients, especially in those with clinical or endoscopic activity despite optimized therapy. Our data suggests a link between IFX antibody formation and other antibodies especially anti-dsDNA.
Disclosure of Interest: None declared

P1460 WEIGHT-BASED MAINTENANCE DOSING OF GOLIMUMAB IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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INTRODUCTION: Given that body weight is the most significant covariate affecting golimumab (GLM) pharmacokinetics, a weight-based approach to dosing was evaluated.
AIMS & METHODS: A posthoc analysis evaluated efficacy in the PURSUIT Maintenance study by body weight (<80kg v ≥80kg; 90 and 100kg cutoffs were also evaluated). Outcomes included clinical response (≥30% and ≥3 points decrease from induction baseline Mayo score, with either a rectal bleeding subscore of 0/ 1 or a decrease of ≥1), clinical remission (Mayo score ≤2 points; no subscore >1), and mucosal healing (endoscopy subscore 0/1). The analysis included patients (pts) with moderately to severely active ulcerative colitis (UC) who were in clinical response to GLM induction therapy and were randomized (1:1:1) to receive placebo (PBO) or subcutaneous GLM 50mg or 100mg every 4 wks through wk 52. *P* values were not adjusted for multiplicity.
RESULTS: 456 pts had clinical response to GLM induction, were randomized, and included in efficacy analyses (8 pts excluded owing to site misconduct); 29% discontinued before wk 52. In the <80kg group, the percentage of pts who maintained clinical response through wk 54, remission at both wk 30 and 54, and mucosal healing at both wk 30 and 54 was generally greater for GLM than PBO; the 2 GLM dose groups had similar magnitudes of response (table). In the ≥80kg group, all outcomes were better for the 100mg dose than the 50mg dose, which had outcomes similar to the PBO group. Similar patterns of efficacy were observed using a 90kg cutoff. A 100kg cutoff was also evaluated, but very few pts had weight >100kg. Given the smaller number of pts ≥90kg or ≥ 100kg, the results should be interpreted with caution. An 80kg cutoff resulted in a greater percentage of patients achieving GLM concentrations favorable for efficacy in UC.
Table. Efficacy Outcomes by Treatment Type and Body Weight.

	Body Weight <80kg			Body Weight ≥80kg		
Outcome, n (%)	PBO n = 105	GLM 50mg n = 108	GLM 100mg n = 100	PBO n = 49	GLM 50mg n = 43	GLM 100mg n = 51
Clinical response through wk 54	31 (29.5)	53 (49.1)[b]	49 (49.0)[a]	17 (34.7)	18 (41.9)[d]	26 (51.0)[c]
Clinical remission at wk 30 and 54	15 (14.3)	28 (25.9)[c]	29 (29.0)[a]	9 (18.4)	7 (16.3)[d]	13 (25.5)[d]
Mucosal healing at wk 30 and 54	27 (25.7)	47 (43.5)[b]	41 (41.0)[a]	14 (28.6)	16 (37.2)[d]	23 (45.1)[d]

CONCLUSION: In patients with UC with body weight ≥80kg, achievement of optimal efficacy outcomes, including sustained remission, with GLM treatment was more likely with a 100mg maintenance dose than a 50mg dose. Overall, the safety profile for GLM in UC was similar to previous reports for GLM in other indications; no new adverse events were identified. (Financial support for this study was provided by Janssen Research & Development, LLC., Spring House, PA, USA.)
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P1461 AZATHIOPRINE FOR THE TREATMENT OF PERIANAL CROHN'S DISEASE

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INTRODUCTION: Crohn's disease may be complicated by perianal disease, which can lead to faecal incontinence, abscess formation and stricturing. The management of perianal lesions is complex, with surgery often performed in conjunction with medical therapy. Thiopurines have been employed in the management of perianal Crohn's disease, although evidence of their efficacy is rare.
AIMS & METHODS: The aim of this study was to evaluate whether azathioprine healed perianal Crohn's disease.
Thirty-five patients (20 males and 15 females, mean age: 31 years) with active perianal Crohn's disease were treated with azathioprine for more than 6 months. The evolution of perianal lesions during azathioprine therapy was analyzed retrospectively. Patients who had a clear anatomic improvement (fistula closure, fissure healing, and stricture dilatation) were considered responders regarding their perianal disease.
RESULTS: There were 28 patients (80%) with an anal fistula, 13 patients (37.1%) with anal ulcerations, and five patients (14.3%) with an anal stricture. In 43% of patients, the anal manifestations preceded any evidence of intestinal disease.
Twelve patients (34.2%) required surgical drainage and three patients (8.5%) required anal dilatation.
Response to azathioprine was noted in 28 of the 35 patients (80%), with complete healing in 16 patients (45.7%). Subsequently, five patients (14.3%) relapsed to some degree on azathioprine.
CONCLUSION: Azathioprine is an effective and useful drug in the treatment of perianal Crohn's disease.
Disclosure of Interest: None declared

P1462 LONG TERM EFFICACY OF GRANULOCYTE-MONOCYTE-APHERESIS IN ULCERATIVE COLITIS. THE ITALIAN REGISTRY OF THERAPEUTIC APHERESIS

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INTRODUCTION: Granulocyte-monocyte-apheresis (GMA) is effective in the treatment of ulcerative colitis (UC). However, all published studies evaluated a low number of patients, with an overall limited follow-up. This observational study investigates the long-term efficacy of GMA in a large number of patients included in the Italian Registry of Therapeutic Apheresis.
AIMS & METHODS: Data of patients with mild/moderate UC treated with a standard protocol of GMA (5 sessions in 5 weeks) were evaluated. All patients had failed to respond to mesalamine or sulphasalazine, and were under steroid treatment. Clinical evaluations were performed at 3, 12 and 24 months since the end of GMA session. The following parameters were assessed: incidence of clinical remission (CAI [Colits Active Index] <4); CAI; erythrocyte sedimentation rate (ESR); c-reactive protein (CRP); white cells blood count (WBC). Endoscopical evaluations were performed at a 3-month follow-up: the incidence of endoscopical remission (EAI [endoscopical activity index] 0/1) was assessed.
RESULTS: Data for 347 patients (214 males, age 46.3 years; CAI 7.47) were available; 288 patients were either steroid-resistant or steroid-dependent. The proportion of patients with remission of disease was 66% at 3 months, 77% at 12 months and 78% at 24 months. At 24 months, all other efficacy parameters had improved from baseline: CAI (7.47 vs 3.47), ESR (35.87 vs 24.1 mm/h), CRP (4.31 vs 2.75 mg/dl) and WBC (8.61 vs 7.19) ($p<0.001$ for all comparisons). Endoscopic data were available for 107 patients. The incidence of mucosal healing was 47% and all patients with mucosal healing presented a clinical remission over the entire follow-up period. No major adverse events were reported during GMA sessions.
CONCLUSION: Data collected on a large sample of steroid-resistant or steroid-refractory patients included in the Italian Registry of Therapeutic Apheresis show that GMA is a safe and effective procedure over a long-term follow-up. Mucosal healing appears strongly associated with clinical remission.
Disclosure of Interest: None declared

P1463 IDENTIFICATION OF NEUTRALIZING ANTI-INFLIXIMAB ANTIBODIES

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INTRODUCTION: About 60% of Infliximab (IFX)-treated inflammatory bowel disease patients (IBD) develop anti-drug antibodies (ADA) with a sizable population suffering from loss of response (LOR). However, these antibodies were shown to be heterogeneous, some of which have no therapeutic consequences. Defining their neutralizing potential has marked therapeutic significance.
AIMS & METHODS: The aim of the study is to assess the neutralizing capability of infliximab ADA.
A biological assay in which TNF-α induced IL-8 secretion from HT-29 cells followed by application of IFX and control pooled IBD sera, or ADA-containing sera was developed. Thereafter, IL8 amplification ratio was determined for each serum relative to controls. In parallel, an immune test was developed in which the IFX concentration in a standard solution was determined before and after its incubation with ADA positive sera compared to control.
RESULTS: Forty seven infliximab ADA positive patients (43% female, 68% Crohn's disease) were tested. Of those, sera of 41 patients (87%) contained biologically active antibodies that inhibited IFX activity in both the cellular and immune models. No difference in the ability to detect the ADA neutralizing effect was noted between assays. Using the immune assay, the average IFX reduction ratio of 31 serums from patients with clinical LOR was 4.7 ± 3.1 compared to 2.1 ± 1.5 in patients without LOR ($p=0.0003$). Notably, the ADA concentration measured by anti-lambda ELISA of both groups was similar (13.9 and 11.6 μg/ml respectively $p=0.38$). Using a cutoff value of 2.5, the test had sensitivity and specificity of 77% and 72% respectively and positive and negative predictive values of 82% and 65% respectively. Antibody extraction lead to loss of the neutralizing effect in the bioassay pointing to its immune specificity. When early sera from IFX-treated patients with no detected ADA and no IFX (double negatives) obtained from patients without, or with subsequent LOR were compared, the IFX reduction ratios were 0.64 and 1.27 respectively ($p=0.01$). Sera from patients with transient antibodies who maintained clinical remission had no inhibitory effect as well (ratio of 0.55; $p=0.004$ compared to the LOR group).
CONCLUSION: Two assays for detection of neutralizing ADA were developed and compared. No advantage was found for the more complex bioassay. A predictive potential of the test was identified, allowing to identify patients prone to develop immunogenic LOR. These findings may assist in optimizing infliximab therapy in IBD patients.
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P1464 5-AMINOSALICYLIC ACID IS EFFECTIVE AS REMISSION INDUCTION THERAPY IN PATIENTS WITH MODERATE TO SEVERE INTESTINAL BEHÇET'S DISEASE

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INTRODUCTION: Behçet's disease (BD), the so-called silk road disease is a chronic relapsing-remitting autoimmune disorder with multiple organ system involvement characterized clinically by oral and genital aphthae, cutaneous lesions, ophthalmological, neurological, or gastrointestinal manifestations. Up to 16% of patients with BD have gastrointestinal (GI) involvement, discrete ulcerations are most often seen in the terminal ileum, caecum, and ascending colon, responsible for intestinal complications like severe bleeding and perforation. Various drugs including 5-aminosalicylic acid (5-ASA) preparations, systemic corticosteroids, and immunosuppressive agents have been applied anecdotally to treat intestinal BD. However, the clinical evidence regarding the management of intestinal BD is very limited.
AIMS & METHODS: We were interested to evaluate the efficacy and safety of 5-ASA as a remission induction therapy in patients with intestinal BD, in a retrospective cohort study. Data were obtained using a retrospective chart review of 54 consecutive patients with intestinal BD who were visiting a single centre in Japan between 2004 and 2013. The patients were clinically and endoscopically evaluated before treatment, then assessed after 12 weeks for a clinical response to 5-ASA, defined as a significant improvement of intestinal symptoms, and a reduction in C-reactive protein (CRP) level, as well as the disease activity index for intestinal BD (DAIBD). Clinical remission was defined as complete disappearance of GI symptoms, including abdominal discomfort, GI bleeding and diarrhoea, followed by normalization of serum CRP level. Clinical response was defined as a significant improvement in GI symptoms accompanied by a lower CRP level. To determine factors predictive of clinical response to 5-ASA therapy, we used the chi squared test for nominal variables and the t-test for continuous variables. We also assessed adverse events during 5-ASA therapy.

RESULTS: A total of 13 patients were treated for active intestinal BD with oral 5-ASA as remission induction therapy. Their average age was 26 years at the diagnosis of BD and 34 years at the initiation of 5-ASA therapy. The response rate was 77.0% (remission 30.8%, response 46.2%). Young age, high disease activity at the initiation of 5-ASA therapy, and short disease duration up to the initiation of 5-ASA were predictors for good clinical response to 5-ASA ($P < 0.05$). There was no severe adverse event warranting cessation of 5-ASA therapy.
CONCLUSION: In this study, 5-ASA as remission induction therapy was effective and safe in patients with moderate to severe intestinal BD. Further, use of 5-ASA as first-line medication in this clinical setting is potentially interesting as it spares the patients from exposure to stronger drugs with safety concerns.
Disclosure of Interest: None declared

P1465 PARTHENOLIDE AMELIORATES EXPERIMENTAL COLITIS ASSOCIATED COLON CANCER BY INHIBITION OF NF-KB SIGNALING

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INTRODUCTION: Parthenolide (PT), a NF-kB inhibitor, has recently been demonstrated as a promising anticancer agent that promotes apoptosis of cancer cells. We previously showed that PT suppresses tumor growth in a xenograft model of colorectal cancer cells by regulation of Bcl-2 family. Unfortunately, little is known about its role in the process of tumor development in colitis associated colon cancer (CAC).
AIMS & METHODS: Therefore, this study was designed to investigate the effects of PT on an experimental murine CAC model. Experimental CAC was induced by azoxymethane (AOM) and dextran sulfate sodium (DSS). Mice were divided into 3 groups: AOM+DSS, AOM+DSS+2mg/kg PT and AOM+DSS+4mg/kg PT.
RESULTS: We demonstrated that administration of PT significantly reduced the severity of AOM/DSS-induced CAC as assessed by histological analysis, and resulted in downregulation of phospho-NF-κB p65 expression by the blockade of phosphorylation and subsequent degradation of IκB-a. Administration of PT ameliorated the carcinogenesis through the downregulation of antiapoptotic protein Bcl-2 and Bcl-xL mediated by inhibition of NF-kB activation. Moreover, apoptosis and caspase-3 expression also increased markedly in PT administration group.
CONCLUSION: These findings demonstrate that PT downregulates NF-kB resulting in initiation of apoptosis and eventual suppression of CAC development, suggesting that PT exerts beneficial effects in experimental CAC and could therefore be a potential chemopreventive and therapeutic agent of CAC.
Disclosure of Interest: None declared

P1466 CCR9 INHIBITOR VERCIRNON CLINICAL TRIALS IN CROHN'S DISEASE

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INTRODUCTION: Vercirnon (previously called CCX282-B or Traficet-EN) is an oral, specific C-C chemokine receptor 9 inhibitor that has been studied in Crohn's disease (CD). A Phase 2b clinical trial, PROTECT-1, showed evidence of activity of vercirnon in patients with moderate to severe Crohn's disease. A subsequent Phase 3 trial, SHIELD-1, failed to confirm efficacy. The data from the two trials were examined to determine the potential source for the contrasting outcomes.
AIMS & METHODS: Both trials were randomized, double-blind, placebo controlled. SHIELD-1 recruited 608 and PROTECT-1 436 subjects world-wide; the latter excluded the USA. In SHIELD-1, subjects had CDAI 220-450, and endoscopically confirmed disease, or an elevated CRP and fecal calprotectin. Subjects received placebo, 500 mg QD or BID vercirnon for 12 weeks. In PROTECT-1, entry criteria were CDAI 250-450 and CRP $\geq$7.5mg/L. Subjects received placebo or CCX282-B 500 mg QD, 250 mg QD or BID for 12 weeks. Key endpoints: CDAI $\geq$100-point response, CDAI remission, and CDAI $\geq$70-point response.
RESULTS: Areas of differences between the two trials are summarized in the table.
Table to abstract P1466

	PROTECT-1 (N = 436)	SHIELD-1 (N = 608)
Prior TNF inhibitor use	26%	69%
CDAI median (range)	330 (249-471)	317 (123-450)
CRP (mg/L) median (range)	22 (3-200)	14 (0.2-157)
Drop-out rate	16%	25%
Gastrointestinal adverse events	Placebo: 40%, 500 mg QD: 41%	Placebo: 30%, 500 mg QD: 37%, 500 mg BID: 48%
Abdominal pain	Placebo: 13%, 500 mg QD: 12%	Placebo: 7%, 500 mg QD: 9%, 500 mg BID: 11%
Diarrhea	Placebo: 8%, 500 mg QD: 7%	Placebo: 1%, 500 mg QD: 4%, 500 mg BID: 5%
Vomiting	Placebo: 4%, 500 mg QD: 3%	Placebo: 2%, 500 mg QD: 6%, 500 mg BID: 9%

The most significant difference was the higher incidence of prior TNF inhibitor use in SHIELD-1 (69%) compared to PROTECT-1 (26%). Also, PROTECT-1 enrolled patients with more severe disease at baseline (CRP and CDAI higher). Lastly, more GI adverse events were found in SHIELD-1, in particular at the highest dose, 500 mg BID, which was not tested in PROTECT-1.
In the 244 patients from SHIELD-1 who would have met entry criteria for PROTECT-1, i.e., CDAI 250-450 and CRP $\geq$7.5 mg/L, the CDAI $\geq$100-point response at Week 12 was 31%, 45%, and 28% in the placebo, 500 mg QD, and BID groups, respectively. CDAI remission was 13%, 21%, and 9%, respectively, and CDAI $\geq$70-point response was 38%, 56% ($p = 0.02$ vs. placebo), and 39%, respectively. These results suggest activity at the 500 mg QD dose, shown efficacious in PROTECT-1. The higher 500 mg BID dose was associated with a higher incidence of GI AEs (see table), which may increase the CDAI.
CONCLUSION: PROTECT-1 and SHIELD-1 enrolled patient populations that differed mostly in terms of prior TNFI use, disease activity at baseline, and GI AEs. These differences, may at least partly account for the divergent outcomes.
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P1467 DISSOLUTION OF COMMERCIALLY AVAILABLE 5-AMINOSALICYLIC ACID (5-ASA) FORMULATIONS AT VARIOUS PH LEVELS

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INTRODUCTION: Ulcerative colitis (UC) is a chronic inflammatory condition that can affect any part of the colon and is characterized by relapsing–remitting gastrointestinal (GI) and systemic symptoms. Treatment with 5-ASA, a topical, locally acting compound that reduces inflammation of the colonic mucosa, is recommended as first-line therapy in patients (pts) with active mild-to-moderate UC. Minimum systemic absorption in the upper GI tract is desired in order to maximize the amount of drug available for local action in the colon. Thus, many 5-ASA formulations employ a pH-dependent release mechanism, designed to dissolve in the more basic environment of the distal small intestine. The pH levels in the GI tract of pts with UC may be lower and more variable than that of unaffected individuals. This in vitro study compared the release of mesalazine from multimatrix mesalazine (Mezavant® XL; Shire Development LLC, USA) and 5 other commercially available 5-ASA formulations.
AIMS & METHODS: The release of 5-ASA from 12 tablets each of multimatrix mesalazine 1.2 g, Mesalazin-Kohlpharma 500 mg (Kohlpharma, Germany), Mesalazin-Eurim 500 mg (Eurimpharm, Germany), Claversal 500 mg (Faes Farma, Spain), Mesalazine EC 500 mg (Actavis, Netherlands), and Mesalazine EC 500 PCH 500 mg (Pharmachemie, Netherlands) was monitored separately at 3 different pH conditions using United States Pharmacopeia dissolution apparatus II, with a paddle speed of 100 rpm. Tablets of each formulation were individually exposed to dissolution medium at pH 1 for 2 h, pH 6.4 for an additional 1 h, and pH 7.2 monitored until complete drug release. After the first 2 h, samples were collected every hour and analyzed by UV spectroscopy at 330 nm. The dissolution percentage was calculated as a mean of 12 units for each formulation.
RESULTS: At pH 1 and pH 6.4, <1% 5-ASA release was observed for each of the 5-ASA formulations. Dissolution profiles for each of the formulations at pH 7.2 (after exposure to pH 1 for 2 h and pH 6.4 for 1 h) are shown in the **Table**. At pH 7.2, 5-ASA was completely released from all generic 5-ASA formulations in about 2 h. Release of 5-ASA from multimatrix mesalazine occurred in a sustained manner over 7 h.

Time at pH 7.2, h	Mesalazin-Kohlpharma 500 mg (% dissolution)	Mesalazin-Eurim 500 mg	Claversal 500 mg	Mesalazine EC 500 mg	Mesalazine EC 500 PCH 500 mg	Multimatrix mesalazine 1.2 g
0	<1	<1	<1	<1	<1	<1
1	36	26	51	102	103	8
2	102	100	101	101	103	26
3	102	101	101	101	103	43
4	102	101	101	101	103	63
5	102	101	101	101	103	84
6	102	101	101	101	102	98
7	102	101	101	101	102	102
8	102	101	101	101	102	102

CONCLUSION: Results of this in vitro study indicate little to no drug release at more acidic pH conditions for all products. At pH 7.2, differences in the respective dissolution profiles suggest that multimatrix mesalazine would result in roughly 5 more hours of sustained release of the drug compared with any of the other examined commercially available 5-ASA formulations.
Disclosure of Interest: S. Tenjarla Shareholder of: Shire, Other: Employee of Shire.

P1468 PROSPECTIVE, LONGITUDINAL OBSERVATIONAL STUDY IN THERAPEUTIC MANAGEMENT OF MILD TO MODERATE ULCERATIVE COLITIS (OPTIMUM): FOLLOW-UP AT ONE YEAR

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INTRODUCTION: OPTIMUM study was set up in France in 2011. Its objective was to describe the progression and methods of therapeutic management of mild to moderate ulcerative colitis (UC), to assess remission rate, duration of remissions and prognostic factors for relapse in patients with a flare-up.
AIMS & METHODS: From June 2011 to June 2012, 812 patients over 18 years of age with a mild to moderate flare-up of UC (51% women, average age of 45 ± 15 years) were included in the observational study by 130 gastroenterologists (64% office based). A three-years monitoring is planned. The time period selected for a visit to one year is 365 ± 100 days after the inclusion visit.
RESULTS: In July 2013, the one-year visit data (time period of 369 ± 42 days) was available for 504 patients (62%); 419 (83%) were in remission during the first year. According to the UCCS score (Ulcerative Colitis Clinical Score), at one-year visit, 397 (79%) patients were in remission, 67 (13%) had mild activity and 33 (7%) had moderate activity. Remission was achieved after a median period of 59 days (95% CI [53–77 days]) after the inclusion consultation. At the end of the visit, treatment with 5-ASA alone was prescribed in 479 patients (59%), treatment combining 5-ASA and another UC treatment in 175 patients (22%) and another UC-treatment not including 5-ASA in 99 patients (12%). The UC treatment at the period of remission was the one prescribed at the end of the inclusion visit in 366 patients (87%). After adjusting for the UCCS score and the level of injury at visit, the patients treated solely with 5-ASA at the end of the inclusion visit were in remission faster than the patients treated without 5-ASA ($p = 0.013$); but the difference with patients treated with 5-ASA in combination with another treatment was not statistically significant ($p = 0.062$). At one year, the remission rate was 82.5% (95% IC [78.0%–86.6%]) in the group treated with 5-ASA alone prescribed at the end of the inclusion visit vs 71.4% (95% IC [64.0%–78.4%]) in the group treated with 5-ASA in combination with another treatment. At the one-year visit, a UC treatment was in on going in 426 patients (84%). Compliance was good in 92 of 394 patients (23%). In total, at least one adverse event was reported in 15 patients (3%). Colorectal cancer or dysplasia was diagnosed in three patients (0.6%).
CONCLUSION: During treatment, the period of remission of mild to moderate UC flare-up is about two months. After one year of monitoring, about 80% of patients are in remission. The continuation of the OPTIMUM observational study will help refine these results and, in particular, analyse possible relapses over three years of monitoring.
Disclosure of Interest: G. BONNAUD Consultancy for: Honorarium, S. NAHON Consultancy for: Honorarium (Coordinator of the study), G. TUCAT Consultancy for: Honorarium, P. NIEZ Directorship (s) for: Medical Director Ferring France.

P1469 DISCORDANCE BETWEEN PATIENTS AND PHYSICIANS IN LONG-TERM USE OF STEROIDS: RESULTS FROM A PATIENT- AND PHYSICIAN-REPORTED SURVEY

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INTRODUCTION: POLARIS, a cross-sectional study employing paper-based questionnaires, assessed treatment patterns from the patients with Crohn's disease (CD) and their health care providers (HCPs). We assessed the concordance in patients and their HCPs' responses regarding the use of steroids, immunosuppressants, and biologics.
AIMS & METHODS: Surveys were administered at inflammatory bowel disease (IBD) centres and community practices in Canada and Germany. Patients ≥18 years old with a confirmed diagnosis of CD, disease duration ≥1 year and ≥2 visits with a participating HCP (consulting gastroenterologist, nurse practitioner, or physician's nurse) were eligible. Patients and their HCPs provided information on steroid use (oral steroids excluding budesonide), steroid monotherapy use, long-term (≥3 months) use of steroids, long-term use of steroid monotherapy, immunosuppressant use, and biologics use. Data were summarised overall, and by IBD centres and community practices using descriptive statistics. Agreement between patients' and HCPs' responses to survey questions was tested using kappa statistics.
RESULTS: Surveys from 809 patients and 798 HCPs were available for this analysis. Overall, a greater percentage of patients vs. HCPs reported use of any steroid (25.9% vs. 20.8%, kappa = 0.735), steroid monotherapy (4.4% vs. 3.7%, kappa = 0.514), long-term steroids (67.7% vs. 63.8%, kappa = 0.598), and long-term steroid monotherapy (11.6% vs. 7.2%, kappa = 0.433). It should be noted that the agreements between patients and HCPs were much lower in community practices than in IBD centres in all measures: use of any steroid (kappa = 0.609 vs. 0.781), steroid monotherapy (0.425 vs. 0.575), long-term steroid use (0.263 vs. 0.663), and long-term steroid monotherapy (0.250 vs. 0.520). Overall, responses from patients and their HCPs were similar regarding use of immunosuppressants (52.4% vs. 51.1%, kappa = 0.784) and biologics (49.5% vs. 47.0%, kappa = 0.909) with lower agreements observed in community practices than in IBD centres (use of immunosuppressants: kappa = 0.715 vs 0.807; use of biologics: kappa = 0.861 vs. 0.928).
Medication Use for CD in Past 12 Months.

	IBD Centres				Community Practices			
	HCPs		PTs		HCPs		PTs	
	N	%	N	%	N	%	N	%
Any steroid used	550	22.4	546	27.3	249	17.3	229	22.7
Steroid monotherapy	547	2.7	539	3.5	247	5.7	207	6.8
Long-term (≥3 months) steroid use	116	61.2	141	64.5	36	72.2	48	77.1
Long-term (≥3 months) steroid monotherapy	116	6.0	141	8.5	36	11.1	48	20.8
Immunosuppressant use	557	57.1	551	56.1	251	37.9	232	43.5
Biologics use	558	51.4	558	52.9	251	37.1	240	41.7

CONCLUSION: Results of this cross-sectional survey revealed a discordance between patients and their HCPs regarding the long-term use of steroids. The discordance was more severe in community practices than in IBD centres. These findings suggest a need to improve the care management, e.g., more coordinated follow-up visits by patients, or enhanced communication between patients and their HCPs.
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P1470 DIFFERENT METHODOLOGIES FOR DETERMINING MAYO SCORE IN CLINICAL STUDIES CAN INFLUENCE DISEASE ACTIVITY ASSESSMENTS IN ULCERATIVE COLITIS

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INTRODUCTION: There is no standard method to determine stool frequency (SFS) and rectal bleeding (RBS) subscores of the Mayo score in ulcerative colitis (UC) clinical trials. In adalimumab (ADA) clinical trials, SFS and RBS were calculated using the worst value from 3 days of patient diary entries (ie, worst-rank methodology).[1,2] Other clinical trials in UC have calculated RBS and SFS using the average of each subscore from the past 3 days of patient diary entries.[3,4] Recently, data from a placebo-controlled study of ADA in Japanese patients suggested that the Mayo subscore calculation method used can influence the effect size of remission rates by several percentage points.[5] The impact of the use of different Mayo score determination methods on Mayo scores in ULTRA 2[2] has not been described.
AIMS & METHODS: In this exploratory analysis, we evaluated the impact of worst vs average score methodology for SFS and RBS by recalculating Mayo scores in ULTRA 2 using the average scoring methodology for patients from sites with readily-available daily diary data. In ULTRA 2, adults with UC and a Mayo score of 6–12 with endoscopy score ≥2 were randomised to ADA (160 mg/80 mg at wks 0/2 followed by 40 mg every other wk to Wk 52) or placebo (PBO).[2] Daily diary data of 16 patients who completed the Wk 52 study visit on their originally randomised treatment (PBO: n = 7; ADA: n = 9) were evaluated. Means for full Mayo scores (FMS) at baseline and Wk 52 were recalculated using the average of daily SFS and RBS from the 3 prior days and compared to FMS obtained using the worst-rank methodology. For the average calculations, SFS and RBS were rounded to the nearest integer.
RESULTS: Average scoring methodology led to greater reduction in mean FMS from baseline to Wk 52 than worst-rank methodology in ADA-treated patients compared to PBO-treated patients (**Table**). The absolute difference in change in FMS from baseline to Wk 52 between ADA and PBO was 0.59 points greater using average scoring methodology than worst-rank methodology.

	ADA (n = 9)			PBO (n = 7)			Absolute difference between overall Δ of ADA and PBO
	FMS		Δ	FMS		Δ	
Methodology	**Baseline**	**Wk 52**		**Baseline**	**Wk 52**		
Worst	9.11	2.89	6.22[a]	9.57	4.29	5.28[a]	
Average	9.00	2.33	6.67[a]	9.00	3.86	5.14[a]	
Overall Δ			−0.45[b]			0.14[b]	0.59

Δ, difference between scores. [a]Difference between baseline and Wk 52. [b]Difference between Δ of worst-rank and average scores.

CONCLUSION: These preliminary results suggest that differences between Mayo scores calculated using worst-rank vs average scoring methodology for SFS and RBS may have a disproportionate effect between active treatment and PBO arms. These results should be confirmed in larger and more diverse data sets.

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P1471 VACCINATION GUIDELINES: ARE WE MISSING THE TARGET WHEN INJECTING OUR PATIENTS?

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INTRODUCTION: Early and increasing use of Immunomodulators (IM) and biological agents in IBD can lead to an increase in the risk of opportunistic infections (OI). The RR of OI is 2.9 with one IM and increases to Odds ratio of 14.5 with ≥2 concomitant IMs. Age (>50 years) is an independent risk factor for OI. Vaccinations are recommended by the European Crohn's and Colitis Organisation (ECCO) to minimise OI in immunocompromised IBD patients after initial screening.

The current recommendation is to screen for Varicella Zoster Virus (VZV), latent or active Tuberculosis (TB) and Hepatitis-B and to administer annual inactivated Influenza vaccine, Pneumococcal (0 & 5 year) and Hepatitis-B (if seronegative) vaccinations. Swine Flu vaccination was also recommended following the outbreak in 2009.

AIMS & METHODS: Retrospective data was collected on the serology status for Hepatitis-B, Hepatitis-C, Varicella zoster and T-spot/ IGRA of our patients receiving biologics from pathology results reporting system. Chest X-rays were picked up from PACS, BCG vaccination status and history of Chicken pox was obtained from the clinic letters.

Information about vaccination status was obtained by contacting the general practioners, directly from patients visiting for their infliximab infusions and IBD MDT minutes.

RESULTS: Retrospective data from our 144 patients (70 (48%) female and 74 (52%) male) showed a total of 479 patient years of biologics exposure (infliximab-319 and adalimumab-160) in our cohort of Crohns 112 (78%) and Ulcerative colitis 32 (22%) patients. Combination therapy (Biologics and IM) was noted in 48 (33%) (45 azathioprine and 3 methotrexate) and biologic monotherapy in 98 (67%) patients.

TB screening with IGRA was done in 144 (100%) and CXR in 53 (37%). Hep B, Hep C and VZV serology/history of chicken pox was noted in 26 (18%), 19 (13%) and 12 (8%) respectively.

Yearly flu vaccination was given to 16% of the patients and pneumococcal vaccine was administered in less than 11% of patients.

CONCLUSION: Relevant serological screening and appropriate vaccination history pre-IM therapy was available in a minority of patients only. This may represent either non/poor-adherence to ECCO guidelines or poor documentation. Information leaflets on the ECCO-recommended vaccines directed at GPs and patients may improve compliance. Adoption of IBD registry will enable clinicians and IBD nurses to empower patients with relevant personalised information delivered at diagnosis and during the course of their treatment. This may increase the appropriate screening and vaccination of these patients at highest risk of developing opportunistic infections.

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P1472 TIME TO SYMPTOM RESOLUTION IN PATIENTS WITH ULCERATIVE COLITIS ON MULTIMATRIX MESALAZINE TREATMENT: A POOLED ANALYSIS

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INTRODUCTION: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by relapsing-remitting symptoms of abdominal pain, stool urgency, and rectal bleeding. While endoscopic remission is the ultimate treatment goal for patients with UC, alleviation of clinical symptoms (mainly rectal bleeding and stool frequency) is a signal that physicians can use to assess remission status. Improvements in UC symptom scores have also been shown to correlate with improvements in patients' quality of life. Mesalazine (5-aminosalicylic acid; 5-ASA) is standard first-line therapy for treatment of mild-to-moderate UC. This study examined pooled data from several clinical trials of multimatrix mesalazine, a once-daily (QD) formulation of 5-ASA, in patients with UC to assess time to symptom resolution in acute treatment, and for those achieving clinical remission, the proportion of patients remaining in remission after 12 months of maintenance treatment.

AIMS & METHODS: Data from three phase 3 (NCT00503243; NCT00548574; NCT00151944) and two phase 4 (NCT00446849; NCT01124149) trials were pooled for this analysis. During acute treatment, patients were randomized to receive either placebo or multimatrix mesalazine 2.4 g/day QD or twice-daily (BID), or 4.8 g/day QD or BID for a period of 8 weeks. All patients achieving symptom resolution (scores of 0 for both stool frequency and rectal bleeding on a modified UC Disease Activity Index on each of the last available 3 days immediately prior to a study visit) by the end of the acute phase were eligible for 12 months of continued treatment with multimatrix mesalazine 2.4 g/day in a maintenance phase. In 1 study (NCT01124149), those in partial remission (including combined scores ≤1 on stool frequency and rectal bleeding) at the end of the acute phase were also allowed to enroll in the maintenance phase; however, those patients were excluded from the pooled maintenance phase analysis.

RESULTS: In the acute phase, median (95% confidence interval) time to resolution for placebo and multimatrix mesalazine 2.4 g/day, 4.8 g/day, and 2.4 + 4.8 g/day, respectively, for stool frequency symptoms was: 52 days (45, not estimable

[NE]); 33 days (23, 46); 38 days (35, 43); and 38 days (34, 41). For rectal bleeding, median time to resolution was: 35 days (20, NE); 14 days (12, 18); 16 days (14, 17); and 15 days (14, 17). For stool frequency and rectal bleeding combined, median time to resolution was: NE (56, NE); 41 days (30, 48); 45 days (42, 50); and 45 days (41, 48). Of those who achieved symptom resolution at the end of acute phase, the following percentages of patients maintained scores of 0 after 12 months of maintenance treatment: 68.2% (462/677) for stool frequency; 68.3% (721/1055) for rectal bleeding; and 67.4% (438/650) for combined symptoms.
CONCLUSION: Overall, acute phase treatment with multimatrix mesalazine (either dose) led to symptom resolution in a shorter time compared with placebo (38 vs 52 days for stool frequency; 15 vs 35 days for rectal bleeding). In addition, more than 6 in 10 patients were able to maintain symptom resolution after 12 months of maintenance treatment with multimatrix mesalazine.
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P1473 PROTEOGLYCAN IS EFFECTIVE AND SAFE IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Proteoglycan (PG) is a component of extracellular matrix materials that exist in connective tissues, such as skin, bone, cartilage and vascular wall. PG has been reported to potently suppress the inflammatory responses induced by heat-killed *Escherichia coli* in mouse macrophages.
AIMS & METHODS: We aimed to evaluate the efficacy and safety of oral PG intake in the treatment of ulcerative colitis (UC). In a placebo-controlled, double-blind study, 40 patients with UC were randomized into either a PG group or a placebo group for 8 weeks. PG was extracted from salmon nasal cartilage. All patients were treated with conventional medications prior to entry. Colonoscopy was done before and at the end of 8 weeks of treatment. Efficacy of treatment was assessed from clinical symptoms using the clinical activity index (CAI), which covers stool consistency, rectal bleeding, abdominal pain and global assessment, with a maximum score of 20. Endoscopic findings were assessed using the endoscopic index (EI), which is derived from a 12-point scale from observations at the most severe area of disease involvement within the area 5–15 cm from the anal verge.
RESULTS: EI scores significantly decreased ($P < 0.05$) in patients in the PG group, but showed no significant change in patients in the placebo group. CAI score significantly ($P < 0.05$) improved among patients with mild UC (CAI score < 6 at enrollment). No side effects were noted in any patient in either the PG or placebo group.
CONCLUSION: PG was safe and useful in these patients with UC as an additional therapy to conventional therapies, particularly in those at the mild stage.
Disclosure of Interest: None declared

P1474 THE IMPACT OF MUCOSAL HEALING ON SUBSEQUENT CLINICAL COURSE IN THE MANAGEMENT OF ULCERATIVE COLITIS: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: In clinical trials of ulcerative colitis (UC), mucosal healing (MH) has been achieved with medical treatment such as 5-aminosalicylates (5-ASAs), corticosteroids, immunosuppressive drugs, and biologic agents. However, clinical implications of MH remain unclear.
AIMS & METHODS: This study was to prospectively evaluate the impact of MH on the subsequent clinical course in the management of UC. We included 112 UC patients who achieved clinical remission (normal stool frequency and no rectal bleeding) with medical treatment (5-ASAs, corticosteroids, leukocytapheresis, immunosuppressants, and/or biologics), and who underwent endoscopic examination when the clinical remission was confirmed. MH was defined as a Mayo endoscopic subscore of either 0 (no lesions) or 1 (mild activity). All patients were followed up for $>$ 1 year.
RESULTS: Of the 112 patients, 62 (55%) achieved MH and 50 (45%) did not. During the 1-year follow-up, 74 patients (66%) maintained clinical remission, while 38 patients (34%) relapsed. Overall, the clinical remission rate was significantly higher in patients who achieved MH (52/62, 84%) than in those who did not (22/50, 44%) ($p = 0.00001$). In a subgroup analysis of patients who received 5-ASA for remission maintenance therapy, the clinical remission rate was significantly higher in patients with MH (25/32, 78%) than in those without MH (13/32, 41%) ($p = 0.002$). Similarly, among patients who received immunosuppressive drugs and/or biologic agents during maintenance therapy, the clinical remission rate was significantly higher in patients with MH (27/30, 90%) than in those without MH (9/18, 50%) ($p = 0.002$).
CONCLUSION: Patients who achieve clinical remission with MH have a reduced risk of future clinical relapse as compared with those without MH in the management of UC.
Disclosure of Interest: None declared

P1475 SHORT AND MEDIUM TERM EFFICACY OF ADALIMUMAB IN ULCERATIVE COLITIS – A MULTICENTRE, PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: Adalimumab is a relatively new therapeutic option in ulcerative colitis (UC). After the ULTRA trials only a few data have been published from the real clinical practice.
AIMS & METHODS: The aim of this study was to prospectively follow the disease course in adalimumab-treated UC patients in Hungary. Primary endpoints were the remission and response rates at week 12 and 30; while secondary endpoints were the changes of C-reactive protein (CRP) levels and the clinical symptoms during the therapy.79 patients who was treated with adalimumab at 10 tertiary Hungarian IBD centres were prospectively enrolled from May 2013 [male/female: 43/36; mean age: 41.7 years (in range: 19-68 years)]. 65.8% of the patients previously received infliximab therapy. Switch to adalimumab in these patients was due to loss of response or intolerance. Clinical data, partial Mayo (pMayo) score and CRP levels were collected at the beginning of adalimumab therapy, at week 12 and at week 30. Colonoscopy was performed before drug administration. Endoscopic Mayo subscore was used to assess the mucosal activity. Clinical remission was defined as $\leq$2 points in pMayo score; response to adalimumab was specified as decreasing 3 or more points.
RESULTS: Adalimumab induction was administered at doses of 160 mg and 80 mg at week 0 and week 2. The mean value of Mayo score at the beginning of adalimumab therapy was 9.7 points. The mean values of pMayo subscores and CRP were 3.5 points, 6.6 mg/l at week 12, and 3.2 points, 7.8 mg/l at week 30, respectively. CRP levels and pMayo subscores decreased significantly at week 12 ($p < 0.001$, $p < 0.001$), and at week 30 remained significant also ($p = 0.027$, $p < 0.001$). Remission, response and non-response rates were 28.8 %, 43.9%, and 27.3% at week 12, and remission, response, loss of response rates were 50%, 40.9% and 9.1% at week 30. No significant difference was detected between patients previously treated with biologicals or naive to them. In addition, we did not find significant association between previous infliximab use and frequency of adalimumab side effects. Adalimumab therapy needed to be discontinued in 12 subjects.
CONCLUSION: Our results suggest that adalimumab is an effective drug for the induction of remission and for the maintenance therapy of UC.
Disclosure of Interest: None declared

P1476 SENSITIVITY ANALYSES OF DISEASE CONTROL AMONG MODERATE TO SEVERE ULCERATIVE COLITIS PATIENTS TREATED WITH CONVENTIONAL THERAPIES IN EUROPE: THE UC CARES (ULCERATIVE COLITIS CONDITION, ATTITUDE, RESOURCE AND EDUCATIONAL STUDY)

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INTRODUCTION: A large proportion of moderate to severe ulcerative colitis (UC) patients rely on conventional therapies (5-ASA, steroids and/or thiopurines) to maintain remission. However, use of UC therapies among biologic naïve patients varies considerably in clinical practice, and it is unknown whether disease is well controlled.
AIMS & METHODS: This analysis is to comprehensively describe rates of disease control in moderate to severe UC patients who were biologics naïve and treated with conventional therapies.
Biologics-naïve patients with moderate to severe active UC (Mayo score $\geq$6), aged $\geq$18 years who received conventional therapies during the 12 months prior to enrollment were recruited from 11 European countries. Patients who underwent colectomy procedure or ileo-anal J-pouch reconstruction were excluded. Medical charts for the 12 months prior to enrollment were reviewed to collect clinical data. The primary endpoint was disease control, defined as maintaining remission status, measured by full or partial Mayo scores, and patients had to have no corticosteroid use the 2 months prior to enrollment.
Sensitivity analyses were conducted according to the criteria whether the patients had thiopurines for at least 4 months in 12 months prior to enrollment and the timeline (within 2 weeks vs. 2 weeks before; winthin 1 month vs. 1 month before) when endoscopy was taken for the patients.
RESULTS: A total of 250 patients were included in the final analysis. Patients' mean age was 46.6 (SD = 16.3) and 59% were male. The median duration of UC was 6.9 years (IQR 2.3-14.4). Extent of UC included 21.6% proctitis, 28.4% left-sided, and 49.6% extensive colitis. At the enrollment date, the percentages of patients receiving thiopurines, aminosalicylates, corticosteroids and other types

of immunosuppressants were 63.2%, 75.2%, 23.6% and 3.6%, respectively. According to the study definition, 87.2% of patients did not achieve disease control. Specifically, 87.3% of patients (55 out of 63) with endoscopy score within the 2 weeks prior to enrollment and 87.2% of patients (163 out of 187) with endoscopy score more than 2 weeks prior to enrollment had uncontrolled disease ($p = 0.98$). In addition, 86 out of 98 patients (87.8%) with endoscopy score within 1 month prior to enrollment and 132 out of 152 patients (86.8%) with endoscopy score more than 1 month were not in disease control ($p = 0.83$). Patients who had thiopurines for at least 4 months in 12 months prior to enrollment had numerically higher percentage of uncontrolled UC (89.1% vs. 85.9%, $p = 0.46$)

CONCLUSION: The majority of biologics naïve UC patients (87%) were not under control. Sensitivity analyses show that patients who had thiopurines for at least 4 months in 12 months prior to enrollment had numerically higher percentage of uncontrolled UC, but not significant difference. Disease control did not vary much according to the time of endoscopy measurement, noting that patients who had more than one endoscopy may be counted in each applicable group.

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P1477 ESOPHAGEAL ULCER FEATURES OF BEHCET'S DISEASE WITH GASTROINTESTINAL LESIONS?

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INTRODUCTION: The Japanese diagnostic criteria for Behcet's disease (BD) define it as a systemic inflammatory disorder characterized by 4 hallmark symptoms (recurrent oral aphthosis, skin symptoms, ocular symptoms, and vulvar ulceration), which can coexist with other accessory/variant symptoms (such as arthritis) that develop metachronously. BD is categorized as complete, incomplete, or suspected according to the extent of this symptom tetrad, while BD with ileocecal ulcer, vascular, and/or nervous system involvement is categorized under special types. That is, if ileocecal ulcer, vascular, or neurological symptoms are present in patients with BD, the disease is classified as gastrointestinal BD, vascular BD, or CNS-BD, respectively. Gastrointestinal lesions associated with Behcet's disease typically develop in the ileocecal ulcer, but atypical gastrointestinal lesions also often occur. This article presents our patients who had BD with esophageal ulcers, which is an atypical gastrointestinal lesion, and outlines the clinical and endoscopic features of their esophageal involvement.

AIMS & METHODS: At our hospital, 33 patients were diagnosed as having BD with gastrointestinal lesions and drug-induced mucosal injury was ruled out (sex ratio = 17:16; 3 patients with complete BD, 25 patients with incomplete BD, and 5 patients with suspected BD; special types = 14 with gastrointestinal BD, 3 with vascular BD, and 1 with CNS-BD (some patients duplicated)). Among these 33 patients, those who had esophageal lesions were retrospectively reviewed to assess their disease types and endoscopic features.

RESULTS: Among the 33 patients, esophageal lesions were found in 4 patients (12.1%). Their sex ratio was 1:1 and their mean age was 35.75±22.42 years. They had incomplete BD, although all 4 patients had oral aphthosis (skin symptoms in 2, ocular symptoms in 2, vulvar ulceration in 0, arthritis in 3, and vascular lesions in 1 patient). They all complained of chest pain. Ileocecal ulcers were found in 3 of the 4 patients. Their esophageal ulcers were located in the mid-esophagus at a mean of 33±4.27 cm from the incisors. These ulcers were generally round and punched-out in all 4 patients, although fused bead-like lesions were also observed. Three patients had multiple esophageal lesions, and one had a single lesion. Three of the 4 patients suffered relapse of esophageal ulcers that was clearly associated with exacerbation of BD. All 4 patients were treated with corticosteroids, and adalimumab was also administered to one patient to control other symptoms. With corticosteroid therapy, chest pain did not relapse, and upper gastrointestinal endoscopy confirmed healing of the esophageal lesions after 44 weeks of treatment.

CONCLUSION: Esophageal ulcers were mostly located at the mid-esophagus in BD. Their ulcers were generally round and punched-out, and also tended to be fused. The ulcers relapsed repeatedly as occurs with ileocecal lesions, which may be a characteristic of BD.

Disclosure of Interest: None declared

P1478 IS MUCOSAL HEALING ACHIEVED AFTER ADALIMUMAB TREATMENT IN ULCERATIVE COLITIS?

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INTRODUCTION: Because Crohn's disease (CD) is described as corresponding to a Th1-proinflammatory, TNF-α-mediated response and ulcerative colitis (UC) is considered to be mediated by a Th2 immune response is adalimumab just as suitable in UC as in CD?

AIMS & METHODS: To evaluate mucosal healing in UC by examining the intracellular changes of colonic mucosa, before and after adalimumab treatment. We studied sixteen patients (14 women, 21-65 years) previously diagnosed with UC of moderate-severe form (Disease Activity Index-UCDAI > 6, Endoscopic Index-EI > 4). All patients were treated with adalimumab (Humira) subcutaneous, at standard doses as it follows: 160 mg at week 0.80 mg at week 2 and afterwards 40 mg at a 2 week interval. We performed a colonoscopy before and 6 months after the first administration of adalimumab. During colonoscopy we collected biopsies that were later processed specifically, stained with uranyl acetate and lead citrate and examined with a JEM-1010 transmission electron microscope.

RESULTS: Before treatment we noticed severe alterations of the epithelium-depletion of microvilli, shattering of epithelial junctions, cytoplasmic vacuolization, dilatation of the endoplasmic reticulum, pycnotic nuclei, destruction of mitochondria and Golgi complexes which conducted to drastic reduction of cell metabolism. Rarefaction of the goblet cells, together with abnormal mucus formation and secretion was observed. The corresponding chorion showed degeneration of collagen fibres and smooth muscle cells, obstructed capillaries, neutrophilic and mononuclear infiltration. After adalimumab therapy, we noticed improvement in morphology and function of epithelial organelles, rich mucus secretion and recovery of the chorionic components. The clinical response observed in all our patients was supported by a descent in UCDAI. Endoscopic severity diminished as well- with 14 out of 16 cases entering remission (EI≤4).

CONCLUSION: Our study clearly demonstrated signs of epithelial barrier recovery at the end of treatment which is one of the main goals of UC treatment. Also the ultrastructural features that we described, might help to a deeper understanding of UC pathogenicity and mechanism of action of the anti-TNF-alpha therapies.

Disclosure of Interest: None declared

P1479 CYCLOSPORIN A IN ACUTE STEROID-REFRACTORY OR DEPENDENT ULCERATIVE COLITIS: A PROSPECTIVE STUDY ON LONG TERM OUTCOME

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INTRODUCTION: In severe corticosteroid refractory ulcerative colitis (UC) cyclosporine A (CsA) or infliximab (IFX) are advantageous to avoid colectomy, and their effectiveness is comparable (*Laherie et al. Lancet 2012*).

AIMS & METHODS: The aim of this prospective study (IBD-HOT) was to evaluate the use, efficacy, and safety of CsA in treatment of acute flare of UC. All consecutive patients with moderate to severe CU refractory, intolerant to or dependent on corticosteroids and treated with CsA between Jan-2007 and Dec-2009 were enrolled. Inclusion criteria were active ulcerative colitis with a total Mayo score of 6 to 12 and moderate-to-severe active disease at colonoscopy. Patients' outcome and adverse effects were followed-up for three years or until colectomy as the major endpoint. Clinical and laboratory data were collected at the beginning of CsA therapy and at routine scheduled visits. Patients' survival w/o colectomy was analysed by Kaplan-Meier survival analysis.

RESULTS: 61 patients (28 female) fulfilled the inclusion criteria. Mean age was 35 years (MED 33, Range 18-64). CsA induction therapy was given intravenously to 40 patients for seven days (MED 7, Range 4-8), and mean dose was 2.15 mg/kg (MED 2.0, Range 1.8-3.6). Oral induction was given to 21 patients with mean dose of 3.8 mg/kg (MED 3.8, Range 2.4-5.5). Eight patients had used thiopurins before CsA longer than two weeks, but only three of them longer than 2 months. Other patients started thiopurins during CsA induction (46 pts) or soon thereafter (7 pts). The mean MAYO scores declined significantly during the beginning of the follow-up period and stayed low thereafter. The clinical response to CsA during the one-week induction period was scored as good in 18 (29.5%), moderate in 26 (42.6%), only partial in 15 (24.6%) and poor in 2 (3.3%) patients.

Colectomy-free survival at 3 years was 72.1 % (95% CI 60.9 – 83.4). Number of colectomies during the 3-year follow-up period was 17 (27.9 %) due to continuously active colitis (14 pts) or colonic mucosal dysplasia (3 pts). All colectomised patients had disease duration under 5 years, and short disease duration was the only independent risk factor for colectomy in multivariate regression analysis including gender, hemoglobin, albumin, C-reactive protein and disease duration. Disease duration had marginally significant predictive value for colectomy ($p = 0.049$; Odds Ratio 0.74, 95% CI 0.54 - 1.00).

In addition to colectomies, two patients were re-treated with CsA during the follow-up, and twelve with infliximab due to active disease. Seven (58.3 %) of IFX treated patients needed colectomy subsequently. Thus outcome after CsA rescue therapy without colectomy or need for CsA re-treatment or infliximab was 62.3 % (95% CI 50.1 – 74.5).

Adverse events were registered in seven patients: *Cytomegalo* viral infection (3), *Pneumocystis jirovecii* infection (1), *Clostridium difficile* colitis (1), transaminase elevation (1), venous thrombosis (1).

CONCLUSION: CsA treatment was successful in 72% of patient who avoided colectomy, and we see CsA as good option in moderate-to-severe acute corticosteroid refractory or corticosteroid resistant thiopurin naïve UC. Short disease duration was independent risk factor for colectomy. Risk of infection under high immunosuppression must be remembered.

Disclosure of Interest: None declared

P1480 ACCEPTANCE OF INFLAMMATORY BOWEL DISEASE TREATMENT RECOMMENDATIONS BASED ON APPROPRIATENESS RATINGS: DO PRACTICING GASTROENTEROLOGISTS AGREE WITH EXPERTS?

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INTRODUCTION: Appropriateness criteria for the treatment of Crohn's disease (CD) and ulcerative colitis (UC) have been developed by experts' panels. Little is known about the acceptance of such recommendations by care providers. We aimed to explore how treatment decisions of practicing gastroenterologists differ from experts using a vignette case study and a focus group.
AIMS & METHODS: Seventeen clinical vignettes were drawn from clinical indications evaluated by the expert panel. A vignette case questionnaire asking for treatment options in 9-10 clinical situations was submitted to 26 practicing gastroenterologists. For each vignette case, practitioners' answers were compared to panel decisions by calculating the proportions of treatments judged by the panels as being appropriate, uncertain and inappropriate. Qualitative analysis was made based on focus group discussion to explore acceptance and divergence reasons.
RESULTS: 239 clinical vignettes were completed, 98 for CD and 141 for UC. Proposed treatments were more frequently considered inappropriate as compared to results from panels for CD (45%) than for UC (27%). Among UC clinical vignettes, the main divergences with the panel were linked to 5-ASA failure assessment and to situations where stopping treatment was the main decision. For CD, the care provider propositions diverged with the panel in mild-to-moderate active disease, where practitioners were more aggressive than the panel's recommendations and in stenotic complications management.
CONCLUSION: In about one third of vignettes cases, IBD treatment propositions by practicing gastroenterologists were considered inappropriate as compared to expert recommendations. Practicing gastroenterologists may not always know current evidence and guidelines, but are often aware of the difficulties of applying recommendations in real IBD patients.
Disclosure of Interest: None declared

P1481 TEN YEARS PROSPECTIVE STUDY OF INFLIXIMAB TREATMENT IN ULCERATIVE COLITIS PERFORMING AN ALGORITHM OF DISCONTINUATION

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INTRODUCTION: Anti-tumor necrosis factor (TNF) has the last decade become an important part of the treatment of severe ulcerative colitis (UC), but there is no international consensus of discontinuation of the therapy.
AIMS & METHODS: To study the long term time of remission performing a prospective study using an algorithm of discontinuation of the anti-TNF drug infliximab (IFX) in UC
UC patients with moderate to severe disease activity admitted at the University Hospital of North Norway in the period 2002-2011 were enrolled. Patients in the need of IFX were enrolled in a prospective study performing the following algorithm: intensive induction therapy (week 0, 2, 6, later each 4 week) until remission according the UCD activity index score (UCDAI) (score 0-2), discontinuation of treatment with subsequent re-induction of IFX treatment if relapse.
RESULTS: Of the 132 patients enrolled in the study 116 patients were evaluated according to the protocol. The mean total observation time was 43 (6-117) months and the patients were in remission 70% of the total observation time. Of the 3 first inductions therapies 96/116 (83 %), 37/61 (61 %) and 10/19 (53 %) were treated to remission, respectively. The mean time of remission was 20, 19 and 12 moths in the 3 first induction therapies, respectively, and predictors of long term remission was sex (woman) and non-smoking. The number of patients in remission that never relapsed was 58/96 (60 %), and sex (woman) was a predictor for never relapse. Eighteen patients (18 %) were withdrawn due to need of colectomi, 10 (8 %) patients were withdrawn due to severe allergic reactions.
CONCLUSION: An intensified IFX induction regime of treatment to remission in patients with UC followed by a discontinuation of treatment showed high efficacy even in the re-treatments, and a high overall time being in remission. There was no tendency of increased allergic reaction to IFX during repeated induction therapies.
Disclosure of Interest: None declared

P1482 SUSTAINED USE OF THIOPURINES REDUCES THE RISK OF PERIANAL SURGERY IN CROHN'S DISEASE

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INTRODUCTION: The thiopurine (TP) analogues, azathioprine and mercaptopurine are widely used in the management of Crohn's disease (CD). Recent studies suggest they reduce the risk of intestinal resection, but their impact on perianal surgery is unknown.
AIMS & METHODS: Our aim was to determine if TPs reduced the risk of perianal surgery in CD.
We conducted a population based study using electronic primary care records in the UK using a validated research database, the Clinical Practice Research Datalink (CPRD) which represents an 8% sample of the UK population. We identified incident cases of CD between 1995 and 2009 by selecting patients registered with a practice for at least 12 months prior to diagnosis. We excluded patients who had perianal surgery before or at the time of diagnosis. We grouped patients according to treatment duration and compared rates of first perianal surgery using Kaplan-Meier survival analysis. We used a multivariable Cox proportional hazards model to adjust for confounders and compare outcomes according to duration of treatment. We used separate models for each duration of use: $\geq$12 months vs $<$12 months, $\geq$18 months vs $<$18months and $\geq$24 months vs $<$24 months. We also evaluated early TP use, within 12 months of diagnosis.
RESULTS: Overall, 5235 patients met our inclusion criteria, of whom 124 had perianal surgery during 15 years of follow up. 56.3% were female and the median age at diagnosis was 38.5 years (IQR: 24.8 – 57.1). TP use for $\geq$12 months duration did not impact on the 5 year cumulative probability of perianal surgery when compared with TP use for $<$12 months. However, the unadjusted 5 year cumulative probability of perianal surgery for those using TPs for $\geq$18 months was 2.9% (95% CI: 2.0 – 4.3%) compared to 5.8% (95% CI: 4.0 – 8.2%) for those using TPs for less than $<$18 months (log-rank test for trend $p = 0.02$). After adjustment, sustained TP use for $\geq$18 months had a 40% reduction in risk of perianal surgery (HR 0.60, 95% CI: 0.39 – 0.95, $p = 0.03$) which improved to 49% (HR 0.51, 95% CI: 0.32 – 0.99, $p = 0.004$) at 2 years. Early TP use did not offer any additional benefit.
CONCLUSION: Sustained TP use in patients with CD halves the risk of perianal surgery at 2 years, although a long duration of treatment is required. We suggest sustained use of TPs for greater than 18 months duration in patients with perianal CD and propose further study to evaluate rates of perianal surgery in CD which at present is unknown.
Disclosure of Interest: None declared

P1483 IN IBD OUTPATIENTS KNOWLEDGE OF FECAL CALPROTECTIN AND INFLIXIMAB TROUGH LEVELS SIGNIFICANTLY ALTERS CLINICAL DECISION MAKING

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INTRODUCTION: Infliximab is an effective, but costly, therapy for inflammatory bowel disease (IBD). Loss of response to infliximab will occur in over 50% of patients within 3 ys, resulting in infliximab dose intensification. One third of patients with symptoms do not have actual disease recurrence.
AIMS & METHODS: Aim: The aim of this study was to determine if objective measures of inflammation using fecal calprotectin (FCP), and infliximab trough levels (ITL) would lead to different management decisions of patients on infliximab than those made when only clinical assessment was available.
Methods: IBD patients receiving maintenance infliximab at the University of Alberta IBD infusion center were consented to provide stool and blood samples for measurement of FCP and ITL prior to their infusion. FCP and ITL levels were determined by immunodiagnostic ELISA. At the time of the infusion clinical HBI and Mayo scores were recorded. An IBD panel made a "clinical decision" based on the clinical assessment recorded. The decision options were no action or an action (scope, increase dose or switch drug, decrease dose). The panel then incorporated FCP to the "clinical decision" to determine "clinical + FCP decision"; and ITL to the "clinical + FCP decision" to determine the "clinical + FCP + ITL decision". The "clinical decision" was compared to the "clinical + FCP decision" or "clinical + FCP + ITL decision", and actions analyzed for concordance.

Table to abstract P1483
Table 1 Contingency Table Showing Impact of Adding FCP and ITL to Expert Panel Clinical Decisions

			Expert Panel Decision (Clinical plus FCP)			
N = 36			No change N = 19	Investigate (Scope) N = 16	Dose escalation N = 1	Dose de-escalation N = 0
Expert Panel Clinical Decision	**No change**	N = 29	19/36 (52.8%)	**10/36 (27.8%)**	0	0
	Investigate (scope)	N = 6	0	6/36 (16.7%)	0	0
	Dose escalation	N = 1	0	0	1/36 (2.8%)	0
	Dose de-escalation	N = 0	0	0	0	0

RESULTS: A total of 36 patients were included (25 CD and 11 UC). As shown in Table 1, the addition of FCP to expert panel clinical decisions led to a change in decisions 10/36 (27.8%) of the cases – all of which were from no change to investigate (scope). The addition of ITL to the expert panel clinical plus FCP decision led to a change in decisions 10/36 (27.8%) of the cases – 6/36 (16.7%) were from no change to infliximab dose de-escalation.
CONCLUSION: The addition of an infliximab trough level or a fecal calprotectin level, incorporated via a fixed algorithm or an expert IBD panel, frequently led to different management decisions compared to clinical assessment alone. The incorporation of fecal calprotectin and infliximab trough levels into daily care requires careful assessment of their effect on outcomes.
Disclosure of Interest: None declared

P1484 CHARACTERIZATION OF MUCOSAL HEALING WITH ADALIMUMAB TREATMENT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE FROM EXTEND

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INTRODUCTION: Patients (Pts) continuously treated with adalimumab (ADA) in the EXTEND trial were more likely to achieve and maintain mucosal healing (MH) than pts receiving induction ADA only/placebo (PBO) treatment.[1] MH of the individual ileocolonic segments with ADA maintenance therapy is evaluated in pts from EXTEND.
AIMS & METHODS: In EXTEND, pts with Crohn's disease (CD), CDAI 220-450, and documented mucosal ulceration at study screening, received open-label (OL) ADA (160/80 mg) at wks 0/2. Pts were randomized at wk 4 to double-blind maintenance ADA (40 mg every other wk) or PBO to wk 52. Pts with flare/non-response could move to OL ADA at or after wk 8. Change from baseline (BL) in the CDEIS variables surface involved and ulcerated surface were assessed in each of the five ileocolonic segments at wks 12 and 52 only in pts who had measurements at all three time points. The presence of deep and superficial ulcers was assessed at wks 12 and 52 in pts who had deep and superficial ulcers at BL. All scores were based on central reading data. Pts were analyzed according to randomized treatment group. For pts who moved to OL ADA after wk 12, the CDEIS variable score at time of moving to OL ADA was used as the wk 52 data point. Pts who moved to OL ADA before wk 12 are not included in this analysis.
RESULTS: Improvement in surface involved was observed in all segments at wk 12 in induction ADA/PBO pts and at wks 12 and 52 in ADA randomized pts (Table). Statistically significant greater mean change from BL in surface involved was observed in the rectum, sigmoid/left colon, and transverse colon at wk 52 in ADA randomized pts compared to induction ADA/PBO pts (Table). Similar results were observed for CDEIS ulcerated surface. Of the pts with deep or superficial ulcers at BL, more ADA randomized pts were without deep (13/20, 65.0%) and superficial ulcers (11/24, 45.8%) relative to induction ADA/PBO pts at wk 52 (no deep 5/20, 25.0%; no superficial ulcers 2/20, 10.0%).
Table. Mean BL values of CDEIS surface involved by segment and randomized treatment group and mean change from BL at wks 12 and 52.

	Induction ADA/PBO			ADA maintenance		
	BL mean, cm	Δweek 12, cm	Δweek 52, cm	BL mean, cm	Δweek 12, cm	Δweek 52, cm
Rectum	5.0 (N = 14)	-2.3	-0.5	3.9 (N = 12)	-3.8*	-3.6**
Sigmoid/left colon	5.5 (N = 14)	-3.0	1.4	3.6 (N = 15)	-3.4	-3.2***
Transverse colon	4.0 (N = 10)	-0.5	0.5	4.9 (N = 12)	-4.6**	-3.7**
Right colon	4.8 (N = 9)	-2.7	-2.7	3.7 (N = 7)	-3.1	-2.6
Ileum	5.2 (N = 8)	-1.1	-0.1	4.0 (N = 13)	-2.4	-2.2

CONCLUSION: ADA maintenance therapy was beneficial in healing deep and superficial ulcers in pts with moderately to severely active CD. Although continuous ADA treatment improved the mucosal surface of all ileocolonic segments, the greatest improvement was in the rectum, left colon, and transverse colon.
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Disclosure of Interest: W. Reinisch Consultancy for: AbbVie, Aesca, Amgen, Astellas, Astra Zeneca, Biogen IDEC, Bristol-Myers Squibb, Cellerix, Chemocentryx, Celgene, Janssen, Danone Austria, Elan, Ferring, Genentech, Grünenthal, Johnson & Johnson, Kyowa Hakko Kirin Pharma, Lipid Therapeutics, Millenium, Mitsubishi Tanabe Pharma Corporation, MSD, Novartis, Ocera, Otsuka, PDL, Pharmacosmos, Pfizer, Procter & Gamble, Prometheus, Robarts Clinical Trial, Schering-Plough, Setpointmedical, Shire, Takeda, Therakos, Tigenix, UCB, Vifor, Yakult, Zyngenia, Austria and 4SC., J.-F. Colombel Consultancy for: for AbbVie, Bristol Meyers Squibb, Ferring, Genentech, Giuliani SPA, Given Imaging, Merck & Co., Millenium Pharmaceuticals Inc., Pfizer Inc. Prometheus Laboratories, Sanofi, Schering Plough Corporation, Takeda, Teva Pharmaceuticals, UCB Pharma (previously named Celltech Therapeutics, Ltd)., G. D'Haens Financial support for research from: Abbott Laboratories, Janssen Biologics, Given Imaging, MSD, DrFalk Pharma, Photopill, Lecture fee(s) from: Abbott Laboratories, Tillotts, Tramedico, Ferring, MSD, UCB, Norgine, Shire, Consultancy for: AbbVie, ActoGeniX, AM Pharma, Boehringer Ingelheim GmbH, Centocor, ChemoCentryx, Cosmo Technologies, Elan Pharmaceuticals, Engene, Dr Falf Pharma, Ferring, Galapagos, Giuliani SpA, Given Imaging, GlaxoSmithKline, Jansen Biologics, Merck Sharp and Dohme Corp, Millennium Pharmaceuticals Inc. (now Takeda), Neovacs, Novonordisk, Otsuka, PDL Biopharma, Pfizer, Receptos, Salix, Setpoint, Shire Pharmaceuticals, Schering-Plough, Tillotts Pharma, UCB Pharma, Versant and Vifor Pharma, W. Sandborn Financial support for research from: AbbVie, Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Janssen, Millennium, Novartis, Pfizer, Procter and Gamble Pharmaceuticals, Shire Pharmaceuticals, and UCB Pharma., Lecture fee(s) from: AbbVie, Bristol-Myers Squibb, and Janssen, Consultancy for: AbbVie, ActoGeniX NV, AGI Therapeutics, Inc., Alba Therapeutics Corporation, Albireo, Alfa Wasserman, Amgen, AM-Pharma BV, Anaphore, Astellas, Athersys, Inc., Atlantic Healthcare Limited, Aptalis, BioBalance Corporation, Boehringer-Ingelheim Inc, Bristol-Myers Squibb, Celgene, Celek Pharmaceuticals, Cellerix SL, Cerimon Pharmaceuticals, ChemoCentryx, CoMentis, Cosmo Technologies, Coronado Biosciences, Cytokine Pharmasciences, Eagle Pharmaceuticals, Eisai Medical Research Inc, Elan Pharmaceuticals, EnGene, Inc., Eli Lilly, Enteromedics, Exagen Diagnostics, Inc., Ferring Pharmaceuticals, Flexion Therapeutics, Inc., Funxional Therapeutics Limited, Genzyme Corporation, Genentech, Gilead Sciences, Given Imaging, GlaxoSmithKline, Human Genome Sciences, Ironwood Pharmaceuticals, Janssen, KaloBios Pharmaceuticals, Inc., Lexicon Pharmaceuticals, Lycera Corporation, Meda Pharmaceuticals, Merck Research Laboratories, MerckSerono, Merck & Co., Millennium, Nisshin Kyorin Pharmaceuticals Co., Ltd., Novo Nordisk A/S, NPS Pharmaceuticals, Optimer Pharmaceuticals, Orexigen Therapeutics, Inc., PDL Biopharma, Pfizer, Procter and Gamble, Prometheus Laboratories, ProtAb Limited, Purgenesis Technologies, Inc., Receptos, Relypsa, Inc., Salient Pharmaceuticals, Salix Pharmaceuticals, Inc., Santarus, Shire Pharmaceuticals, Sigmoid Pharma Limited, Sirtris Pharmaceuticals, Inc. (a GSK company), S. L. A. Pharma (UK) Limited, Targacept, Teva Pharmaceuticals, Therakos, Tillotts Pharma AG, TxCell SA, UCB Pharma, Viamet Pharmaceuticals, Vascular Biogenics Limited (VBL), Warner Chilcott UK Limited, P. Rutgeerts Financial support for research from: AbbVie, Centocor, Merck and UCB Pharma, Lecture fee(s) from: AbbVie, Centocor, Merck and UCB Pharma, Consultancy for: AbbVie, Bristol-Myers Squibb, Centocor, Merck, Millennium Pharmaceuticals Inc. (now Takeda) and UCB Pharma, J. Petersson Shareholder of: AbbVie, Other: Employee: AbbVie, S. Eichner Shareholder of: AbbVie, Other: Employee: AbbVie, Q. Zhou Shareholder of: AbbVie, Other: Employee: AbbVie, A. Iezzi Shareholder of: AbbVie, Other: Employee: AbbVie, R. Thakkar Shareholder of: AbbVie, Other: Employee: AbbVie.

P1485 DURABILITY OF CLINICAL REMISSION WITH VEDOLIZUMAB IN CROHN'S DISEASE

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INTRODUCTION: Efficacy and safety of vedolizumab (VDZ) in patients with Crohn's disease (CD) were demonstrated in the GEMINI 2 study.[1] However, the proportion of patients with durable clinical remission (secondary end point; Crohn's Disease Activity Index [CDAI] score ≤150 points at 11 of 13 [80%] visits from wks 6-52) was not significantly different between the VDZ and placebo (PBO) groups. To account for factors that may have led to this result (eg, previous VDZ induction therapy in maintenance PBO patients coupled with the long half-life of VDZ), we defined alternative post hoc end points to further evaluate the effects of VDZ on durable clinical remission.
AIMS & METHODS: In GEMINI 2, patients with CD were randomly assigned to receive blinded VDZ 300 mg or PBO or open-label VDZ 300 mg at wks 0 and 2 of the induction phase (wks 0-6). Wk 6 VDZ responders were rerandomized to receive VDZ 300 mg every 8 wks (Q8W; n = 154) or every 4 wks (Q4W; n = 154) or PBO (n = 153) during the maintenance phase (wks 6-52). In post hoc analyses, durable clinical remission end points were defined as a CDAI score of ≤150 points at 60% (8/13) of maintenance phase visits, at wks 6 and 52, and at 10 of 12 visits from wks 10 to 52.
RESULTS: Mean baseline (wk 0) CD duration was 8.4 y in the VDZ Q8W group, 7.7 y in the VDZ Q4W group, and 9.6 y in the PBO group. Mean baseline CDAI score (Q8W, 325.5; Q4W, 317.0; PBO, 325.2) and previous failure of tumor necrosis factor (TNF) antagonists (Q8W, 55%; Q4W, 50%; PBO, 51%), immunosuppressants but not TNF antagonists (Q8W, 32%; Q4W, 35%; PBO, 32%), and corticosteroids only (Q8W, 13%; Q4W, 14%; PBO, 16%) were similar among the groups. Percentages of patients with durable clinical remission based on 60% (8/13) of visits and at both wks 6 and 52 were significantly higher with Q8W and Q4W than with PBO (Table). Percentages of patients with durable remission based on >80% (10/12) of visits from wks 10 to 52 were significantly higher for Q4W and numerically higher for Q8W than for PBO (Table).

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	VDZ		
	Q8W n = 154	Q4W n = 154	PBO n = 153
Durable remission based on 60% (8/13) of visits[a]	49 (31.8)	42 (27.3)	30 (19.6)
P value	0.003	0.022	-
Remission at wks 6 and 52[b]	30 (57.7)	26 (60.5)	22 (39.3)
P value	0.040	0.020	-
Durable remission based on 10 of 12 visits from wks 10-52	37 (24.0)	33 (21.4)	24 (15.7)
P value	0.060	0.044	-

CONCLUSION: The definition of *durable clinical remission* has not been standardized. These post hoc analyses of patients with CD, including those with previous TNF antagonist failure, showed that VDZ (vs PBO) led to durable clinical remission through wk 52 as defined by multiple clinically relevant alternative end points.

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P1486 RELATIONSHIP BETWEEN CLINICAL OUTCOMES AND DISEASE DURATION, EXTENT, AND SEVERITY IN PATIENTS WITH ULCERATIVE COLITIS WHO RECEIVED 6 WEEKS OF TREATMENT WITH GOLIMUMAB

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INTRODUCTION: To determine the relationship between baseline disease characteristics and efficacy of golimumab (GLM) treatment in patients with moderately to severely active ulcerative colitis (UC).

AIMS & METHODS: The PURSUIT induction study included patients with Mayo scores of 6–12 inclusive, including endoscopic subscore ≥2. Patients were randomized to receive at wk 0/2 either placebo (PBO)/PBO; GLM 200mg/100mg; or GLM 400mg/200mg. At wk 6, clinical response (≥30% and ≥3 points decrease from baseline Mayo score, with a decrease in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1) was analyzed by disease duration (≤5 y, >5 to ≤15 y, or >15 y), extent (limited v extensive), and severity (Mayo <9 v ≥9) at baseline. Missing data were considered nonresponse. *P* values were not adjusted for multiplicity.

RESULTS: 761 patients were randomized and included in efficacy analyses (13 patients were excluded owing to site misconduct). 98% of patients completed to wk 6. Overall, a greater percentage of patients had clinical response in both GLM dose groups than the PBO group (200/100mg: 51%, 400/200mg: 55%, PBO: 30%). This pattern was similar for patients in each category of disease duration, disease extent, and Mayo score (table). Excluding the longest disease duration group that had the smallest number of patients, odds ratios for differences between the GLM and PBO groups varied from 2.0–3.5; all differences from PBO were statistically significant.

CONCLUSION: Clinical response to 2 doses of GLM treatment (200/100mg or 400/200mg at wks 0/2) was consistently achieved in approximately 50% of patients at wk 6 regardless of UC disease duration, extent, or severity at baseline. Overall, safety was comparable among treatment groups through wk 6.

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Table Percentage of Patients With Clinical Response at Wk 6 by Disease Characteristics at Baseline

		PBO N, (% response)	200/100mg N, (% response)	OR vs PBO (95% CI)	400/200mg N, (% response)	OR vs PBO (95% CI)
All patients		251 (30)	253 (51)	2.4 (1.66, 3.45)[a]	257 (55)	2.8 (1.94, 4.03)[a]
UC duration, y	≤5	143 (32)	143 (52)	2.3 (1.44, 3.76)[a]	139 (51)	2.2 (1.36, 3.57)[a]
	>5 to ≤15	84 (29)	91 (53)	2.8 (1.49, 5.23)[a]	93 (58)	3.5 (1.85, 6.48)[a]
	>15	24 (25)	19 (32)	1.4 (0.36, 5.28)	25 (64)	5.3 (1.55, 18.30)[a]
Extent of disease	Limited	143 (33)	148 (49)	2.0 (1.24, 3.20)[a]	146 (58)	2.8 (1.71, 4.47)[a]
	Extensive	107 (27)	105 (53)	3.1 (1.73, 5.45)[a]	111 (51)	2.8 (1.61, 5.00)[a]
Mayo score	<9	141 (31)	117 (54)	2.6 (1.55, 4.28)[a]	129 (57)	2.9 (1.75, 4.73)[a]
	≥9	110 (29)	136 (49)	2.3 (1.35, 3.91)[a]	128 (53)	2.8 (1.61, 4.73)[a]

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P1487 ADHERENCE TO ULCERATIVE COLITIS TREATMENT: DETAILS MATTER

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INTRODUCTION: The adherence of patients to their therapy is essential for the success of treatment. Many determinants of adherence, especially in the long-term treatment of ulcerative colitis (UC), are, however, still inadequately understood. There is some evidence that frequency of administration and dosage form affect acceptance and compliance with mesalazine therapy.
AIMS & METHODS: The aim of this prospective, non-interventional study was to identify factors that influence adherence to mesalazine therapy in patients with UC.
In 113 specialized private gastroenterology practices, patients with UC who received mesalazine for acute treatment or maintenance of remission, rated their own compliance at time 0 (A), after 4-8 months (B) and after 12 months (C) on a visual analogue scale, where 0 signified "I have taken all medication correctly" and 10 "I have taken no medication". At the outset, patients were asked about their preference regarding the oral dosage form (tablets/granules/no preference). It was recorded whether the doctor's prescription matched the patient's wishes. The results were shown as median values.
RESULTS: 520 patients (47% female) were enrolled and observed prospectively for up to 12 months. 76% of the patients preferred granules, 14% tablets, and 10% had no preference. Almost all patients received their preferred dosage form. Among patients who preferred and received granules, compliance improved during the observation period (0.50 (A), 0.30 (B) and 0.25 (C)). Patients who preferred and received tablets rated their compliance at all times worse than those taking granules. However, their compliance also improved during the study (1.80; 0.70; 1.0). The group with no preference initially rated compliance as high, but this worsened with time (0.45; 0.70; 0.78). No evidence of other influencing factors such as age, sex, duration of disease or UC severity was found.
CONCLUSION: Documentation by the patient and consideration of the preferred dosage form of mesalazine increase adherence. Indifference of the patient is associated with poorer compliance. The dosage form of mesalazine should be discussed with the patient at the start of treatment.
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P1488 SAFETY AND EFFECTIVENESS OF SEQUENTIAL INTRAVENOUS ADMINISTRATIONS IN A SINGLE SESSION OF IRON CARBOXYMALTOSE AND INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND IRON DEFICIENCY

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INTRODUCTION: The objective of this study was to evaluate the safety and effectiveness of combined intravenous (IV) administration in a single session of ferric carboxymaltose [Ferinject®] and infliximab [Remicade®] in patients with inflammatory bowel disease (IBD) treated with infliximab for the combined management of underlying disease and iron deficiency anemia (IDA) or iron deficiency (ID), in contrast to the usual pattern of two or more hospital visits to administer both treatments.
AIMS & METHODS: Prospective observational study which included 22 consecutive patients with IBD of $\geq$ 6 months evolution (mean age 40.5 $\pm$ 10.7 years; 50% women). 16 patients had Crohn's Disease and 6 Ulcerative Colitis, all treated with infliximab and diagnosed with ID or IDA according to WHO criteria. After completion of IV administration of 5 mg/kg infliximab, 50 ml of saline were injected using the same venous access, followed by the Ferinject® infusion (accordance with Ganzoni formula). 63.4% of patients received Ferinject® infusions of 500 mg and 36.6 % received 1000 mg iron. Laboratory analyses of the ferric profile and inflammatory activity index (modified Truelove I. or Harvey-Brasdshaw I.) pre-infusion and at 2 months were performed. Presence of adverse events was evaluated at 7 and 60 days after the sequential infusions. Ferinject® effectiveness was measured after a mean of 69.0 $\pm$ 41.3 days after infusions.
RESULTS: At the end of the evaluation period no adverse events associated with sequential IV infusion of ferric carboxymaltose or infliximab were recorded. After this period, the mean hemoglobin levels increased from 11.5 $\pm$ 2.5 to 12.5 $\pm$ 1.9 g/dL ($p = 0.143$). Increases in mean levels of serum iron (41.1 $\pm$ 19.5 to 69.6 $\pm$ 33.8 µg/dL, $p = 0.002$), ferritin (73.4 $\pm$ 122.8 to 304.9 $\pm$ 390.7 ng/mL, $p = 0.001$) and mean transferrin saturation (12.3 $\pm$ 4.3 to 21.5 $\pm$ 11.4%, $p = 0.004$) were statistically significant.
CONCLUSION: Sequential IV administration of infliximab following IV ferric carboxymaltose [Ferinject®] in a single session was well tolerated and effective. Contrary to the usual practice of infusing infliximab and IV iron on separate days, this sequential regimen can offer a good cost- benefit ratio and could improve treatment adherence and patients' quality of life.
Disclosure of Interest: None declared

P1489 INTEREST OF COMBINATION THERAPY WITH IMMUNOSUPPRESSIVE TREATMENT IN IBD PATIENTS IN LOSS OF RESPONSE TO INFLIXIMAB AND EXHIBITING VERY HIGH ANTI-INFLIXIMAB ANTIBODY (ATI) LEVELS

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INTRODUCTION: For IBD patients treated with IFX as monotherapy and exhibiting undetectable IFX levels combined with high anti-IFX levels (ATI), the recommended course is to switch to another anti TNF. A single case study has however reported a potential benefit of the addition of immunosuppressants (IS). In this study we studied the clinical and pharmacological impact of adding an IS in patients treated with IFX and exhibiting undetectable trough levels of IFX concurrent with high ATI levels.
AIMS & METHODS: Within a prospective cohort of patients with IBD, all patients receiving IFX as monotherapy at the dose of 5mg/kg were identified. Inclusion was restricted to patients exhibiting undetectable IFX levels and high levels of ATI (> 200 ng/ml) measured using ELISA LISA-TRACKER (Theradiag) technique and detected at least twice. In cases of declining clinical response an IS was added to the prescription of IFX at the same dose, for a minimum period of 6 months.
RESULTS: 15 patients (13 with Crohn's disease (CD)), sex ratio = 1, mean age = 36 years) were included. All patients had IFX levels < 0.1µg/ml and ATI > 200ng/ml. Loss of clinical response was moderate in 10 and minimal in 5, all with faecal calprotectin > 450 µg/g of stools or with an endoscopic Mayo score = 2. The addition of IS (thiopurines in 13 cases) was proposed. Pharmacological data revealed a median IFX level which increased from 0.015 µg/ml [0.01-0.02] to 0.9 µg/ml [0.01-2.2] after 6 months of combination therapy. Median ATI levels decreased from 320 ng/ml [200-600] to 60 ng/ml [20-500]. At 6 months, 8 patients out of 15 exhibited IFX levels greater than 1.5 µg/ml. assoiciated with ATI below 20ng/mL Clinically, 7 of the 13 patients with CD and in relapse on inclusion were in clinical remission at 6 months with normal faecal calprotectin values and in all cases a favourable pharmacological outcome (IFX > 1.5µg/ml with ATI < 20 ng/ml). The pharmacological profile of the 7 other patients remained unchanged.
CONCLUSION: The addition of IS in patients relapsing during IFX treatment and having high ATI levels lead to remission, in 54% of cases as evidenced by clinical, pharmacological and biomarker data. This clinical response is slow: 6 months for a pharmacological effect, 4 months for an effect on the biomarkers and 5 months for a favourable clinical outcome to be observed.
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Disclosure of Interest: None declared

P1490 INDIRECT COMPARISON OF ADALIMUMAB AND VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE IN THE UNITED KINGDOM: COST PER RESPONDER/REMITTER ANALYSIS

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INTRODUCTION: Adalimumab (ADA) and vedolizumab (VDZ) have been shown to induce and maintain clinical remission in patients with moderate to severe inflammatory bowel disease (IBD). The objective was to calculate cost per responder and remitter associated with ADA and VDZ from the perspective of the National Health Service in the United Kingdom (UK).
AIMS & METHODS: RCTs comparing ADA (CHARM and ULTRA 2) or VDZ (GEMINI 1 and 2) to placebo in ulcerative colitis (UC) or Crohn's disease (CD) at 1 year were included. Relative response and remission of each biologic therapy was estimated using a network meta-analysis (NMA) in UC and CD separately. The number needed to treat (NNT) was estimated for each biologic based on the results of the NMA. In CD, the annual cost of ADA (£10,564) assumed all patients were on therapy for 1 year. In UC, the annual cost of ADA (£6,722) assumed patients not in response at week 8 discontinued therapy, as per the European Medicines Agency product information. Because VDZ is not yet approved in the UK, annual cost was assumed to be equal to the indication-specific cost of treating with ADA or the 2013 average annual cost of anti-TNF therapies in the UK (£17,915). The cost of VDZ was assumed to be the same for both VDZ 300mg every 8 weeks (Q8) and every 4 weeks (Q4) dosing regimens. The 1-year costs per responder and remitter were estimated in UC and CD by multiplying the NNT by the annual cost. Blended costs per responder and

remitter in IBD were estimated by weighting the UC and CD results by their respective market size.
RESULTS: When VDZ's annual cost was assumed to equal ADA's, the 1-year treatment costs per responder in patients with IBD were numerically lower for ADA (£60,370) than VDZ Q8 (£146,255) and VDZ Q4 (£128,462). 1-year treatment costs per remitter were also numerically lower for ADA (£60,996) than VDZ Q8 (£118,814) and VDZ Q4 (£137,521). When VDZ's annual cost was assumed to be £17,915 in IBD, the cost per responder of ADA compared to both VDZ dosing regimens was significantly different (Table).

Treatment	Cost per responder Mean (95% Credible Interval)	Cost per remitter Mean (95% Credible Interval)	Cost assumption for VDZ
ADA	£60,370 (£41,174, £98,167)	£60,996 (£38,865, £106,716)	
VDZ Q8	£146,255 (£58,751, £491,114)	£118,814 (£58,724, £271,587)	VDZ treatment costs equal ADA's
VDZ Q4	£128,462 (£58,980, £346,582)	£137,521 (£60,944, £369,964)	
VDZ Q8	£252,800 (£104,360, £836,914)	£208,382 (£102,409, £465,272)	VDZ treatment costs equal the average of all anti-TNF therapies
VDZ Q4	£223,428 (£104,808, £593,699)	£239,344 (£108,709, £635,055)	

CONCLUSION: Costs per responder and remitter in IBD in the UK were numerically lower for ADA-treated patients compared to VDZ-treated patients, indicating that ADA may have better economic value than VDZ in patients with IBD.
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P1491 WHAT IS OUR SUCCESS ON COMPLEX PERIANAL FISTULA HEALING IN THE CLINIC?: FROM ANTIBIOTIC TO COMBINED ANTI-TNF BASED TREATMENT, ENDING WITH OR WITHOUT ILEOSTOMY

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INTRODUCTION: Our aim was to determine overall treatment (Tx) success and factors influencing the medical Tx (MedTx) response in complex perianal fistulas (Cpfis).
AIMS & METHODS: Patients' charts between 1999-13 retrospectively were reviewed. There were 51/705 (7%) CD patients with Cpfis. All patients were treated with different combinations of antibiotics, azathioprine (AZA) and anti-TNFs but our aim was to put them on triple MedTx if there was no drug intolerance. In case of an abscess, drainage and seton was applied remaining between 3 to 6 mo. in case of no recurrence. Tx success was stratified as complete discharge cessation or additional closure of external orifice, and ultimately radiological disappearance by MRI. In case of MedTx failure a diverting stoma was applied. Age, sex, disease duration, location, behaviour, rectal involvement, age at fistula onset, fistula duration, number of fistula, smoking, number of setons, duration of each MedTx, time with seton, total durations of drugs, and type of surgery was noted. Each patient's fistula status at the last visit was determined and re-opening and re-closing events and closure time after seton removal were noted.
RESULTS: There were 51 Cpfis pts., 20 (39%) being female with a mean age of 35.66±11.66 yrs. The mean fistula follow-up time was 41.68±31.31 mo., 19/51 (37%) patients had one fistula the remaining multiple. 34 patients (66%) were complicated by abscesses and loose seton was applied to 30/34 (88%), four of them with permanent setons for repeating abscesses. During whole follow up 50 abscesses (12 of them while having a seton) were observed. Fistula closure after seton removal was achieved between 1-21 (median 8) mo. Ileostomy was performed in 14 (28%) patients and fistula closure was achieved in only 4/14 (30%) between 2-9 mo. At the last visit 27/51 (53%) were in remission, and only 7/51 (14%) achieved radiological. The follow up Tx time was significantly longer in response-positive group (50.33 vs. 31.95 mo., $p=0.031$), and total anti-TNF Tx time significantly correlated with Tx success ($r=-0.339$, $p=0.021$). An age-sex adjusted Cox regression analysis disclosed total anti-TNF Tx time as the only independent predictor of Tx response ($p=0.001$).
CONCLUSION: Anti-TNFs necessary for even small success of complex fistula closure. Clinical response rate within the mean 41 mo. of follow up was 53% with it's own re-opening risk. Only 14% had radiological tract closure reaching our ultimate aim. Long term antibiotic use either solo or combined did not show any effect on perianal fistula closure.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
OTHER LOWER GI DISORDERS III – POSTER EXHIBITION – HALL XL

P1492 RISK OF MICROSCOPIC COLITIS DURING USE OF PPIS, NSAIDS, BETA-BLOCKERS AND OTHER DRUGS

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INTRODUCTION: Microscopic colitis (MC) is a disease characterized by chronic watery diarrhea, normal radiological and endoscopic appearance but microscopic inflammation. MC includes two distinct entities: lymphocytic (LC) and collagenous colitis (CC). In recent years, several drugs were reported to increase the risk of MC. However, these studies lacked a clear exposure definition or did not address dose- and duration-relationships. Aim of this study was to estimate the risk of MC during use of several drugs, such as NSAIDs, PPIs, beta-blockers and SSRIs.
AIMS & METHODS: Case-control study nested within a population based cohort using a primary care database from the Netherlands (1999- 2013). MC cases were identified using free text search with manual validation to ensure histological confirmation. Cases were persons aged≥18 years with incident MC diagnosis. Controls (community-based and patients with negative colonoscopy results), being MC and colorectal cancer-free, were matched to cases on age, sex and primary care practice. Drug use was determined within 1 and 2 years prior to date of earliest symptoms leading to MC diagnosis (matching date). Odds ratios (OR) with 95% CI were calculated by conditional logistic regression, while adjusting for confounders (ORa), including auto-immune diseases, type 2 diabetes mellitus, polyarthritis, colonoscopy and concomitant drug exposure.
RESULTS: From the source population of 1,458,410 subjects we identified 218 incident MC cases (92 CC, 70 LC, 56 unspecified) that were matched to 15,045 community controls. Current use (≤ 3 months) of proton pump inhibitors (PPIs), NSAIDs, selective serotonin re-uptake inhibitors (SSRIs), low-dose aspirin (LDA), ACE-inhibitors (ACEI) and beta-blockers (BBL) significantly increased the risk of MC compared to never use, with adjusted ORs ranging from 2.6 (95%CI:1.5-4.4) for BBL to 7.2 (95%CI:4.4-11.9) for PPIs when evaluating 1 year prior to date of earliest symptoms. At 2 years prior to the matching date, accounting for diagnostic delay, only current use of NSAIDs, PPIs, LDA and ACEI showed increased risk of MC. Statins did not increase the risk of MC. Increasing doses did not show higher risks for MC. When estimating the risk of MC compared to colonoscopy-test negative controls, only current use of PPIs and beta-blockers significantly increased the risk of MC (ORa 4.3 and 6.8, respectively).
CONCLUSION: The risk of microscopic colitis increases from 3 up to 7-fold with current use of drugs, including NSAIDS, PPIs, low-dose aspirin, ACE-inhibitors and beta-blockers when compared to community-based controls. When compared to colonoscopy negative controls, however, only PPIs and beta-blockers increased the risk of MC, suggesting that use of NSAIDs, low-dose aspirin, ACE-inhibitors increases the likelihood of receiving a colonoscopy or worsen underlying colonic diseases or diarrhea rather than increases the risk of MC.
Disclosure of Interest: None declared

P1491

	Response positive(n)	Response positive(%)	Response negative(n)	Response negative(%)	p
Age of the fistula in months	36.4 ±30.5		32.5 ±20.1		NS
Sex (Female/male)	12 /15	44.5%/ 55.5%	8 /16	33%/ 66%	NS
Rectal involvement(absent/present)	12/15	44.5%/ 55.5%	11/13	46%/54%	NS
Treatment duration(follow up in month)	27	50.3 ±36.3	24	31.9 ±21.2	0.031
Number of fistula (1/2/3/4)	12/10/4/1	44%/37%/15%/4%	7/9/8/0	29%/38%/33%/0	NS
Perianal absecess during follow up (no/yes)	12/15	45%/55%	5/19	21%/79%	0.074
Total anti-TNF duration in month	24	31.5 ±19	22	19.4 ±10.8	0.011
Total AZA duration in month	20	35.1 ±26.1	22	21.6 ±11.5	0.040
Total antiobiotic duration in month	27	11.1 ±10.3	24	14.3 ±10.4	NS

P1493 ADMINISTRATION OF IRT-5, MIXTURE OF FIVE PROBIOTICS AMELIORATES COLITIS AND PROTECTS COLITIS –ASSOCIATED CANCER IN MICE MODELS

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INTRODUCTION: The aim of this study is to define the effect of IRT-5, new probiotics combination on the mice colitis and colitis associated cancers using mice colitis and colitis associated cancer (CAG) models.
AIMS & METHODS: IRT-5 was composed of five probiotics *(L.acidophilus, L. casei, L.reuteri, B.bifidum and S. thermophilus*). We used two mice colitis models (DSS and IL-10-/-piroxicam). After 2.5% DSS induction for 5 days, normal chow or IRT-5 (5x108 cfu/day) was administrated for 7 days and B6 mice were sacrificed at day 12. 8- to 10-week-old IL-$10^{-/-}$ mice were fed pellet-chow containing piroxicam for 2 weeks. Then normal chow or IRT-5 mixed chow was administered for 2 weeks after piroxicam induction. Four-weeks old Apc min/+ mice were given 2% DSS for 7 days and normal chow or IRT-5 was administrated for 6 weeks after the initiation of DSS. IL-$10^{-/-}$ mice were fed normal chow or IRT-5 mixed chow was administered for 6 weeks after piroxicam induction. Macroscopic tumors were measured and histologic analyses were done. Real-time PCRfor inflammatory cytokines and immunohistochemistry (IHC) for CD 163 and F4/80 were performed.
RESULTS: IRT-5 reduced the colonic inflammations in both DSS-colitis and colitis in IL-10 -/- mice. Mean tumor incidence (9.55±2.51 vs 4.72±3.09, $p<0.05$), tumor size (3.87±1.69 vs 2.63±1.01 $p< 0.05$) and the tumor portion in >3mm were significantly decreased in IRT-5 treated Apc min/+ mice compared with control mice. Histologic grade was more severe in control IL-10 -/- mice compared with IRT-5 treated IL-10 -/- mice (invasive caricinoma, 70% vs 40%). The activities of CD 163, and F4/80 were decreased in the tumor of IRT-5 treated Apc min/+ in IHC analyses.
CONCLUSION: IRT-5, combination of probiotics ameliorated mice colitis and inhibits CAC in Apc min/+-DSS model and IL-10 -/- mice by the modulation of macrophage activation.
Disclosure of Interest: None declared

P1494 CLINICOPATHOLOGICAL FEATURES OF ACUTE GRAFT-VERSUS-HOST DISEASE IN LOWER GASTROINTESTINAL TRACT

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INTRODUCTION: Acute graft-versus-host disease (GVHD), which typically occurs within 100 days of transplantation, is an important factor influencing prognosis in transplant resipients. In this study, we retrospectively investigated the diagnostic accuracy of acute GVHD that developed in the lower gastrointestinal tract.
AIMS & METHODS: Of the 660 patients who underwent allogeneic hematopoietic stem cell transplantation at our hospital between January 2008 and June 2013, 335 developed acute GVHD-like symptoms such as watery diarrhea. Subsequently, 107 of these patients underwent lower gastrointestinal endoscopy within 100 days of transplantation, as well as biopsy for histological diagnosis. The frequency of each endoscopic findings and their probability of indicating GVHD were assessed in these 107 patients.
RESULTS: Endoscopic observation up to the terminal ileum was possible in 86 (80.4%) patients, and 98 patients were diagnosed as having GVHD based on histological findings, accounting for 29.3% of the 335 patients initially suspected of having GVHD and 91.6% of the 107 patients who underwent endoscopic examination. Of 12 patients infected with cytomegalovirus, 10 also showed the coexistence of GVHD. After excluding these 10 patients, GVHD was observed in the terminal ileum of 59 patients, with endoscopic findings of redness in 27, villous atrophy in 25, edema in 20, erosion in 19, ulcer in 4, and mucosal exfoliation in 5. GVHD was also observed in the colon of 88 patients, with endoscopic findings of reduction or loss of vascular visibility or ''orange peel'' appearance of the mucosa in 76 patients, edema in 68, redness in 42, erosion in 34, ulcer in 10, and mucosal exfoliation in 6. The diagnostic accuracy of each finding as an indicator of GVHD was 100% for villous atrophy, ulcer, and mucosal exfoliation, 97.7% for redness, and 96.3% for erosion in the terminal ilium. In the colon, the accuracy was 100% for ''orange peel'' appearance of the mucosa and mucosal exfoliation, 97.1% for erosion, and 96.2% for reduction or loss of vascular visibility. Six patients had GVHD only in the terminal ilium, and 5 had GVHD only in the right colon. The remaining 86 (87.8%) patients were diagnosed with GVHD in the left colon based on the biopsy results.
CONCLUSION: The characteristic endoscopic findings of GVHD were villous atrophy, turtleback-like appearance of the mucosa, and mucosal exfoliation. Approximately 90% of patients who underwent biopsy of the left colon were accurately diagnosed with GVHD, indicating that biopsy should be performed of the left colon regardless of poor bowel preparation.
Disclosure of Interest: None declared

P1495 EFFECTS OF POLY (I:C), A LIGAND FOR TOLL-LIKE RECEPTOR 3, IN COLON BARRIER FUNCTION

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INTRODUCTION: The gastrointestinal (GI) tract and especially the gut wall act as a barrier to prevent translocation of harmful biological and chemical entities from the lumen. Accordingly, intestinal and colonic barrier functions depend on an adequate response to pathogens by immune but also epithelial cells. Toll-like receptor 3 (TLR-3) recognizes pathogen-associated molecular patterns, particularly double-stranded RNA. TLR-3 activation is noxious to nasal epithelial cells and perturbs blood brain barrier. Although it has been shown that systemic activation of TLR-3 induces intestinal damage, there is little information regarding the mechanisms for TLR-3 actions on epithelial cells in the GI tract. In addition, the effects of direct TLR-3 activation on gut barrier function are unknown.
AIMS & METHODS: We aimed to evaluate the effects of TLR-3 activation on rat colon permeability *ex vivo* as well as *in vivo*. For the *ex vivo* approach, we used the everted gut sac technique. The synthetic ligand for TLR-3, Poly (I:C), was applied at the mucosal side of the colon at doses of 0, 0.5, 5, 50 and 200 ug/mL, and the transit of fluorescent probes (TRITC-dextran 4.4 kD, TD4.4 and FITC-dextran 40 kD, FD40) from the mucosal to the serosal side was measured for up to 3 hours. At the end of this protocol RNA was extracted from the mucosa in order to quantify the mRNA expression of tight junction proteins ZO-1 and Occludin. The effects of Poly (I:C) on colon mucosal morphology and ZO-1 immunostaining were evaluated in another set of tissues. For the *in vivo* experiments, either saline or 100 ug of Poly (I:C) were applied along 7 cm into the colorectal cavity of adult male rats. Six hours later the colon was removed and subjected to the everted gut sac permeability test as described before.
RESULTS: Tissues exposed to 200 ug/mL Poly (I:C) *ex vivo* displayed a decreased thinning of mucosal layer after 2 hours and a decrease in the transit of FD40 (but not of TD4.4) from the mucosal to the serosal side after 3 hours, in comparison to controls. No changes were found in mRNA levels of ZO-1 and Occludin or in the immunostaining for ZO-1 in the mucosa. Colons removed from rats that received Poly (I:C) intrarrectally also showed decreased permeability to FD40 in the everted gut sac assay at 3 hours post-extraction.
CONCLUSION: Our results suggest that an acute exposure to the TLR-3 ligand Poly (I:C) reduces colon permeability to a 40 kD molecule, both *ex vivo* and *in vivo*. This effect is accompanied by a reduction in mucosal thinning *ex vivo* but not by a modification in the expression of ZO-1 or Occludin. Although the mechanism and significance of this potentially protective effect need further investigation, to our knowledge this is the first report showing a direct effect of a TLR-3 ligand in colon barrier function. FUNDED BY: Conicyt 79112017, Fondecyt 1130213.
Disclosure of Interest: None declared

P1496 GUT REGION-SPECIFIC ALTERATIONS IN THE COMPOSITION OF THE INTESTINAL MICROBIOTA IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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INTRODUCTION: Among the potential environmental triggers that are implicated in the development of the diabetes-related myenteric neuropathy, the intestinal microbiome is considered as primary candidate.
AIMS & METHODS: Therefore, the aim of this study was to map the alterations of the composition of microbiota along the gut in diabetic rats. Luminal samples of streptozotocin-induced diabetic and insulin-treated diabetic rats were compared with healthy controls. Segments of duodenum, ileum and colon were dissected and microbiomes of the luminal contents were analyzed by next generation DNA sequencing from phylum to genus level.
RESULTS: No significant differences in the bacterial composition were observed in luminal contents derived from the duodenum of different experimental groups. However, distinct patterns of microbiomes were recognized in the ileum and colon, depending on the history of the luminal samples. Ileal samples from diabetics exhibited particularly striking alterations while the richness and diversity obscured some of these in the colon. Proteobacteria displayed most pronounced shifts, while the dominating phyla (Firmicutes and Bacteroidetes) apparently were modified to smaller degree. Characteristic rearrangements and diversity in the microbiome were detected after insulin replacement, although the normal gut flora was not restored.
CONCLUSION: Diabetes and also insulin treatment affect the composition of the intestinal microbiota on a different but strictly gut region-specific way. The luminal samples from the ileum appear more suitable for diagnostic purposes than the colon/faeces. Proteobacteria should be in the center of diagnosis and potential therapy.
Disclosure of Interest: None declared

P1497 THE LEAKY GUT IN PATIENTS WITH CRONIC KIDNEY DISEASE

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INTRODUCTION: Bacterial infections and sepsis are common complications leading to high morbidity and mortality in patients with chronic kidney disease (CKD). A defective gastrointestinal barrier may contribute to increased translocation of bacterial products.
The aim of this study was to investigate gut permeability, oxidative stress and phagocytic capacity of neutrophils in CKD patients.
AIMS & METHODS: Diamine oxidase (DAO),a marker of gut permeability, was measured by ELISA (DAO, Immundiagnostic, Germany). The LPS surrogate markers lipopolysaccheride binding protein (LBP) and soluble (s)CD14 were measured by ELISA (Human LBP, Human sCD14, Hycult biotech, Netherlands). Advanced Oxidation Protein Products (AOPP) were determined by HPLC. Neutrophil function was determined by co-incubating whole blood with FITC labelled E. coli (Phagotest, Glycotope, Germany) and analysed by flow cytometry.
RESULTS: Predialysis (PDL, n = 73), hemodialysis/hemodiafiltration (HD, n = 32), peritoneal dialysis (PD, n = 28) patients as well as peritoneal dialysis patients with peritonitis (PDP, n = 14) were studied and compared to healthy controls (Ctrl, n = 33). DAO levels were significantly higher patient groups (except PDP patients) compared to Ctrl (see Tab.1). LBP and sCD14 were significantly higher in patient groups compared to Ctrl (see Tab.1). Among the patient groups LBP and sCD14 were highest in the PDP group. AOPP were significantly increased in patient groups (see Tab.1). Neutrophil phagocytosis was significantly reduced in the HD group (see Tab.1).
Tab. 1 Results are shown as median (interquartile range). Significance is shown as [a] $p<0.001$, [b] $p<0.01$, [c] $p<0.05$ compared to ctrl. [A] $p<0.001$, [B] $p<0.01$, [C] $p<0.05$ compared to patient groups (DAO: compared to PDL; LBP: compared to PDP; sCD14: compared to PDP; AOPP: compared to HD; phagocytosis: compared to HD).

parameters		ctrl	PDL	HD	PD	PDP
DAO	[ng/ml]	21.0 (13.1)	33.8 (16.9)[a]	31.9 (23.0)[a]	25.6 (.10.3)[c, B]	27.5 (20.9)
LBP	[µg/ml]	16.7 (9.9)	34.1 (21.1)[a, A]	28.3 (26.3)[a, A]	28.35 (17.7)[a, A]	59.9 (48.2)[a]
sCD14	[µg/ml]	1.5 (0.8)	2.7 (2.1)[a, A]	3.3 (1.6) [a, A]	2.8 (0.7)[a]	6.3 (5.1)[a]
AOPP	[µmol/l]	31.1 (12.9)	53.2 (40.9)[a, A]	90.5 (50.3)[a]	67.9 (30.3)[a, C]	70.2 (38.4)[a]
phagocytosis	[%]	96.0 (57.4)	110.8 (60.5)[A]	75.7 (40.2)[a]	98.8 (74.5)[C]	96.8 (79.8)

CONCLUSION: These results reveal an increased gut permeability in CKD patients. It can therefore be hypothesized that translocation of bacterial products may be increased, leading to an increase in the LPS surrogate markers LBP and sCD14. Additionally, protein oxidation as measured by AOPP is increased in patient serum. Our findings are akin with previous studies showing that CKD patients are exposed to circulating endotoxemia and systemic inflammation on the basis of a leaky gut, altered intestinal microbiota and ultrafiltration- induced splanchnic ischemia. A pathophysiological role of the type of renal replacement therapy is underlined by the fact that neutrophil phagocytosis is impaired in patients undergoing hemodialysis/hemodiafiltration but not in PDL and PD-patients.
Disclosure of Interest: None declared

P1498 INCREASED LEVELS OF PROINFLAMMATORY SERUM CYTOKINES AND LOWER MUCOSAL EXPRESSION OF TLR4 IN IBS PATIENTS

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INTRODUCTION: Alterations in immune function by means of increased activity and potential low-grade inflammation have been suggested as being important in irritable bowel syndrome (IBS). We therefore studied the serum cytokine profile as well as expression of mucosal host mRNA targets of relevance to inflammation and bacterial recognition in IBS patients.
AIMS & METHODS: MesoScale Discovery (MSD) multiplex immunoassay analysis was used for the measurement of serum cytokines, IL-12p70, IL-13, IL-2, IL-4, IL-6, IL-17A, IL-5, IFN-g, IL-1β,IL-8, IL-10 and TNF in 154 IBS patients (female = 105, median age 29 years (24-40)), (Rome III; IBS-C = 16, IBS-D = 38, IBS-M = 98) and 45 healthy controls (female = 30, median age 27 years (23-41)). Mucosal expression of FOXP3, TLR4, TLR6, TLR9, NOX1, IL-8, IL-10 and TNF was determined by qRT-PCR in sigmoid colon biopsies from 114 IBS patients (female = 72, median age 32 years (27-39)), (Rome III; IBS-C = 14, IBS-D = 26, IBS-M = 73) and healthy controls (female = 25, median age 27 years (23-35)). The qRT-PCR results were normalized to the mean expression level of housekeeping (HK) genes 18s, POLR2A and RPLP0, or HPRT, and expressed as $2^{\text{-target-HK}}$. Data is shown as median, range 25-75 percentile.
RESULTS: IBS patients had higher serum levels of TNF compared to healthy controls (Table 1) with higher levels in IBS-D compared to IBS-M (2.7 pg/mL (2.2-3) vs. 2.1 pg/mL (1.7-2.5); $p = 0.02$) and healthy controls (2.7 pg/mL (2.2-3) vs. 2.2 pg/mL (1.5-2.5); $p = <0.001$), respectively. Also levels of IL-6 and IL-8 tended to be higher in serum of IBS patients (Table 1), without differences between IBS subgroups. In contrast, serum levels of IFN-g were lower in IBS patients compared to healthy controls (Table 1). Remaining serum cytokines were similarly expressed in IBS and healthy controls. In colon biopsies, the expression of NOX1 and FOXP3 tended to be lower in IBS than in healthy controls (0.02 (0.02-0.03) vs. (0.03 (0.02-0.03) arbitrary units; $p = 0.06$) and (2.5e-4 (1.8e-4-3.5e-4) vs. 3.1e-4 (2.9e-4-3.7e-4); $p = 0.1$) respectively. The expression of TLR4 was lower in IBS patients than healthy controls (2.1e-3 (1.6e-3-2.5e-3) vs. 2.4e-3 (2.0e-3-2.8e-3); $p = 0.02$), with IBS-M having lower expression of TLR4 compared to healthy controls ($1.9e^{-3}$($1.6e^{-3}$-$2.4e^{-3}$) vs. $2.4e^{-3}$($2.0e^{-3}$-$2.8e^{-2}$); $p = 0.003$). The mucosal expression of TNF, IL-8, IL-10, TLR6 and TLR9 was similar in IBS patients and healthy controls.
Table 1. Levels of serum cytokines in IBS patients and healthy controls.

Target (pg/mL)	IBS (n = 151)	Healthy (n = 48)	
TNF	2.3 (1.8-2.8)	2.2 (1.6-2.5)	$p = 0.03$
IFNg	8.0 (5.1-11.7)	11.2 (6.2-16.2)	$p = 0.01$
IL-6	0.4 (0.3-0.7)	0.4 (0.2-0.6)	$p = 0.1$
IL-8	11.4 (7.6-14.5)	9.5 (6.5-13.2)	$p = 0.1$

CONCLUSION: This study supports the notion that a subset of IBS patients has a low-grade inflammation with higher serum levels of pro-inflammatory cytokines. Also, lower mucosal expression of TLR4 and NOX1 RNA suggest impaired recognition and subsequent clearance of bacteria in intestinal tissue.
Disclosure of Interest: None declared

P1499 THE BURDEN OF CLOSTRIDIUM DIFFICILE INFECTION BETWEEN 2010 AND 2013: TRENDS AND OUTCOMES FROM AN ACADEMIC CENTER IN EAST EUROPE

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INTRODUCTION: Clostridium difficile infection (CDI) is one of the most important healthcare associated infections (HAI). Increasing incidence of CDI were reported.
AIMS & METHODS: Our aim was to analyze incidence and possible risk factors in inpatients treated with CDI between 1 January 2010 and 1 May 2013 at 1st Department of Medicine, Semmelweis University, Budapest, Hungary. A total of 11751 inpatients were treated in our clinic in the follow-up period. 247 inpatients were diagnosed with a CDI infection. For the risk analysis a 1:3 matching was used. Data of 732 matched for age, gender, inpatient care period and unit were compared to the CDI population. Inpatient records were collected and comprehensively reviewed.
RESULTS: The incidence of CDI infection was 21.0/1000 admissions (2.1% of all cause-hospitalizations and 4.45% of total inpatient days). The incidence of severe CDI was 126/1000 admission (12.55% 31/247 cases), Distribution of CDI cases was different according to the unit type, with highest incidence rates in hematology, gastroenterology and nephrology units (32.9, 25 and 24.6/1000 admissions) and lowest rates in 1.4% (33/2312) in endocrinology and general internal medicine (14.2 and 16.9/1000 admissions) units. Recurrence of CDI infection was 11.34%/12 week after discharge. Duration of hospital stay was longer (17.66 (SD:10.78) vs. 12.4 (SD: 7.71) days) in patients with CDI infection. CDI accounted for 6.3% of all-inpatient deaths, 30 day mortality rate was 21.86% (54/247 cases). Risk factors for CDI infection were: antibiotic therapy (including 3rd generational cephalosporins or fluoroquinolons, OR:4.559, $p<0.001$), use of proton pump inhibitors (OR:2.082, $p<0.001$), previous hospitalization within 12 months (OR:3.167, $p<0.001$), previous CDI infection (OR:15.32, $p<0.001$), while presence of diabetes mellitus was identified as a protective factor against CDI (OR:0.484, $p<0.001$). Treatment but not outcome of relapsing cases was significantly different with more frequent use of vancomycine alone or in combination ($p<0.001$) and longer ($p<0.02$) antibiotic therapy.
CONCLUSION: Incidence of CDI was high and CDI accounted for a significant burden with longer hospital stay and adverse outcomes. Antibiotic therapy, proton pump inhibitor therapy and previous hospitalization/CDI infection were identified as risk factors for CDI
Disclosure of Interest: None declared

P1500 UTILITY OF AN INTERFERON GAMMA RELEASE ASSAY, TB-FERON GOLD (TBG), IN DIAGNOSING ILEOCOLONIC TUBERCULOSIS

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INTRODUCTION: Both Ileocolonic tuberculosis and Crohns disease are common in developing world. In spite of all present day gadgetries at times it is difficult to differentiate Ileocolonic tuberculosis from Crohns disease.
AIMS & METHODS: Aim - The aim of our study was to assess the utility of an Interferon Gamma Release Assay, Quantiferon TB Gold in tube test (TBG), in diagnosing Ileocolonic tuberculosis.

Methods: We prospectively included 18 patients with Ileocolonic tuberculosis (ITB) and 30 patients with IBS (as per ROME III Criteria) who had a normal chest X-ray and Ileocolonoscopy and biopsy as controls. Demographic, clinical, laboratory, chest x-ray, endoscopic and histological features were noted in all the patients. All patients were evaluated with a TBG test. Diagnosis of ITB was made combining established clinical, endoscopic and histologic criteria. Patients were followed up and a repeat colonoscopy was performed at 3 months to look for response and at the end of 6 months of therapy to ensure mucosal healing. The diagnosis was revised if no healing was noted at 3 months.
RESULTS: Results: Eight of the 18 patients (44%) were male, and the mean age was 42.9 years (Range 16-81 years). All 30 control subjects had a negative TBG test. Seventeen out of the 18 ITB patients (94.4%) had a positive TBG test. The sensitivity was 94.4%, Specificity was 100%. Positive predictive value was 100% and a negative predictive value of 96.7%.

	IBS (n = 30)	TB (n = 18)	
Male/Female	18/12	8/10	
Mean Age in years (Range)	41.9 (16-80)	44 (18-81)	
TBG Positive	0	17 (94.4%)	
Abdominal pain	30	17 (94.4%)	
Diarrhoea	8 (26.7%)	9 (50%)	
Hb	12.4 ± 1.55	10.97 ± 1.83	0.016
Platelet	2.85 ± 0.75	2.67 ± 0.89	0.38
CRP	9	57	0.09
Alb	3.66 ± 0.29	2.7 ± 0.7	0.5

CONCLUSION: The TBG Test is both specific and sensitive for diagnosing ilieocolonic Tuberculosis, and can be can be added to the armamentarium for diagnosing Ileocolonic tuberculosis.
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Disclosure of Interest: None declared

P1501 ASYMPTOMATIC CARRIAGE OF CLOSTRIDIUM DIFFICILE IN A JAPANESE LONG-TERM CARE FACILITY FOR THE ELDERLY: PREVALENCE AND RISK FACTORS

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INTRODUCTION: *Clostridium difficile* (CD) is the most frequent cause of nosocomial infectious diarrhea in developed countries. Recent studies suggest asymptomatic carrier may be a major source of CD in healthcare settings. The aim of this study was to identify the prevalence and risk factors for asymptomatic CD carriage in a long-term care facility for the elderly.
AIMS & METHODS: Fecal samples were collected from 171 asymptomatic patients (68.4% woman) with a median age of 83 (range 43 to 101 years). Data on demographic or clinical information, including age, sex, body mass index, major diagnosis leading to admission, duration of facility stay, medication use of antibiotics, proton pump inhibitors (PPI), H_2 blockers, or probiotics, and concurrent diabetes mellitus were studied.
RESULTS: CD was isolated from 61 (35.7%) of 171 asymptomatic patients. 26 (42.6%) of the 61 isolates were toxin A-, B+, 18 (29.5%) were toxin A+, B+, and 17 (27.9%) were toxin A-, B-. Demographic or clinical data were analyzed between CD carriers and CD noncarriers. Multivariate analysis showed only PPI use was significant risk factor for CD carriage (odds ratio 2.193, 95% confidence interval 1.026-4.687, p = 0.043).
CONCLUSION: This study showed asymptomatic CD carriage was common in a Japanese long-term care facility for the elderly and was significant association with PPI use. The findings add to the understanding of CD carriage and have implication for prevention.
Disclosure of Interest: None declared

P1502 AGE IS THE MAIN RISK FACTOR OF MORTALITY AMONG PATIENTS WITH CLOSTRIDIUM DIFFICILE INFECTION

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INTRODUCTION: Clostridium difficile infection (CDI) has become important cause of hospital morbidity and mortality during last decade. Recurrent CDI is difficult to treat and novel therapies (i.e. fecal transplantation) are evaluated in this group of patients. In our retrospective study we have decided to analyze group of patients with CDI from last three years in our hospital.
AIMS & METHODS: All patients with CDI from all hospital departments diagnosed during period from 1/2011 to 12/2013 were included in the study. Information about sex, age, previous antibiotic treatment, PPI therapy, various comorbidities (trauma, imobility, diabetes, dementia, COPD, IBD) and type of department (surgical/internal) were obtained. Community onset of CDI and recurrent CDI were also recorded. Hospital mortality and risk of recurrence were analyzed in univariate analysis.
RESULTS: Our group consists of 174 patients, 84 men, 90 women, average age 74 years. 27 patients had a recurrent disease (up to 4 recurrences). 51 patients died during hospital stay (hospital mortality 29%). Majority of patients stayed in internal medicine department (100/174, 57%). 39 patients (22%) had onset of disease in the community. In univariate analysis only patients with age ≥70 years (121/174) had significantly higher mortality than those with age under 70 (53/174) (OR 2.599, 95%CI 1.158-5.836, p = 0.021). Other variables were not significant. No risk factor for recurrent CDI was statistically significant.
CONCLUSION: Patients with CDI had overal hospital mortality 29%. 22% of patients had onset of their disease in the community. Age over 70 was the only significant risk factor of mortality in our group of patients. We believe that novel treatment strategies should be considered preferably in elderly patients.
Disclosure of Interest: None declared

P1503 NECESSITY OF COLONOSCOPY AFTER COMPUTED TOMOGRAPHY- DIAGNOSED ACUTE RIGHT-SIDED DIVERTICULITIS

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INTRODUCTION: Several recent studies have reported that screening colonoscopy is not necessary after computed tomography (CT)-diagnosed uncomplicated diverticulitis in Western countries where most diverticulitis are left-sided. In Japan, as in other Asian countries, more than half of the diverticulitis cases are right-sided. No study has reported on the need for screening colonoscopy after diagnosing diverticulitis in Asian patients.
AIMS & METHODS: The aim of this study was to determine if screening colonoscopy is required in patients with CT-diagnosed diverticulitis. A retrospective cohort study was carried out in a tertiary hospital using hospital registry codes for diverticulitis. All patients diagnosed with acute diverticulitis between April 2008 and January 2014, confirmed by CT, were included.
RESULTS: A radiological diagnosis of acute diverticulitis was made in 173 patients. Six patients (1 right-sided and 5 left-sided) underwent emergency resection at hospital admission, whereas 167 were treated conservatively. Among the conservatively treated patients, 146 (93 right-sided and 53 left-sided) underwent colonoscopy during follow up. The mean age of right-sided diverticulitis patients was significantly lower than that of left-sided diverticulitis patients (46.9 ± 14.1 years vs. 60.7 ± 15.5 years, p < 0.01). There was no colorectal cancer in both groups. There were 8 patients with advanced adenoma (6/93 [6.5%] and 2/53 [3.8%], p = 0.49) and 35 with non-malignant colonic polyp (19/93 [20.4%] and 16/53 [30.2%], p = 0.32).
CONCLUSION: This study showed that the prevalence of colorectal cancer/advanced adenoma/non-malignant colonic polyp in patients with diverticulitis, regardless of the involved side, may be similar to that of asymptomatic average-risk individuals which has been previously reported. In the absence of other indications, routine colonoscopy after CT-diagnosed diverticulitis, even if it was right-sided, may be unnecessary.
Disclosure of Interest: None declared

P1504 DIGESTIVE TUBERCULOSIS IN THE REGION OF CASABLANCA. EPIDEMIOLOGICAL, DIAGNOSTIC AND THERAPEUTIC ASPECTS

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INTRODUCTION: Tuberculosis remains a public health problem in Morocco despite the introduction of the vaccination program. Digestive tuberculosis is a common site of extrapulmonary locations.
It can affect any segment of the gastrointestinal tract; however, peritoneal and intestinal locations remain the most frequent. Symptoms are highly variable and non specific, not necessarily referring to the diagnosis of tuberculosis. Diagnosis confirmation is based on microbiological or histological examinations. The treatment is essentially medical.
AIMS & METHODS: This is a retrospective study including 32 patients with tuberculosis over a period of 72 months in the departement of Gastroentérologie in the university hospital of Casablanca:Ibn Rochd. The data have been selected from medical records.
The diagnosis of gastrointestinal tuberculosis was selected on histological or bacteriological evidence.
RESULTS: The average age of patients was 39 years, the sex ratio: 1.8 with a male predominance. Tuberculosis contagion was found in 27% of patients. Clinically all patients had pain and abdominal distention, fever in 36% of cases, a pleural effusion syndrome in 27% and diarrhea in 34% of cases.
Abdominal ultrasonography and computed tomography have objectivied peritoneal effusion in all patients, thickening of digestive handles with lymphadenopathy in 30% of cases.
The ascites puncture revealed liquid rich in proteins in all cases with an average of 57 g/l proteins (40-94 g / l) with lymphocytic predominance.
Search of Mycobacterium tuberculosis was positive in one patient in a rectal biopsy.
At the end of this report 13 cases of peritoneal tuberculosis were isolated and the others were associated with intestinal disease in 10 patients, pleuro-peritoneal localization in 9 patients and one case of hepato-splenic tuberculosis.

Patients with tuberculosis received an antituberculous treatment for 6 months; the outcome was favorable in 82% of cases.
CONCLUSION: Digestive Tuberculosis is a common location of extra pulmonary locations (4th rank) with a predominance of peritoneal involvement, the gastrointestinal tract and solid organs.
Diagnosis is suggested by clinical, biological and radiologic arguments. The diagnosis confirmation is histological or bacteriological.
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Disclosure of Interest: None declared

P1505 THE COST OF ANTIBIOTICS-ASSOCIATED DIARRHOEA IN HOSPITALIZED PATIENTS

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INTRODUCTION: Antibiotic-associated diarrhoea (AAD) is a common adverse event of antibiotic (AB) treatment. Symptoms range from mild and self-limiting to severe diarrhoea, particularly in the case of a *Clostridium difficile* infection (CDI). The cost – be it from a societal, healthcare payer or hospital perspective – for a hospitalized patient experiencing AAD (including non-CDI) is not well established. A better insight in the cost of AAD in hospitalized patients is essential for robust health-economic evaluations of interventions aiming to prevent AAD.
AIMS & METHODS: A cost model was developed for determining the cost of AAD from a societal, healthcare payer and hospital perspective using two complementary approaches: (a) a top-down approach comparing the total (invoice) cost for hospitalization of AAD and non-AAD patients and (b) a bottom-up approach establishing the additional cost for a hospitalized patient with AAD as compared to a hospitalized patient without AAD based on additional resources used in AAD patients.
Data for the top-down and bottom-up models were obtained as part of a study investigating the prevalence of AAD in 743 patients on antibiotics therapy admitted to internal medicine wards in 4 Belgian hospitals. As part of the study protocol, hospital invoices for all included patients (both AAD and non-AAD) were collected and additional resource use specifically attributable to the occurrence of AAD was registered. Resource use registrations included medical acts, lab tests, drugs, number of days in isolation and extra nursing time for the treatment of diarrhoea. Additionally, length of stay differences were calculated from the invoice registrations comparing AAD to non-AAD patients.
For the bottom-up analysis, the cost of hospitalization was calculated by assigning unit costs to the registered additional resource use applicable for the Belgian context based on local health-economic evaluation guidelines. A literature review was performed to determine the cost per day of isolation for the hospital perspective. Length of stay and total invoice cost differences between AAD and non-AAD patients were corrected for confounders using logistic regression analysis, including age, number of AB treatments, type of ward and known risk factors for development of diarrhoea after exclusion of outlier results.
RESULTS: Using the top-down analysis approach, from a healthcare payer perspective, a hospitalization where AAD occurs is 811 EUR more expensive than a hospitalization where no AAD occurs (4,101 EUR AAD; 3,290 EUR non-AAD). Using a bottom-up analysis approach, this cost difference amounts to 1,253 EUR from a healthcare payer perspective; 2,133 EUR from a societal perspective and 274 EUR from a hospital perspective.
CONCLUSION: The results from this study using two complementary cost calculation approaches - one based on total invoice data, one based on additional resource use registrations for AAD – clearly demonstrate the significant impact of the occurrence of AAD on hospitalization cost.
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P1506 VALIDATION OF A NEW IN VITRO COLONIC FERMENTATION MODEL WITH IMMOBILIZED ELDER MICROBIOTA FOR CLOSTRIDIUM DIFFICILE INFECTION AND ANTIBIOTIC TREATMENT TESTING

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INTRODUCTION: *C. difficile* infection (CDI) is a frequent hospital acquired infection in the elderly often associated with broad-spectrum antibiotics treatments. Currently, vancomycin and metronidazole are the standard therapies for CDI but increasing antibiotic resistances and high recurrence rates emphasizes the need for alternative treatments. *In vitro* intestinal fermentation and cell models are useful platforms for studying separately the interactions between complex microbiota and cell responses.
AIMS & METHODS: The objective of this study is to validate novel intestinal *in vitro* fermentation models of the elderly gut microbiota for the investigation of CDI and antibiotic treatment.
The PolyFermS models were designed to allow parallel testing under highly controlled conditions of treatments applied in test reactors simulating the conditions of the proximal or distal colon reactor. The test reactors were continuously inoculated with the same intestinal microbiota composition produced in a first stage immobilized cell reactor operated under conditions of the proximal colon. CDI was induced in test reactors by spiking *C. difficile* vegetative cells of ribotype 001 or by addition of spores of ribotypes 001 and 012. The elderly models with CDI were validated through antibiotic treatments with the application of daily 150 mg/l ceftriaxone or twice daily 330 mg/l metronidazole. The main bacterial groups (qPCR), metabolite production (HPLC), gut microbiota profiles (pyrosequencing) and cytotoxin titre (Vero cell assay) were determined.
RESULTS: The elderly PolyFermS models showed very high stability for all tested bacterial groups and metabolites over the fermentation period (two models run for 70 and 80 days). V5-V6 sequencing showed that the diversity of the fecal inoculum was maintained in the inoculum reactor while the ratios among the bacterial groups differed. Upon inoculation *C. difficile* colonized in the distal (pH 6.8) but not in the proximal intestinal reactors (pH 5.7), reaching high and stable copy numbers of up to log 8 per ml fermentation effluent and increasing toxin titre over time. Metronidazole administration during ten days strongly impaired growth of butyrate producing bacteria and decreased the *C. difficile* numbers to below the detection limit of qPCR. Two days after cessation of metronidazole treatment *C. difficile* started to re-colonize the reactors.
CONCLUSION: The new PolyFermS model of the elderly gut microbiota and CDI is especially suitable for assessing the potential and mechanisms of new antimicrobials and alternative strategies (e.g. probiotics) to prevent and/or treat CDI.
Disclosure of Interest: None declared

P1507 AEROMONAS SPECIES: AN OPPORTUNISTIC ENTEROPATHOGEN IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES? A SINGLE CENTER COHORT STUDY

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INTRODUCTION: Exacerbation of inflammatory bowel disease (IBD) has been classically linked to pathogens such as *Clostridium difficile* (*C.diff*) and cytomegalovirus. We recently observed 4 cases with a positive *Aeromonas* stool culture at the time of a severe IBD flare or diagnosis. Its role as an enteropathogen is debated.
AIMS & METHODS: Aim: To explore the significance of positive *Aeromonas* stool cultures in IBD patients and controls.**Methods:** Observational prospective study. All patients with positive *Aeromonas* stool cultures between 1-1-2011 (start of massaspectrometry detection) to 30-10-2013 were indentified in the microbiology database at a referral hospital. Demographics, clinical, biological and endoscopic data were extracted from medical records. Ethics approval was obtained.
RESULTS: 77 patients (11 IBD) were identified. Baseline characteristics are summarized in **Table 1**. Symptoms were diarrhea in 87%, abdominal pain in 51%, fever in 35% and vomiting in 26%. Median (IQR) C-reactive protein was 28 (9-98) mg/L. In 48% of the cases, *Aeromonas* caused a very mild self-limited gastrointestinal infection (GII) and no antibiotics (ATB) were given. Among the 40 cases needing ATB, 20 had a mild-moderate GII; 4 a severe GII with complications; 4 a co-infection by *Campylobacter* and 2 *de novo* Crohn's disease (CD). Hospitalization was needed in 31 cases and in other 21 *Aeromonas* was detected during the hospitalization for other reasons. *A.caviae* and *A.veronii* were isolated in 32 and 27 cases respectively. *A.veronii* was more frequent in IBD patients (50 vs. 32%) and was isolated in 7/18 and 3/4 of the moderate and severe GII whereas *A.caviae* was found in 12/20 of mild self-limited GII. Among the IBD patients, *Aeromonas* triggered a moderate-severe flare in 2 cases of silent ulcerative colitis (UC) on 5-ASA, and appeared in the context of *de novo* CD in 2 more cases. In contrast, *Aeromonas* appeared in 3 CD patients (1 on infliximab (IFX) and azathioprine (AZA) and the other 2 with an ileostoma without treatment) with already active disease;in 3 IBD patients in remission (1 UC on 5-ASA, 1 CD with ileostoma on IFX and 1 CD on AZA) it presented as a mild GII and in 1 asymptomatic CD patient it appeared in a control culture after *C.diff* infection. IBD cases were treated more often with ATB (82 vs. 37%, $P = 0.005$) and had more complications (45 vs. 12%, $P = 0.025$).
Table 1. Baseline characteristics.
Table to abstract P1507

	N = 77
Median (IQR) age (years)	65 (27-78)
Female (%)	35 (46)
IBD: CD/UC/IBDU (%)	7/3/1 (64/27/9)
Previous chronic diarrhea/ Reflux esophafgitis/GI surgery (%)	14/8/8 (18/10/10)
Active oncologic disease (%)	22 (29)
Solid organ Transplant (%)	7 (9)
Previous hospitalization within previous 3m (%)	35 (46)
Previous ATB within previous 3m (%)	19 (25)

CONCLUSION: *Aeromonas* infection presented as a milder infection in non-IBD patients. A.*veronii* was more prevalent in IBD and was associated with worse clinical outcomes. Prospective case controlled data in larger cohorts are needed to establish the true significance of *Aeromonas* as an opportunistic enteropathogen in IBD.
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P1508 COLORECTAL CANCER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN UPPSALA COUNTY, SWEDEN 1970-2010

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INTRODUCTION: Inflammatory bowel disease (IBD), ulcerative colitis as well as Crohn's disease, is associated with an increased risk of colorectal cancer (CRC). The level of lifetime risk of malignant development does however differ between studies and conditions in different countries over time.
AIMS & METHODS: The aim of our study was to review historic cases of IBD-related CRC in the Uppsala region, Sweden, and analyse the clinical characteristics of the cases in question.
From the patient diagnosis registry of Uppsala University Hospital, all patients with a diagnosis of IBD were scrutinized over a period spanning 40 years from 1970 to 2010. The outcome of CRC cases were retrieved and reviewed for clinical information in association with development of malignant disease.
RESULTS: Over the period of 40 years, 49 cases of CRC were found. Out of these, 37 were males and 12 females. The median age for diagnosis of CRC was 46 years, as compared to 72 years for CRC in non IBD-patients ($p<0.001$). The standardized incidence ration (SIR) calculated from 38 patients in the Uppsala region was for the whole CRC group 0.97 (95% confidence interval (CI) 0.92-1.03). For males, SIR was 1.23 (CI 1.18-1.27) and for females SIR was 0.65 (CI 0.59-0.71). There was no preponderance for CRC in smokers or patients with high BMI. The overall 5-year survival was 43.3% with no significant difference between men and women ($p=0.54$). Of note, the younger cases with CRC diagnosis before 30 years of age had a 14.3% 5-year survival, whereas those diagnosed between 30-60 years had a 49.2% 5-year survival, $p<0.013$). The 5-year survival of those diagnosed after 60 years was 44.9% ($p=0.20$).
Mortality from CRC was numerically higher for those diagnosed between 1970-1990 with a 31.7% 5-year survival rate, whereas cases between 1991-2010 had a 47.9% 5-year survival rate ($p=0.25$).
CONCLUSION: Patients with IBD are prone to develop CRC at a much younger age than the population in general. Albeit, the overall lifetime risk for CRC in IBD is similar to that of the general population. However, men seem to be at a higher risk, almost twice that of women for developing CRC in IBD. There was a considerably higher 5-year mortality among those diagnosed at an early age before 30 years of age.
Disclosure of Interest: None declared

P1509 THE PREDICTORS FOR METACHRONOUS ADVANCED NEOPLASMS AFTER INITIAL COLONOSCOPIC RESECTIONS OF SPORADIC ADENOMA AND CARCINOMA

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INTRODUCTION: We aimed to investigate the major predictors for developing metachronous colorectal advanced neoplasms during colonoscopic surveillance after initial resections of sporadic adenoma and carcinoma.
AIMS & METHODS: The study included 403 patients (mean age 66.2±9.9yr, M:F = 1.55:1) with initial endoscopic resections of colorectal adenomas and/or intramucosal carcinomas with repeated follow up colonoscopies (an average time of surveillance: 73.9 months). During surveillance colorectal lesions less than 5mm in diameter were not resected. The patients were divided into two groups according to the following risk factors at initial resections; age of patients (less or more than 65 yr), gender (male or female), number of colorectal lesions (single or multiple), size (less or more than 10mm), location (left or right/both), histology (adenoma with low grade dysplasia or high grade dysplasia / cancer). The statistical comparisons were made by Logrank test between 2 groups as for the cumurative incidences of patients with metachronous lesions, and those with metachronous advanced lesions (larger than 10mm, adenoma with high grade dysplasia or cancer). The hazard ratio (HR) values of risk factors for metachronous lesions and those for metachronous advanced lesions according to Cox proportional hazard models were also investigated.
RESULTS: The cumurative incidences of patients with metachronous lesions were significantly higher in male patients ($p<0.001$), those with multiple lesions ($p<0.0001$), those with large lesions more than 10mm ($p<0.001$), those with right/both sided-lesions ($p<0.05$), and those with lesions of high grade dysplasia or cancer ($p<0.005$). The cumurative incidences of patients with metachronous advanced lesions were significantly higher in male patients ($p<0.01$), those with multiple lesions ($p<0.01$), those with large lesions more than 10mm ($p<0.0001$), and those with lesions of high grade dysplasia or cancer ($p<0.0001$). Multivariate analysis showed that male gender (HR 1.78, 95%CI 1.25-2.55), multiple lesions (HR 2.01, 95%CI 1.46-2.77), large lesion (HR 1.88, 95%CI 1.31-2.69), right/both sided-lesion (HR 1.38, 95%CI 1.01-1.90), and lesions of high grade dysplasia or cancer (HR 1.49, 95%CI 1.04-2.14) were statistically significant factors for metachronous lesions, and male gender (HR 2.11, 95%CI 1.18-3.75), multiple lesions (HR 1.70, 95%CI 1.02-2.82), large lesion (HR 2.26, 95%CI 1.28-3.98), and lesions of high grade dysplasia or cancer (HR 1.75, 95%CI 0.99-3.08) were statistically significant factors for metachronous advanced lesions.
CONCLUSION: Male gender and patients with multiple lesions, large lesions more than 10 mm, lesions with advanced pathology at initial resections were confirmed as the major predictors of metachronous advanced lesions during colonoscopic surveillance.
Disclosure of Interest: None declared

P1510 METABOLIC FACTORS WHICH ASSOCIATE WITH PATIENTS HAVING METACHRONOUS COLORECTAL NEOPLASMS DURING SURVEILLANCE AFTER INITIAL COLONOSCOPIC RESECTIONS

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INTRODUCTION: Recently visceral obesity, insulin resistance, and metabolic syndrome are considered to be important risk factors for developing colorectal neoplasms. After initial resections of colorectal adenoma and carcinoma many metachronous neoplasms requiring endoscopic or surgical resections were detected during surveillance. In this study we aimed to determine the risk factors for occurrence of metachronous colorectal tumors using health examination data of patients undergoing colonoscopic surveillance.
AIMS & METHODS: The study included 348 patients with initial endoscopic resections of colorectal adenomas and/or intramucosal cancers with follow-up repeated colonoscopies after at least one year interval (a median follow-up period 63.2 months). They were classified into 156 patients with subsequent resections of metachronous colorectal lesions (group A), and 192 patients with no metachronous lesions during surveillance (group B). 306 subjects with normal colorectum were also studied as a control group (group C). Health examination data in group A, B, and C were statistically compared to determine the risk factors for developing metachronous neoplasms during surveillance.
RESULTS: Mean age and gender ratio were 66.1 yr, 113:43 (group A), 67.5 yr, 100:92 (group B), 66.4 yr, 181:125 (group C), respectively. No difference of age between 3 groups, but male to female ratio was higher in group A than group B and C ($p<0.01$). Body mass index (kg/m^2) were 24.5 (group A), 23.7 (group B), and 23.5 (group C), demonstrating higher BMI in group A than group B and C ($p<0.05$). The percentages of drinking and smoking were 31.4%, 23.7% (group A), 18.8%, 15.6% (group B), and 22.2%, 14.7% (group C), disclosing higher percentages of drinking in group A than group B and C ($p<0.05$). Mean blood pressures (mmHg) were 139.4/80.4 (group A), 136.9/79.2 (group B), and 135.1/79.1 (group C), respectively. Systolic pressure in group A was significantly higher than that in group C ($p<0.05$) but no difference from group B. Serum total cholesterol and triglyceride (mg/dl) were 203.7, 128.1 (group A), 201.0, 122.0 (group B), 200.8, 103.3 (group C), respectively. Serum triglycerides showed higher serum levels of group A and B than group C ($p<0.005$), although no significant difference of serum cholesterol. Liver function test disclosed higher serum level of γGTP in group A (59.7IU/L) than that in group B (41.6IU/L) and C (34.4IU/L) ($p< 0.005$), although no significant difference of AST and ALT levels. The prevalence of fatty liver evaluated by ultrasound were 38.3% (group A), 26.2% (group B), and 24.1% (group C), respectively. Fatty liver was significantly frequent in group A than group B and C ($p<0.05$). Fasting blood sugars (mg/dl) were 109.2 (group A), 105.6 (group B), 103.0 (group C), disclosing higher level in group A than group C ($p<0.01$) but no difference from group B.
CONCLUSION: Health examination data disclosed that male gender, obesity, high percentage of drinking, high serum level of γGTP, and high prevalence of fatty liver were considered to be the risk factors for developing metachronous colorectal tumors during surveillance after initial colonoscopic resections.
Disclosure of Interest: None declared

P1511 CONTRASTING COLON/RECTAL CANCER RATIOS IN TWO CHINESE CITIES WITH DIFFERENT BACKGROUND COLORECTAL CANCER INCIDENCES

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INTRODUCTION: The incidences of colorectal cancer (CRC) are rising rapidly in Chinese, particularly in Hong Kong (HK) where it has emerged as the most common cancer. In contrast, some cities in West China like Chongqing (CQ) are still having a relatively low CRC incidence.
AIMS & METHODS: We studied the epidemiology of colon and rectal cancers in these two Chinese cities (HK and CQ) with different background CRC incidences to gain further insight into the changing CRC epidemiology in Chinese. Data on CRC incidences were retrieved from the HK Cancer Registry and from two large regional hospitals in CQ (West China). We included all patients newly diagnosed to have CRC in a 10-year period (2003-2012). The baseline demographic of CRC patients and the Colon/Rectal cancer ratios (CR ratio) of the two cities were compared.

RESULTS: There was no significant change in CRC incidence over the study period in both cities. The mean age at diagnosis of CRC was significantly younger in the lower prevalent area (CQ) than in the higher prevalent area (HK) (61 vs 71 years; P <0.001). Although the proportion of young (<40 years) CRC patients was significantly higher in CQ than in HK (6.7% vs 2.1%, P <0.001), there was a significantly higher proportion of older (≥70 years) CRC patients in HK (53.1% vs 36.3%; P <0.001). CRC was more common in men in both cities (M:F ratio, 1:3). There was also a remarkable difference in the distribution of colon and rectal cancer between the two cities. Colon cancer was more prevalent in the higher prevalent area (HK) with an overall CR ratio of 1.34, whereas rectal cancer is the predominant cancer in CQ (CR ratio 0.63; P <0.0001). In all age groups, colon cancer is more prevalent than rectal cancer in the high prevalent area (HK) with the CR ratios ≥1. In HK, the CR ratio was significantly higher in female than in male (1.79 vs 1.34; P <0.0001) and progressively increased with ages with the highest CR ratio in the ≥80 years' group (women: 2.18; men: 1.74). In contrast, rectal cancer is more prevalent than colon cancer in lower prevalent area (CQ) in all age groups (CR ratio <1). Similar patterns of rising CR ratios with age and sex were not obvious in the lower prevalent region.
CONCLUSION: When comparing two Chinese regions with different background CRC incidences, there are significantly higher proportions of rectal cancer and young patients with CRC in the lower prevalent region. The increase in CRC in higher prevalent region is attributed to the older population and the marked increase in colon rather than rectal cancer. These findings have important ramifications on the pathogenesis, screening and treatment of CRC in Chinese. The CR ratio may serve as a surrogate marker for monitoring the rapidly changing epidemiology of CRC in developing regions.
Disclosure of Interest: None declared

P1512 LOWER RISK OF ADVANCED ADENOMA (AA) AND COLORECTAL CANCER (CRC) AMONG PATIENTS WITH A PREVIOUS NEGATIVE RESULT FROM A FECAL IMMUNOCHEMICAL TEST (FIT) FOR CRC. PRELIMINARY DATA ON SECOND ROUND SCREENING

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INTRODUCTION: Screening for colorectal cancer by FIT is based on consecutive rounds to detect precursor lesions or CRC in early stages. Data on consecutive rounds of FIT screening are limited and based mostly on small population studies.
AIMS & METHODS: We assessed the preliminary data regarding positivity predictive values (PPVs) for advanced adenoma (AA) and CRC among patients with a previous negative result from a FIT.
Methods: Data were collected from 2 rounds of FIT screening in population-based CRC screening program (50 to 70 years old). The PPV for AA and CRC were compared among the first-round participants and second-round participants with a previous negative FIT result.
RESULTS: The rate of positive results from FIT was significantly superior in the first vs. second round screening (6.2% vs. 4.1%, p< 0.0001). Data comparing all participants in the first and preliminary results on second round participants who tested FIT positive and were eligible for colonoscopy were compared (4.195 vs. 1.890 colonoscopy studies performed, respectively). A significant decrease in the PPV was observed for AA and CRC between the first and second round (33.3% to 23.5%; p<0.0001 and 6.29% to 3.1%; p<0.0001), respectively. There were no significant differences in stages (I+II vs. III+IV) of CRC detected in the first and second round (p<0.408). Although not achieving statistical significance, proximal AA were more frequent in the first round (9.0% vs. 7.6%, p<0.083). A significantly increase in proximal location of detected CRC were observed on second round (20.1% vs. 34.5%, p< 0.031)
CONCLUSION: In our population-based CRC screening program the rate of positive results from FIT decrease after a first round, and PPVs of FIT for AA and CRC are significantly lower among second-round participants who tested negative in the first round. Although no differences are observed in CRC stage, more proximal CRC are detected on second round screening for CRC. These results could have a significant impact on the provision cost for population-based CRC screening programs.
Disclosure of Interest: None declared

P1513 THE DIAGNOSTIC RELEVANCE OF FAECAL LACTOFERRIN TEST IN COLORECTAL CANCER SCREENING

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INTRODUCTION: Faecal haemoglobin (Hb) and transferrin (Tf) tests are often used in colorectal cancer screening. However, these tests are inadequate when the amount of blood in the test sample is very low. Lactoferrin (LF) is a glycoprotein secreted by most mucosal cells and predominantly by neutrophils as a component of inflammatory response.
AIMS & METHODS: Between June 2011 and June 2012, faecal Lf along with the conventional faecal Hb and Tf tests were undertaken in 2,012 consecutive subjects who underwent screening for colorectal cancer at our hospital. Nescauto® Hemo Plus, Nescauto® Transferrin Plus, and Nescauto® Lactoferrin Plus test reagents were used to assay faecal Hb, Tf and Lf, respectively by using the NS-PlusC15 instrument (all from Alfresa Pharma). Any subject with at least one positive test result underwent colonoscopy as an additional screening test.
RESULTS: There were 477 subjects (23.7%) with two or three positive test results. The positive rates were 6.6% for faecal Hb, 5.7% for Tf, and 17.2% for Lf, reflecting markedly better sensitivity for faecal Lf assay. Further, among the 183 subjects who underwent colonoscopy, 107 had colorectal cancer, ulcerative colitis, or other colonic lesions like diverticula or haemorrhoids. Of the 107 subjects with lesions, 79 were positive in the faecal Lf test; in 64 of these, only Lf test was positive. In contrast, in the conventional faecal Hb and Tf tests, only 43 of the 107 subjects were positive. Additionally, 3 subjects had colorectal cancer, and only one of these was positive for faecal Hb or Tf test, while all 3 were positive in the faecal Lf test.
CONCLUSION: In this comparative study, the positive rate for faecal Lf was about 3 times higher than for either faecal Hb or Tf. This led to more precise cut-off value for faecal Tf test. Therefore, in the screening for colorectal cancer and other colonic lesions that cannot be detected by using the occult blood test, faecal Lf should yield better screening outcome, and serve as a clinically relevant biomarker in this clinical setting.
Disclosure of Interest: None declared

P1514 LOW PREVALENCE OF SERRATED POLYPOSIS SYNDROME IN SCREENING POPULATIONS – A SYSTEMATIC REVIEW

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INTRODUCTION: Population screening programs offer unique opportunities to study prevalence of less common polyposis syndromes in relatively unbiased populations. For serrated polyposis syndrome (SPS) the most cited prevalence is 1 patient in every 3000 persons (Lockett et al. 2001), but this number has been subject of debate. The change of WHO criteria for diagnosis of SPS in 2010 might also affect the prevalence. An up-to-date estimate of the prevalence of SPS is necessary to predict the number of cases in screening programs.
AIMS & METHODS: A systematic literature search was conducted in the electronic databases Cochrane Library, PubMed, EMBASE and Web of Science up to February 2014 using a search strategy including the terms *serrated, hyperplastic, metaplastic, polyp, polyposis* and *syndrome*. Studies reporting the prevalence of SPS defined by the WHO criteria in screening populations were selected. Two reviewers independently calculated prevalence numbers and appraised risk of bias[1].
RESULTS: Prevalence of SPS in screening populations was reported in six studies (Table 1) and varied between 0 – 0.66%. The highest prevalence (0.34% and 0.66%) was seen in studies (2-3) based on screening programmes preselecting patients with a positive stool test. Colonoscopy based screening programmes (4-6) have the lowest risk of bias reporting prevalences ranging from 0 to 0.09%. The most cited study (1) reporting a prevalence of 0.03%, has a high risk of bias because it is based on data from a sigmoidoscopy based screening trial. Only patients with high risk adenomas or ≥ 20 distal hyperplastic polyps were referred for colonoscopy. Therefore it is likely that patients presenting with proximal serrated polyps were missed.

	Screening method	WHO criteria	SPS patients/ participants	Prevalence, *(95% CI)*	Risk of bias
1 Lockett et al, 2001	Sigmoidoscopy	2000	12/40674	0.03% (0.01-0.05)	High
2 Biswas et al, 2013	gFOBT	2010	5/755	0.66% (0.08-1.24)	High
3 Moreira et al, 2013	FIT	2010	8/2355	0.34% (0.10-0.57)	High
4 Orlowska et al, 2009	Colonoscopy	2000	28/50148	0.06% (0.04-0.08)	Intermediate
5 Kahi et al, 2012	Colonoscopy	2010	3/3170	0.09% (0 – 0.20)	Intermediate
6 Hazewinkel et al, 2014	Colonoscopy	2010	0/1426	0% (NA)	Low

Table 1. Overview of included studies. CI = Confidence Interval, gFOBT = guaiac Fecal Occult Blood Testing, FIT = Faecal Immunochemical Testing, NA = Not Applicable.
CONCLUSION: Due to the low number of high quality studies, true prevalence of SPS is unclear but is likely to be below 0.09%. Prevalence in preselected screening populations after positive stool testing are higher with reported range between 0.34 and 0.66%.
REFERENCES
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P1515 EFFECT OF VISCERAL OBESITY ON LYMPH NODE METASTASIS IN COLON CANCER

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INTRODUCTION: An association between obesity and unfavorable outcomes for various types of malignancy has been established. However, the relationship between fat distribution and lymph node metastasis has not been well studied.
AIMS & METHODS: The aim of our study is to determine the impact of visceral obesity on lymph node metastasis and overall survival in colon cancer. This study reviewed medical records for consecutive patients who underwent radical resection for colon cancer between 2003 and 2008. Metastatic lymph node ratio (MLR) was defined as the number of involved nodes by tumor divided to the total number of resected lymph nodes. Visceral obesity was determined by measuring abdominal fat volume distribution via CT scan and then calculating the percentage of visceral fat (VF%) to total fat area.
RESULTS: 278 patients were divided into two groups: VFs (VF% $\leq$ 29, n = 81) and VFv (VF% $>$ 29, n = 197). The baseline characteristics showed some differences between two groups with respect to body mass index, total cholesterol and the proportion of MLR. In the multivariate analysis, MLR significantly decreased with the higher VF% (OR = 0.406, 95% CI = 0.206–0.801, $P = 0.009$). In addition, MLR was significantly associated with HbA1c, differentiation, lymphovascular invasion and perineural invasion. There was significant difference in overall survival between patients with VF% $\leq$ 29 and those with VF% $>$ 29 ($P = 0.009$).
CONCLUSION: Visceral obesity was associated with a lower ratio of metastatic lymph nodes and higher overall survival.
Disclosure of Interest: None declared

P1516 MEK5/ERK5 SIGNALLING ACTIVATES NF-KB AND PROMOTES A MORE AGGRESSIVE PHENOTYPE IN HUMAN COLON CANCER CELLS

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INTRODUCTION: ERK5 and its direct activator, MEK5, are overexpressed in prostate and breast cancer, correlating with overall poorer disease prognosis, and leading to increased proliferation, metastasis and chemoresistance. In addition, we have previously demonstrated that ERK5 silencing increases colon cancer (CC) cell apoptosis and 5-FU-sensitivity, highlighting the relevance of ERK5 signalling in CC.
AIMS & METHODS: In the present study, we evaluated the expression of MEK5, ERK5, NF-kB and IkB in 284 human CC samples, including normal colonic mucosa, tubulovillous adenomas, and adenocarcinomas with proficient or deficient DNA mismatch repair system (pMMR and dMMR, respectively). In addition, to further evaluate ERK5 signalling in CC, we produced a stable cell line model with differential ERK5 activation via lentiviral transduction and cell sorting of SW620 colon carcinoma cells, to overexpress constitutively active MEK5 (MEK5-CA), dominant-negative (MEK5-DN), or empty vector control. Next, we evaluated the impact of MEK5/ERK5 signalling in cell cycle progression, by flow cytometry following PI staining, and cell migration, by wound healing and Boyden assay. NF-kB activation was estimated by the ratio of NF-kB and IkB expression levels, NF-kB nuclear translocation, and also by luciferase reporter assay. Finally, we performed cecum orthotopic xenografts in NOD. SCID mice and evaluated tumor cell metastization.
RESULTS: Our results show that ERK5 and MEK5 are overexpressed in human adenomas ($p < 0.01$) and pMMR and dMMR adenocarcinomas ($p < 0.05$). Similarly, NF-kB is overexpressed in adenomas, pMMR and dMMR adenocarcinomas, and significantly overactivated in pMMR and dMMR adenocarcinomas ($p < 0.05$). According to TNM staging, more aggressive tumors displayed higher ERK5 overexpression and NF-kB activation ($p < 0.05$), suggesting that ERK5 might be relevant in CC progression and to the acquisition of more invasive and metastatic potential. Interestingly, we observed a significant correlation between ERK5 expression and NF-kB activation, in human adenocarcinoma samples ($p < 0.05$). We also showed that *in vitro,* ERK5 overactivation (MEK5-CA) significantly accelerates cell cycle progression ($p < 0.01$) and increases cell migration ($p < 0.001$), as compared to inactive ERK5 (MEK5-DN) and empty control cell lines. In parallel, MEK5-CA cells displayed increased NF-kB nuclear translocation and transcriptional activity ($p < 0.05$), together with increased expression of mesenchymal marker Vimentin ($p < 0.05$). Finally, we observed that 6-weeks post tumor cell injection into the cecum wall of NOD. SCID mice, MEK5-CA-injected mice presented increased incidence of lymph node metastasis (2/4), compared to MEK-DN mice (0/5).
CONCLUSION: Our results suggest that ERK5/NF-kB signalling pathway is important for tumor onset, progression and metastization, possibly representing a novel therapeutic target in CC treatment.
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Disclosure of Interest: None declared

P1517 SYSTEMATIC, ROBUST, REVERSIBLE DNA METHYLATION PRECEDE SPORADIC, RANDOM MUTATIONS IN COLORECTAL ADENOMA-DYSPLASIA-CANCER DEVELOPMENT

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INTRODUCTION: Colorectal adenoma-dysplasia-cancer (AD-CRC) development is characterised by sequential, random and sporadic ($<45\%$ frequency) mutations of certain genes. Recent epigenetic investigations showed that methylation of selected genes occurs in high frequency ($>95\%$) in early stages of cancer already. New generation sequencing and array technologies now allow the systematic investigation and comparison of genetic or epigenetic alterations in AD-CRC.
AIMS & METHODS: We aimed to evalate the role of epigenetic and genetic alterations in the AD-CRC development using new generation sequencing and DNA methylation arrays. DNA was isolated from fresh frozen biopsy specimens (20 normals; 33 adenomas; 17 CRCs). First, a multiplex PCR panel was designed to amplify mutation hot spots of 12 selected genes (APC, BRAF, CTNNB1, EGFR, FBXW7, KRAS, MSH6, NRAS, PIK3CA, SMAD2, SMAD4, TP53). Amplicons of eight samples were sequenced together at once by a GS Junior instrument (Roche) using ligated, barcoded adaptors for library preparation. Further methylation analysis of 94 genes was performed on Human Colon Cancer EpiTect Methyl II Signature PCR Array (Qiagen) from the same DNA specimen. After RNA isolation whole genome expression analysis was performed with HGU133plus2 microarrays (Affymetrix) from 49 normal, 49 adenoma and 49 CRC specimens and on HT-29 cells with and without 5-aza-deoxycytidin treatment. Immunohistochemistry confirmation of expression changes on protein level was performed using tissue microarrays.
RESULTS: Mutations were found in 76% of adenomas and 78% of the cancer cases. The average number of mutations found in mutated samples was 1; 1,8; 1,9 and 2,3 in low grade adenomas, high grade adenomas, carcinomas and serrated adenomas, respectively. The only mutation found in normal samples was a germ line APC mutation. The APC suppressor gene was mutated in adenomas more frequently than in carcinomas (36% vs. 24%). The most frequently mutated genes were APC, TP53 and KRAS with 36%, 18% and 26% frequencies in adenomas and 24%, 47% and 45% frequencies in carcinomas. Interestingly, no sample was found bearing APC and TP53 mutations together. DNA methylation was found in 100 % of the investigated colorectal adenoma and cancer specimens. Eight genes were found to be methylated in all of the cases. This gen set included SFRP1, MAL, SLIT2, SST, VIM; another set of genes (DKK1, SLI3, TMEFF2) was found to be hypermethylated in adenomas and cancers in $>75\%$ of the cases. In adenomas 56 genes, in dysplasias 40 in cancer 37 genes were methylated ($>50\%$ of the cases). The effect of methylation could be confirmed by decreased mRNA and protein expression. Demethylation treatment successfully restored the expression profile of the top methylated genes.
CONCLUSION: Methylation occurred in early premalignant stages in parallel followed by somatic random mutations in increasing number through the AD-CRC development. Demethylation treatment could reverse the systematic, robust methylation alterations. Epigenetic alterations precede the somatic mutations of the AD-CRC and show higher significance in CRC development than genetic.
Disclosure of Interest: None declared

P1518 AN ABNORMAL BODY MASS INDEX IS ASSOCIATED WITH AN INCREASED RISK OF RECTOSIGMOID CANCER RISK: INTEREST A SHORT RECTO-SIGMOIDOSCOPY FOR EARLY DETECTION

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INTRODUCTION: Obesity is a well-known risk factor for colorectal cancer (CRC) and is associated with underweight with a poor prognosis. The French CRC screening is based on cancer register which allow diagnosing one cancer for 2000 performed colonoscopy. We studied the influence of body mass index (BMI), which is evolving during past decades, on the location of CRC and its relevance to adapt the screening.
AIMS & METHODS: From January 2008 to December 2010, all patients consecutively operated for CRC in 20 Parisian centres were collected in a prospective database (COINCIDE project). Data analysis was done through its proprietary algorithm clustering supervised non-parametric (Q-Finder®).
RESULTS: Of the 1908 patients, CRC primary localization was sigmoid or rectal in 1095 patients. Six subgroups of patients with an excess risk of developing rectosigmoid cancer were linked to abnormal BMI. For example, 142 patients from 42 to 69 years, with a BMI from 24 to 33 (overweight and obese) had a surrisk of 1.8. Another subgroup of 123 patients from 53 to 63 years, with a BMI from 14 to 22.4 (underweight) had a 1.9 times higher risk.
CONCLUSION: COINCIDE database is representative, on a very recent period, of the Parisian population of CCR. Abnormal BMI (overweight and underweight) is associated with an excess risk of rectosigmoid CRC. We discuss an intensification of CRC screening for this population by achieving a sigmoidoscopy at the age of 45 years. The validation of the cost and effectiveness of such a practice should be performed prospectively.
Disclosure of Interest: None declared

P1519 MEK5-ERK5 SIGNALLING INHIBITION DECREASES PROLIFERATION AND INCREASES 5-FLUOROURACIL-INDUCED APOPTOSIS IN COLON CANCER CELLS

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INTRODUCTION: Aberrant MEK5-ERK5 signalling has been reported in several types of human cancer, being established as a critical player in cancer development, and as a key survival signal for chemoresistance in response to several antitumor agents. In colon cancer (CC), MEK5 overactivation was correlated with disease stage progression. Moreover, recent data from our group demonstrated that MEK5 and ERK5 expression is increased in human colon adenomas and adenocarcinomas. Importantly, we have also demonstrated that ERK5 silencing enhances CC cell sensitivity to 5-fluorouracil (5-FU), the most widely used chemotherapeutic for CC treatment.
AIMS & METHODS: In the present study, we aimed to investigate the role of MEK5-ERK5 signalling in CC cell proliferation and sensitivity to 5-FU exposure. For this purpose, HCT116 and SW620 cell lines expressing a constitutively active (CA) or a dominant negative (DN) form of MEK5 were produced by lentiviral transduction, followed by sorting of stably transduced cells.
RESULTS: Our results demonstrate that CA-MEK5 increased cell proliferation ($p < 0.05$) and KRAS expression ($p < 0.01$), in both HCT116 and SW620 cells. In turn, in the HCT116 model, DN-MEK5 increased the expression of p53 ($p < 0.05$) and its transcriptional targets p21 and Puma ($p < 0.01$), as well as cell death following 5-FU exposure ($p < 0.05$). This was further associated with increased caspase-3/7 activation and apoptosis ($p < 0.05$). Conversely, CA-MEK5 reduced 5-FU-induced cytotoxicity and apoptosis ($p < 0.05$). Furthermore, 5-FU exposure markedly decreased the levels of endogenous MEK5 and ERK5 expression and activation ($p < 0.05$). Finally, our results show that MEK5-ERK5 activation may modulate cell proliferation and sensitivity to 5-FU through downregulation of the expression of the tumour suppressor miRNAS, miRNA-143, -145, and -34a ($p < 0.05$).
CONCLUSION: Overall, our results indicate that MEK5/ERK5 pathway overactivation may contribute to CC aggressiveness and chemoresistance, suggesting ERK5-targeted inhibition, via siRNA, miRNA or small-molecule inhibitors, may provide a promising therapeutic approach for CC treatment.
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Disclosure of Interest: None declared

P1520 PTP1B EXPRESSION AND PHOSPHATASE ACTIVITY ARE INCREASED IN PRIMARY COLORECTAL CANCER WHICH LEADS TO A MORE INVASIVE PHENOTYPE

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INTRODUCTION: Cell signaling is dependent on the balance between phosphorylation of proteins by kinases and dephosphorylation by phosphatases. This balance if often disrupted in colorectal cancer (CRC), leading to increased cell proliferation and invasion. For many years research has focused on the role of kinases as potential oncogenes in cancer, while phosphatases were commonly assumed to be tumor suppressive. However, this dogma is currently changing as phosphatases have also been shown to positively affect cancer growth. One of these phosphatases is protein tyrosine phosphatase 1B (PTP1B).
AIMS & METHODS: The aim of this study was to investigate the expression and phosphatase activity of PTP1B in CRC, and elucidate its effects on cellular functions and signaling. PTP1B expression was analysed by immunohistochemistry on microsections from biopsies of dysplasia (n = 6), adenocarcinoma (n = 9) and control (inactive ulcerative colitis, n = 5), as well as by western blotting of paired freshly frozen CRC and normal adjacent tissue (n = 10). Phosphatase activity was also assessed in these latter samples by immunoprecipitating PTP1B under saturating conditions, followed by a phosphatase activity assay using PNPP as substrate. To investigate the effects of PTP1B on proliferation, adhesion, migration, and elucidate its downstream targets, we manipulated the PTP1B expression *in vitro* by lentiviral transduction of HCT116 and Caco-2 cells with 2 different shRNAs against PTP1B.
RESULTS: PTP1B expression in intestinal epithelial cells (IECs) is low in normal colon (14% positive; mean intensity 0.2±0.1) and increases from dysplasia to carcinoma (100% positive IECs; with mean intensity rising from 1.4±0.3 to 1.8±0.3 respectively). These results were confirmed by western blot analysis. The intrinsic enzymatic activity of the PTP1B protein is significantly increased in cancer compared to adjacent normal tissue (mean OD 1.0 in CRC compared to 0.2 in normal tissue) (p = 0.001). Knocking down PTP1B in CRC cells reduced the phosphorylation of the mitogenic kinase ERK by approximately 50%, and decreased mRNA levels of downstream targets involved in proliferation; i.e. c-MYC and CyclinD1. Furthermore, adhesion, migration, and proliferation were significantly reduced in PTP1B knockdown cells.
CONCLUSION: Not only is the expression of PTP1B is increased in colorectal cancer as compared to normal tissue, but strikingly, the intrinsic enzymatic activity of the protein is also enhanced, suggesting a role for PTP1B phosphatase activity in CRC progression. Knocking down PTP1B in CRC cell lines results in a less invasive phenotype with lower adhesion, migration and proliferation capabilities, by interfering in the RAS-RAF-ERK pathway. Together these results suggest that inhibition of PTP1B activity is a promising new target in the treatment of colorectal cancer and the prevention of metastasis.
Disclosure of Interest: None declared

P1521 REVERSIBLE DNA METHYLATION OF SFRP1 IN STROMAL MYOFIBROBLASTS IS A FINAL STEP IN EPITHELIAL CELL GROWTH BLOCKADE IN COLORECTAL CANCER DEVELOPMENT

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INTRODUCTION: Loss of stroma-mediated inhibitory mechanisms can contribute to uncontrolled proliferation and growth of tumor cells. Expression changes of stromal secreted frizzled-related protein 1 (*SFRP1*) Wnt pathway inhibitor were not evaluated in colorectal carcinoma (CRC) development yet.
AIMS & METHODS: Our aims were to evaluate *SFRP1* expression changes in CRC development by mRNA analysis and immunohistochemistry (IHC). We also aimed to analyse SFRP1 promoter DNA methylation levels in order to identify epigenetic alterations from laser microdissected epithelial and stromal components as well as from isolated myofibroblasts. We aimed to examine the effect of recombinant SFRP1 protein administration and demethylation treatment to CRC cell lines harboring different mutations. For *SFRP1* gene expression examination biopsy samples from CRC (moderately differentiated tumors from sigmoid colon and rectum; n = 49) areas and paired histologically normal colonic mucosa (n = 49) were analyzed by HGU133Plus2.0 microarrays (Affymetrix) and were validated with real-time PCR. SFRP1 IHC was detected on normal biopsy samples (n = 20), surgically removed CRC (n = 35) and colonic tissues containing normal adjacent tumor (NAT), adenoma and CRC areas on the same slide (n = 14). We microdissected at least 10^4 cells from epithelial and stromal components, furthermore, approx. 10^3 α-smooth muscle actin immunopositive myofibroblasts from similar stromal areas of consecutive slides. SFRP1 promoter DNA methylation was evaluated by bisulfite sequencing. Effect of recombinant SFRP1 protein treatment to cell proliferation and apoptosis were examined on SW480 (APC mutant) and HCT116 (APC wild type, β-catenin mutant) cell lines. SFRP1 gene expression analysis was performed on HT-29 (p53 mutant) cells with or without 5-aza-2-deoxycitidine demethylation treatment.
RESULTS: SFRP1 showed decreased expression in mRNA and no expression on protein level in parallel in adenoma and CRC epithelium. We identified α-smooth muscle actin positive myofibroblasts as the main source of stromal SFRP1 protein in NAT areas and adenomas, but this protein expression disappeared along the transition into the malignant stage. DNA hypermethylation of the *SFRP1* promoter was detected in microdissected epithelium in adenoma and CRC and in CRC only in myofibroblasts. Recombinant SFRP1 treatment induced apoptosis and inhibition of proliferation in SW480 and less in HCT116 cells. Demethylation treatment could increase SFRP1 expression significantly in HT-29 CRC cell line.
CONCLUSION: Decreased expression of SFRP1 in CRC development is related to DNA hypermethylation. Epithelial methylation of SFRP1 could be observed in NAT, adenoma and cancer, but myofibroblast SFRP1 methylation could be detected in cancer stage only. The restored expression of SFRP1 in colorectal cancer cell lines leads to decrease in proliferation and apoptosis induction. 5-aza-deoxycytidin is a potential demethylation agent for SFRP1 with consecutive increase in gene expression.
Disclosure of Interest: None declared

P1522 THE S100B-P53 PROTEIN-PROTEIN INTERACTION: A NOVEL ROLE FOR ENTERIC GLIA IN COLON CANCER

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INTRODUCTION: The connection between intestinal inflammation and tumorigenesis is well-established. We previously showed that upregulation of the enteroglial-derived S100B protein amplifies intestinal inflammation via its interaction with the Receptor for Advanced Glycation Endproducts (RAGE). Recently, S100B-p53 protein-protein interaction has been described to be involved in the melanoma. Our aim is to investigate the role of S100B and its interactions with the tumor suppressor p53 in human sporadic colon cancer.
AIMS & METHODS: The expression of S100B, RAGE, p53 was evaluated in cancer and control colonic tissues (n = 8 and 6 subjects, respectively); secretion of VEGF and Filamin was also assessed to estimate cancer cell invasion and angiogenesis, respectively. In order to investigate the direct involvement of the enteroglial protein in tumorigenesis, control colonic tissues were challenged with increasing concentration of S100B (0.05, 0.5 and 5μM, for 48 h) and expression of RAGE, p53, VEGF and Filamin were analysed. Similarly, the effect of Pentamidine (0.05, 0.5 and 5μM, for 48 h), that was previously demonstrated to disrupts the S100B-p53 protein-protein interaction, on p53 expression was assessed on control colon tissues.
RESULTS: In colon cancer the expression of p53 was significantly reduced (18±2 vs. 0.8± 0.1 mm^2, $p < 0.001$), while S100B, RAGE, VEGF and Filamin A were all significantly higher than in control tissues (28±2 vs. 6±0.8 mm^2, 18±3 vs. 2±1 mm^2, 7±1 vs. 1.8±0.9 ng/ml and 7±2 vs. 2.5±1ng/ml, all $p < 0.001$).

In vitro challenge with 5μM of S100B induced a tenfold decrease of p53 (15±0.4 vs. 2.2±0.6 mm^2, $p<0.01$) and a significant increase of RAGE VEGF and Filamin (12±3 vs. 1.3±0.2 mm^2, 1.9±0.3 vs. 5±1 and 1.3±0.2 vs. 8±2 ng/ml, respectively, all $p<0.01$ vs. control); data with S100B 0.05 and 0.5 μM are not shown. Most interestingly, pentamidine treatment yields to a concentration-dependent (0.05-5μM) and significant increase of p53 (8±0.3, 10±3 and 18±3 vs. 3±0.3 mm^2, $p<0.05$, <0.01 and <0.001, respectively).

CONCLUSION: We showed that the S100B protein is significantly increased in human sporadic colon cancer. We also showed that exogenous S100B is able to significantly reduce the expression of p53 protein, together with a consistent increase of RAGE, VEGF and Filamin A and that these effects were completely abolished by pentamidine, that is known to disrupts the S100B-p53 protein-protein interaction. Our data for the first time indicate that the enteric glia is likely involved in the tumorigenesis of colon cancer; at the same time we indicate in the disruption of S100B-p53 protein-protein interaction a new potential target of intervention for colon cancer.

Disclosure of Interest: None declared

P1523 ENTERIC GLIAL CELLS ACTIVATE COLON CANCER STEM CELLS TO PROMOTE TUMORIGENESIS

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INTRODUCTION: Similar to the cellular hierarchy that drives normal/healthy intestinal crypts, only a limited number of colon cancer cells possess the ability to self-renew and to give rise to all the different cancer cell types of the tumor[1, 2]. These cells, called cancer stem cells (CSCs), are thought to be responsible for colorectal cancer (CRC) initiation, propagation and recurrence. Current views in the field suggest that similar to normal intestinal stem cells, CSCs are regulated by their niche composed of resident or recruited cells that have been hijacked/altered by the tumor in order to exploit them as nurturing cells delivering paracrine signals crucial to CSC maintenance and tumor growth. Among CSC neighboring cells are enteric glial cells (EGCs) that are potent regulators of intestinal epithelial barrier functions[3], but whose impact on CSCs has not yet been studied. We hypothesized that EGCs modulate CSC functions and associated tumorigenesis.

AIMS & METHODS: *In vitro*. CSCs have been FACS-isolated from HT29 CRC cell line based on CD44 and CD133 expression ($CD133^{High}/CD44^{High}$), and cultured in 3D Matrigel in presence of EGCs seeded on Transwell filters. Two types of EGCs were used: a non-transformed EGC line purified from rat embryo (EGC-JUG) and primary cultures of human EGCs (EGC-HOG). Impact of EGCs was assessed on numbers and size of tumorspheres grown from CSCs, and compared to non-transformed human fibroblast CCD-18Co cells as well as known glial-derived soluble factors. *In vivo*. CSCs were injected alone *vs*. concomitantly with EGCs subcutaneously in immunodeficient mice.

RESULTS: Our data demonstrate that *in vitro* EGC-JUG massively increased numbers and size of tumorspheres grown from CSCs. These results were recapitulated by EGC-HOG. In contrast, CCD-18Co fibroblasts induced an increase in tumorspheres size but not in numbers. *In vivo*, concomitant injection of CSCs and EGCs increased tumor load as compared with CSCs injected alone. Furthermore, our *in vitro* preliminary data indicate that EGC-conditioned medium (CM) did not impact CSCs, suggesting that at basal state, EGCs do not release pro-tumorigenic factors. However, CM of EGCs that have been pre-incubated with CRC cells exhibited similar impact on CSCs than direct co-culture with EGCs, indicating that tumor cells activate EGCs to acquire pro-tumorigenic abilities. Among all known EGC-derived soluble factors tested, only prostaglandin E2 (PGE2) reproduced EGC effects on CSC-derived tumorsphere growth *in vitro*. Furthermore, RT-qPCR data show that CRC cells induced increased expression of mPGES-1, the terminal synthase responsible for generating PGE2, in EGCs. Finally, CM of EGCs that have been first pre-incubated with CRC cell-CM and then treated with a specific inhibitor of mPGES-1 (CAY10526), did not impact CSCs, indicating that CAY10526 abolished pro-tumorigenic properties induced by CRC cells in EGCs.

CONCLUSION: Altogether these results strongly suggest that CRC cells activate EGCs to acquire pro-tumorigenic abilities, and that tumor-activated EGCs stimulate CSC clonogenicity and tumorigenicity *via* PGE2-dependent pathways.

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P1524 ESTABLISHMENT OF AN ENDOSCOPY-BASED MURINE ORTHOTOPIC TUMOR IMPLANTATION MODEL TO STUDY COLORECTAL CANCER

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INTRODUCTION: Despite recent advances in diagnostics and therapy of colorectal cancer (CRC) the prognosis is still limited, especially in patients with advanced stages of the disease. New diagnostic and therapeutic approaches are therefore highly desirable. Aim of this study was to establish an orthotopic tumor model for CRC by endoscopy-guided implantation of tumor cells in the colon of immunodeficient mice.

AIMS & METHODS: The implantation of CRC tumor cells (Caco-2 and HT29) was primarily performed either subcutaneously or orthotopic by submucosal injection during murine colonoscopy (coloview miniendoscopic system) in CD1 nude mice (n = 6) as well as in NOD/SCID mice (n = 10). For monitoring of tumor development, matrixmetalloproteinases (MMP) expression of tumors was assessed 24h after i.v.-injection of a Cy5.5-labeled MMP-selective tracer (Cy5.5-AF443) by *Fluorescence Reflectance Imaging (FRI)* and *Fluorescence Endoscopy*. Finally, tumors were histologically evaluated.

RESULTS: Subcutaneaously implanted HT-29 cells resulted in a marked tumor growth 14 days after implantation. In contrast, orthotopic implantation in the colon of CD1 mice lead to decelerated tumor development after 17 weeks. In the NOD/SCID mice, distinct tumor growth could already be detected beginning at day 14 after submucosal cell injection. Subsequently, rapid tumors growth with occupation of the entire colonic circumference could be observed. Notably, post mortem analysis revealed suspect liver lesions, which were confirmed to be metastasis by histological evaluation. Pathology revealed CRC limited to the submucosa, explaining the low signal detected by fluorescence endoscopy.

As opposed to HT-29 cells, successful implantation of Caco-2-cells could not be achieved, neither by s.c. nor by orthotopic implantation.

FRI revealed only a discreet tracer uptake in s.c. implanted tumors with a target-to-background ratio of 1.55 ± 0.49. Confirmatively, western blot analysis and IHC proved no significant MMP-2/-9 expression in s.c. implanted tumors. In contrast, MMP-tracer uptake was markedly enhanced in orthotopic implanted tumors.

CONCLUSION: Orthotopic, endoscopy-guided implantation of HT-29 colorectal carcinoma cells was successful in immunodeficient NOD/SCID mice. Therefore, this model appears to be promising for examination of tumor biology and preclinical evaluation of novel diagnostic and therapeutic approaches in the future.

Disclosure of Interest: None declared

P1525 MISMATCH REPAIR GENES INHIBITION ENHANCE CD80 EXPRESSION IN COLORECTAL CANCER CELL LINE AND SPORADIC DEFECTS ARE ASSOCIATED TO HICD80+ LAMINA PROPRIA MONUCLEAR CELLS INFILTRATION AND BETTER SURVIVAL

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INTRODUCTION: Genomic defects in DNA mismatch repair (MMR) genes (MSH2, MLH1, PSM2 or MSH6) characterize the hereditary non polyposis colon cancer (HNPCC). Moreover, most colorectal cancers (CRC) have MMR defect caused by DNA methylation. Several studies demonstrated that patients with MMR-deficient colon cancers have a more favourable stage-adjusted prognosis. Since the immune environment has been demonstrated to influence CRC prognosis, we aimed to investigate whether MMR genes modulate the immune response in CRC.

AIMS & METHODS: A group of 108 consecutive patients operated on for CRC was retrospectively analysed. The presence of Bethesda criteria for HNPCC diagnosis was assessed. Inflammatory infiltration was quantified by standard histology. Immunohistochemistry for costimulatory molecule CD80, innate immunity (TLR4 and MyD88), tumor infiltrating lymphocytes (CD4, CD8) and MMR genes was performed. Patients were stratified in three groups: no MMR genes defect, MMR genes defects alone and MMR genes defects and at least one positive Bethesda criteria. HT29 (CRC cell line) cells were cultured and transfected with specific siRNAs (siMSH2, siMLH1, siMSH6 and siPSM2) and the rate of CD80+ positive cells was quantified by flow cytometry in presence and in absence of oxidative stress condition. Non parametric statistics and survival analysis were used.

RESULTS: Patients with at least one MMR gene defect had more frequently a high CD8+ lymphocytes infiltration ($p = 0.01$) and more frequently a high CD8/CD4 ratio ($p = 0.01$). Patients with MMR defects alone had a better survival than patients with no defects (HR = 0.40 (95% CI 0.06-1.03), $p = 0.051$). LPMC infiltration, frequency of highCD8+ lymphocytes infiltration and frequency of highCD8/CD4 ratio were significantly higher in patients who had a MMR genes defect alone compared to those who had no MMR genes defect and to those with MMR genes defect and positive Bethesda criteria ($p = 0.014$, $p = 0.01$ and $p = 0.05$). A significantly greater frequency of patients with high CD80 expression was observed in patients who had a MMR genes defect alone compared to patients who had no MMR gene defect and to those with MMR genes defect and positive Bethesda criteria ($p = 0.048$). In standard condition, RNA silencing of MSH2, MLH1 and MSH6 significantly increased CD80+ cells rate ($p = 0.007$, $p = 0.023$ and $p = 0.015$). In oxidative condition, RNA silencing of MSH2 and MSH6 further increased CD80+ cells rate ($p = 0.031$ and $p = 0.015$).

CONCLUSION: Patients with MMR defects and no Bethesda criteria have a better survival. In this group, the antigen presenting cells and CD8+ tumor infiltrating lylmphocyte cross talk was enhanced as shown by higher LPMC infiltration and higher frequency of hiCD80+ and hiCD8+ patients. In vitro silencing of MMR genes expression significantly increase CD80 expression in CRC cells. All together these data support the view that a more effective immune activation in CRC may be responsible of a better prognosis in patients with MMR defects.

Disclosure of Interest: None declared

P1526 HIGH NITRIC OXIDE PRODUCTION, SECONDARY TO HIGH INDUCIBLE- NITRIC OXIDE SYNTHASE EXPRESSION, IS ESSENTIAL IN REGULATING TUMOUR INITIATING PROPERTIES OF COLON CANCER STEM CELLS

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INTRODUCTION: Several studies have indicated that continuous exposure to high concentrations of Nitric Oxide (NO), produced by inducibile-NO synthase (iNOS), promote neoplastic transformation in many human cancers and especially in colon cancer (CC). Recently, it has also been suggested that high NO synthesis is a distinctive feature of "cancer stem cells" (CSC), a tumor subpopulation with self-renewal capacity, that may be identified by the expression of the CD133 surface marker.
AIMS & METHODS: Aims of this study were to explore the contribution of NO in the definition of colon CSC features and evaluate potential strategies to treat CC by modulating NO production. By immunohistochemistry analysis we evaluated iNOS and CD133 expression in 30 samples of human CC. Using the DAF-2DA detection system, we assayed the production of intracellular NO in 5 colon CSC lines obtained from human CC tissues. By FACS sorter, we purified the NO^{high} and NO^{low} fractions from all colon CSC lines. We compared the tumorigenic potential of both cell fractions by *in vitro* and *in vivo* assays. To tested the potential antitumor effects of iNOS modulation, we treated colon CSCs with the selective iNOS inhibitor 1400W or we stably transfected these cells with two distinct iNOS-directed short-harpin RNA (shRNAs).
RESULTS: NO^{high} CSCs display an overespression of stem cell markers and higher expression levels of iNOS than NO^{low} cells. Interestingly, immunohistochemistry analysis confirmed that, regardless of tumor differentiation grade and TNM stage, there was a significant association between iNOS overexpression and higher expression level of the stem cell marker CD133, in human CC.
Moreover, we demonstrated, by *in vitro* and *in vivo* assays, that NO^{high} cells displayed higher tumorigenic abilities than NO^{low} fractions. The blockade of endogenous NO availability using a specific iNOS inhibitor and genetic knockdown of iNOS resulted in a significant reduction of colon CSC growth and tumorigenic capacity: a lower capacity to give rise to colonies in soft agar, a dramatic decrease of invasivness and *in vivo* tumor growth (xenotransplantations in nude mice). These data confirmed an integral role for endogenous NO and iNOS activity in the biology of colon CSCs. Interestingly, analysis of the genes altered by iNOS-directed shRNA showed that the knockdown of iNOS expression was associated with a significant down regulation of a wide range of signaling pathways in colon CSCs, especially genes involved in stemness and tumor progression (such as CD133, BMI, b-Catenin and NF-kB pathway).
CONCLUSION: These findings have demonstrated for the first time that endogenous NO plays an important role in defining the stemness properties of colon CSCs through cross-regulation of several cellular signaling pathways. This discovery could shed light on the mechanisms by which NO induces the growth and invasiveness of CC gathering new insights on the link between inflammation and colon tumorigenesis.
Disclosure of Interest: None declared

P1527 PROGRESSION OF AZOXYMETHANE-INDUCED COLON CARCINOGENESIS IS AFFECTED BY CD80 SIGNALING MODULATION

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INTRODUCTION: In patients with ulcerative colitis, the inconsistency between cumulative risk of colon cancer and cumulative rate of dysplasia suggested the presence of an immune surveillance mechanism. In non inflammatory colorectal cancer, T cell populations were demonstrated to play a significant role in the patients prognosis although it is not clear the trigger of this immune response and its efficiency. Costimulatory interactions are decisive in sensitization of T cells by antigen presenting cells and important for the elicitation of the immune responses. In previous studies, we observed a significant overexpression of CD80 costimulatory molecule in the colonic mucosa of patients with UC with dysplasia and its down-regulation at more advanced stages of carcinogenesis [1,2].
AIMS & METHODS: The aim of this study was to explore the effect of CD80 signaling modulation in a murine model of sporadic carcinogenesis of the colon. Male C57/Bl6 mice (12 weeks old) were injected i.p. with AOM (10 mg/Kg) once a week for 6 weeks. Neutralizing antibodies against CD80 or its inhibitory receptor CTLA4 were administered in order to inhibit or enhance CD80 signaling, respectively. Mice were randomized into three groups and treated i.p. with specific abs or isotype control twice, 3 and 4 months after the first AOM injection. Mice were euthanized 6 months after the first AOM injection. Colons were removed, flushed with PBS, fixed as "Swiss rolls" in formalin and paraffin embedded for histology. Hematoxylin and eosin colonic sections were examined for high grade dysplasia (HGD), low grade dysplasia (LGD), adenoma and inflammation. Non parametric statistics was used.
RESULTS: Invasive carcinoma was absent in all the three groups while adenoma was more frequent in mice injected with anti-CD80 compared to control and anti-CTLA4 treated mice ($p = 0.10$). HGD frequency was significantly augmented in mice treated with anti-CD80 antibody compared to the other two groups ($p = 0.02$). Moreover, HGD extension resulted increased in mice administered with anti-CD80 antibody and minimal in anti-CTLA4 treated mice ($p = 0.034$). LGD foci number and extension were significantly reduced in mice injected with anti-CTLA4 ($p = 0.005$). The inflammatory score resulted lower in mice treated with anti-CD80 but it was similar in control mice and those who received anti-CTLA4.
CONCLUSION: CD80 signaling inhibition caused a significant increase in HGD frequency and extension while its enhancement triggered a complete elimination of HGD and a dramatic reduction of LGD extension. These data suggest that CD80 signaling may control the immune surveillance mechanism in sporadic colon carcinogenesis.
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Disclosure of Interest: None declared

P1528 SUPPRESSION OF INTESTINAL TUMOR-INITIATING CELLS BY INHIBITION OF DNA METHYLATION

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INTRODUCTION: Cancer stem cells with self-renewal and multipotent capacity play critical roles in refractory cancers with high metastatic and invasive potential. Although DNA methylation inhibitors such as 5-aza-2'-deoxycytidine (5-Aza-CdR) are emerged as promising drugs in the treatment of malignant disorders, little is known about the effect of DNA methylation inhibition on cancer stem cells. Recently, the new 3-D culture system for stem cells called organoid culture has been developed (Sato T. *et al*. Nature; 459: 262-5, 2009).
AIMS & METHODS: To investigate the effect of DNA methylation inhibition on colon cancer stem cells, treatment with 5-Aza-CdR and knockdown of *Dnmt1* were performed in organoids derived from intestinal tumors of $Apc^{Min/+}$ (*Min*) mice, which is an animal model of colon cancer. *Min* mice were treated with 5-Aza-CdR (1 μg/body weight, $n = 12$) or PBS ($n = 11$) by subcutaneous injection weekly from 6 weeks of age. At 21 weeks of age, mice were dissected and number of intestinal polyps was counted. Stem cells were isolated from intestinal tumors of *Min* mice and maintained by organoid culture. Treatment with 5-Aza-CdR and lentivirus-mediated knockdown of *Dnmt1* were performed in organoids derived from intestinal tumors. Expression profiles of genes including microRNAs after treatment with 5-Aza-CdR and *Dnmt1*-knockdown were analyzed.
RESULTS: Treatment of *Min* mice with 5-Aza-CdR significantly reduced the average number of intestinal adenomas from 66 to 44 (male) and from 65 to 47 (female). The average number of large adenomas ($\geq$ 3 mm) in *Min* mice treated with 5-Aza-CdR was significantly decreased from 24 to11, whereas there was no significant difference in the average number of small adenomas ($<$ 3 mm). We successfully established organoids containing stem cells from intestinal adenomas of *Min* mice by 3-D culture with serum-free medium including epidermal growth factor (EGF) and Noggin. Treatment with 5-Aza-CdR and *Dnmt1*-knockdown significantly reduced the cell proliferation activity of tumor organoids. Microarray analyses of tumor organoids after treatment with 5-Aza-CdR and knockdown of *Dnmt1* revealed that interferon-related genes including *interferon regulatory factor 7 (IRF7)* were activated by inhibition of DNA methylation.
CONCLUSION: These findings indicate that inhibition of DNA methylation prominently suppresses the growth of intestinal tumor-initiating cells through activation of interferon-related genes. Treatment of colon cancers with DNA methylation inhibitors such as 5-Aza-CdR may be a novel therapeutic strategy targeting cancer stem cells.
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Disclosure of Interest: None declared

P1529 CHARACTERISTIC AND VERIFIED MICRORNA EXPRESSION PATTERNS IN COLORECTAL ADENOMA-CARCINOMA SEQUENCE

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INTRODUCTION: miRNA expression alterations can be observed in colorectal cancer (CRC), however dysregulation of miRNA might be present in various stages of precancerous lesions, such as adenoma. High-throughput screening platforms became available recently: whole genome miRNA expression microarrays and RT-qPCR panels with hundreds of miRNA specific oligos.
AIMS & METHODS: Our primary aim was to identify the microRNA expression alterations between normal colonic tissue (N), tubular adenoma (AD$<$SUB$>$T$<$/SUB$>$), tubulovillous adenoma (AD$<$SUB$>$TV$<$/SUB$>$) and colorectal cancer (CRC) samples. Another purpose was to determine the

level of miRNA by different methods and in several types of samples such as fresh frozen, FFPET.
Sixty fresh frozen biopsy samples (n = 20 N, n = 11 AD_T, n = 9 AD_{TV}, n = 20 CRC) were collected; and, total RNA were isolated. A miRNA microarray experiment was performed. Then, a series of pools of RNA from the same groups of samples was made to validate the data of microarray by RT-qPCR. Then, RT-qPCR data of FFPET tissues (N n = 3, AD_{TV} n = 3, CRC n = 3) were compared to the microarray and PCR results from fresh-frozen samples. miRNA-mRNA interactions were predicted based on four algorithm and validated by biopsy mRNA microarray data. miRNA-126 was selected to be visualized by in situ hybridization.
RESULTS: Out of the 1733, the detectable number of miRNAs, which could be detected in each group was only a small percentage (N n = 442, AD n = 460, CRC n = 441). 12 miRNA were upregulated (miR-31 logFC = 3, p < 0.001) and 11 miRNA were downregulated only (e.g. miR-10b, logFC = -1.7 p < 0,001) in neoplastic lesions (AD+CRC) compared to N samples. 11 miRNA showed altered expression between AD_T and AD_{TV} (e.g. miR-183 LogFC = 1.5 p < 0.007). Expression levels of 9 miRNA were found to be changed between AD_{T,TV} and CRC groups based on microarray data (e.g. miR-196a logFC = -1.8 p < 0.001). MiRNA expression data could be confirmed by RT-PCR in both FFPE and fresh frozen samples. miRNA-126 array expression results could be confirmed by in situ hybridization. MAP3K1 were identified as the targets of miR-196a in the MAPK signaling pathway.
CONCLUSION: A small number (n = 23) miRNA showed characteristic alteration during neoplastic development, but their impact is remarkable and systematic as a key control element of the upstream mRNA pathways. The identified miRNA expression changes are reproducible through adenoma-dysplasia-carcinoma sequence and in the FFPE tissues as well.
Disclosure of Interest: None declared

P1530 TEXTURE ANALYSIS AS IMAGING BIOMARKER OF TUMORAL RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY IN RECTAL CANCER PATIENTS STUDIED WITH 3T MR

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INTRODUCTION: To determine whether texture features of rectal cancer on T2-weighted MR images can predict tumoral response in patients treated with neoadjuvant chemoradiotherapy (CRT)
AIMS & METHODS: We prospectively enrolled 15 consecutive patients (6 females, 63.2±13.4 years) with rectal cancer, who underwent pre- and post-treatment 3T MRI. Treatment protocol consisted of neoadjuvant chemoradiotherapy (CRT) with oxaliplatin and 5-Fluorouracile. Texture analysis using a filtration-histogram technique was performed using a commercial research software algorithm (TexRAD Ltd, Somerset, England, UK) on unenhanced axial T2-weigthed images by manually delineating a region-of-interest (ROI) around the tumor outline for the largest cross-sectional area. The technique selectively filters and extracts textures at different anatomic scales followed by quantification of the histogram using kurtosis, entropy, skewness and mean value of positive pixels (MPP). After chemoradiotherapy, all patients underwent complete surgical resection and the surgical specimen served as the gold standard.
RESULTS: Six patients showed pathological complete response (pCR) and 4 patients, partial response (PR). Five patients were classified as non-responders (NR). Baseline medium texture-scale quantified as kurtosis was significantly lower in the pCR sub-group in comparison with PR+NR (p = .01). Post-treatment kurtosis without filtration was significantly higher in pCR in comparison with PR+NR (p = .045). The change in kurtosis between post-treatment and pre-treatment images was significantly lower in the PR+NR sub-group compared to pCR (p = .038). At baseline, the area under the ROC curves (AUC), to discriminate between pCR and PR+NR, was significantly higher for kurtosis (0.907, p < 0.001) compared to all others parameters. The optimal cut-off value for baseline kurtosis was ≤0.19. Using this value, the sensitivity and specificity for pCR prediction were 100% and 77.8%.
CONCLUSION: Texture parameters derived from T2w images of rectal cancer have the potential to act as imaging biomarkers of tumoral response to neoadjuvant chemoradiotherapy.
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Disclosure of Interest: None declared

P1531 THE IMMUNOCHROMATOGRAPHIC FECAL TUMOR M2 PYRUVATE KINASE TEST DETECTS COLORECTAL CANCER WITH HIGHER SENSITIVITY THAN FECAL OCCULT BLOOD TEST

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INTRODUCTION: The M2 pyruvate kinase (M2-PK) is known a specific enzyme produced in undifferentiated and proliferating tissues. This study aims to evaluate the usefulness of the immunochromatographic M2 pyruvate kinase (iM2-PK) for screening of colorectal cancer (CRC) and premalignant lesions.
AIMS & METHODS: Healthy volunteers and patients with colorectal neoplasms were enrolled in six academic hospitals in capital province of Korea. The value of iM2-PK was compared with immunochromatographic fecal occult blood test (iFOBT) and fecal tumor M2-PK enzme-linked immunosorbent assay (ELISA).
RESULTS: A total of 323 subjects were enrolled. The sensitivity of iM2-PK for CRC was 92.8%, and was superior to that of iFOBT, 47.5% (p < 0.0001). For adenomatous lesions, the sensitivity of iM2-PK was 69.4% and was also superior to 12.1% of iFOBT (p < 0.001). In comparison with M2-PK ELISA, iM2-PK proved significantly better sensitivity for CRC, 97.5% and 80.0% (p = 0.0289). The sensitivity of iM2-PK was higher in advanced stage of CRC compared to cancers confined to mucosa and submucosa (p < 0.05), however, lymph node metastasis had no influence on the sensitivity of iM2-PK.
CONCLUSION: The iM2-PK proved higher sensitivity for CRC and adenomatous lesions than iFOBT. With rapidity and convenience, CRC screening using iM2-PK is promising.
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Disclosure of Interest: None declared

P1532 EFFECT OF ANTIPLATELET AND ANTICOAGULANT TREATMENTS ON THE DIAGNOSTIC ACCURACY OF FECAL IMMUNOCHEMICAL TEST IN COLORECTAL CANCER DETECTION IN SYMPTOMATIC PATIENTS

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INTRODUCTION: There are discrepancies regarding the effect of antiplatelet and/or anticoagulant therapies in the diagnostic accuracy of fecal immunochemical test (FIT) for colorectal cancer (CRC) detection.
AIMS & METHODS: The aim of this analysis is to assess the influence of anticoagulant and/or antiplatelet treatments in FIT diagnostic accuracy for CRC detection in symptomatic patients. COLONPREDICT study is a prospective blind study of diagnostic tests that has evaluated FIT diagnostic accuracy for CRC detection in symptomatic individuals undergoing a colonoscopy. In the 1567 patients included chronic treatment with acetylsalicylic acid (ASA), clopidogrel and/or acenocumarol was collected. The overall diagnostic accuracy was compared with ROC curves, area under the curve (AUC) and homogeneity test areas and the sensitivity and specificity (at a 100 ng/ml cutoff) was compared using the chi-square test.
RESULTS: 426 (27%) patients were receiving antiplatelet and/or anticoagulant treatments. 215 CCR were detected no difference in prevalence between the two groups (treatment = 12%, control = 14.3%; p = 0.2). FIT diagnostic accuracy for CRC was statistically lower in the treatment group (treatment AUC = 0.81, control AUC = 0.88; p = 0.04). With a 100ng/ml cutoff, 175 (41.1%) patients in the treatment group and 434 (38%) in the control group had a positive result (p = 0.2). At this cutoff, treatment with antiplatelet and/or anticoagulant treatments produced a non significant reduction of FIT sensitivity (90.2%, 91.5%, p = 0.7) and specificity (65.6%, 71%; p = 0.05) for CRC detection. Comparisons of the diagnostic accuracy according to the treatment received are shown in the accompanying table.

Table to abstract P1532

Treatment		AUC	p	Sensitivity	P	Specificity	p
ASA	Yes (16.2%)	0.78	0.04	84.6%	0.2	64%	0.05
	No (83.8%)	0.87		92.1%		70.6%	
Clopidogrel	Yes (3.8%)	0.79	0.2	90%	0.9	70%	0.9
	No (96.2%)	0.86		91.2%		69.4%	
Acenocumarol	Yes (7.9%)	0.80	0.3	94.1%	0.6	62.6%	0.1
	No (92.1%)	0.86		91%		70%	

CONCLUSION: Treatment with acetylsalicylic acid reduces FIT diagnostic accuracy for CRC detection in symptomatic patients.
Disclosure of Interest: None declared

P1533 THE GROWTH PATHWAY AND THE PATHOLOGICAL FEATURES OF DEPRESSED-TYPE COLORECTAL CARCINOMAS

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INTRODUCTION: Advanced colorectal cancers were conventionally considered to develop from sessile-type "polyps". And it has been maintained as the mainstream of development of cancers in colorectum.
But recently advances in endoscopic diagnosis and colonoscopy technology have revealed the existence of many depressed-type cancers, which have a growth pathway different from "*adenoma-carcinoma sequence*".
AIMS & METHODS: The aim is to clarify the pathological features of depressed-type colorectal carcinomas compared with flat- and sessile-type. A total of 20160 colorectal neoplasms excluding advanced carcinomas were resected endoscopically or surgically in our Center from April 2001 to September 2013. Of these, 847 lesions were T1 carcinomas. According to the morphological/development classification, 194 lesions (22.9%) were depressed-type, 281 lesions (33.2%) were flat-type and 372 lesions (43.9%) were sessile-type. We analyzed the pathological features of these lesions.
RESULTS: The rate of submucosal invasion in all the lesions was 45.9% in depressed-type, 2.7% in flat-type and 2.8% in sessile-type. Within under 5mm in diameter, that was 8.8%, 0.02% and 0.02% respectively. In T1 carcinomas, the rate of vessel permeation was 65.0% in depressed-type, 32.4% in flat-type and 37.6% in sessile-type, that of tumor budding was 37.6%, 15.7% and 17.7%, and that of poorly differentiated adenocarcinoma was 9.8%, 3.9% and 4.6% respectively. The rates of these pathological factors were significantly higher in the depressed-type lesions. On the other hand, the rate of adenomatous component was 6.2%, 51.2% and 55.4%, respectively. This was significantly lower in depressed-type lesions, suggesting that they emerge directly from the normal epithelium without going through the adenoma stage.
CONCLUSION: Depressed-type early colorectal carcinomas tend to invade submucosal layer and grow downward even when they are small in size and show the worth pathological characteristics than the other types. Therefore, more careful endoscopic diagnosis - whether the lesion is depressed type or not - would be needed.
Disclosure of Interest: None declared

P1534 GENE EXPRESSION PROFILING OF LATERAL SPREADING COLORECTAL TUMORS

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INTRODUCTION: Laterally spreading tumors (LSTs) are generally defined as lesions >10 mm in diameter, characterized by lateral expansion along the luminal wall with a low vertical axis. In contrast to other forms of tumor, LSTs are generally considered to have a superficial growth pattern and the potential for malignancy.
AIMS & METHODS: We focused on this morphological character of LSTs, and analyzed the gene expression profile of LSTs. The expression of 168 genes in 41 colorectal tumor samples (17 LST-adenoma, 12 LST-carcinoma, 12 Ip (pedunculated type of the Paris classification)-adenoma, all of which were 10 mm or more in diameter) was analyzed by PCR array. Based on the results, we investigated the expression levels of genes up-regulated in LST-adenoma, compared to Ip-adenoma, by hierarchical and K-means clustering. Next, using an additional 61 samples (39 LST-adenoma, 22 Ip-adenoma), we confirmed the results of the array analysis and determined the localization of the gene product by immunohistochemical staining.
RESULTS: The expression of 129 genes differed in colorectal tumors from normal mucosa by PCR array analysis. As a result of K-means clustering, the expression levels of 5 genes, AKT1, BCL2L1, ERBB2, MTA2 and TNFRSF25, were found to be significantly up-regulated ($p<0.01$) in LST-adenoma, compared to Ip-adenoma. Analysis by immunohistochemical analysis showed that the BCL2L1 protein was significantly up-regulated in LST-adenoma compared to Ip-adenoma ($p=0.0089$).
CONCLUSION: Our findings suggest that LSTs have an unusual profile of gene expression compared to other tumors. BCL2L1 might be an important gene for the organization of LST.
Disclosure of Interest: None declared

P1535 EVALUATION OF FECAL TUMOR M2-PYRUVATE KINASE (M2-PK) AS A SCREENING TOOL FOR ORGANIC BOWEL DISEASES – PRELIMINARY RESULTS

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INTRODUCTION: Evaluation of the potential role of fecal M2 pyruvate kinase (M2-PK) test as a screening tool for colorectal cancer (CRC), inflammatory bowel disease (IBD) and colonic polyps and to compare the rapid chromatographic qualitative and ELISA quantitative test for M2-PK determination.
AIMS & METHODS: Fecal samples of 40 patients (19 male, 21 female) at mean age 56±17 were collected in our centre for the period March – November 2013. Ten patients had CRC, 11 patients – IBD (3 had Crohn's disease, 7 ulcerative colitis), 8 had colon adenomas (4pts >1 cm), 11 had normal colonoscopy findings. We also subdivided patients according to disease burden – subgroup A comprised of CRC, IBD and adenomas > 1cm and subgroup B - of small polyps and controls. Rapid M2-PK immunochromatographic test, M2-PK ELISA test and immunological fecal occult blood test (FOBT) were performed in all samples.
RESULTS: In the CRC group Rapid M2-PK test results were positive in 100%, in IBD group – 72.7%, in adenomas group – 50% positive (all >1cm), controls - 18.2%. The M2-PK ELISA test results were positive in 100%, 63.6%, 37.5% and 18.2% respectively. The FOBT resulted positive in 90% of CRC, 72.7% of IBD, 12.5% in polyps group and 0% of controls. In the subgroup analysis the Rapid test was positive in 88% of patients in subgroup A, and negative in 86.7% of subgroup B ($p<0.001$), while the FOBT was positive in 72% of subgroup A and negative in 100% of subgroup B. When comparing the immunochromatographic qualitative test with M2-PK ELISA test we found statistically significant correlation – 91.7% of patients with positive Rapid test had positive ELISA test ($p<0.001$). The estimated sensitivity and specificity of Rapid M2-PK for patients in subgroup A is 91% with a positive predictive value of 92%. The sensitivity and specificity of M2-PK ELISA in the same subgroup is 90% and 81% respectively with a positive predictive value of 90%.
CONCLUSION: Fecal rapid M2-PK test is an easily performed and reliable tool for screening of bowel pathology. The Rapid test correlates with the quantitative ELISA for the determination of M2-PK
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Disclosure of Interest: S. Siminkovitch Other: M2-PK immunohrmatographikc tests were contributed from Naturpharma, _Biotech AG, Giessen, Germany representative in Bulgaria.

P1536 RELATIONSHIP BETWEEN THE EXPRESSION OF ONCO-RELATED MIRNAS AND ENDOSCOPIC APPEARANCE IN COLORECTAL TUMORS

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INTRODUCTION: Accumulating data indicate that some microRNAs (miRNAs or miRs) function as tumor suppressors or oncogenes in cancer development. The certain miRNAs (miR-143, -145, -34a, -7) were differently expressed in the samples between the tumor and the paired non-tumorous samples in the same patient in colorectal tumors, which was reported by us and others. On the other hand, recent studies indicated that exophytic tumors and flat elevated tumors were different for the expression profile of genome. In the current study, we demonstrated the difference in the miRNA expression profile between exophytic tumors and flat elevated tumors in colorectal tumors.
AIMS & METHODS: We examined the expression of these miRNAs in 131 sporadic exophytic adenomas or early cancers, and 52 sporadic flat elevated adenomas or early cancers to clarify the relationship between the expression of the miRNAs and the endoscopic morphological appearance in the colorectal tumors.
RESULTS: The expression levels of miRs-143, -145, and 34a were significantly reduced in exophytic tumors compared with those in flat elevated tumors. The expression levels of miR-7 and were significantly up-regulated in flat elevated adenomas compared with those in exophytic adenomas.
CONCLUSION: These findings indicated that the expression of onco-related miRNA associated with the morphological appearance of colorectal tumors.
Disclosure of Interest: None declared

P1537 IMMUNOHISTOCHEMICAL ANALYSIS USING D2-40 AND EVG ENHANCE THE DETECTABILITY OF LYMPHOVASCULAR INVASION IN RECTAL NETS LESS THAN 10MM IN DIAMETER

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INTRODUCTION: Rectal neuroendocrine tumors less than 10mm in diameter (RNETs≦10mm), confined to submucosal layer (SM), are usually treated by endoscopic resection (ER), and ER is reported to successfully achieve clear resection margin [1]. Previous studies have demonstrated that RNETs≦10mm had relatively low incidence of lymphovascular invasion [2]. Nonetheless, we often detect lymphovascular invasion by immunohistochemical analysis using D2-40 and EVG in addition to HE stain.
AIMS & METHODS: This study aimed to demonstrate enhancement of detection rate of lymphovascular invasion in RNETs≦10mm using D2-40 and EVG stain. We retrospectively reviewed consecutive RNETs≦10mm patients treated by EMR or ESD between November 2005 and March 2014 at Chiba Cancer Center Hospital. Specific data extracted from the medical records included patient sex, age, tumor site, tumor size, depression in the lesion, margin status, depth of SM invasion, mitotic rate, and lymphovascular invasion. According to World Health Organization 2010 classification, tumors were divided into the two groups: G1 (<2/10 high-power fields [HPF]) or G2 (2≧10HPF). In addition to conventional HE stain, lymphatic invasion was identified by D2-40 and venous invasion by EVG stain.
RESULTS: Thirty three patients were recruited in the study (18 male, 15 female; median age 59 years). Characters of the tumor were as below: 3 located in upper rectum, 30 in lower; median size 5 mm (range 1-10); no surface depression in all. On histopathological examination, resection margin was free in 23 patients, indeterminate in 7 and positive in 3. The median depth of SM invasion was 1500μm (range 800-7000) and all tumors were classified as G1. Regarding lymphatic and venous invasion, they were 0% (0/33) and 3.0% (1/33) by HE stain, respectively. While by D2-40 and EVG stain, lymphatic and venous invasion were detected in 6.1% (2/33) and 36.4% (12/33), respectively. Finally, the rate of lymphovascular invasion detected by D2-40 and EVG stain was increased to 36.4% (12/33) as compared to 3.0% (1/33) by HE stain. Assessing the rate of lymphovascular invasion according to tumor size, lymphatic and venous invasion were 7.1% (1/14) and 42.9% (6/14) in the size of >5mm, and 5.3% (1/19) and 31.6% (6/19) in the size of ≦5mm, respectively, showing no significant difference. Similarly assessing the rate according to SM invasion, lymphatic and venous invasion were 11.1% (2/18) and 33.3% (6/18) in the depth of SM invasion >1500μm, and 0% (0/15) and 40% (6/15) in ≦1500μm, respectively, showing no difference.
CONCLUSION: Compared to HE stain, D2-40 and EVG stain is proved to significantly increase detection rate of lymphovascular invasion in RNETs≦10mm. Therefore, application of D2-40 and EVG stain is considered to be indispensable to RNETs≦10mm after ER.
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Disclosure of Interest: None declared

P1538 INDIVIDUALIZED CHEMOTHERAPY FOR ADVANCED COLORECTAL CANCER (CRC) BASED ON COLLAGEN GEL DROPLET-EMBEDDED DRUG SENSITIVITY TEST (CD-DST) IN CLINICAL SETTING

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INTRODUCTION: The leucovorin (FOL) and fluorouracil (5-FU) plus oxaliplatin (*l*-OHP; FOLFOX) or FOL and 5-FU plus irinotecan (SN-38; FOLFIRI) regimens with or without molecularly-targeted drugs are widely used as first-line chemotherapy in the treatment of advanced colorectal cancer (CRC). Whether FOLFOX or FOLFIRI is administered first is not significant, however, it is essential that full administration of the targeted dosages of all 3 drugs, 5-FU, *l*-OHP, and SN-38 is achieved. However, this is not always possible and second-line chemotherapy must be abandoned in certain cases due to disease progression, adverse effects or high medical cost in clinical setting. Where possible, the most effective regimen should be selected as the first line of treatment.
AIMS & METHODS: The aim of this study was to determine whether first-line chemotherapy mat be individualized using the collagen gel droplet-embedded drug sensitivity test (CD-DST).
Specimens of primary tumors were obtained between March 2008 and November 2013 from 87 CRC patients who had received no preoperative chemotherapy. Informed consent to measure drug sensitivity was obtained from all patients. The CD-DST allows evaluation of drug sensitivity using isolated, 3-dimensionally cultured tumor cells in a small collagen gel droplet. The CD-DST was performed and the growth inhibition rate (IR) obtained under incubation conditions (5-FU with *l*-OHP at 6.0 and 3.0 μg/ml, or 5-FU with SN-38 at 6.0 and 0.2 μg/ml, respectively, for 24 h). The cumulative distributions of the IR under each condition were evaluated based on evidence that the clinical response rates to FOLFOX and FOLFIRI were almost the same; approximately 50%, respectively. The histogram of individual discrepancy of antitumor effects between FOLFOX and FOLFIRI was also evaluated. Histogram was analyzed with D'Agostino-Pearson omunibus normality test.
RESULTS: Individualization of first line treatment was possible in all patients. FOLFOX and FOLFIRI were recommended as first line chemotherapy in 37 and 44 patients, respectively, and equal efficacy in 6 cases. The histogram of the individual discrepancy showed normal distribution ($p = 0.00679$). The standard deviation (SD) was 15.82.
CONCLUSION: This method has the potential to facilitate the establishment of individualized first line chemotherapy for CRC patients. Improvement in the further prognosis is expected by selection of more effective regimen for advanced CRC patients whose discrepancy of anti-tumor effects between two regimens is greater than one SD in clinical setting.
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Disclosure of Interest: None declared

P1539 PREDICTIVE VALUE OF VEGFR AND EGFR PATHWAYS FOR ADJUVANT TREATMENT WITH FLUOROURACIL, LEUCOVORIN +/- IRINOTECAN IN PATIENTS WITH LOCAL ADVANCED COLORECTAL CANCER: TRANSLATIONAL RESULTS OF THE FOGT-4 STUDY

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INTRODUCTION: The introduction of molecular biomarkers as predictive factors for palliative chemotherapy improved the clinical outcome and led to efficient treatment personalization in metastatic colorectal cancer (CRC). However, such a predictive value has not yet been established in patients with locally advanced CRC receiving adjuvant chemotherapy. Since EGFR- and VEGFR-signalling cascades are fundamental for the development of cancer, we assessed correlations of VEGF-C, VEGF-D, VEGFR-3, Hif-1 alpha, PTEN, amphiregulin (AREG) and epiregulin (EREG) expression levels with the clinical outcome in a randomized phase III study of patients with stage II/III CRC receiving adjuvant treatment.
AIMS & METHODS: The patients' data examined in this study were from the collective of the 5-FU/FA versus 5-FU/FA/irinotecan phase III FOGT-4 trial. Tumor tissues from 269 patients were stained via immunohistochemistry for VEGF-C, VEGF-D, VEGFR-3, Hif-1 alpha, PTEN, AREG and EREG expression. The results were evaluated by two independent, blinded investigators. Survival analyses were calculated for all patients receiving 5-FU/FA vs. 5-FU/FA/irinotecan in relation to expression of all makers above.
RESULTS: Patients with negative AREG and EREG expression had a significant longer disease free survival (DFS) in comparison to AREG/EREG positive ones ($p < 0.05$). The benefit on DFS in AREG-/EREG- patients compared to AREG+/EREG+ patients was even stronger under 5-FU/FA/irinotecan ($p = 0.002$). Patients expressing PTEN on their tumor tissues lived longer receiving adjuvant treatment including irinotecan than PTEN- ones ($p < 0.05$). No correlation between clinical outcome and markers related with the VEGFR-pathway was found. Patients with negative VEGF-D expression had a trend for a loobger DFS when treated with 5-FU/FA ($p = 0.106$). Patients with lack of Hif-1 alpha expression remained longer disease free than Hif-1 alpha+ ($p = 0.007$) and profited more treated with the triple adjuvant regime ($p = 0.026$). Finally, patients who were AREG-/EREG-/PTEN+ showed a trend for better overall survival (OS) under 5-FU/FA/irinotecan than without irinotecan ($p = 0.071$).
CONCLUSION: Patients with AREG/EREG negative, PTEN positive and Hif-1 alpha negative CRC tumors might profit in terms of DFS from a treatment containing fluoropyrimidines and irinotecan. Our results suggest a predictive value of these biomarkers concerning adjuvant chemotherapy with 5-FU/FA +/- irinotecan in stage II/III colorectal cancer.
Disclosure of Interest: None declared

P1540 A PRO-ACTIVE MODEL TO IDENTIFY PATIENTS AT HIGH RISK FOR FAMILIAL CANCER SYNDROMES – RESULTS OF A HIGH YIELD OUTREACH PROGRAM

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INTRODUCTION: Identifying patients with familial colorectal cancer syndromes is of great importance, for both patients and their family members. Some centers have utilized a reflex testing system, in which every colorectal cancer (CRC) patient is screened for Lynch syndrome (LS). However, the associated cost of such programs hampers their widespread implementation. One possible alternative is to refer only high risk patient for genetic evaluation. We present the results of a proactive outreach program, set to identify patients at risk for familiar colorectal cancer.
AIMS & METHODS: Aim: To evaluate the yield of a proactive outreach program designed to identify patients at high risk for familial colorectal cancer, using discharge letters following surgery for colorectal cancer.
Methods: Charts of patients hospitalized in our tertiary center during 2011-2013 with the diagnosis of CRC were identified. For each case, the discharge letter

from the hospitalization during which they underwent surgery was identified. Un-operated patients were excluded. Then, patients were alphabetically contacted by phone to complete follow up and personal details to ascertain their Bethesda criteria status. We then compared the data from the discharge letters to the follow-up, mainly – the recommendation to complete genetic counseling for either LS or polyposis syndromes.
RESULTS: The program included 96 patients (M:F ratio of 1:1), with a mean age of 67.79. The mean age at diagnosis was 66.29y (31-93y). Mean time to follow up was 545 days after surgery, during which 13 patients had died, one patient was admitted to hospice and 4 were lost to follow up.
After revising the clinical and pathological data of the 96 patients, 26 (27%) have had an indication to complete genetic counseling. Two patients had an indication to complete evaluation for polyposis syndromes, while the other 24 qualified for testing for LS according to the modified Bethesda criteria (16 were under the age of 50y at diagnosis, 4 patients had synchronous or metachronous tumors of the colon, 1 patient had a metachronous Lynch associated tumor, 1 patient was known to have LS, 1 had a suggestive family history and in 1 patient's evaluation was recommended according to tumor's biopsy). From the entire study groups, 2 patient were already after genetic counseling (1 with known LS), and only two patients with indication were referred to genetic counseling (ages 31 and 43y at diagnosis). This means that out of the patients with indication to complete genetic evaluation who have not received previous counseling, approximately 90% of cases did not receive the recommendation.
CONCLUSION: The rate of identification of high risk patients for familial CRC in surgical departments is sub-optimal, even when the indication is obvious at the time of discharge after surgery for CRC. We present a high yield out-reach program which can be easily implemented in any center, and offers a potential for identifying missed cases of LS.
Furthermore, identification of high risk patients and adequate referral for genetic counseling following surgery for CRC should be considered a quality control measurement for surgical departments.
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P1541 COLONIC STENTING AS BRIDGE TO SURGERY VERSUS EMERGENCY SURGERY IN OBSTRUCTIVE COLORECTAL CANCER

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INTRODUCTION: About 7-29 % of the colorectal cancers presents with acute obstruction. Acute obstruction is an emergency situation with risk for necrosis, perforation due to colonic distention, bacterial translocation and intracorporal electrolytic fluid imbalance. The situation calls for decompression, traditionally emergency surgery (ES) is performed. ES is associated with a high mortality in 15-34 % of patients and morbidity in 32-64 %, compared to $<5\%$ for elective surgery.
AIMS & METHODS: Comparing patients with malignant obstruction treated with self-expanding metal stent (SEMS) versus primary surgery. Endpoints: 30 days mortality, technical and clinical success. Tumor placement and cancer related death.
Method: Retrospective register study done in the period of 1.1.2008-1.9.2013. 364 patients from the surgical department Køge-Roskilde. 99 treated with SEMS and 256 had surgery.
RESULTS: 130 patients, median age 72 years, 66 women and 64 men. ASA 1: 19.5 %, ASA 2: 79.7% and ASA 3: 0.8 %. Median follow-up 22 months (5-56). There is a significant difference between patient groups and tumor placement. Most patients with palliative stent and patients with bridge to surgery without later surgery, had tumor placed in the sigmoid colon 41.5 %, and the recto sigmoid colon 17 %. Technical and clinical success is respectively 94.6 % and 93.8 %. 6.9 % had complications after SEMS, no significant difference between patient groups. No significant difference in 30 days complications between SEMS versus primary surgery. Overall survival SEMS versus primary surgery shows no significant difference. 15.4 % died before 30 days. No significant difference between patient groups. The number of dead is larger among patients with primary operation, patients with SEMS 9.6 % versus 31.4 % patients with primary operation. Cancer related mortality sjows no significant difference, $p=0.6$. Regarding adjuvant chemotherapy and cancer related mortality no significant difference found between the patient groups.
CONCLUSION: Colonic stenting followed by elective surgery shows no significant difference compared to primary surgery regarding 30 days mortality and complications, but a trend towards higher mortality in the group who went through primary surgery.
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Disclosure of Interest: None declared

P1542 CRC SCREENING USING FEACAL IMMUNOCHEMICAL TEST (FIT) IN IBARAKI PREFECTURE, JAPAN -AN ADVANTAGE OF A TWO-DAY SAMPLING METHOD-

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INTRODUCTION: A two-day method was shown to have higher sensitivity than a one-day method in 1988, therefore a two-day sampling method through immunological fecal occult blood test (FIT) has been widely accepted by colorectal cancer screening program according to Japanese Colorectal Cancer (CRC) screening guidelines.
AIMS & METHODS: The purpose of this study is to evaluate the positive predictive values and Dukes classification of identified colorectal cancer between the first day positive and the first day negative group. For Regional Screening Program from 2007 to 2012, FIT participants, who were over 40 years old, were screened with 2 samples of stool measured by the OC-SENSOR (Eiken, Japan) with a cut-off value of 100ng/mL (20μg Hb/g stool). The number of participants was 750,839. The participant gender was 41.3% male and 58.7% female. The FIT positive participants were classified into the first day positive group (++) (+-) (+) and negative group (-+).
RESULTS: The positive FIT participants was 53,847 in number, and the total FIT positive rate was 7.17%. The number of the first day positive and negative participants were 33.172 (61.6%) and 20.675 (38.4%) respectively. Work-up examination rates were 72.8% and 74.3% respectively. The number of two-day positive participants was 10.163 (18.8%). CRCs were identified in 1,330 cases. One thousand and forty-one (1,041) cases were from the first day positive group and 289 cases were from the first day negative group. The positive predictive values between the first day positive and negative group were 3.138% and 1.398% respectively. The positive predictive value of FIT-positivity in both days was 6.839%. Identified CRCs were classified according to Dukes classification. Those were 632 (Dukes A intra-mucosal carcinoma), 387 (Dukes A invasive carcinoma), 128 (Dukes B), 153 (Dukes C), 23 (Dukes D) and 7 (unknown). Seventy-eight % of total identified CRCs were from the first day positive group; 459/632 (Dukes A intra-mucosal carcinoma), 72.6%; 310 /387 (Dukes A invasive carcinoma), 80.1%; 116/128 (Dukes B), 90.6%; 130/153 (Dukes C), 85.0%; and 20/ 23 (Dukes D), 87.0%.
CONCLUSION: If one-day sampling of FIT were adopted in the screening program, 27.4% (173/632) of Dukes A intra-mucosal carcinoma and 19.9% (77/387) of Dukes A invasive one would be missed. The highest positive predictive value was shown in the FIT both days-positive group.
Disclosure of Interest: None declared

P1543 ENDOSCOPIC TREATMENT IN RECTAL NEUROENDOCRINE TUMOR- NET REGISTRY MULTICENTER STUDY

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INTRODUCTION: Rectal neuroendocrine tumor (NET) incidence is low. So previous studies of Endoscopic treatment in rectal NET have been small sample size studies.

AIMS & METHODS: The aim of this study was to investigate effectiveness of endoscopic treatment in rectal NET below 2cm. From Jan. 2003 to Dec. 2012. 1366 patients diagnosed Rectal NET in 24center was enrolled. Inclusion criteria were endoscopic treatment, under 2cm size, over 18 age. Exclusion criteria included no treatment, treatment, operation, chemotherapy, octreotide therapy, imcomplete data. After exclusion, 411 patients was enrolled. We analyzed the clinicopathologic data and factors affecting incomplete resection. We used Ki-squre, t-test statistically.
RESULTS: In total 411 patients, Age was 49.64±11.33, Male were 238 (57.9%), All symptom were 59 (14.4%), Carcinoid symptom were 13 (3.2%), Family history of NET were 4 (1%), Multiple lesion were 15 (3.6%), Elevated /Flat/ Depressed lesions were 407 (99)/2 (0.5%)/2 (0.5%), Lesion size was 0.58 ± 0.32cm, In histology, Well differentiated neuroendocrine tumor/Well differentiated neuroendocrine carcinoma wred 403 (98.1%)/8 (1.9%), Mucosa/ Submucosa/Proper muscle invasion were 117 (28.5%)/288 (70.1%)/6 (1.5%), Lymphovascular invasion were 4 (1%), EMR/ESD were 300 (73%)/111 (27%), Complete/Incomplete resection were 344 (83.7%)/67 (16.3%), Additional treatment after incomplete resection were 5 (1.5%), Recurrence were 8 (1.9%). The lymphovascular invasion, ESD, Recurrence were significant factor in Incomplete resection.
CONCLUSION: We suggest endoscopic treatment was effective in rectal neuroendocrine tumor below 2cm size. But further study including complication result will be needed.
Disclosure of Interest: None declared

P1544 INCREASED ZONULIN SERUM LEVELS AND CORRELATION WITH SYMPTOMS IN NON-CELIAC GLUTEN SENSITIVITY AND IRRITABLE BOWEL SYNDROME WITH DIARRHEA

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INTRODUCTION: Increased intestinal permeability plays a role in the pathophysiology and symptom generation in celiac disease (CD), non-celiac gluten sensitivity (NCGS) and irritable bowel syndrome (IBS). The pre-haptoglobin 2, also known as zonulin, is an endogenous modulator of epithelial tight junctions (TJs) and intestinal permeability. Zonulin is the human homolog of the zonula occludens toxin secreted by Vibrio cholerae. Intestinal bacterial infections and gluten evoke zonulin release in the intestinal milieu and in the bloodstream. Zonulin serum levels, their correlation with symptoms and diagnostic value as a disease biomarker in NCGS and IBS remain undetermined.
AIMS & METHODS: In the present study, we aim at characterizing zonulin serum levels in patients with NCGS (n = 11) and IBS-D (n = 9) compared with CD (n = 7; positive control) and healthy controls (n = 7; HC, negative control). NCGS patients were diagnosed based on the presence of gastrointestinal symptoms referable to the ingestion of gluten and in the absence of serological and histological criteria for celiac disease. IBS patients were diagnosed according to Rome III criteria. Celiac disease patients were identified on the basis of symptoms, antibodies and confirmation with duodenal biopsy. ELISA assay was used to evaluate zonulin serum levels; total protein amount was evaluated spectrophotometrically using Nanodrop (Thermo Scientific) and used to normalize data. Clinical data were recorded for each patient including: anti-transglutaminase (TTG) antibodies, anti-deamidated gliadin peptide (DPG) antibodies, IgE, abdominal symptoms and bowel habit.
RESULTS: Zonulin serum levels were significantly different among the four groups ($p < 0.001$). CD patients showed significantly higher serum zonulin levels compared to HC (0.044 ± 0.003 vs 0.01 ± 0.002, $p < 0.001$) and to IBS-D patients (0.018 ± 0.003, $p < 0.05$). NCGS zonulin serum levels were significantly higher than HC (0.01 ± 0.002 vs 0.036 ± 0.007, $p < 0.05$). Compared to all other subgroups, zonulin values in NCGS patients showed a broader range of distribution. Compared to IBS-D, NCGS zonulin values were higher although did not reach statistical significance ($p = 0.06$). Zonulin levels were positively correlated with the titer of anti-DPG antibodies (r:0.6; $p < 0.05$,) and anti-TTG antibodies (r:0.6; $p < 0.05$). In NCGS patients zonulin levels were positively correlated to total serum IgE levels (r:0.6; $p < 0.05$).
CONCLUSION: Our results suggest that zonulin could play a role in the pathophysiology of NCGS and IBS-D. Further studies are needed to assess its role as a biomarker with diagnostic potential in conditions characterized by increased intestinal permeability.
Disclosure of Interest: None declared

P1545 SACCHAROMYCES BOULARDII SUPPLEMENTATION REDUCES THE SEVERITY OF HERPES SIMPLEX VIRUS TYPE 1-INDUCED GASTROINTESTINAL DYSFUNCTION

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INTRODUCTION: The development of effective treatments for Irritable bowel syndrome (IBS), a functional gastrointestinal (GI) disorder, have been hampered by the lack of animal models. We have established a model of anomalous GI contractility secondary to persistent infection *of Herpes simplex* virus type 1 (HSV-1) in enteric nervous system (ENS) (Gastroenterology 2010;138:1790).
AIMS & METHODS: Since previous studies have suggested that *S. boulardii* may improve quality of life in IBS patients we assessed its effects on HSV-1-induced GI neuromuscular dysfunctions. Male C57/Bl6 mice were inoculated intranasally with HSV-1 and 4 weeks (W) later intragastrically (IG). Mice were allocated to receive IG either *S. boulardii* or vehicle. In an experimental group, the treatment started 1W before IG viral inoculum and lasted until the sacrifice (1W after viral inoculum). The second experimental group were treated from 6W to 10W after IG viral inoculum. At the time of sacrifice (1 or 10W after viral IG inoculum) we determined a) GI motility, fecal pellet expulsion and water content, and distal colonic transit; b) ENS integrity by immunohistochemistry and WB; c) changes in isometric muscle tension following electric field stimulation of ileal segments; d) inflammation by IL-1$\beta\alpha$, TNFα and MCP-1 ELISA in LMMP.
RESULTS: After 1 W, HSV -1 infection of ENS caused delayed GI transit time, impaired cholinergic neuromuscular transmission, altered expression and distribution of the neurofilaments peripherin and βIII-tubulin, and increased expression of MCP-1. Even if supplementation with *S. boulardii* reduced the production of inflammatory cytokines and the deregulated expression of neurofilaments, the treatment failed to influence HSV-1-induced GI neuromuscular dysfunction. However, 10 W after HSV-1 IG administration, *S. boulardii* supplementation almost completely corrected the severity of GI neuromuscular anomalies, restoring GI transit time, cholinergic neuromuscular contractility, faecal water content and colonic expulsion time to levels comparable to those obtained from control mice. Furthermore, *S. boulardii* completely abolished ENS structural alterations and the mild inflammation in ileal LMMP.
CONCLUSION: Dietary *S. boulardii* ameliorates GI neuromuscular dysfunction and ENS anomalies secondary to chronic but not acute HSV-1 infection, underlying its beneficial effects for the treatment of enteric dysmotility disorders associated to mild inflammatory conditions.
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P1546 IMMUNE ACTIVATION IS ASSOCIATED WITH SYMPTOM FLARE IN DIARRHOEA PREDOMINANT IRRITABLE BOWEL SYNDROME

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INTRODUCTION: IBS has historically been described as a functional neurological motility disorder resulting from alterations in the brain-gut axis, but the underlying mechanisms remain unclear. There is increasing evidence that the immune system is also altered in IBS patients, consistent with a chronic low grade immune activation (Hughes et al. Am. J. Gastro. 2013). However the nature of the immune response remains controversial with conflicting findings as to whether it comprises a predominantly typical or atypical allergic or autoimmune type response. Much of this controversy stems from grouping of all IBS patient subtypes and the use of cross-sectional data.
AIMS & METHODS: We aimed to investigate immune activation in IBS patients longitudinally, comparing immune responses in patient flare vs. when symptom free. 5 IBS-D patients were enrolled in the study and blood samples were taken quarterly (baseline) over a 1 year period and again whenever the patient self-reported symptom flare (flare). Questionnaires related to symptom severity (IBSS) were completed at each blood sample. PBMC were isolated from whole blood via density centrifugation and $1*10^6$/ml cells were cultured in culture media only (unstimulated) overnight, in the presence of PMA/ionomycin for 4 hours or LPS overnight. Cell culture supernatants were collected and analysed for cytokine concentrations using multiplex bead based assay (eBioscience). Baseline cytokine concentrations and IBSS scores were averaged and compared against cytokine concentrations and IBSS scores from patients in flare using paired student t-test.
RESULTS: IBSS scores were significantly increased during self-reported symptom flare compared to baseline. PMA/ionomycin stimulation increased concentrations of IFN-gamma, IL-2, IL-13, IL-21, GMCSF and TNF-alpha and decreased concentrations of IL-4, IL-5, IL-9, IL-10, IL-22, IL-23 and IL-27 relative to concentrations in unstimulated supernatants. LPS stimulation increased concentrations of GMCSF, IFN-gamma, IL-10, IL-13, IL-17, IL-18, IL-21, IL-22, IL-23, IL-27 and TNF-alpha, and decreased concentrations of IL-4 relative to unstimulated supernatants. Cytokine concentrations varied considerably between patients but remained stable at baseline within patient samples. The concentration of unstimulated cytokines did not differ between baseline and flare. The concentration of PMA/ionomycin stimulated IFN-gamma, IL-2, IL-4, IL-5, IL-18 and IL-23 were significantly increased during flare relative to baseline. The concentration of LPS stimulated GMCSF and IL-10 were significantly increased during patient flare vs baseline.
CONCLUSION: Our preliminary findings indicate both innate and adaptive arms of the immune response are altered in IBS-D patients in symptom flare vs baseline. Future investigations with more patients, including IBS-C and IBS-A subtypes, will indicate whether these alterations are IBS-D specific. These studies will potentially identify biomarkers for IBS patients in symptom flare and also novel treatments targeting specific aspects of the immune response.
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Disclosure of Interest: None declared

P1547 LOW SERUM LEVELS OF SHORT-CHAIN FATTY ACIDS AFTER LACTULOSE INGESTION MAY INDICATE IMPAIRED MICROBIAL FERMENTATION IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Poorly absorbable, but fermentable carbohydrates may provoke symptoms in patients with irritable bowel syndrome (IBS). This indicates that fermentation plays a role in symptom generation.
AIMS & METHODS: We aimed to measure microbial fermentation products before and after ingestion of an unabsorbable carbohydrate (lactulose) in IBS patients compared to healthy subjects.
Patients with IBS according to Rome III criteria (n = 22) and healthy controls (n = 20) ingested a 10 gram lactulose solution. Short chain fatty acids (SCFA) were measured in serum in fasted state and 90 minutes after lactulose intake, using hollow fiber supported liquid membrane extraction coupled with gas chromatography (1). Symptoms following lactulose ingestion were also assessed.
RESULTS: Lactulose induced more symptoms in patients with IBS than in healthy controls ($p = 0.0004$). Fasting serum levels of SCFA were not different in patients and controls ($p = 0.1$). Levels of SCFA in serum obtained after 90 minutes were significantly lower in patients with IBS compared to healthy controls, both for total SCFA ($p = 0.0002$), acetic acid ($p = 0.0049$), propionic acid ($p = 0.0204$) and butyric acid ($p = 0.0111$).
CONCLUSION: Patients with IBS had lower serum levels of SCFA in response to lactulose ingestion than healthy controls. The results suggest a failure of colonic salvage of carbohydrates in IBS that may be involved in abdominal symptom development.
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Disclosure of Interest: None declared

P1548 DEVELOPMENTAL LEVEL OF DEFENSE MECHANISMS AND TENDENCY OF CORPORAL DISCOURSE IN IRRITABLE BOWEL SYNDROME – A COMPARATIVE PILOT STUDY

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INTRODUCTION: Corporal discourse is the pronounced utilization of somatic modalities as a mean of communication and emotional expression. The maturity level of defense mechanisms allows the quantification and understanding of developmental level of psychological defenses used by an individual. In irritable bowel syndrome (IBS), both, the developmental level of defense mechanisms and the tendency of corporal discourse have not been extensively assessed.
AIMS & METHODS: To evaluate the developmental level of defense mechanisms and the tendency of corporal discourse among IBS patients compared to healthy volunteers and medical staff members.
We performed a survey assessing for the maturity level of defense mechanisms and the tendency of corporal discourse in 40 adult patients with IBS, 40 adult healthy volunteers and 39 local medical staff members. All participants completed the Defense Style Questionnaire (DSQ-40) and the Corporal Discourse questionnaire. Responses were statistically analyzed by group using one way ANOVA and the Pearson correlation coefficient.
RESULTS: IBS patients tended to use a lower order of defense mechanisms compared to medical staff, but not to healthy volunteers ($F(2.116) = 3.27$, $p = 0.04$). Compared to the other groups, IBS patients tended to use more extensively a corporal discourse ($F(2.116) = 28.36$, $p < 0.01$). In IBS patients, correlations were found between maturity level of defense mechanisms and tendency of corporal discourse (mature factor $r = -0.41$, $p < 0.01$; neurotic factor $r = -0.35$, $p = 0.03$) and between tendency to use somatization as a defense mechanism and tendency to use corporal discourse ($r = -0.38$, $p = 0.01$). Finally, a correlation between situational anxiety/depression and the tendency of corporal discourse was found in both IBS patients and medical staff, (IBS: $r = 0.65$, $p < 0.01$; $r = 0.59$, $p < 0.01$ respectively. Medical staff: $r = 0.42$, $p < 0.01$; $r = 0.41$, $p < 0.01$ respectively).
CONCLUSION: A lower developmental level of defense mechanisms and a higher tendency of corporal discourse are more pronounced in IBS patients. Furthermore, medical staff members and IBS patients share a relation between situational anxiety/depression and the tendency of corporal discourse.
Disclosure of Interest: None declared

P1549 INFLUENCE OF A LOW-FODMAP DIET ON SYMPTOMS AND GUT MICROBIOTA IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Reducing intake of fermentable oligo-, di- and monosaccharides and polyols (FODMAP) may improve functional bowel symptoms. We aimed to investigate the effect of such a dietary change on intestinal and extra-intestinal symptoms and gut microbiota in patients with irritable bowel syndrome (IBS).
AIMS & METHODS: IBS patients admitted to Lovisenberg Diakonale Hospital were investigated consecutively from April 2013 to January 2014. Symptoms were assessed by using validated questionnaires to measure both intestinal (IBS-SSS) and extra-intestinal symptoms (HADS, FIS) before and after 4 weeks on a low-FODMAP diet. Fecal gut bacteria DNA analysis was performed by using the GA-map™ Dysbiosis Test (Genetic Analysis AS, Oslo, Norway). This 16S rRNA DNA test utilizes DNA probes to recognize gut bacteria (1) found to best correlate with dysbiosis in patients with IBD and IBS. Dysbiosis index is an index calculated by an algorithm based on bacterial abundance and profile in a fecal sample, measured on a scale from 1 to 10, where values above 2 are considered abnormal. Change in dysbiosis index between week 0 and 4 were investigated.
RESULTS: Forty-eight patients (4 M, 44 F) completed the study. At baseline, 23 and 25 patients had a dysbiosis index classified as "normal" and "abnormal", respectively. These two groups were significantly different regarding intestinal symptom severity (mean IBS-SSS scores 263 versus 304, respectively; $p = 0.04$), but similar regarding extra-intestinal symptom severity. A correlation between dysbiosis index and IBS-SSS was demonstrated ($r = 0.29$, $p = 0.04$), including the subscale measuring pain ($r = 0.30$; $p = 0.04$). Following dietary intervention, symptomatic improvement was demonstrated as a reduction in IBS-SSS (from 285 to 157; $P < 0.0001$), HADS (from 14 to 9; $P < 0.0001$) and FIS (from 72 to 38; $P < 0.0001$). The dysbiosis index changed in 31 (65%) patients while it remained unchanged in 17 (35%) patients. There was no correlation between change in dysbiosis index and change in symptoms following diet.
CONCLUSION: A low-FODMAP diet seems to improve not only intestinal, but also extra-intestinal symptoms in patients with IBS. The GA-map™ Dysbiosis Test showed that patients with higher dysbiosis indices had more severe intestinal symptoms at baseline. The test thus provides information on alterations in bacterial abundance and profiles that may prove valuable for individual patients. However, we did not demonstrate any associations between change in dysbiosis indices and symptoms following dietary intervention.
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Disclosure of Interest: None declared

P1550 TREATMENT SATISFACTION AFTER RETREATMENT AND LONG-TERM THERAPY WITH LINACLOTIDE

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INTRODUCTION: The chronic nature of irritable bowel syndrome (IBS) requires pharmacological treatments to achieve long-term sustained symptom control. As IBS symptoms fluctuate over time, it is important that symptom control with pharmacological treatment can be re-established if treatment is re-introduced after a period of discontinuation. Linaclotide (LIN) is a first-in-class, minimally absorbed, guanylate cyclase-C agonist for the treatment of adults with IBS with constipation (IBS-C). One of the pivotal Phase 3 LIN trials (Trial 31) included a 4-week post-treatment randomised withdrawal period (RWP); upon completion of the trial, including the RWP, patients were allowed to continue treatment in an open-label, long-term study (LTS).
AIMS & METHODS: This post-hoc analysis examined the impact on treatment satisfaction of reintroducing LIN after 4 weeks off treatment in patients who were randomised to LIN 290μg once daily in the initial 12-week treatment period in Trial 31. Of these, 158 were subsequently re-randomised to LIN (LIN-LIN) and 154 were re-randomised to PBO (LIN-PBO) in the 4-week RWP. Eligible patients could then receive LIN for a further 78 weeks in the LTS. Patient-reported treatment satisfaction was used as an efficacy measure in the LTS, measured at study visits during Weeks 2, 4, 8, 12, 14 and 16 during Trial 31 and at Weeks 2, 6, 14, 26, 39, 52, 65 and 78 during the LTS. Patients were asked to rate how satisfied they were with the ability of the study medication to relieve their IBS symptoms on a 1-5 point scale (1 = not at all satisfied, 2 = a little satisfied, 3 = moderately satisfied, 4 = quite satisfied, 5 = very satisfied). Data were analysed using a last observation carried forward approach.
RESULTS: At the end of the 12-week treatment period in Trial 31, treatment satisfaction was similar for LIN patients who were re-randomised to PBO and patients who remained on LIN (mean [standard deviation, SD] treatment satisfaction at Week 12: 3.42 [1.34] vs 3.37 [1.34]). During the 4-week RWP, patients re-randomised from LIN to PBO (LIN-PBO) showed a statistically significant ($P < 0.05$) mean reduction in treatment satisfaction compared to patients who remained on LIN (LIN-LIN) and at the end of the RWP the mean (SD) treatment satisfaction for patients in the LIN-PBO group was 3.18 [1.34] vs 3.47 [1.37] for patients in the LIN-LIN group. Following reintroduction of LIN during the

LTS, mean (SD) treatment satisfaction increased to previous levels in the LIN-PBO treatment group within 2 weeks of starting LIN (LIN-PBO, 3.69 [1.17] vs LIN-LIN, 3.70 [1.05]) and this effect was sustained to the end of the 78-week follow-up period (LIN-PBO, 3.93 [1.32] vs LIN-LIN, 3.81 [1.21]). LIN treatment satisfaction increased throughout the long-term study. Similar to the Phase 3 trials, the most common AE observed during the LTS among LIN-treated patients was diarrhoea.

CONCLUSION: Patients with IBS-C who discontinued LIN therapy for a 4-week period experienced a significant reduction in treatment satisfaction; however, subsequent reintroduction of these patients to LIN therapy resulted in a similar, relatively high level of treatment satisfaction to patients who remained on LIN during long-term therapy.

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P1551 BASELINE CHARACTERISTICS AS A PREDICTOR OF RESPONSE TO LINACLOTIDE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: A POOLED ANALYSIS OF 2 PHASE 3 TRIALS

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INTRODUCTION: In 2 Phase 3 trials in irritable bowel syndrome with constipation (IBS-C), linaclotide (LIN) treatment was superior to placebo (PBO) based on European Medicines Agency co-primary endpoints (rate of abdominal pain/discomfort responders [Trial 31: 54.8% vs 41.8%; Trial 302: 54.1% vs 38.5%; $P<0.001$] and IBS degree-of-relief responders [Trial 31: 37.0% vs 18.5%; Trial 302: 39.4% vs. 16.6%; $P<0.0001$]). Improvements after 1 month of LIN therapy were highly likely to be maintained at 3 months.[1] A potential association between baseline patient characteristics and likelihood of therapeutic response to LIN is unclear.

AIMS & METHODS: This pooled analysis evaluated potential predictive value of baseline characteristics in 2 pivotal Phase 3 IBS-C trials by comparing demographics (age, sex, body mass index [BMI]) and baseline symptoms (Complete Spontaneous Bowel Movements [CSBM] rate, Bristol Stool Form Scale [BSFS], straining, abdominal pain, discomfort, and bloating) for LIN non-responders vs responders, defined as (1) 12-week abdominal pain/discomfort responders (≥30% reduction in abdominal pain and/or discomfort score [11-point scales], with neither worsening from baseline, for ≥6/12 weeks) and (2) 12-week IBS degree-of-relief responders (symptoms 'considerably' or 'completely' relieved for ≥6/12 weeks).

RESULTS: The pooled analysis included 1602 patients (LIN, n = 805; PBO, n = 797). Baseline characteristics were similar for responders and non-responders in the LIN group and the PBO group (Table). Abdominal discomfort scores and BMI were also similar for responders and non-responders (not shown).

CONCLUSION: Baseline demographics and disease characteristics did not predict treatment response to LIN or PBO in patients with IBS-C in the Phase 3 pivotal trials.

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P1552 PINAVERIUM BROMIDE PLUS SIMETHICONE IMPROVES BLOATING IN IBS PATIENTS INDEPENDENTLY OF BMI WHILE DAY/NIGHT VARIABILITY IN DISTENSION IS RELATED TO WEIGHT

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INTRODUCTION: In IBS, bloating seems related to visceral hypersensitivity, while visible abdominal distension to related to hyposensitivity due to delayed intestinal transit.[1] We have previously shown that pinaverium bromide 100 mg + simethicone 300 mg (PB+S), bid, improves bloating but not distension in IBS.[2] However, the relationship of BMI over these responses is unknown. Therefore, in this *post hoc* analysis, we explored the effect PB+S on bloating/distension according to BMI.

AIMS & METHODS: In this *post hoc* analysis, we explored the effect PB+S on bloating/distension according to BMI.

IBS-Rome III patients were randomly allocated to PB+S (n = 127) or placebo (n = 128) during 12-weeks in a double-blind placebo-controlled trial. A 10-cm VAS was used to evaluate the severity of bloating. Abdominal girth was measured twice a day (morning and night) during 7 consecutive days in weeks 1, 6 and 12. Abdominal volume (V) was calculated as: V = (girth cm)3/[6 p2] and day/night differences were determined. Partial etha^2 was calculated by ANCOVA for abdominal volume differences due to treatment and body weight adjusted by the initial volume differences and sex.

RESULTS: Patients were (mean±SD) 35.9±8.9 years old, women: 83.2% and BMI: 26.5±5.3 (Normal: 43%, Overweight: 36%, Obesity: 21%). IBS-subtypes were classified as IBS-C: 44%, IBS-D: 23%, IBS-M: 31% and IBS-U: 2%. At 12 weeks, bloating severity decreased by 18% in the overweight patients and 22% in the obese with respect to normal-weight subjects ($p = 0.32$); PB+S had a 37% effect size vs. placebo ($p < 0.006$). Also, a higher variability in the day/night change of abdominal volume was found in the overweight (39%) and obese (42%) patients compared to the normal ones ($p < 0.03$); the effect size of PB+S was 13% vs. placebo ($p < 0.39$).

CONCLUSION: While PB+S improved bloating in IBS patients independently of BMI, variability in abdominal volume was higher in overweight and obese patients compared to those with normal-weight with a low treatment effect.

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P1553 BLOATING IN IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: BASELINE SEVERITY AND RESPONSE TO TREATMENT IN 2 PHASE 3 TRIALS OF LINACLOTIDE

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INTRODUCTION: Irritable bowel syndrome with constipation (IBS-C) is defined by the presence of abdominal pain or discomfort in association with symptoms of constipation; another common symptom of IBS-C is bloating, but its severity and association with bowel movements (BMs) are not well defined. Linaclotide (LIN) is a guanylate cyclase C agonist approved in the United States and European Union for the treatment of IBS-C.

AIMS & METHODS: The aim of this post-hoc analysis was to: (1) characterise the severity of bloating in IBS-C patients; (2) describe the effect of LIN on bloating; and (3) assess the relationship between bloating and complete spontaneous BMs (CSBMs). Data from 2 LIN phase 3 IBS-C trials (Trials 302 and 31) were pooled for this analysis. Both trials randomised patients to oral once-daily LIN 290 μg or placebo (PBO) after a 2-week pretreatment period. Trial 302 had a 26-week treatment period; Trial 31 had a 12-week treatment period. Patients rated their bloating on a 0-10 point scale (0 = none; 10 = very severe) daily during the pretreatment and treatment periods. Patients also reported spontaneous BM (SBM) and CSBM frequency, stool consistency, straining, and other abdominal symptoms (pain, discomfort, fullness, cramping). Effect of CSBMs on bloating

Table to abstract P1553
Table Pooled responder rates in Phase 3 trials stratified by baseline characteristics

Characteristic	Abdominal pain/discomfort		IBS degree of relief		Abdominal pain/discomfort		IBS degree of relief	
	LIN R	LIN NR	LIN R	LIN NR	PBO R	PBO NR	PBO R	PBO NR
Age, years*	44.50 (12.05)	43.36 (13.91)	45.03 (12.08)	43.33 (13.41)	43.61 (13.75)	43.96 (12.71)	42.34 (13.45)	44.13 (13.05)
Female, n (%)	408 (92.9)	327 (89.3)	287 (93.2)	448 (90.1)	288 (90.0)	420 (88.1)	125 (89.9)	583 (88.6)
CSBM* (no. per week)	0.19 (0.44)	0.19 (0.42)	0.20 (0.44)	0.19 (0.43)	0.25 (0.49)	0.21 (0.47)	0.31 (0.51)	0.21 (0.47)
BSFS* (1-7)	2.34 (1.01)	2.31 (1.08)	2.41 (0.99)	2.27 (1.07)	2.32 (1.00)	2.38 (1.00)	2.25 (0.89)	2.38 (1.02)
Straining* (0-5)	3.60 (0.79)	3.53 (0.80)	3.53 (0.76)	3.59 (0.82)	3.49 (0.79)	3.48 (0.80)	3.42 (0.81)	3.50 (0.79)
Abdominal pain* (0-10)	5.63 (1.67)	5.65 (1.72)	5.66 (1.70)	5.63 (1.69)	5.27 (1.68)	5.79 (1.71)	5.42 (1.70)	5.61 (1.72)
Abdominal bloating* (0-10)	6.73 (1.83)	6.62 (1.81)	6.63 (1.82)	6.71 (1.82)	6.22 (1.79)	6.67 (1.87)	6.26 (1.80)	6.54 (1.86)

was assessed by stratifying the patient's change in daily bloating score by number of days since the patient had a CSBM.
RESULTS: The pooled intent-to-treat (ITT) population consisted of 1602 patients; 98% had baseline bloating scores ≥3. During pretreatment, ≥50% of patients had an average bloating score ≥6.5; only 6% of patients reported ≥1 day with no bloating (score of 0). LIN significantly reduced bloating within the first week of treatment compared with PBO and provided sustained benefit across 26 weeks of treatment. Mean percentage reduction in bloating from baseline for LIN vs PBO was 16% vs 7% at Week 1, 39% vs 24% at Week 12 and 44% vs 24% at Week 26. During the treatment period, the number of days since a patient had a CSBM was strongly associated with a patient's bloating score (i.e. a greater reduction in bloating was associated with more recently having had a CSBM), in both LIN and PBO patients. When controlling for days since last CSBM, the percent decrease in bloating for the LIN group was consistently greater than the PBO group (with non-overlapping 95% confidence intervals). For patients with 0 days since last CSBM, mean percentage improvement in bloating from baseline was 42% vs 33% in the LIN vs PBO treatment groups; this decreased to 35% vs 28% for patients with 2 days since last CSBM and to 21% vs 13% for patients with 4+ days since last CSBM.
CONCLUSION: Bloating is a significant issue in IBS-C patients, as evidenced by high baseline scores. LIN provides sustained reduction in bloating over PBO starting at Week 1 of treatment. Having a CSBM was associated with reduced bloating for LIN and PBO patients, with greater decreases in bloating on LIN vs PBO regardless of time since last CSBM.
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P1554 EFFECT OF NICKEL FREE DIET IN IBS PATIENTS WITH NICKEL SENSITIZATION

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INTRODUCTION: Irritable bowel syndrome (IBS) is characterized by chronic abdominal pain or discomfort accompanied by abnormal bowel movements, such as diarrhoea or constipation.
In sensitized subjects, the ingested nickel may induce gastrointestinal symptoms similar to IBS, in addition to typical systemic cutaneous lesions.
This clinical picture is known as Systemic Nickel Allergy Syndrome (SNAS).
Although there is no general agreement, a low nickel diet could improve the systemic manifestations. The prevalence of nickel allergy and the effect of nickel-free diet on IBS symptoms are not known.
AIMS & METHODS: To evaluate the prevalence of nickel allergy among IBS patients and to evaluate the effect of nickel-free diet on gastrointestinal symptoms in patients with IBS and nickel-sensitized patients. We selected *35 consecutive patients* affected by IBS defined by Rome III criteria and tested them with nickel patch tests. Patients positive for nickel allergy and meeting criteria for suspected SNAS (history for abdominal symptoms and nickel patch-test) underwent intestinal permeability test. Gastrointestinal symptoms (bloating, abdominal pain, flatulence, cramps, constipation, diarrhoea, epigastric pain, nausea, vomiting) were evaluated using visual analogue scale (VAS–IBS: 0–10) before and after diet. Gut permeability was evaluated by measuring 24-hour urine excretion of orally administered ^{51}Cr-EDTA and expressed as percentage of urinary excretion of the orally administered dose of ^{51}Cr-EDTA (%, cut off < 3%/24h). Then, all patients started a three months low nickel diet. Subjects with increased intestinal permeability at baseline repeated nuclear exam after the diet.
RESULTS: Thirteen patients (M/F: 3/10; age: 39±9) met inclusion criteria. The most frequent profile was diarrhoea predominant IBS (IBS-D, 10/13) compared to mixed (IBS-M, 2/13) and constipation (IBS-C, 1/13). Lactose intolerance was found in 9 patients. 6 subjects showed also sensitization to other haptens (palladium, cobalt, kathon). Mean urinary output of ^{51}Cr-EDTA was 5.88%/24h (±1.44). There was a variable and inconstant behaviour of the change of intestinal permeability after treatment. Conversely, low nickel diet induced a significant and constant improvement of gastrointestinal symptoms (i.e. a reduction of VAS–IBS) in all patients.
CONCLUSION: There is a high prevalence of suspected SNAS and intestinal permeability impairment in patients with IBS. Low nickel diet has significant beneficial effects on gastrointestinal symptoms in subjects with IBS and positive nickel patch test. The effect of such diet on gastrointestinal permeability requires further investigation.
Disclosure of Interest: None declared

P1555 HOW DO IBS PATIENTS TREAT THEIR SYMPTOMS UNDER REAL LIFE CONDITIONS? RESULTS FROM A SURVEY AMONG THE MEMBERS OF A GERMAN IBS PATIENT ORGANIZATION (DEUTSCHE REIZDARMSELBSTHILFE E. V.)

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INTRODUCTION: Irritable bowel syndrome (IBS) is a chronic, relapsing and often life-long gastrointestinal disorder[1]. Although not being life-threating, patients suffering from IBS report a significant impact on quality of life by their various symptoms which consist of abdominal discomfort (stomach cramps and bloating) and disordered defaecation (constipation, diarrhea, or both)[1,2]. Besides dietary and lifestyle advices, guidelines recommend pharmacological treatment, adjusted to individual symptoms and patient preferrences[2]. Little data is yet available about patient preferences and treatment habits.
AIMS & METHODS: To investigate the prevalence and severity of the main IBS complaints, as well as the preferred treatment options among the members of a German IBS patient organization (Deutsche Reizdarmselbsthilfe e. V.).
In 2013, non-personalized questionnaires were sent to all the members of the Deutsche Reizdarmselbsthilfe e. V., and returned questionnaires were analyzed by the patient organization.
RESULTS: 717 questionnaires were returned. 62% of respondents were female; on average, IBS patients were 54 years old and over 73% suffered from IBS symptoms for at least 10 years. 87% reported abdominal cramping and pain at least several times per month (categories: up to once every three months/once per month/several times per month/once per week/every day or several times per week), followed by 84% reporting flatulence with the same frequency. There were fewer patients reporting diarrhea, gastric cramps and constipation (several times per month or more often: 69%, 62% and 61%, respectively).
When asked "Do abdominal pain and spasms affect your quality of life permanently and massively? (categories: very strong/strong/moderate/weak/not at all)", 93% of patients answered with "moderate", "strong", or" very strong".
Open questions were asked concerning the preferred therapeutics. Abdominal cramping and pain, as well as gastric cramps were most often treated with the antispasmodic hyoscine butylbromide (N = 318 and 172, respectively), flatulence with simethicone (N = 320). The preferred treatment for diarrhea was loperamide (N = 205), and constipation was treated most often with bisacodyl (N = 138). 68% of hyoscine butylbromide users report ''good'' or ''very good'' efficacy against their abdominal cramps, 86% at least moderate efficacy (categories: very good/ good/ moderate/ not sufficient/ very bad).
CONCLUSION: Abdominal cramping and pain was reported most often and had a high and sustainable influence on quality of life among IBS patients. The preferred treatment options for all symptoms consisted of classical OTC drugs. Hyoscine butylbromide was the most often named and best rated treatment option for the most frequent symptom abdominal cramping and pain.
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P1556 SAMPLE SIZE CALCULATION IN CONFIRMATORY TRIALS IN IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: EXPERIENCE WITH LINACLOTIDE

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INTRODUCTION: Calculation of sample size (SS) with sufficient power to detect expected meaningful significant differences vs placebo is necessary for the success of confirmatory pivotal trials in irritable bowel syndrome with constipation (IBS-C). Phase 2b trial data on linaclotide in IBS-C were used as a benchmark to simulate different approaches for SS calculation in Phase 3 linaclotide trials to identify the best option for obtaining sufficiently powered results, and to assess the corresponding power to reject the null hypothesis that no difference in effect exists between active treatment and placebo.
AIMS & METHODS: Protocol design, patient population and endpoint assessments of a pilot Phase 2b (Trial 202) and two Phase 3 pivotal trials (Trial 302; Trial 31) of linaclotide in IBS-C were compared. Two statistical assumptions for the Phase 3 SS calculation for European Medicines Agency (EMA) co-primary endpoints were compared: 1) replication of Phase 2b 290 μg/day results and 2) minimally important clinical differences (MICD).
RESULTS: No relevant differences in protocol design or patient population were identified in the Phase 2b/3 trials. For endpoint assessments, only the range of the pain/discomfort scale differed (Phase 2b: range 1-5; Phase 3: range 0-10). For both clinical endpoints, Phase 2b data showed a non-statistically significant higher placebo effect and a non-statistically significant higher improvement over placebo compared with Phase 3 data (Table). The SS for the Phase 3

Table to abstract P1556
Table Responder rates in Phase 2b/3 studies of linaclotide

Endpoint	Study	Linaclotide 290 μg/day (%)	Placebo (%)	Delta
12-week abdominal pain or discomfort responder rate Patient with ≥30% improvement from baseline in either abdominal pain or abdominal discomfort (with neither getting worse) for ≥50% of the treatment period	Phase 2b (Trial 202) N=169	68	45	23 ($P<0.001$)
	Phase 3 (Trial 302) N=804	54.11	38.46	15.65 ($P<0.0001$)
	Phase 3 (Trial 31) N=800	54.81	41.77	13.04 ($P=0.0002$)
12-week IBS degree-of-relief responder rate Patients who are 'considerably relieved' or 'completely relieved' (score ≤2/5) for ≥50% of the treatment period	Phase 2b (Trial 202) N=169	47	21	26 ($P<0.0001$)
	Phase 3 (Trial 302) N=804	39.40	16.63	22.77 ($P<0.0001$)
	Phase 3 (Trial 31) N=800	37.04	18.48	18.56 ($P<0.0001$)

trials was estimated to have ≥95% power to detect a MICD of 15% in both co-primary endpoints. Based on replication of Phase 2b results for SS calculation assumptions, an SS of 134 patients per treatment arm in Phase 3 trials would have been sufficient to achieve ≥95% power to detect the expected efficacy (i.e. comparable efficacy to Phase 2b). However, this SS would have only 46% and 67% overall power to detect the actual observed results of Trial 31 and Trial 302, respectively, and even less overall power (13% and 47%, respectively) when the MICD is reduced to 10%.
CONCLUSION: In the linaclotide IBS-C clinical programme, Phase 2b results were not a good predictor of Phase 3 outcome, even without major differences in study design. Caution should be exercised when calculating SS for Phase 3 pivotal trials in IBS-C to ensure sufficient power to detect clinically relevant differences vs placebo.
Disclosure of Interest: M. Falques Other: Employee Almirall SA, C. Díaz Other: Employee Almirall SA, M. Moya Other: Employee Almirall SA, D. Vilardell Other: Employee Almirall SA, J. Fortea Other: Employee Almirall SA, J. Johnston Shareholder of: Ironwood Pharmaceuticals, Other: Employee Ironwood Pharmaceuticals.

P1557 STATISTICAL APPROACHES TO MISSING DATA IN TRIALS OF IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: EXPERIENCE WITH LINACLOTIDE

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INTRODUCTION: Missing data may affect validity and interpretation of clinical trials and different statistical approaches for handling missing data may lead to different conclusions. As patterns of missing data are often unknown until unblinding, pre-planning the most appropriate method can be difficult but may be guided by experience from similar trials in the same therapeutic area. Information on handling missing data in trials in irritable bowel syndrome with constipation (IBS-C) is limited.
AIMS & METHODS: This post-hoc analysis compared imputation methods for missing data in 2 pivotal Phase 3 clinical trials of linaclotide in IBS-C. Both were randomised, double-blind, placebo-controlled, multicentre trials of linaclotide 290μg once-daily for 12 (Trial 31) or 26 weeks (Trial 302). Pre-specified European Medicines Agency (EMA)-recommended co-primary endpoints were (1) 12-week abdominal pain/discomfort responder rate (patients with ≥30% reduction in abdominal pain and/or discomfort [11-point scales], with neither worsening from baseline, for ≥6/12 weeks) and (2) 12-week IBS degree-of-relief responder rate (patients with symptoms 'considerably'/'completely' relieved for ≥6/12 weeks). These endpoints were analysed using observed cases (OC), last observation carried forward (LOCF), baseline observation carried forward (BOCF), drop-out as non-responder and multiple imputation analysis.
RESULTS: In Trial 302, the different imputation methods for missing data yielded results consistent with the initial OC approach for both co-primary endpoints (Table). Results were similar for Trial 31, with statistically significant treatment differences for all imputation methods for both endpoints ($P<0.0001$ for all except for 12-week abdominal pain/discomfort responder: OC, $P=0.0002$ and drop-out as non-responder, $P=0.0056$).
CONCLUSION: All five imputation methods for handling missing data yielded non-biased results in both linaclotide Phase 3 IBS-C trials, supporting the robustness of linaclotide treatment effects on EMA endpoints. The approach that could be considered to be the most conservative, if any, was 'drop-out as non-responder' because using this method, the treatment effect estimates for both co-primary endpoints were numerically lower than those obtained by other methods.
Disclosure of Interest: M. Falques Other: Employee Almirall SA, C. Díaz Other: Employee Almirall SA, M. Moya Other: Employee Almirall SA, D. Vilardell Other: Employee Almirall SA, J. Fortea Other: Employee Almirall SA, J. Johnston Shareholder of: Ironwood Pharmaceuticals, Other: Employee Ironwood Pharmaceuticals.

P1558 REGION-SPECIFIC EFFECTS OF THE HERBAL MEDICINE STW 5 (IBEROGAST®) AND ITS INDIVIDUAL EXTRACTS ON HUMAN INTESTINAL MOTILITY

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INTRODUCTION: The multiherbal drug STW5 (Iberogast® a hydroethanolic extract ofangelica, peppermint, liquorice, greater celandine, caraway, lemon balm, chamomile, bittercandy tuft and milk thistle) is approved in Germany to treat functional dyspepsia and IBS. Recently, we reported region-specific effects in guinea pig and human stomach. Additionallywe demonstrated prosecretory effects on human intestinal epithelium and proposed thatthese effects may be involved in its clinical efficacy.
AIMS & METHODS: Now we investigated the effects ofSTW5 and its individual extracts on smooth muscle from different regions of human gut, alsoto address its mode of action. Methods: We recorded changes in muscle strip activity due to STW5 in 575 circular (CM) orlongitudinal muscle (LM) strips of small or large human intestine from 114 patientsundergoing abdominal surgery. Measured parameters were muscle tone (MT) and phasiccontractions (Motility index, MI).
RESULTS: STW5 induced significantly and dose dependently MT inhibition (64-5120μg/ml). Relaxation was significantly higher in large vs. small intestine and in CM vs. LM. STW5. At aconcentration of 5120μg/ml (which is still subtherapeutic) duodenum and jejunum (D+J) CMshowed comparable spasmolytic effect compared to ileum CM (-5.5±2.2 vs. -6.8±1.1mNrespectively $n=6$, $p=0.6$). However, they showed region-specific responses to MI reduction (ΔMI; -147.5±68.4mN/min, $n=6$, $p=0.004$ vs. -20.6±54.2mN/min, $n=6$, $p=0.6$). MT relaxationof large intestinal CM was significantly higher than in small intestine by 224.2% ($n=12$, $p=0.01$). In large intestinal CM STW5 changed the pattern of contractions into clusters with ahuge transient increase in MI (ΔMI; 292.4±150.4 mN/min; $n=11$, $p<0.05$) followed byinhibition of phasic contractility. Apart from milk thistle and bitter candy tuft, all extractscontributed to inhibitory actions of STW5 on MT and MI of small intestine. G.

Table to abstract P1557
Table Imputation methods for Trial 302

Analysis	12-week abdominal pain/discomfort responder, n (%)			12-week IBS degree-of-relief responder, n (%)		
	Placebo (N=403)	Linaclotide (N=401)	Δ; OR (95% CI)	Placebo (N=403)	Linaclotide (N=401)	Δ; OR (95% CI)
OC	155 (38.5)	217 (54.1)	15.6; 1.89 (1.43;2.51)*	67 (16.6)	158 (39.4)	22.8; 3.26 (2.34;4.53)*
LOCF	172 (42.7)	246 (61.3)	18.7; 2.15 (1.62;2.85)*	74 (18.4)	174 (43.4)	25.0; 3.39 (2.46;4.67)*
BOCF	132 (32.8)	191 (47.6)	14.8; 1.88 (1.41;2.51)*	68 (16.9)	158 (39.4)	22.5; 3.20 (2.30;4.44)*
Drop-out as non-responder	134 (33.3)	186 (46.4)	13.1; 1.75 (1.31;2.33)*	65 (16.1)	139 (34.7)	18.6; 2.75 (1.97;3.84)*
Multiple imputation approach	177 (43.8)	246 (61.3)	17.5; 2.05 (1.53;2.74)*	70 (17.4)	167 (41.7)	24.3; 3.40 (2.42;4.76)*

celandineincreased MI in D+J vs. reduction of ileum contractility (ΔMI; 74.7±29.0mN/min, n = 9, p = 0.001vs. -76.6±20.7mN/min, n = 7, p = 0.001 respectively). In large intestine, additionally caraway had no influence on MT. Peppermint, liquorice and angelica mimicked STW5 effect on MI. G. celandine increased MT without affecting MI. STW5 effects on MT and MI were reduced by blockade of TRPA1 channels (HC030031, by 50.4 and 74.0%, respectively), SOCs blocker (SK&F96365, by 35.2% and 69.5%), and TRPC3 antagonist (Pyr3, by 39.3% and 100.0%)(all 10μM).

CONCLUSION: *Our experiments identified region and layer specific effects of STW5 in human intestinal smooth muscle. The inhibitory effects were mediated by a closure of SOCs belonging to the TRPC3/TRPA1 family, resulting in decreased intracellular calcium levels. With the exception of milk thistle and iberis amara all extracts contributed to the effects of STW5. Peppermint, angelica and liquorice mimicked its inhibitory action on muscle activity. Due to the region and target specific effects of STW5 and its components we propose a potential to treat motility disorders of small and large intestine.*

Disclosure of Interest: S. Allam: None declared, D. Krueger: None declared, O. Kelber Other: Employee, I. E. Demir: None declared, G. Ceyhan: None declared, F. Zeller: None declared, M. Schemann: None declared

P1559 REDUCED QUALITY OF LIFE (QOL) IN SUBJECTS WITH IRRITABLE BOWEL SYNDROME (IBS) – HOW COULD IT BE IMPROVED?

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INTRODUCTION: Reduced Quality of Life (QoL) is common and often the main problem for subjects with Irritable Bowel Syndrome (IBS), and treatment should focus more on this problem to improve and individualize the treatment of these patients.

AIMS & METHODS: This study aimed at finding predictors of reduced physical and mental QoL in patients with IBS. Consecutive subjects with IBS (Rome II criteria) in general practice were included in this cross-sectional study. Information about gender, age (years), smoking habits (daily: yes/no), alcohol (more or less than twice a week), education (more or less than 10 years), duration of IBS (years), and severity of IBS-symptoms (a product of severity and frequency, score 0-12) were noted. Short Form 12 (SF12) was used for the measurement of physical QoL (SF-12 PCS, reference value 50) and mental QoL (SF-12 MCS, reference value 50). Somatic comorbidity was measured as the number of organic diseases and unspecified organic symptoms with Subjective Health Complaints 17 (SHC-17, reference value 6.2). Mental health complaints (anxiety, depression and somatization) was measured with Hopkin Symptom Checklist 10 (SCL-10, score 1-4, reference value < 1.85), hypochondria with Whiteley index (WI, score 14-70, ref. value < 40), and personality with Eysenck Personality Questionnaire (EPQ) short form 10 with focus on neuroticism (score 0-10). The study conforms to the principles of the Declaration of Helsinki and was approved by the Norwegian Regional Committees for Medical and Health Research Ethics. Results are given as mean (SD) or median (range), and multivariable analyses as partial correlation (pc) and p-values (p).

RESULTS: Out of 208 consecutive subjects with IBS, 149 were included in the study. Demographics; age: 52 years (SD 15.3); women: 105 (70%); daily smokers: 49 (36%); alcohol ≥ twice a week: 23 (17%); duration of IBS: 10 years (1-55); and IBS symptom score: 2 (0-12). Somatic comorbidity: number of organic diseases: 2 (0-9); and SHC-17: 12 (0-42). Psychiatric comorbidity: SCL-10: 1.7 (1.0-3.8); WI: 25 (14-60); and EPQ: 4 (0-10). QoL: SF-12 PCS: 38.4 (11.9); and SF-12 MCS: 45.0 (11.3). Independent predictors (multivariable analyses) of high SF-12 PCS were number of organic diseases (pc = - 0.168; p = 0.046) and SHC-17 (subjective health complaints, pc = - 0.304; p < 0.001). Independent predictors of high SF-12 MCS were SCL-10 (anxiety, depression and somatization, pc = - 0. 421, p < 0.001) and EPQ (neuroticism, pc = - 0.174, p = 0.050). Neither duration nor severity of IBS symptoms was independent predictors of QoL.

CONCLUSION: Somatic comorbidity and subjective health complaints were significant predictors of physical QoL, and anxiety/depression, somatization and neuroticism were significant predictors of mental QoL. Neither duration nor severity of IBS symptoms was associated with QoL. The study indicates that treatment of patients with IBS and reduced QoL should focus more on comorbidity than on IBS symptoms.

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P1560 FECAL CALPROTECTIN IN PREDICTING RECURRENCE AFTER ATTACK OF COLONIC DIVERTICULITIS

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INTRODUCTION: Colonic diverticulitis shows a high recurrence rate, but the role of fecal markers in predicting recurrence is unknown.

AIMS & METHODS: The aim of this study was to investigate the role of fecal calprotectin (FC) in predicting recurrence of diverticulitis.

A prospective cohort study was performed on 54 patients suffering from Acute Uncomplicated Diverticulitis (AUD) and treated with antibiotics to obtain remission. After remission, patients underwent to clinical follow-up every 2 months. During the follow-up, C-reactive protein (CRP) and FC was analysed at each medical control visit starting 2 weeks after the end of the antibiotic therapy. Recurrence of diverticulitis was defined as return to our observation due to left lower quadrant pain with or without other symptoms (e.g. fever), associated with leucocytosis and/or increased CRP, and confirmed by means of Computerized Tomography (CT).

RESULTS: The mean follow-up was 20 months (range 12-24 months). Forty-eight patients were available for the final evaluation, and 6 patients were lost to follow-up.

During the follow-up, increased FC was detected in 17 (35.4%) patients. Diverticulitis recurred in 8 (16.7%) patients: 7 (87.5%) patients showed increased FC during the follow-up, and only 1 (12.5%) patient with recurrent diverticulitis didn't show increased FC.

FC sensitivity, specificity, positive predictive value and negative predictive value were 87.5%, 75.0%, 41.2%, and 96.8%, respectively.

Only higher FC values (>60 μg/g) correlated with CRP levels (rho = 0.351, 95% CI 0.163 to 0.5267; p = 0.001). Finally, extension of diverticulosis showed correlation with FC expression (rho = 0.632, 95% CI 0.515 to 0.791; p = 0.000).

CONCLUSION: Increased FC was found to be predictive of diverticulitis recurrence.

Disclosure of Interest: None declared

P1561 DEVELOPMENT AND VALIDATION OF AN ENDOSCOPIC CLASSIFICATION OF DIVERTICULAR DISEASE OF THE COLON: THE DICA CLASSIFICATION

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INTRODUCTION: A validated endoscopic score on Diverticular disease (DD) of the colon is lacking at present.

AIMS & METHODS: We developed a simple endoscopic score of DD, the Diverticular Inflammation and Complication Assessment (DICA) score. The DICA score for DD resulted in the sum of the scores for extension of diverticulosis (left and right colon), number of diverticula per district (up to 15 and >15 diverticula), presence and type of inflammation (edema, hyperemia, erosions), and presence and type of complications (rigidity, pus, stenosis, bleeding): DICA 1 (up to 3 points); DICA 2 (score from 4 to 7 points); DICA 3 (over 7 points).

Videos of 70 consecutive patient at first diagnosis of DD were visualized during plenary session and classified by endoscopists that did not know the DICA classification.

Validation was carried out by estimating the correlation between DICA score and symptoms, Erythro-Sedimentation Rate (ESR) and C-Reactive Protein (CRP) expression. Finally, 50 videos of DD patients not involved in the development of DICA were reassessed in order to investigate the predictive role of DICA on the outcome of the disease.

RESULTS: A total of 960 ratings were performed. Overall agreement in using DICA was 0.847 (95% CI 0.812 to 0.893). It was 0.878 (95% CI 0.832 to 0.895) for DICA 1, 0.765 (95% CI 0.735 to 0.786) for DICA 2, and 0.891 (95% CI 0.845 to 0.7923) for DICA 3. Intra-observer agreement kappa was 0.91 (95% CI 0.886 to 0.947).

A significant correlation was found between DICA score and both ESR (p = 0.0001) and CRP values (p = 0.0001), as well as between median pain score and DICA score (p = 0.0001).

With respect to the 50 patients reassessed, recurrence or occurrence of disease complications were recorded in 10 pts (34.5%) classified as DICA 1 and 19 pts (65.5%) as DICA 2 (p = 0.036).

CONCLUSION: Diverticular Inflammation and Complication Assessment (DICA) score is a simple, reproducible, validated, and easy-to-use endoscopic scoring system for diverticular disease of the colon.
Disclosure of Interest: None declared

P1562 POSSIBLE ASSOCIATIONS BETWEEN COLONIC DIVERTICULA AND BOWEL HABITS: A MULTICENTER STUDY IN JAPAN

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INTRODUCTION: The association of diverticula on bowel habits are unclear. We therefore analyzed the association between diverticula and bowel habits in over 1000 Japanese individuals.
AIMS & METHODS: Japanese subjects who underwent total colonoscopies at seven centers in Japan from June to September 2013 were analyzed. Bowel habits were evaluated using the Gastrointestinal Symptom Rating Scale, and stool form was assessed using the Bristol Scale. Diverticula were diagnosed by colonoscopy with a transparent soft-short hood.
RESULTS: The study evaluated 1066 subjects, 648 males and 418 females (ratio, 1.55:1), of mean age 63.9 ± 13.0 years. After adjusting for age and gender, the presence of constipation was associated with a significantly reduced likelihood of diverticula (odds ratio [OR] = 0.70, 95% confidence interval [CI] 0.52–0.93, p = 0.0152). When assessed according to the location of diverticula, the presence of constipation was associated with a significantly decreased likelihood of left-sided (OR = 0.39, 95% CI 0.16–0.93, p = 0.0338), but not right-sided (OR = 1.10, 95% CI 0.48-2.53, p = 0.8230), diverticula. Furthermore, stool form was unrelated with the presence or absence of diverticula.
CONCLUSION: The wide-spread hypothesis that hard, small caliber stools could lead to colonic diverticula was not supported. Rather, we found that the absence of diverticula was associated with constipation, suggesting the need to reassess the etiology of colonic diverticula.
Disclosure of Interest: None declared

P1563 ARE CT SCAN BASED SCORING SYSTEMS OF ANY USE IN THE PRACTICAL MANAGEMENT OF ACUTE DIVERTICULAR DISEASE?

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INTRODUCTION: A large number of emergency patients are admitted with complaints of pain in the left lower quadrant, fever, and soiling and labeled 'acute diverticulitis'. Contrast enhanced CT scans are the most important imaging modality for acute diverticular disease in today's clinical practice. A CT scan can demonstrate an associated abscess and assist with direct percutaneous drainage. In the case of diverticular bleeding, CT angio may demonstrate a contrast blush. Hinchey described a traditional classification for 'acute diverticulitis' in 1978; since then, several CT based modifications have been presented to display a more contemporary overview of the disease; these translate into management strategies for the patient. However, not all patients admitted with left iliac fossa pain undergo a CT scan; far fewer have CT scoring.
AIMS & METHODS: We aimed to look at patients diagnosed with 'acute diverticulitis' in our Hospital, with specific reference to CT scans, classification, management and outcomes.
Methods: Data was retrospectively collected for all patients admitted with a diagnosis of 'acute diverticulitis', during the period November 2013 to February 2014. Data collected included CT scans, surgery/ radiological drainage, outcomes etc. All CT scans were then reviewed by a single GI radiologist and scored using a modified Hinchey scoring system.
RESULTS: 271 patients were identified with a diagnosis of acute'diverticulitis; of these, only 144 had had a CT scan. Of these, only 29 had a CT diagnosis of diverticulitis, with no scoring used. On review by the GI radiologist, this number further dwindled to 21. Of these, 18 had a modified Hinchey score assigned- 8 patients were IA, 5 were IB, 2 were II and 3 were III. 5 of these underwent Hartmans procedure/ sigmoid colectomy. One patient was successfully managed with CT guided drainage, while 1 underwent attempted drainage. There was no mortality. Of the 24 patients with an original CT diagnosis of diverticulitis who did not undergo surgery/ drainage, 15 were followed up with a colonoscopy later.
CONCLUSION: Since the introduction of the CT in the 1980s, this imaging modality has established itself as the primary diagnostic tool in the assessment of diverticular disease, leading on to the use of new treatment strategies, such as CT-guided percutaneous drainage of abscesses. A good CT scan based classification system of acute diverticular disease helps guide clinical decision making and management; unfortunately, we found this lacked a translation into daily clinical practice. Many patients with diverticulosis were therefore unnecessarily treated as acute diverticulitis; fortunately, pelvic abscesses, purulent and fecal peritonitis were accurately diagnosed clinically and managed appropriately. We emphasise the importance of performing a CT scan at acute presentation of diverticular disease to diagnose/ rule out/ manage complicated disease; this baseline scan is also crucial if the patient deteriorates during conservative treatment.
Disclosure of Interest: None declared

P1564 ARE ANTIPLATELET AGENTS OR HEMODIALYSIS RISK FACTORS FOR COLONIC DIVERTICULAR RE-BLEEDING?

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INTRODUCTION: Colonic diverticular bleeding is frequently encountered, but there have been few reports of its recurrence. In general, antiplatelet and hemodialysis are reported to be risk factors of gastrointestinal bleeding of various situations.
AIMS & METHODS: The aim of this study was to identify risk factors for diverticular rebreeding, especially whether antiplatelet and hemodialysis contributed or not.131 hospitalized patients, who were diagnosed with diverticular bleeding on the basis of colonoscopy findings between April 2002 and May 2013, were analyzed. The cumulative bleeding recurrence rate and potential risk factors for rebleeding, such as patient attributes (Age, sex, underlying conditions, and medication), treatment methods, were retrospectively investigated.
RESULTS: The 131 patients diagnosed with colonic diverticular bleeding included 96 men (73 %) and 35 women (27 %). The mean age was 62.5 ± 3.5 years, and the location of the diverticulum was the right colon in 31 cases, left colon in 21 cases, and both sides in 79 cases. 57 patients used antiplatelets and 9 underwent hemodialysis for end-stage renal failure. The method of hemostasis for first bleeding was clipping in 31 patients (23 %), local injection in 23 (17 %), surgery in 2, and conservative treatment in 91 (69 %). Rebleeding was noted in 51 patients (38 %), with the mean period before recurrence being 54 ± 30 months (mean follow up periods: 43.5±38.5 months). By multivariate analysis, conservative treatment (hazard ratio, 2.57; $p = 0.02$) is the only significant risk factor of rebleeding. But antiplatelet (hazard ratio, 1.51; $p = 0.27$) or hemodialysis (hazard ratio, 1.05; $p = 0.94$) were not significant.
CONCLUSION: In this study, antiplatelet or hemodyalysis were proven to be not significant risk factors for colonic diverticular rebleeding. Conservative treatment was identified as only independent risk factor.
Disclosure of Interest: None declared

P1565 THE PRESENCE OF DIVERTICULOSIS IS NEGATIVELY ASSOCIATED WITH POLYP DETECTION RATE

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INTRODUCTION: The association between diverticulosis and colorectal cancer (CRC) is controversial, since some of the data indicated a positive association, whereas some studies could not confirm this. Addressing this issue is very important since finding an association between diverticulosis and CRC may have implications for CRC prevention.
AIMS & METHODS: Therefore, we aimed to examine the association between the presence of diverticulosis and polyp detection rate (PDR).
Methods: We included 13,554 subjects aged 50 years and above (mean 65.4±10.3y) who underwent their first colonoscopy with acceptable preparation at our endoscopy unit between the years 2003-2010. Multivariable logistic regression analysis including the patients' age and gender, the examination hour, the quality of preparation and the presence of diverticulosis, were carried out to assess the association between diverticulosis and the presence of the polyps that were detected.
RESULTS: Polyp was detected in 4,667 (34.4%) subjects and increased from 26.2% at age 50-54y to 38.3% at age ≥84y. Diverticulosis was reported in 2,229 (16.4%), and increased from 6.9% at age 50-54 to 32.8% at age ≥84y. Both diverticulosis and PDR were increased significantly with age ($p < 0.001$ for both). Among 11,325 subjects without diverticulosis, 4,048 (35.7%) had polyps, as compared to 2,029 subjects with diverticulosis, out of them only 619 (27.8%) had polyps ($p < 0.001$). Using multivariable logistic regression analysis the presence of diverticulosis was negatively associated with PDR, (OR: 0.60 95% confidence interval 0.53-0.66, $p < 0.001$). An older age, male gender and the preparation quality were all significantly associated with PDR.
CONCLUSION: Although both diverticulosis and PDR were increased with age, the presence of diverticulosis was negatively associated with PDR. Whether this finding reflects a true phenomenon or could the presence of diverticulosis interferes with detecting polyps, should be further investigated.
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Disclosure of Interest: None declared

P1566 ASSOCIATION BETWEEN THE LOCATION OF DIVERTICULAR DISEASE AND IRRITABLE BOWEL SYNDROME: A MULTICENTER STUDY IN JAPAN

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INTRODUCTION: No previous reports have shown an association between location of diverticular disease (DD) and irritable bowel syndrome (IBS).
AIMS & METHODS: We included 1009 consecutive patients undergoing total colonoscopy in 7 centers in Japan from June 2013 to September 2013. IBS was diagnosed using Rome III criteria and diverticulosis was diagnosed by colonoscopy with transparent soft-short-hood. Left-sided colon was defined as sigmoid colon, descending colon, and rectum. Right-sided colon was defined as cecum, ascending colon, and transverse colon. We divided the patients into IBS and non-IBS groups and compared characteristics.
RESULTS: Patient characteristics included: mean age, 64.2 ± 12.9 years and male: female ratio, 1.62:1. Right-sided DD was identified in 21.6% of subjects. Left-sided and bilateral DD was identified in 6.6% and 12.0% of subjects, respectively. IBS was observed in 7.5% of subjects. Multiple logistic regression analysis showed left-sided DD (odds ratio, 3.1; 95% confidence interval (CI), 1.4–7.1; $P = 0.0060$) and bilateral DD (odds ratio, 2.6; 95% CI, 1.3–5.2; $P = 0.0070$) were independent risk factors for IBS. Right-sided DD was not a risk factor for IBS.
CONCLUSION: Our data showed that the presence of left-sided and bilateral DD, but not right-sided disease, were associated with a higher risk of IBS, indicating that differences in pathological factors caused by the location of the DD is important in the development of IBS. Clarifying the specific changes associated with left-sided DD could lead to elucidation of the pathogenesis of IBS.
Disclosure of Interest: None declared

P1567 NSAIDS, HYPERURICEMIA, AND CARDIOVASCULAR DISEASE WERE INDEPENDENT RISK FACTORS FOR DIVERTICULAR BLEEDING: ANALYSIS BY MATCHED CASE CONTROL STUDY

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INTRODUCTION: Colonic diverticulum is one of the common diseases especially in elderly patients. However diverticular bleeding occasionally causes massive bleeding that requires urgent colonoscopy (CS) and treatment.
AIMS & METHODS: The aim of this study is to clarify the significant risk factors for the diverticular hemorrhage in the colorectum.
Between January 2009 and December 2012, 26602 patients had a CS in our institution. One hundred twenty three patients had an urgent CS with the symptom of acute lower gastrointestinal hemorrhage. Seventy-two (72) patients of them received diagnosis with colonic diverticular hemorrhage. Age and sex matched 149 controls were selected from non-bleeding diverticulum patients who underwent CS by other reasons during the same period. The information checked were included the presence of cerebrovascular disease, ischemic heart disease, hypertension, hyperlipidemia, diabetes mellitus, chronic renal disease, osteoporosis, hyperuricemia. The information also contained medication including NSAIDs, antithrombotic agents. The relationship between these factors and diverticular bleeding were compared between cases and controls.
RESULTS: Among the 123 patients, 72 patients were diagnosed as colonic hemorrhage caused by colon diverticular. Age range of patients was from 33 years to 93 years old (average70±12.8). Sex ratio of men versus women of patients was 51:21. In the result of the univariate analysis, the factors of cerebrovascular disease, hypertension, hyperuricemia, chronic renal disease and usage of antithrombotic agents, and NSAIDs were significant to increase of ORs. Using these factors, we performed multivariate conditional logistic regression with stepwise variable selection. Finally, present usage of NSAIDs (OR = 14.70, 95% CI: 3.890-55.800, P < 0.0001), cerebrovascular disease (OR = 8.66, 95% CI: 2.330-32.100, p = 0.00126), and hyperuricemia (OR = 15.5, 95% CI: 1.740-138.000, p = 0.014) remained statistically significant.
CONCLUSION: This study indicated the present usage of NSAIDs, cerebrovascular disease, and hyperuricemia were significant risk factors for colonic diverticular hemorrhage. The knowledge obtained by this study may give some insight in the diagnostic process for the patients with acute lower gastrointestinal bleeding.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
NERVE GUT AND MOTILITY III – POSTER EXHIBITION – HALL XL

P1568 ENDOFLIP: A NEW DIAGNOSTIC MODALITY FOR MEASURING ANAL CANAL FUNCTION

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INTRODUCTION: Anorectal manometry is a commonly used technique to assess patients with fecal incontinence, but is known to have low reproducibility and poor validation in assessment of anal sphincter function. We report a pilot study on a novel technique using Functional Lumen Imaging Probe (FLIP) to improve assessment. Although FLIP has been used in upper GI studies its use in anorectal region is limited to three published studies, all of which used a 12 cm probe (as in upper GI studies). We used a purpose built shorter catheter to demonstrate bio-mechanical properties of the anus.
AIMS & METHODS: Aims: Primary objective was to demonstrate reproducibility of measurement taken by EndoFLIP. Secondary objective was to demonstarte its utility in assessment of anal canal. Methods: 19 healthy volunteers were recruited (9 females), mean age 34 (20-75). Catheters were purpose built, incorporating a rectal and anal canal balloon (three different sizes 2, 3 and 4cm long). Appropriate sized catheter corresponding to the length of subject's anal canal (based on manometry) was used. Participants underwent standard water-perfused anal manometry followed by FLIP on the same day. To test repeatability the FLIP was repeated after 30 minutes on the same day. The parameters checked for repeatability included CSA during rest, squeeze, endurance squeeze and cough in addition to the intra balloon pressure during these phases. Anal canal was divided into three parts- distal, mid and proximal based on anatomy and preliminary data analysis. There were different inflation volumes used, according to the balloon size, determined by analysing the pre-study test results.
RESULTS: 3 cross sectional area (CSA) readings were obtained with 2cm balloon, 5 with 3cm and 10 with 4cm balloon. Study established the test-retest and intra-observer repeatability for CSA using Bland-Altman plot and Intra-class correlation coefficient (ICC). Pearson correlation coefficient (PCC) was used to establish a correlation between CSA and pressure.
Bland Altmans plots showed measurement points for all parameters to be within 2 SD of line of equality. ICC calculated individually for each part of anal canal showed high levels of repeatability for CSA measurements (Table 1). Pressure readings were also repeatable (Table 1). Pearson correlation coefficient esablished a negative correlation between CSA and pressure during resting phase, at all the balloon volumes apart from the highest.

Measured phase	ICC for proximal anal canal	ICC for proximal anal canal	ICC for proximal anal canal	ICC for pressure readings
Resting	.960	.960	.928	.806
Squeeze	.978	.960	.919	.776
Cough	.970	.970	.943	.867
Endurance squeeze	.965	.960	.937	.868

Table 1

CONCLUSION: By allowing determination of serial CSAs during distension EndoFLIP allows detailed and segmental description of geometric and mechanical properties of the anal canal. The CSA and intra balloon pressure were repeatable and lower CSA was associated with higher pressure across all balloon volumes apart from the highest. Most likely cause for this was excessive distension of anal canal at higher balloon volumes. Validity and repeatability of EndoFLIP have been demonstrated by this study and future work will assess its utility in patients with faecal incontinence.
Disclosure of Interest: None declared

P1569 PERCUTANEOUS TIBIAL NERVE STIMULATION IS INEFFECTIVE FOR PATIENTS WITH CONSTIPATION

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INTRODUCTION: The efficacy of percutaneous tibial nerve stimulation (PTNS) in faecal incontinence has been well proven. However its value in managing constipation has not been studied. Current literature search (Pubmed & Embase) brings up only one study assessing its effect in managing constipation. Chronic constipation can be aetiopathogenically classified into slow transit (STC), rectal evacuation difficulty (RED) or a combination (BOTH). We studied the effects of PTNS in these patient subgroups.
AIMS & METHODS: Aims: We aimed to evaluate the effectiveness of PTNS in patients with range of constipation aetiologies by measuring change in wexner score, atransit study and anorectal physiology. Methods: 34 patients (30 women, median age 50 years, range 20-79) with constipation previously failing maximal laxative and biofeedback therapy participated in the study. All patients underwent baseline transit study and anorectal physiology to identify constipation subtype. All patients had 12 sessions of 30 minutes of PTNS. Responder rate (judged by Wexner constipation score fall to ≤15 or by ≥5points) was the primary outcome. Transit study and anorectal physiology were evaluated post-treatment.
RESULTS: There were 11 STC, 14 RED and 9 BOTH patients. Response was seen in 5 patients (2/11 STC, 2/14 RED and 1/9 BOTH). Comparing pre- vs post-PTNS, change in mean wexner scores was not significant (p = 0.10). There was no change in colonic transit time in the whole population (p = 0.56) or those with STC (p = 0.47). Balloon expulsion did not significantly improve in the whole group (p = 0.73) or those with RED (p = 0.69).
CONCLUSION: The data available from single study done so far, evaluating PTNS response in constipation, demonstrated a response rate of 33% based on reduction of improvement in constipation score of ≥ 5 points. However, this was not replicated in our study which had a response rate of only 15% based on the same criteria. Common finding in both the studies was a lack of improvement in transit time. Percutaneous tibial nerve stimulation is not of benefit in patients with constipation, whatever aetiopathogenic mechanism is responsible for their symptoms.
Disclosure of Interest: None declared

P1570 RECTAL HYPOSENSITIVITY TO BALLOON DISTENSION IS INFLUENCED BY RATE OF INFLATION

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INTRODUCTION: Impaired rectal sensation to mechanical distension, rectal hyposensitivity (RH), has been suggested to be causally linked to constipation in a quarter of patients. Although the exact mechanism of rectal distension sensitivity remains uncertain it is postulated to relate to populations of slow- and fast- adapting mechanoreceptor populations in the rectal wall. In clinical practice the measurement is elicited by manual inflation of a balloon, rather than the more predictable (but cumbersome) use of barostat-driven inflation. Interventions such as behavioural retraining, neuromodulation and rectal surgery have suggested that 'normalising' distension volume thresholds, is a desirable biomarker of treatment outcome. In an attempt to standardise protocols, we conducted a study to investigate the influence of rate of ramp rectal distension on volume thresholds.
AIMS & METHODS: Aims - To investigate the influence of rate of ramp rectal distension on rectal volume thresholds. Methods: We studied 49 patients (42 female, mean age 40 [21-74]) and 23 asymptomatic controls (18 female, mean age 36 [22-60]). Patients underwent transit studies and MR proctography, and accordingly stratified in to slow transit, ST (n = 18, 15 female, mean age 38 [21-60]) and puborectalis dyssynergia, PD (n = 21, 16 female, mean age 41 [23-74]): 10 patients had combined abnormalities and were excluded from further analysis. The participants underwent anorectal physiology test in the following sequence: rectal distension – manometry – RAIR – expulsion – rectal distension. Rectal distension was done by hand at rate of 1ml/sec and 5ml/sec in random order. Patients were asked to report first sensory awareness, urge to defaecate and maximal tolerable thresholds.
RESULTS: Results are shown in the table. There was no order effect, and no difference in thresholds between constipation subtypes. At 1ml/sec distension 5/18 and 6/21 ST and PD patients, respectively, were determined to have rectal hyposensitivity; this fell to 1/18 and 1/21 at 5ml/sec. Amongst controls 4 had elevated volumes at 1ml/sec and none at 5ml/sec.

	1ml/sec	5ml/sec	p value
FS in healthy controls (n = 23)	115 ± 61	49 ±23	0.01
FS in slow transit (n = 18)	142 ±64	71 ±33	0.04
FS in puborectalis dyssynergia (n = 21)	131 ±74	78 ±34	0.07
DDV in healthy controls (n = 23)	165 ±79	91 ±37	0.08
DDV in slow transit (n = 18)	202 ±87	129 ±49	0.03
DDV in puborectalis dyssynergia (n = 21)	189 ±90	128 ±51	0.05
MTV in healthy controls (n = 23)	304 ±111	202 ±93	0.03
MTV in slow transit (n = 18)	349 ±150	221 ±101	0.03
MTV in puborectalis dyssynergia (n = 21)	333 ±145	223 ±105	0.05

CONCLUSION: We have shown a significant difference in thresholds between slow and rapid distension rates. Slower rate of distension was associated with higher thresholds across all the three sensory volumes. Rectal hyposensitivity is identified less often at more rapid distension rate. Distension rates play a crucial part in diagnosing RH and standardised of protocol is required in future studies.
Disclosure of Interest: None declared

P1571 DIMINISHED THE UPPER-GUT MOTILITY AND ENTEROHORMONES LEVEL IN THE CELIAC DISEASE PATIENTS

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INTRODUCTION: The chronic inflammation in gastrointestinal tract in celiac disease (CD) patients may cause alterations of the upper-gut motility. The aim of study was to investigate the influence of CD on the upper-gut motility and release of enterohormones.
AIMS & METHODS: We studied 25 CD patients (8 males, 17 females, aged 42.4±15.8 years). CD was diagnosed by serological (serum level of anti-endomysial antibodies) and histological evaluation of duodenal mucosa. The gastric myoelectric activities (EGG), performed by 4-channels electrogastrography, were measured in fasted and fed subjects. The ghrelin and pancreatic polypeptide (PP) plasma level were measured. The results obtained were compared with a healthy, asymptomatic control group (9 males and 21 females, aged 42.1 ± 9.2 years).
RESULTS: Fasting CD patients showed decreased parameters of % of normogastria (54.8±24.5 vs. 86±12.3, p = 0.02) and SWC (61.1±17 vs. 67±18, p = 0.01) with increased dominant power (log DP) (13.3±1 vs. 11.1±1.1, p = 0.0001) compared to control group. In fed CD patients: % of normogastria, log DP, dominant frequency (DF), slow wave coupling (SWC) did not improve on the contrary for the control group in which log DP, DF, SWC and percent of normogastria increased ($p < 0.05$). Fasting ghrelin plasma level was lower in CD in comparison to control group 156.8±86.7 pg/ml vs 260.2±87.6 pg/ml ($p < 0.05$) but PP level was higher 265.2±123.1 pg/ml vs 211.4±114.6 pg/ml ($p < 0.05$) consequently.
CONCLUSION: CD causes subsequent disturbances of gastric myoelectric activity and fasting enterohormones levels. CD patients demonstrated diminished response to food. Observed diminished responsiveness suggests dysfunction of autonomic nervous system as common pathophysiological mechanisms.
Disclosure of Interest: None declared

P1572 INVESTIGATION OF DYSPHAGIA AND REFLUX SYMPTOMS AFTER ANTIREFLUX SURGERY BY HIGH RESOLUTION MANOMETRY: IMPACT OF MULTIPLE WATER SWALLOWS AND A SOLID TEST MEAL ON DIAGNOSIS, MANAGEMENT AND CLINICAL OUTCOME

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INTRODUCTION: Management of patients with persistent dysphagia and / or recurrent reflux after anti-reflux surgery is challenging [1,2]. This prospective, case-control study tested the hypothesis that, compared to standard high resolution manometry (HRM) with single water swallows (SWS), adding multiple water swallows (MWS) and solid swallows increase diagnostic yield and clinical impact of physiological investigation after fundoplication surgery.
AIMS & METHODS: 57 symptomatic and 12 asymptomatic control patients underwent HRM with SWS, MWS and a solid test meal. Diagnostic yield of standard and full HRM studies with 24hr pH-impedance monitoring was compared. Clinical outcome of pneumatic dilatation for outlet obstruction on HRM studies was assessed on an analogue scale from inadequate <40%, satisfactory 40-60%, good 60-80% to excellent >80% improvement. A "satisfactory" response was defined by a clear improvement in symptoms from baseline to a level where no further treatment was necessary.
RESULTS: Baseline EGJ pressure was similar in all groups. Abnormal EGJ morphology ("double high pressure band") was more common in symptomatic than control patients (13/57 vs. 0/12; p = 0.004). Overall diagnostic yield of HRM was 11 (19%), 11 (19%) and 33/57 (58%) with SWS, MWS and solids respectively ($p < 0.001$), being greatest for solids in patients with dysphagia (19/27 (70%)), see table. Outlet obstruction was present in 4 (7%), 11 (19%) and 15/57 (26%) patients with SWS, MWS and solids respectively ($p < 0.009$). Note that 4 patients that presented with reflux had outlet obstruction on HRM and negative pH-impedance studies. No asymptomatic control had clinically relevant dysfunction on solid swallows. Dilatation was performed in 12/15 patients with symptomatic outlet obstruction during the test meal. Symptom response was satisfactory, good or excellent in 7/12 (58%) with no serious complications.
Table: Diagnosis based on SWS and solid test meal (*$p < 0.05$, ** $p < 0.01$)

Main Symptom		Overall HRM	Outlet Obstruction	Peristaltic Dysfunction	Reflux	Functional (no cause)
Dysphagia n = 27	SWS	8 (30%)	4 (15%)	4 (15%)	2 (7%)	17 (63%)
	Meal	19 (70%)**	11 (41%)*	8 (29%)		6 (22%)**
Reflux n = 30	SWS	3 (10%)				
	Meal					
		14 (46%)**	0 (0%)	3 (10%)	10 (33%)	17 (57%)
		4 (13%)	10 (33%)*			9 (30%)*
Asymptomatic n = 12	SWS	1 (8%)	0 (0%)	1 (8%)	0 (0%)	n/a
	Meal	0 (0%)	0 (0%)	0 (0%)		

CONCLUSION: The addition of MWS and a solid test meal increases the diagnostic yield of HRM studies in patients with symptoms post-fundoplication and identifies additional patients with clinically relevant, symptomatic esophageal dysfunction. This includes patients with outlet obstruction post-fundoplication that benefit from endoscopic dilatation.
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Disclosure of Interest: None declared

P1573 THE ASSOCIATION OF SOMATIZATION WITH IRRITABLE BOWEL SYNDROME (IBS) AND UNINVESTIGATED DYSPEPSIA IN THE U. S. GENERAL POPULATION

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INTRODUCTION: Multiple studies have reported elevated somatization, i.e., excess frequency of general non-gastrointestinal physical symptoms, in clinical samples of IBS and functional dyspepsia (FD) patients. Much less is known about whether somatization is associated with these disorders in the general community.
AIMS & METHODS: Data from a nationwide U. S. internet survey of 1,665 adults were used to assess somatization in FD and IBS in the general population. The survey included the validated Recent Physical Symptoms Inventory (RPSQ)

developed by our team to measure somatization in IBS (MacLean et al. J Psychosom Res. 2012;73 (5):351-5), the SF-12 quality of life scale, the Rome III Diagnostic Questionnaire with new validated response formats (Gastroenterology 2013;144 (5) Suppl.1:S-916) planned for Rome IV, and demographic and health history questions. Responders providing inconsistent survey answers on 3 repeated quality-check questions were excluded from analysis, leaving 1277 response sets. Somatization scores were calculated as the number of different non-GI symptoms (out of the 26 on the RPSQ) experienced more than once in the past month.

RESULTS: The analysis sample was 648 females and 629 males; 701 white, 218 black, 240 hispanic and 118 other or undeclared race/ethnicity. Mean age was 46.4 years (range 18-94). A total of 91 individuals (7.1%) met Rome III IBS criteria (after subjects with organic bowel diagnoses were excluded), 146 (11.4%) met FD criteria, and 57 (4.5%) met both criteria. Mean somatization score was twice as high ($p < 0.0001$) in subjects with IBS (Mean +/- SD: 14.1 +/- 6.4) and FD (13.1 +/- 6.7) compared to those qualifying for neither diagnosis (6.5 +/- 5.7). These subgroup differences were significant even when all individuals reporting physician diagnosis of any upper or lower GI disorders were removed from the analysis, and were found within every race/ethnicity, gender and age group. Whole sample analysis showed that somatization scores were significantly correlated with frequency of each of the key gastrointestinal symptoms defining FD and IBS, including pain anywhere in the abdomen ($r = 0.50$), uncomfortable fullness after meals ($r = 0.49$), pain/burning in the middle of the abdomen ($r = 0.41$), and frequency of hard ($r = 0.38$) and loose ($r = 0.38$) stools; all correlations $p < 0.01$. All 26 non-GI symptoms of the RPSQ were significantly more prevalent in IBS and FD than in other subjects, even after controlling for multiple comparisons. The most common non-GI symptoms were the same in IBS and FD: Sleep difficulties (IBS = 86%,FD = 74%), muscle aches (82%,78%), back pain (81%,75%), headaches (79%,76%), and muscle stiffness (66%,60%). Excess somatization (score above 95th percentile in the comparison subjects meeting neither disorder criteria) was seen in 42.9% of IBS and 30.8% of FD cases. For both IBS and FD, somatization was negatively correlated ($p < 0.01$) with the physical ($r = -0.51, -0.42$) and mental ($r = -0.35, -0.32$) composite SF-12 quality-of-life scales.

CONCLUSION: Increased somatization (excess number of general non-GI symptoms) is robustly associated with both FD and IBS not only in clinic samples but also in the general population, and is seen across all gender, race and age groups. Somatization tendency is associated with higher frequency of functional GI symptoms and impairment in quality of life. [Supported by funding from the Rome Foundation]

Disclosure of Interest: None declared

P1574 DOES PERCEIVED STIGMA AFFECT HEALTHCARE CONSULTING AND QUALITY OF LIFE IN FECAL INCONTINENCE?

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INTRODUCTION: Fecal incontinence (FI) is a sensitive social topic, but it is unknown to what degree the perceived stigma of the condition impairs the quality of life (QoL) of FI sufferers or contributes to the common avoidance of healthcare-seeking for the problem.

AIMS & METHODS: We aimed to quantify the associations of perceived FI stigma with QoL impairment and the tendency to consult doctors about FI. A validated Perceived Stigma Scale (PSS) developed to measure gastrointestinal illness stigma and previously used (Taft et al Qual Life Res 2011;20:1391–1399) in irritable bowel syndrome and inflammatory bowel disease was adapted for FI (FI-PSS). Subjects indicate for each of 10 questions how often on a 5-point frequency scale from 0 = "Never" to 4 = "Always" they perceive potential or actual FI-associated stigma (like concerns that they would be treated differently or their opportunities limited if people knew about their FI) from six categories of people in their life; family members, friends, significant others, healthcare workers, coworkers and boss/supervisor. A nationwide U. S. internet survey that included the FI-PSS, Fecal Incontinence Quality of Life (FI-QOL), Fecal Incontinence Severity Index (FISI) and demographic questionnaires was completed by 234 adults with FI (defined as accidental loss of liquid or solid stool at least once a month in the past 6 months). Subjects who responded inconsistently ($n = 48$) on either of two repeated quality-check questions were excluded from analysis, leaving 186 response sets for analysis.

RESULTS: The 186 FI subjects were 52.2% female. Race/ethnicity was 82.8% white, 9.1% hispanic, and 8.1% black. Subject ages ranged from 20-91; 39.2% under age 40, 38.2% ages 40-65, and 22.6% age 65+. Nearly all subjects (93.5%) reported some perceived FI-related social stigma on the FI-PSS; least stigma was perceived from healthcare providers (mean score 15.6) and most from co-workers and employers (mean score 21.5 for both). Respondents who had consulted doctors about their FI (55.4% of the sample) had substantially greater FI severity (FISI mean +/- SD: 39.5 +/- 15.7 vs. 18.0 +/- 10.2) and higher perceived FI-PSS stigma scores (118.3 +/- 51.9 vs. 91.1 +/- 51.5) than non-consulters, and were also younger, more educated and more affluent ($p < 0.0001$ for all comparisons). However, when these variables were combined in a binary logistic regression equation, FI severity was the only significant predictor of consulting doctors for FI, explaining 53% of the variance (Nagelkerke $R^2 = 0.53$). FI-QOL scores (higher score = better QoL) were negatively correlated with FI severity (Pearson $r = -0.73$), stigma scores ($r = -0.51$), younger age ($r = -0.37$), education ($r = -0.28$) and household income ($r = -0.36$). When these were all combined in a linear regression equation, FI severity was the only significant contributor to the 56% total variance in QoL scores explained (adjusted $R^2 = 0.56$).

CONCLUSION: Perceived stigma is pervasive among FI sufferers. It is robustly associated with symptom severity, but it does not seem to be associated with avoidance of healthcare consultation for FI nor to have an independent effect on quality of life. [Supported by a research grant from Salix Pharmaceuticals]

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P1575 NEUROTRANSMITTER CONCENTRATION IN PREGENUAL ACC IN STOOL CONSISTENCY PATIENT SUBGROUPS WITH IBS

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INTRODUCTION: The Anterior Cingulate Cortex (ACC) is a key region of the central autonomic brain network. Irritable Bowel Syndrome (IBS) is characterized abdominal pain and bowel habit disturbances. Autonomic dysregulation has been reported in IBS as well as altered ACC activation in pregenual ACC during visceral stimulation [1] [2]. Glutamate is the major excitatory and Gamma-aminobutyric acid (GABA) the major inhibitory neurotransmitter in the brain.

AIMS & METHODS: We aimed to measure neurotransmitter concentration in the pregenual ACC, in stool consistency subgroups with IBS by using quantitative neurotransmitter Magnetic Resonance Spectroscopy (qMRS)

Seven patients with IBS-mixed (6 women) and five patients with IBS -diarrhea (4 women) according to Rome 3 were included. Mean age was 34.2 years (SD 5.3) with no significant difference between subgroups. Patients completed symptom severity score (IBS-SSS). Quantitative MRS was measured in a 3T MRI scanner. A water-suppressed MEGA-PRESS sequence (TR 2.0 s, TE 68 ms) was used with the editing pulses placed at 1.90 ppm ('ON-dynamics') and at 7.46 ppm ('OFF-dynamics') with a voxel (3x3x3 cm3) placed in the pACC. Each MEGA-PRESS measurement resulted in a sequence of 40 OFF- and ON-dynamics, where each was computed by 8 phase cycles. Directly after each water-suppressed MEGA-PRESS measurement, a shorter 2-dynamic unsuppressed water MEGA-PRESS measurement was performed within the same voxel, which was used to obtain the concentrations in physically well-defined units of [mM]. The GABA concentrations were computed by averaging the difference spectra obtained by subtracting each OFF-dynamic from subsequent ON-dynamic and using LCModel (Version 6.3) for the final quantification. The Glutamate concentrations were obtained by only averaging the OFF-dynamics, which were not affected by the editing pulses. Additionally, all dynamics were phase and frequency corrected prior to the averaging. For group comparison unpaired T-tests were used.

RESULTS: Patients had moderate to severe symptoms with IBS-SSS of 367 (SD 79.7). There was no significant difference between IBS subgroups in terms of IBS-SSS. Mean pACC GABA concentration was 1.66 (SD 0.17) mM in IBS-M and 1.65 (SD 0.27) mM in IBS-D. There was no significant difference between groups ($p = 0.9$). Mean pACC Glutamate concentration was 4.54 (0.35) mM in IBS-M and 5.13 (SD 0.64) mM in IBS-D. There was no significant difference between groups, although a trend with $p = 0.06$ was observed.

CONCLUSION: Further qMRS data have to be collected in IBS patients as well as healthy controls to evaluate if IBS subgroups demonstrate alterations in pACC glutamate and GABA concentrations.

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Disclosure of Interest: None declared

P1576 GLP-1 INHIBITS PRE- AND POSTPRANDIAL ANTRO-DUODENO-JEJUNAL MOTILITY IN HEALTHY SUBJECTS AND PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Glucagon-like peptide-1 (GLP-1) is secreted from gut endocrine L-cells in response to nutrient ingestion. GLP-1 acts as an incretin to lower blood glucose via stimulation of pancreatic islet beta cells. GLP-1 also exerts actions independent of insulin, including inhibition of gastrointestinal (GI) motility, inhibition of gastric emptying and acid secretion. IBS is characterized by abdominal pain or discomfort, associated with altered bowel habits and motor function in the GI tract. The positive actions of the GLP-1 in preclinical motility research and clinical IBS studies, highlights potential use of GLP-1 for treatment of IBS. Since recent studies indicate IBS symptoms to be prominent postprandially, we found it reasonable to investigate if GLP-1 would have an effect on upper GI motility in the pre- and postprandial period.

AIMS & METHODS: To investigate if GLP-1 can reduce GI motility after a meal.

The motility pattern of the proximal small intestine was monitored using a multichannel polyvinylchloride recording tube with its distal recording site at the angle of Treitz. Pressure transducers were connected via a PC Polygraph HR

(Synectics) to a PC. The software program Polygram Lower GI 6.40 (Synectics) was used with sampling frequency 4 Hz.
The over-all frequency of contractions, their amplitude and duration were computed during the respective 4-h infusion periods with saline and GLP-1 and transferred to a motility index.
Studies in vitro were done with muscle strips mounted between two platinum ring electrodes in 5 mL organ bath chambers containing Krebs solution, continuously bubbled with 5% CO_2 and 95% O_2 and and pH 7.4. Data acquisition was performed using Powerlab hardware and LabChart 7 software (ADInstruments). Tissues were equilibrated to a 2 g tension. After equilibration, muscle strips were studied with GLP-1 alone and in combination with the nitric oxide synthase inhibitor, LNMMA.
RESULTS: After food-intake, GI motility index increased in healthy volunteers and IBS patients. In volunteers, GLP-1 0.7 pmol/kg min^{-1} suppressed motility index in antrum, duodenum and jejunum from 6.2 ±0.4 to 4.8 ±0.7, from 5.6 ±0.6 to 4.9 ±0.6 and from 5.8 ±0.1 to 5.6 ±0.4 $Ln(\Sigma$ (mmHgsmin^{-1})), respectively. In IBS patients, GLP-1 2.5 pmol/kg min^{-1} decreased motility index in antrum from 6.2 ±0.1 to 6.0 ±0.2 $Ln(\Sigma$ (mmHgsmin^{-1})) whereas, in duodenum and jejunum inconsistent motility responses were found. Studies on gastrointestinal smooth muscle strips confirmed our results in by inducing an inhibitory action of GLP-1 on spontaneous motility.
CONCLUSION: Inhibitory motility responses to GLP-1 in healthy volunteers are similar to that in earlier animal studies. In IBS, an inhibitory effect of GLP-1 seems to require higher dosage of the peptide. Studies in vitro confirm our studies by relaxing intestinal smooth muscle strips. The relaxatory effect of GLP-1 on motility together with its inhibitory action on gastric emptying and small intestinal motor activity opens the possibility of using GLP-1 as a plausible treatment of IBS.
Disclosure of Interest: None declared

P1577 COMBAT-TRAINING STRESS MEDIATES METABOTYPIC CHANGES ASSOCIATED WITH GASTROINTESTINAL SYMPTOMS AND ALTERED INTESTINAL PERMEABILITY

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INTRODUCTION: Physical and psychological stress have been shown to precipitate gastrointestinal (GI) symptoms and impair intestinal barrier function. The neuroendocrine and –immune axes, as well as probably modulation of the microbiome, are involved mechanisms, but the molecular basis of stress-induced GI manifestations remains elusive. Global urinary metabolic profiling represents a novel approach for interrogating the multiparametric metabolic fluxes that occur in response to pathophysiologic stimuli such as stress.
AIMS & METHODS: Here, we characterized the stress-induced metabolic phenotype (metabotype) in soldiers during high-intensity combat-training and correlated the metabotype with changes in GI physiology, particularly the development of GI symptoms and alteration in intestinal permeability. In a prospective, longitudinal study, urinary metabotyping was conducted on 38 male soldiers (ages 19-23) during combat training and the subsequent rest period using gas chromatography-mass spectrometry. Stress was measured using the perceived stress scale-10 item (PSS-10) questionnaire, while incidence and severity of GI symptoms were assessed using the irritable bowel syndrome symptom severity score (IBS-SSS). Whole gut intestinal permeability was evaluated by quantifying the 24h urinary excretion of sucralose as a percentage of the orally administered 1g dose.
RESULTS: PSS-10 stress and IBS-SSS scores were higher during the combat-training period than at rest. The urinary metabotype was clearly distinct from the rest period [partial least squares discriminant analysis (PLSDA) $R^2X = 0.386$, $R^2Y = 0.712$, Q^2 (cumulative) = 0.563], confirming the presence of a unique stress-induced metabotype. Based on PLSDA, differential metabolites related to combat stress were uncovered (e.g. elevated pyroglutamate and fructose; reduced gut microbial metabolites such as hippurate and m-hydroxyphenylacetate) [$p < 0.05$]. The extent of pyroglutamate upregulation exhibited a positive correlation with the increase in IBS-SSS in soldiers during combat-training [$r = 0.504$, $p < 0.05$]. Additionally, the rise in fructose levels during combat-training was positively correlated with an increase in intestinal permeability [$r = 0.630$, $p < 0.005$].
CONCLUSION: Protracted and mixed psychological and physical combat-training stress yielded unique metabolic changes that corresponded with the incidence and severity of GI symptoms and alteration in intestinal permeability. Taken together, our data provided new insights into the molecular changes underlying stress-induced GI perturbations which could be exploited for future biomarker research or therapeutic strategies.
Disclosure of Interest: None declared

P1578 DYSMOTILITY IN PARKINSON'S DISEASE CORRELATES TO GUT SYMPTOMS: FINDINGS OF A WIRELESS MOTILITY CAPSULE STUDY

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INTRODUCTION: Parkinson's disease (PD) is a neuro-degenerative disorder with frequent involvement of the gut. Symptoms arise throughout the gastrointestinal tract through dysmotility secondary to autonomic and enteric nervous system involvement, as well from skeletal muscle involvement in the oropharynx and anorectum. It has been speculated that gut involvement may precede motor symptoms. The Wireless Motility Capsule (WMC) yields data on transit and motility throughout the gut.
AIMS & METHODS: We report the first use of WMC to systematically assess motility in PD patients with and without gut symptoms, compared to controls. 15 patients with established PD completed the study: eight (2 f, mean age 70 [47-85]) had GI symptoms and seven (2 f, mean age 61 [49-77]) did not based on history and baseline scores on the Gastroparesis Cardinal Symptom Index (GCSI) and Wexner constipation score. Data comparison with seven controls (3f, mean age 52 [39-63]). Medications affecting GI motility /pH were discontinued for the study and the WMC was ingested following a standardized nutrient bar meal. Data on gastric emptying time (GET), small bowel transit time (SBTT), colonic transit time (CTT) and whole gut transit time (WGTT) were calculated.
RESULTS: PD patients with gut symptoms showed significantly slower transit in the stomach (GET 5.2 vs 2.7h, $p = 0.0003$), colon (CTT 57.8 vs 27.4h, $p = 0.02$) and overall gut (WGTT 67.2 vs 34.7h, $p = 0.02$) compared to asymptomatic patients. Small Bowel transit (mean SBTT 4.17h) did not significantly differ. GET, SBTT, CTT and WGTT did not differ between asymptomatic PD and controls. There was a significant correlation between the Wexner constipation score and CTT in all patients ($p < 0.01$), but no correlation between GCSI and gastric emptying ($p > 0.05$).
CONCLUSION: This study demonstrates that symptomatic PD patients have markedly delayed transit times throughout the whole gut compared to asymptomatic PD patients and controls. The correlation between scores and transit times suggest that WMC is a less useful indicator of gastric emptying than small bowel and colonic transit.
Disclosure of Interest: None declared

P1579 NOVEL METHOD FOR MEASUREMENT GASTRIC EMPTYING USING 3D MICRO-CT IN LIVE SMALL ANIMAL

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INTRODUCTION: Delayed gastric emptying (GE) is one of the important pathogenic mechanisms of functional dyspepsia. Traditionally, oral gavage of phenol red/methylcellulose mixture has been used to measure the change of GE in small animals like rat or mice. However this method has a disadvantage to sacrifice animals at each measurement. 3D micro-CT has been used in the study for bone and soft tissues with the small animal, however it has not been applicated to the functional gastrointestinal study until now.
AIMS & METHODS: We aimed to establish a novel method for measurement of gastric volume and GE without sacrifice of rat using 3D micro-CT (Polaris-G90, NanoFocusRay, Jeonbuk, Korea). Sprague-Dawley rat (210~310g) were used. Rats were divided into Control (vehicle, n = 5), Delayed GE (atropine, n = 6), and Enhanced GE (bethanechol, n = 5) groups. After overnight fasting, distilled water, atropine (7.5mg/kg), and bethanechol (1mg/kg) was given by I. P. route in each group, respectively. After 20 minutes of IP, 3ml of radiopaque semisolid food was fed into stomach by gastric gavage under isoflurane anesthesia. Immediately after gastric gavage, baseline CT (fed volume) was performed, and after 1h freely moving time, 2nd CT (residual volume) was performed. Conventional CT image was converted to 3D image and the volume of radiopaque intragastric food was measured from baseline and 2nd CT. GE was calculated as [(fed volume-residual volume)/residual volumex100].
RESULTS: Fed food volume was 3.0 ± 0,02 ml, 2.99 ± 0.05 ml, and 2.4 ± 0.7 ml and residual volume was 1.33 ± 0.22 ml, 2.59 ± 0.35 ml, and 0.74±0.24 ml in Control, Delayed GE, and Enhanced GE groups, respectively. Fed volume at baseline CT of bethanechol treated rat was lower than 3ml because gastric contraction was very active and food was emptied immediately after gavage. The 1h GE rate, which was calculated using fed volume and residual volume on CT, was 55.9 ± 7.09 %, 13.5 ± 11.9 %, and 68.7 ± 6.64 % in Control, Delayed GE, and Enhanced GE group, respectively. ($P < 0.05$ compared to vehicle).
CONCLUSION: Gastric food volume was measured by 3D micro-CT in live small animal and GE rate was calculated using CT volume. This novel method can measure GE serially in a same animal. It seems that this method will be useful in the functional study for FD with decreasing the sacrifice of animal.
Disclosure of Interest: None declared

P1580 THE MOTILITY RESPONSE OF ESOPHAGUS TO PER-ORAL ENDOSCOPIC MYOTOMY IN PATIENTS WITH ACHALASIA: HIGH-RESOLUTION MANOMETRY APPROACH WITH CHICAGO CLASSIFICATION

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INTRODUCTION: Although per-oral endoscopic myotomy (POEM) is widely studied for achalasia, the motility response has been mainly focused on lower esophageal sphincter (LES). This study investigated the esophageal motility response including upper esophageal sphincter (UES), esophageal body (EB) and LES in subtypes of achalasia.
AIMS & METHODS: Achalasia patients who received POEM were included for analysis. Eckardt score was used to assess symptom improvement. High-resolution manometry was applied for studying motility change. HRM parameters analyzed were (i) LES: resting pressure (restP), 4-second integrated relaxation pressure (4s-IRP), intrabolus pressure (IBP); (ii) EB: contraction amplitude (CA); contraction duration (CD), distal contraction integral (DCI); distal delay (DL); esophageal length; (iii) UES: resting pressure (restP), relaxation pressure (relaxP); relaxation duration (RD).
RESULTS: There were 11 type I achalasia and 21 type II achalasia patients included. (i) LES tone was reduced significantly in both subtypes. (ii) Motility parameters of EB (length, CA, CD and DCI) were all lowered in type II achalasia, but were not in type I achalasia. (iii) UES relaxP was reduced in type II achalasia (13.90±6.76 vs. 5.22±6.80 cm, $p<0.001$); change of UES parameters in type I achalasia was insignificant. (iv) Eckardt score decreased more in type II achalasia without statistical significance [6.00 (3-10) vs. 5.00 (3-9), $p=0.056$]. (v) Proximal segment of esophagus without myotomy changed with distal segment with myotomy in both subtypes.
CONCLUSION: Type I and type II achalasia had different motility response patterns to POEM, which could lead to different clinical outcome. Distal myotomy of POEM would have a feedback l inhibition on proximal esophageal motility such as body contraction and relaxation of upper esophageal sphincter.
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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS III – POSTER EXHIBITION – HALL XL

P1581 THE IMMUNE RESPONSE IN THE LUNGS AND PHENOTYPE OF ALVEOLAR MACROPHAGES IN ASTHMA, GASTROESOPHAGEAL REFLUX DISEASE AND THEIR COMBINATION

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INTRODUCTION: The portion of patients with a combination of bronchial asthma (BA) and gastroesophageal reflux disease (GERD) grows steadily. We must understand particular features of this combined pathology to treat lung symptoms of these diseases. Our hypothesis: immune response abnormalities in the lungs during bronchial asthma (BA), GERD and in their combination is determined by faulty reprogramming of alveolar macrophages.
AIMS & METHODS: To verify the hypothesis and compare changes in immune response in the lungs with changes in phenotype of alveolar macrophages in patients with BA, GERD and their combination.
Methods: We measured the concentration of pro-inflammatory M1 cytokines: IL-1β, IL-8, IL-12, IFN-γ, TNF-α and TNF-β; anti-inflammatory M2 cytokines: IL-4, IL-5 и IL-10 and bivalent cytokines: IL-2 и IL-6 in bronchoalveolar lavage fluid (BALF) and in the alveolar macrophages culture medium. Changes in immune response in the lungs and changes in phenotype (reprogramming) of macrophages were evaluated using M1 cytokines to M2 cytokines ratio (M1/M2 index) in BALF and culture medium, respectively.
RESULTS: Patients with GERD had M1/M2 index of 4.2 in BALF; patients with combined pathology – 0.6; patients with BA – 0.9. So in GERD immune response in the lungs shifts to proinflammatory, in BA and combined pathology – to anti-inflammatory. Pro-inflammatory shift in GERD is due to increased concentration of M1 cytokines and decreased concentration of M2 cytokines in BALF, anti-inflammatory shift in BA is due to decreased concentration of M1 cytokines IL and decreased concentration of M2 cytokines, anti-inflammatory shift in combined pathology is due to decreased M1 cytokines and increased M2 cytokines. Along with specificity of cytokine pattern all three diseases have similar features: increased concentration of TNF-α, IL-6 and IL-2 in BALF. Phenotype of cultivated macrophages isolated from BALF in GERD and BA shifts to M1, in combined pathology shifts to M2. CD markers of phenotype confirmed these shifts. Pro-inflammatory shift of macrophage phenotype in GERD is due to the increased production of M1 cytokines and decreased production of M2 cytokine; pro-inflammatory shift in BA is due to decreased production of M1 cytokines and decreased production of M2 cytokine; anti-inflammatory shift in combined pathology is due to decreased production of M1 cytokines and and increased production of M2 cytokines. Along with specific changes in production of cytokines by macrophages in GERD, BA and their combined pathology, similar features were observed: increased production of M1 cytokines IL-8 and TNF-β, M2 cytokine IL-10 and cytokine IL-6.
CONCLUSION: analysis of cytokine spectrum from BALF and those produced by macrophages proved our hypothesis, that immune response abnormalities in the lungs during BA, GERD and in their combination is determined by faulty reprogramming of alveolar macrophages. This allows us to initiate new clinical direction – abnormalities in reprogramming of immune cells in the pathogenesis of lung diseases. Our results also indicate that the therapy of inflammatory component in the lungs should be conducted with consideration about specificity of the cytokine response abnormality.
Disclosure of Interest: None declared

P1582 ACTIVATION OF CB2 RECEPTORS HAS GASTROPROTECTIVE EFFECT ON EXPERIMENTALLY INDUCED GASTRIC ULCERS IN MICE

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INTRODUCTION: Cannabinoid (CB) receptors type 2, which belong to the endogenous CB system, are distributed in the central nervous system and in the periphery. Recent studies indicated that CB2 receptors are expressed profusely in the non-neuronal systems, including immunocytes and the gastrointestinal (GI) tract. It has therefore been suggested that cannabinoids may be involved in alleviating GI inflammation and the CB2 receptor agonists may represent potential therapeutics in GI inflammatory states, where immune system is activated. The aim of the study was to investigate the effect of the activation of CB2 receptors by a novel and highly selective CB2 agonist, MJ2010, on the development of gastric lesions in two murine models of gastric ulcer.
AIMS & METHODS: We used two well-established mouse models of gastric ulcer, induced by oral administration of acidified ethanol (60% EtOH in 0.3 M HCl) and a non-steroid anti-inflammatory drug (NSAID) diclofenac (30 mg/kg). Clinical parameters for gastroprotection were assessed based on the inhibition of gastric lesion area. To establish the mechanism of gastroprotective action, myeloperoxidase (MPO) and superoxide dismutase (SOD) activity, as well as glutathione (GSH), thiobarbituric acid reactive substances (TBARS), and H_2O_2 levels were assessed in gastric tissues.
RESULTS: CB2 agonist MJ2010 produced a dose-dependent gastroprotective effect in NSAID-induced gastric lesions, as evidenced by significantly lower macroscopic damage score. Moreover, we observed that the administration of MJ2010 (5 mg/kg p.o.), stimulated the oxidative stress protection mechanisms in the tissue, as demonstrated by an increased GSH level. We also found that our compound reduced the superoxide dismutase (SOD) activity, which was followed by lower levels of H_2O_2 in the tissue.
CONCLUSION: Activation of CB2 receptors by MJ2010 reduced gastric lesion through enhancing cell response to oxidative stress. Our data suggest that CB2 receptors are a new potential target in the treatment of gastric ulcers.
Disclosure of Interest: None declared

P1583 GASTROPANEL HELPS TO PREDICT ATROPHIC BODY GASTRITIS IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE

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INTRODUCTION: The prevalence of autoimmune thyroiditis in the general population is high (5-15%) and it is often associated in the same subject with other autoimmune disorders. One of them is the autoimmune atrophic gastritis, which occurs in 20-30% of asymptomatic patients carrying an autoimmune thyroiditis and likely affects 2-8% of the general population. This is a precancerous lesion of the stomach greatly affecting the absorption of vitamins, oligonutrients and some oral given drugs. Diagnosis is currently made by the serum detection of antibodies against parietal cells (APCA) and histology. Gastropanel, a combination of PG-I (pepsinogen-I), PG-II (pepsinogen-II), sG-17 (gastrin-17) and *Helicobacter pylori* antibodies, has been proposed as a simple non-invasive serological test to select patients with a high risk of harboring atrophic gastritis, who deserve endoscopic examination. This study assessed, non-invasively, the presence of chronic atrophic gastritis in patients carrying autoimmune thyroiditis, as managed in the primary care setting.

AIMS & METHODS: Patients (n = 160) with autoimmune thyroiditis were extracted from the database of n = 16 Italian primary care physicians. After exclusion of thyroid cancer, drug-induced hypothyroidism, inability to suspend PPI and contraindications to perform endoscopy, n = 145 of them (females = 130, median age 52 yrs) were further studied for gastric alterations. After overnight fasting, venous blood was taken for APCA and Gastropanel. PG I/II <3 was considered suggestive of moderate to severe body gastric atrophy and an indication to perform an upper gastrointestinal endoscopy.
RESULTS: APCA was positive in n = 22 (15.2%) and PG I/II <3 in n = 20 (13.8%) patients with autoimmune thyroiditis. Fifteen patients (75%) with PG I/II < 3 were also APCA positive. Gastric atrophy was present in 24/145 (16.6%) patients: 11/22 (50%) APCA positive, 13/20 (65%) PG I/II < 3 and in 10/15 (67%) with both APCA positivity and PG I/II <3. Patients (n = 24) with atrophy at histology were 11/24 (46%) APCA positive, 13 (54%) PG I/II <3, 10 (42%) positive and 10 (42%) negative for both markers. By multiple = "multiple" logistic regression, APCA alone showed a positive predictive value for atrophic gastritis of 50%, PG I/II <3 alone had a positive predictive value of 67%, whereas the PG I/II >3 had a negative predictive value of 86%. The presence of both APCA positivity and PG I/II <3 increased to 69% the positive predictive value for chronic atrophic gastritis.
CONCLUSION: Although based on a low number of patients, our results indicate that PG I/II <3 has a higher predictive value than APCA for gastric atrophy. The simultaneous presence of both APCA and PG I/II <3 increases the predictive value for gastric atrophy in patients with autoimmune thyroiditis. Gastropanel together with APCA positivity may represent a promising non-invasive tool to select patients needing endoscopy and histology.
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Disclosure of Interest: None declared

P1584 EXPLORATION OF THE POTENTIAL OF TUMOUR-ASSOCIATED AUTOANTIBODIES AS BIOMARKERS FOR GASTRIC CANCER DETECTION

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INTRODUCTION: Gastric cancer (GC) represents the third leading cause of cancer-related deaths worldwide in both sexes, which is mainly due to the belated diagnosis. Currently there are no reliable non-invasive biomarkers in clinics that could be used for prompt and early GC diagnosis. Research by many research groups including ours has demonstrated that circulating IgG class autoantibodies that are generated against tumour-associated antigens, due to their specificity, stability in serum and production even in early stages of cancer development may serve as promising non-invasive biomarkers for early detection of certain malignancies.
AIMS & METHODS: In a previous study[1], we applied T7 phage display-based SEREX (PhD-SEREX) approach and phage-displayed antigen microarray (PDAM) technology to identify GC-associated antigens and analyse Ag-specific autoantibody responses in patients with GC, which resulted in the identification of 45 autoantibody biomarker panel having promising diagnostic value (AUC = 79). The aim of the current study was to assess the GC-associated antigen repertoire in the proportion of patients that tested negative with the assay, and to evaluate its potential to increase the diagnostic performance of the serological test. We applied PhD-SEREX to identify GC antigen repertoire in 28 patients, and exploited PDAM for serum autoantibody reactivity profiling against the identified antigens in 67 GC patients (from these, 56 tested negative previously) and 54 healthy controls (HC). After microarray data processing and normalisation, each antigen was ranked basing on the detected serum signal intensity and frequency of reactivity in the two groups. For each of the tested serum, a score was calculated by summing up the intensities of sero-positive antigens.
RESULTS: By using serum samples from 28 GC patients, 183 different serum-reactive clones were identified. Clone sequence analyses revealed different antigen repertoire in comparison to that identified in our previous study[1]. According to the serum autoantibody profiling results, positive rank was assigned to 50 antigens, autoantibody responses against which were detected predominantly in GC patients. Autoantibody reactivity to individual antigens ranged from 1-7% of the GC patients. Mean serum score in GC group was 3.19 and 0.6 in HC group. From the top ranked antigens, autoantibody responses against 29 were found only within the group of GC patients that tested negative previously, and thus might represent valuable biomarker candidates. From these, majority represented novel serologically active tumour-associated antigens.
CONCLUSION: The results of this study demonstrate that there might exist different sets of induced autoantibody responses possibly reflecting immunologically distinct processes induced during tumour development in stomach or, alternatively, immune responses to molecularly different types of GC. The addition of the newly identified biomarker candidates to the previously established serological GC test set may substantially increase its diagnostic performance and thus awaits for further testing and validation within larger serum sample sets.
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Disclosure of Interest: None declared

P1585 NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: HOW TO PREDICT THE PRESENCE OF LESIONS WARRANTING ENDOSCOPIC TREATMENT?

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INTRODUCTION: Non-variceal upper gastrointestinal bleeding (NVUGIB) constitutes one of the most frequent emergency presentations in the gastroenterology field. Esophagogastroduodenoscopy (EGD) plays a predominant role in its approach and management.
AIMS & METHODS: Our objective was to identify variables at hospital admission with predictive value for the presence of high risk hemorrhagic lesions in EGD.
We included consecutive patients undergoing emergency EGD for upper gastrointestinal bleeding presenting with hematemesis or melena during a one-year period. Patients with either esophageal or gastric varices as well as portal hypertensive gastropathy were excluded.
Lesions with active hemorrhage, ulcers with a visible vessel and ulcers with adhering clot were defined as high risk hemorrhagic lesions, warranting endoscopic therapy.
Statistical analysis was performed using SPSS 21.0, and a p-value <0.05 was considered statistically significant.
RESULTS: Ninety-two patients were included, 54.3% (n = 50) were male, mean age 69 years (23-93 years). Ulcers (53%) and Mallory-Weiss lesions (12%) were the most frequently observed hemorrhagic lesions; no potentially bleeding lesion was found in 14% of the procedures.
Lesions with high hemorrhagic risk criteria were observed during EGD in 32.6% (n = 30) of the patients. In multivariate analysis, hematemesis (p = 0.026), systolic hypotension (p = 0.022), leukocytosis (p = 0.004) and EGD performed in the first 12 hours after the bleeding event (p = 0.002) were significantly associated with the presence of high risk hemorrhagic lesions.
CONCLUSION: One third of the patients undergoing EGD for non-variceal gastrointestinal bleeding were shown to have a high risk hemorragic lesion. Patients undergoing EGD during the first 12 hours of the hemorrhage, presenting with hematemesis, systolic hypotension or leukocytosis were more frequently diagnosed with high risk hemorrhagic lesions.
Disclosure of Interest: None declared

P1586 THE IMPACT OF MANDATORY INCLUSION OF GLASGOW BLATCHFORD BLEEDING SCORE IN THE INPATIENT REFERRAL PATHWAY TO A TERTIARY ENDOSCOPY UNIT

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INTRODUCTION: The Glasgow Blatchford Bleeding Score (GBS) is a validated pre-endoscopy scoring system, which stratifies patients presenting with acute upper gastrointestinal (GI) haemorrhage according to the likelihood of the need for intervention. Previous research indicates that patients with a low GBS score (0 or 1) are safe to have endoscopy as outpatients. An initial review in our own institution indicated 10% of inpatient endoscopies were in this low risk group. We therefore aimed to assess the impact of the introduction of GBS as standard part of the referral pathway on inpatient endoscopic activity. We also aimed to establish whether patients with a score of 2 could also avoid inpatient endoscopy.
AIMS & METHODS: We undertook a retrospective study of all inpatient referrals over a 6 month period. The GBS scores were completed by the referrer or calculated based on information recorded in patient's notes and electronic patient record. A review of the endoscopic findings and use of proton pump inhibitors (PPI) prior to endoscopy was performed and compared with previous findings.
RESULTS: During the study period (comparative first study data included in parenthesises) there were 140 (97) referrals, 137 (97) patients mean GBS 8.92 +/- 3.79 (6.2 +/- 4.2). Mean difference between the two studies was 2.72 (CI 1.68, 3.75), p < 0.0001. GBS was completed for 48 referrals - 34% (10–10%) and calculated in 92 – 66% (87–90%). Overall GBS was 0 or 1 in 2 patients – 1.5% (18–18.5%), 2 in 5 patients- 3.5% and 2 or more in 138 patients – 98.5% (79 – 81.5%). Of those with GBS 0 or 1, only 1 patient (18) had inpatient endoscopy. Endoscopic findings in the five patients scoring 2 were: normal-2, oesophagitis-2, Barrett's-1 and oesophageal ulcer-1. None had stigmata of recent haemorrhage or required end therapy. Amongst the whole group 21 patients – 15.2% (12 – 15.2%) required endotherapy. 102 patients – 72.8% (69–71.1%) were prescribed PPI prior to endoscopy. Of these, 48 patients – 47% (43–62.3%) had oral PPI, 51 – 50% (22–31.8%) had IV PPI and 3 – 3% (3–5.9%) PPI infusion.
CONCLUSION: Completion of the GBS proformas improved substantially from 10 to 34%. There was also a concurrent significant reduction in the number of inpatient referrals for endoscopy with a low risk score of 0 or 1 from 10% to 1.5 %. It appears the introduction of the GBS score has led to a wider appreciation of the importance of risk stratification amongst referrers in triaging inpatient endoscopy. Our findings also support recent research suggesting low risk stratification may safely be extended to include patients with a score of two.
Disclosure of Interest: None declared

P1587 IMPORTANCE OF ANGIOTENSIN-(1-7), A VASOACTIVE METABOLITE OF ANGIOTENSIN I IN THE MECHANISM OF GASTRIC ADAPTATION TO REPEATED ASPIRIN INSULT. A KEY IN UNDERSTANDING OF GASTRIC ADAPTATION TO ASPIRIN?

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INTRODUCTION: The rodent and human gastric mucosa of the stomach can adapt to damaging action of aspirin (ASA) but the contribution of renin-angiotensin system (RAS) and vasoactive metabolites of angiotensin I, e.g. angiotensin-(1-7) (Ang-(1-7) in phenomenon of gastric adaptation to ASA has been little studied.
AIMS & METHODS: Using advance LC-ESI-MS method we determined whether 1) Ang-(1-7) is detectable in gastric tissue and whether 2) the treatment with Ang II, the blockade of specific Ang-(1-7)/Mas receptor, exogenous Ang-(1-7) or AVE 0991, the agonist of Mas receptor, could influence the gastric damage induced by single and repetitive ASA treatment. Gastric adaptation was induced by daily repeated exposure of acidified ASA (100 mg/kg-d) given p.o. for 5 days to rats treated daily i.g. with or without: 1) Ang II (100 μg/kg), 2) A-779 (50 μg/kg), 3) Ang-(1-7) (20 μg/kg), and 4) AVE 0991 (50 μg/kg i.p.). The area of gastric lesions was determined by planimetry, the gastric blood flow (GBF) was assessed by H_2-gas clearance technique, the mucosal malondialdehyde (MDA) content as an index of lipid peroxidation, the plasma levels of IL-10, IL-1β and TNF-α (ELISA) were assessed. The expression of mRNAs for ACE, HIF-1α, IL-10, IL-1β and TNF-α, cNOS and iNOS was analyzed by RT-PCR.
RESULTS: We found that the rat stomach mounted in organ bath ex vivo is a source of Ang-(1-7) which is abundant metabolite product of Ang I conversion in the gastric mucosa. The single treatment with ASA produced gastric lesions and decreased GBF while raising both the mucosal MDA contents and the plasma IL-1β and TNF-α levels but significantly decreased the plasma IL-10 levels. The lesion area was reduced by 75% at 5 repeated exposures to ASA followed by a significant increase in the GBF and the significant decrease in the MDA content and the plasma IL-1β and TNF-α. Treatment with Ang-(1-7) (50 μg/kg i.g.) significantly reduced ASA-induced gastric lesions and the mucosal MDA content and raised GBF and these effects were reversed by concurrent treatment with A-779 ($p < 0.02$) or Ang II (10 μg/kg i.g.). In ASA-adapted rats the reduction in the lesion area and an increase in GBF were further improved by concomitant treatment with Ang-(1-7) or AVE 0991. Expression of mRNA for ACE was normal in intact mucosa but mRNAs for IL-1β, TNF-α, HIF-1α and iNOS which were negligible in intact gastric mucosa, were strongly upregulated in single ASA-treated mucosa and these effects were significantly attenuated in rats treated 5 times with ASA with or without treatment with AVE 0991.
CONCLUSION: We conclude that 1) Ang-(1-7) produced in excessive amounts by the gastric mucosa of the stomach is involved in the mechanism of gastric mucosal defense and mucosal resistance to subsequent repetitive ASA treatment, 2) blockade of specific Ang-(1-7) Mas receptor impairs the ASA adaptation suggesting that Ang-(1-7) plays an important role in the mechanism of gastric adaptation to repetitive ASA insult, and 3) Ang-(1-7) mediates ASA-induced adaptation *via* its antiinflammatory, vasodilatatory and hyperemic properties resulting in suppression of proinflammatory cytokines, lipid peroxidation and attenuating effect on oxidative stress.
Disclosure of Interest: None declared

P1588 A NEW SIMPLE SCORING SYSTEM FOR UPPER GASTROINTESTINAL BLEEDING – COLOGNE-WATCH RISK PREDICTION (C-WATCH)

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INTRODUCTION: Acute upper gastrointestinal bleeding (UGIB) is the leading indication for emergency endoscopy. Scoring systems have been developed for immediate risk stratification. However most of these scores include endoscopic findings and are based on data from patients with non-variceal bleeding. The aim of our study was to design a pre-endoscopic scoring system for acute UGIB - including variceal bleeding – in order to differentiate between high-risk patients in need of early endoscopy from low-risk patients with justifiable outpatient management.
AIMS & METHODS: The scoring system was developed using a training set consisting of 586 patients with acute UGIB. These patients were recruited from the emergency department as well as all inpatient services at the University Hospital of Cologne within a two year period (01/2007 – 12/2008). A cohort of 322 patients, who presented to our endoscopy unit with acute UGIB in 2009 served as validation set. Clinical, laboratory and endoscopic parameters as well as further data on medical history and medication were retrospectively collected from the electronic clinical documentation system. A multivariate logistic regression was fitted to the data to obtain a predictive risk score using recurrent bleeding, need for intervention (angiography, surgery) or death within 30 days as composite endpoint.
RESULTS: Only **C**RP, **w**hite blood cells, **A**LT, **t**hrombocytes, **c**reatinine, and **h**emoglobin could be identified as significant predictors for the composite endpoint. Based on the odds ratios of these variables an easy to use point scoring scheme (C-WATCH) was derived predicting the risk of complications from 3% to 86% with an AUC of 0.723 in the training set and 0.704 in the validation set. None of the low risk patients (0-1 points) needed any intervention included in our composite endpoint, while 36% of patients in the high risk group ($\geq$ 2 points) experienced a complication.
CONCLUSION: In emergency settings, our easy to use scoring system is able to separate high-risk patients who need hospitalization or immediate upper endoscopy from low-risk cases that are suitable candidates for outpatient management or in whom endoscopy can be postponed. A prospective validation of the C-WATCH risk score in different patient populations outside a university hospital setting seems warranted.
Disclosure of Interest: None declared

P1589 HEALTHCARE COSTS AND QUALITY OF LIFE ASSOCIATED WITH ACUTE UPPER GASTROINTESTINAL BLEEDING IN THE UK

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INTRODUCTION: Acute upper gastrointestinal bleeding (AUGIB) accounts for over 70,000 hospital admissions in the UK annually. Its incidence is likely to rise due to an ageing population and increasing burden of liver disease. Data on the healthcare costs and health related quality of life (HRQoL) associated with this condition are sparse.
AIMS & METHODS: The TRIGGER trial is a cluster randomised feasibility trial evaluating restrictive versus liberal red cell transfusion for patients with AUGIB. The study collected data on resource use, costs and outcomes during hospitalisation and up to day 28 to explore the feasibility of gathering inputs required for a cost-effectiveness analysis. Resource use data were collected during the inpatient episode on the use of laboratory tests, medications, blood components, endoscopy and endoscopic therapy, clinical events including ischaemic/thromboembolic events and length of hospital stay (LOS) by ward type. Data were also collected on primary and secondary care resource use, as well as informal care/days off work, post-discharge to day 28. Resource use for each patient was multiplied by national unit costs to generate an estimate of the costs of AUGIB to 28 days. HRQoL was measured on a scale anchored at 0 (death) and 1 (full health), using the EuroQol EQ-5D-3L questionnaire at day 28.
RESULTS: 936 patients were enrolled into TRIGGER between August 2012 and March 2013 in 6 UK hospitals. Preliminary analyses show that the mean (standard error (SE)) cost of the inpatient episode was £2436 (£87) per patient. LOS was a key cost driver; mean LOS was 5.3 days with an associated cost of £1432. Additional cost drivers included: (1) endoscopy, with mean of 0.8 endoscopies per patient at a cost of £627; (2) red cell transfusion, with a mean of 1.6 units transfused per patient at a cost of £198. Mean (SE) costs from hospital discharge to 28 days were £386 (£25) per patient. The main cost driver post discharge was readmission to hospital; 11% of patients were readmitted within 28 days for a mean of 4.8 days. The mean cost associated with readmission across all patients was £145. HRQoL was on average (SE) 0.68 (0.01) at 28 days.
CONCLUSION: The mean (SE) cost up to 28 days for patients presenting with AUGIB is £2822 (£90). At 28 days, the mean HRQoL in patients who have experienced an AUGIB is well below the average population level of 0.86. This is the first study to provide detailed estimates of the costs and HRQoL associated with AUGIB in the UK. These data can be used by healthcare providers and researchers to inform the design of subsequent cost-effectiveness analyses of interventions for AUGIB.
Disclosure of Interest: None declared

P1590 SIMULTANEOUS COMBINED BALLOON-OCCLUDED RETROGRADE TRANSVENOUS OBLITERATION AND PARTIAL SPLENIC EMBOLIZATION FOR GASTRIC FUNDAL VARICES

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INTRODUCTION: Balloon-occluded retrograde transvenous obliteration (B-RTO) has been widely adopted for the management of gastric fundal varices (GV). We previously reported the efficacy and safety of simultaneous combined B-RTO and partial splenic embolization (PSE) based on the hypothesis that concomitant PSE can diminish the increase in portal venous pressure following B-RTO for GV (JVIR 2012). With more cases and long-term observation, we re-evaluated the efficacy of simultaneous combined B-RTO and PSE.
AIMS & METHODS: We performed B-RTO in 36 consecutive patients with GV between 2005 and 2013 at a single institute. Of these, 8 and 4 patients with ruptured GV were treated emergently and electively, respectively. The remaining 24 patients with unruptured GV were treated prophylactically. Twenty-three patients received simultaneous combined B-RTO and PSE (Group 1) and 13 received B-RTO monotherapy (Group 2). Outcomes were retrospectively assessed.
RESULTS: No significant differences were observed in the baseline characteristics between the two groups except for significantly larger spleen volumes in Group 1. B-RTO was performed successfully in 33 of 36 patients (91.7%). Gastrorenal shunts were well-embolized, and GV resolved in all patients successfully treated by B-RTO. The procedure time was not significantly different between Groups 1 and 2 ($p = 0.2623$). In Group 1, the volume of sclerosing agent required for B-RTO was significantly smaller ($p = 0.0118$) and exacerbation of esophageal varices was significantly less frequent ($p = 0.0013$) than in Group 2.
CONCLUSION: This study indicated that concomitant PSE may improve the success of B-RTO.
Disclosure of Interest: None declared

P1591 NO CORRELATION OF ALARM SYMPTOMS AND CLINICALLY SIGNIFICANT FINDINGS IN UPPER ENDOSCOPY IN AMBULATORY SETTING: CONTINUATION OF THE PROSPECTIVE STUDY

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INTRODUCTION: In our former report (1) we represented the interim results on the correlation of alarm symptoms and clinically significant findings found on EGDS in 502 ambulatory patients. The results raised the doubts if the presence of alarm symptoms yields in much more clinically significant findings. Therefore we continued the study and the amount of patients was doubled.
AIMS & METHODS: Aim. To evaluate the correlation of alarm symptoms and clinically significant findings found on Esophagogastroduodenoscopy (EGDS) in the routine clinical practice in ambulatory setting.
Methods. A prospective study performed in 5 hospitals in Lithuania: Hospital of Lithuanian University of Health Sciences (tertiary level), and 4 secondary level hospitals. The data of ambulatory patients referred to upper endoscopy were collected and analyzed. Alarm symptoms that were evaluated as an indication to perform EGDS were: dysphagia, odynophagia, anemia, signs of upper GI bleeding (suspicion of melena), weight loss, recurrent vomiting, fever. The following endoscopic findings were considered as a clinically significant: erosive esophagitis, gastric ulcer, duodenal ulcer, gastric or duodenal polyps, malignant tumors.
RESULTS: Data from 1010 patients (mean age- 56.4±16.3) were analyzed: 379 (37.5%) males and 631 (62.5%) females. Mean age of males – 53.8±15.9, of females – 58.0 ±16.3 years, $p<0.01$. Alarm symptoms were found in 137 (13.6%) patients: in 75 (11.9%) females and in 62 (16.4%) males, $p<0.05$. Mean age of patients with alarm symptoms- 57.6±18.6, without alarm symptoms- 56.2±15.9, $p>0.05$. Clinically significant findings found in 381 (37.7%) patients. Malignant tumor found only in 7 (0.7%) patients. Mean age of patients with clinically significant findings was 56.3±15.4, without clinically significant findings- 56.5±16.8, $p>0.05$. Among patients with alarm symptoms, clinically significant findings were found in 48 (35.0%) patients, among patients without alarm symptoms– in 333 (38.1%), $p>0.05$. Duodenal or gastric ulcer was found in 4 (26.7%) out of the 15 patients with melena, and in 66 (6.6%) out of 995 patients without melena, $p<0.05$. We did not find any differences in clinically significant findings if the patients were referred to upper endoscopy by gastroeneterologist or not gastroenterologist.
CONCLUSION: The presence of alarm symptoms in our cohort was not associated with the clinically significant findings. Only the presence of signs of upper gastrointestinal bleeding was associated with more frequent detection of peptic ulcer. There is no correlation between the age and alarm symptoms and clinically significant findings in our cohort. The prevalence of esophageal, gastric and duodenal malignancies is extremely low (0.7%) in our studied setting. Therefore it is not feasible to determine the role of alarm symptoms in predicting the malignant diseases.
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P1592 UPPER GASTROINTESTINAL MUCOSAL INJURY AND SYMPTOMS IN ELDERLY PATIENTS TAKING LOW-DOSE ASPIRIN

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INTRODUCTION: It is well known low-dose aspirin (LDA) not only increases the risk of gastrointestinal (GI) mucosal injury but also worsens the quality of life (QOL) because of the symptoms like dyspepsia. Today, many elderly patients are taking LDA to prevent atherosclerosis diseases. Moreover, the number of LDA users is expected to increase in the future.
AIMS & METHODS: To reveal the clinical features of LDA related upper gastrointestinal mucosal injury (u-GI) especially in elderly patients, we investigated the prevalence, severity and symptom of esophageal mucosal injury (EI), gastric mucosal injury (GI) and duodenal mucosal injury (DI) individually between elderly patients (sixty-five years of age or over) LDA users (Users) and non-users (Non-users). Data was extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2008 and December 2013. Among 3162 elderly patients answering Frequency of Scale for Severity of GERD (FSSG) and SF8-QOL (SF8) were analyzed after excluding proton pump inhibitor or histamine type 2 receptor antagonist users. Prevalence was compared between Users and Non-users. Among patients who were diagnosed to have mucosal injuries, symptoms and QOL were compared between Users and Non-users. FSSG items were classified into total score (TS), reflux score (RS) and dyspepsia score (DS). SF8 has physical component summary (PCS) and mental component summary (MCS).
RESULTS: The study included 281 Users (199 men, 82 women; mean age, 72.7 years), and 2881 Non-users (1617 men, 1264 women; mean age, 71.7 years), respectively. Prevalence of EI in Users: Non-users was 10.0% ($n=28$): 9.6% ($n=276$) ($p=0.83$), GI was 35.9% ($n=101$): 27.5% ($n=792$) ($p=0.003$) and DI was 3.2% ($n=9$): 3.4% ($n=99$) ($p=0.84$). Regarding symptoms and QOL, TS, RS and DS of EI were Users: Non-users = 5.8 ± 6.6: 6.4 ± 6.3 ($p=0.61$), 3.3 ± 4.3: 3.7 ± 3.9 ($p=0.57$) and 2.5 ± 3.1: 2.7 ± 2.9 ($p=0.72$), GI were 5.0 ± 5.8: 6.0 ± 6.3 ($p=0.13$), 2.6 ± 3.2: 3.1 ± 3.7 ($p=0.15$) and 2.4 ± 3.1: 2.9 ± 3.1 ($p=0.17$), DI were = 2.6 ± 2.1: 4.8 ± 4.5 ($p=0.13$), 0.7 ± 1.1: 2.6 ± 2.8 ($p=0.04$) and 1.9 ± 1.8: 2.6 ± 2.8 ($p=0.69$). PCS and MCS of EI were Users: Non-users were 44.5 ± 9.1: 48.9 ± 5.8 ($p=0.0004$) and 50.6 ± 5.9: 50.0 ± 6.3 ($p=0.65$), GI were 47.4 ± 7.1: 47.8 ± 6.4 ($p=0.60$) and 50.5 ± 5.4: 49.5 ± 6.6 ($p=0.14$), DI were 48.8 ± 6.7: 49.0 ± 6.6 ($p=0.93$) and 45.3 ± 6.6: 50.3 ± 6.3 ($p=0.02$).
CONCLUSION: Prevalence of gastric mucosal injury in elderly LDA users was significantly higher than Non-users, although the prevalence of esophageal and duodenal mucosal injury was about the same. LDA users diagnosed with duodenal mucosal injury had significantly less symptom score on RS. LDA users diagnosed with esophageal mucosal injury had significantly less PCS score and LDA users diagnosed with duodenal mucosal injury had significantly less MCS score. These results give us the important clinical information that symptom based management was not appropriate in elderly LDA users in terms of upper gastrointestinal mucosal injuries.
Disclosure of Interest: None declared

P1593 ESOPHAGEAL MUSCULAR RING: CLINICAL REVIEW OF 10 CASES

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INTRODUCTION: The lower esophageal muscular ring remains a poorly defined entity. Distinguishing the muscular ring from achalasia and other causes of focal esophageal stenosis is important because of the differences in treatment and outcome.
AIMS & METHODS: The aim of this study is to analyze clinical characteristics of lower esophageal muscular ring. Medical records of 10 cases of lower esophageal muscular ring diagnosed at Daegu Catholic University Hospital from 2002 to 2013 were reviewed and analyzed retrospectively.
RESULTS: 10 patients comprised of 5 men and 5 women, with mean age of 57.4 years (range 43-72 years). The nine patients (90%) had symptoms consisting of chronic, intermittent dysphagia for both liquids and solids. Upper gastrointestinal endoscopic examinations revealed a focal smooth concentric narrowing of esophagus located a few centimeters above the squamocolumnar junctions. Endoscopic ultrasound examination showed a focal thickening of inner circular muscle at the luminal narrowing and mean thickness of muscle ring was 5.2 ± 1.4 mm. Nine patients underwent esophageal manometry and mean lower esophageal sphincter (LES) pressure was 35.2 ± 18.4 mmHg. Five cases showed complete LES relaxation and 8 cases showed well propagated esophageal body peristalsis. Mean amplitude of distal esophageal body contraction was 105.9 ± 43.9 mmHg. Barium esophagogram showed concentric narrowing of distal esophagus or patent esophageal lumen. Mean maximal diameter of luminal narrowing was 6.1 mm (range 2.6 -12 mm). Six cases were treated with calcium channel blocker and 4 cases had significant symptomatic improvement.
CONCLUSION: We have presented a series of 10 cases of patients with lower esophageal muscular rings. Considering a possibility of a muscular ring in the distal esophagus, well propagated esophageal body peristalsis, complete LES relaxation and variable luminal opening at barium esophagogram may help differential diagnosis of focal esophageal stenosis.
Disclosure of Interest: None declared

P1594 THE EFFECT OF K027, A NOVEL OXIME ACETYLCHOLINESTERASE REACTIVATOR, ON GASTRIC MYOELECTRIC ACTIVITY ASSESSED BY ELECTROGASTROGRAPHY IN EXPERIMENTAL PIGS

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INTRODUCTION: Reactivators of acetylcholinesterase (AChE) are essential in the treatment of organophosphate intoxication. Wider clinical use of several AChE modulators is limited because of the significant side effects, including serious gastrointestinal toxicity. Our research team has synthesised our own priority compound K027, 1-(4-carbamoylpyridinium)-3-(4-hydroxyiminomethylpyridinium)-propane dibromide. This novel oxime AChE reactivator was already tested in-vitro and on small laboratory animals with excellent results. K027 might thus be a candidate for human therapeutic use in the event of industrial poisoning or catastrophic situations. The small adult pig can be used in experiments as an omnivorous representative due to its relatively very similar gastrointestinal functions in comparison to man.
AIMS & METHODS: The aim of this study was to evaluate the effect of K027 on porcine electrogastrography (EGG). Six mature female pigs (3 months old, mean weight 23.2±2.1 kg) were included in the study. All EGG recordings were performed under general anaesthesia in the morning after 24 hours of fasting (by means of the MMS EGG System, Enschede, the Netherlands). After 10-minute baseline EGG, K027 (1500 mg i.m.) was administered. The EGG trial recording lasted 150 min. Running spectral analysis was used for initial evaluation of the EGG. The gastric myoelectric activity was estimated by EGG power analysis (areas of amplitudes) and by power ratio assessment (ratio of the areas of amplitudes after and before K027 administration).

RESULTS: After i.m. administration, K027 did not cause any significant changes in EGG dominant frequency. EGG power results displayed non-normal distribution. The power increased from the baseline mean values 648±326 (μV^2) to 4881±7756 (at 5 min.) and 12730±24404 (at 10 min.), p = 0.032, p = 0.151. Afterwards, the power values decreased gradually to those comparable with baseline ones (536±301 μV^2 at 150 min.). The EGG power ratio reached the highest values at 5 min. (11.3±20.3) and 10 min. (31.2±62.7), decreased significantly at 20 min. (3.0±2.9; p < 0.001) and stayed at low values until 150 min. (1.0±0.9).
CONCLUSION: K027, a novel AChE reactivator, caused only a transient increase in the EGG power with quick subsequent equalisation comparable with initial basal myoelectric values.
Acknowledgement: The study was supported by research grant IGA NT/14270-3 from the Ministry of Health.
Disclosure of Interest: None declared

P1595 EFFECTS OF NESFATIN-1 ON GASTRIC DISTENSION SENSITIVE NEURONAL DISCHARGE AND GASTRIC MOTILITY IN THE ARCUATE NUCLEUS OF RATS

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INTRODUCTION: Nesfatin-1, derived from the precursor NEFA/ nucleobinding-2 (NUCB2), is a newly identified 82-amino-acid anorexigenic neuropeptide which was initially discovered in the neurons of the hypothalamus. Several studies have showed that central administration of nesfatin-1 could suppress food intake and body weight gain, underscoring the potential importance of this peptide in the controlling of feeding behavior. Although the novel satiety peptide nesfatin-1 has been revealed to regulate the motor function, the underlying mechanisms have yet to be elucidated.
AIMS & METHODS: The study aims to explore effects of nesfatin-1 in arcuate nucleus (Arc) on gastric distension sensitive neurons (GD) and gastric motility, and the potential regulation mechanisms by lateral hypothalamic area (LHA). Single unit discharges in Arc were recorded extracellularly and gastric motility in conscious rats was monitored when administration of nesfatin-1 to Arc or electrical stimulation of LHA. Retrograde tracing and fluo-immunohistochemistry staining were used to determine NUCB2/nesfatin-1 neuronal projections.
RESULTS: Nesfatin-1 could inhibit most of GD-excitatory neurons (GD-E), but excite GD-inhibitory neurons (GD-I) in Arc. The reduced firing by nesfatin-1 on GD-E neurons could be partly absorbed by SHU9119 (P < 0.05), an antagonist of melanocortin 3/4 receptor. The gastric motility was significantly reduced by administration of nesfatin-1 into Arc (P < 0.05). Electrical stimulation of LHA could excite most of GD neurons in Arc (P < 0.05) and promote gastric motility (P < 0.05). However, pretreatment of anti-NUCB2/nesfatin-1 antibody in Arc could further increase the firing rates of GD-E neurons induced by electrical stimulating LHA (P < 0.05). NUCB2/nesfatin-1/fluorogold-double labeled neurons were observed in the LHA.
CONCLUSION: The results suggested that the effects of nesfatin-1 on GD-E neurons may be related with melanocortin signal pathway. Nesfatin-1 in the LHA perhaps was involved in the regulation of Arc on gastric activity.
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Disclosure of Interest: None declared

P1596 IMPEDANCE PLANIMETRY (ENDOFLIP®) MEASUREMENTS AT THE ESOPHAGO-GASTRIC JUNCTION DISTINGUISH NEUROMUSCULAR DISEASE FROM FIBROTIC LESIONS IN DYSPHAGIA PATIENTS

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INTRODUCTION: Impaired opening of the esophago-gastric-junction (EGJ) is a frequent cause of dysphagia and may be due to neuromuscular disease or fibrosis. Aim of this study was to test whether impedance planimetry parameters can be used to distinguish these etiologies.
AIMS & METHODS: Based on endoscopy, histopathology, HR-manometry and videofluoroscopy dysphagia was ascribed to be of neuromuscular (NM) or fibrotic (F) origin. A catheter fitted with a 25 mm balloon (EndoFLIP® EF-320) was inserted into the stomach transnasally and retracted until it was centered across the esophagogastric junction. The EndoFLIP® catheter acts as a functional imaging probe (FLIP) converting voltage measurements inside the balloon to estimations of balloon diameters at 5 mm intervals over 8 cm length. Intraballoon pressure is monitored by a solid state pressure transducer, facilitating the calculation of compliance data. EGJ distensibility measurements over 30 seconds were performed with balloon filling volumes of 20, 30, 40, and 50 ml volumes, respectively. Estimations of diameter and the distensibility index (DI, cross sectional area in mm2 divided by intraballoon pressure in mm Hg) were used as parameters. Study hypothesis was that DI is inversely correlated with balloon filling volume in patients with fibrotic lesions whereas it remains constant in subjects with neuromuscular disease affecting the esophago-gastric junction. The quotient of DI at 50 ml and at 30 ml volumes (DI 50 ml/DI 30 ml) was used to account for the change of distensibility with balloon filling volume.
RESULTS: The NM group comprised 20 subjects (4 females). Diagnoses were achalasia in 7, hypertensive lower esophageal sphincter (LES) in 4, and impaired LES relaxation upon swallowing in 9 patients. In the F group of patients (1 female) 4 had eosinophilic esophagitis, 5 a Schatzki-ring, and 6 a peptic stenosis.

	NM n = 20	F n = 15	p-value
Age (yrs)	42.1 ± 19.4	52.9 ± 17.8	n.s.
EGJ diameter 30 ml (mm)	6.2 (5.0 - 7.9)	7.2 (6.5 - 10.0)	0.007
EGJ diameter 50 ml (mm)	11.6 (8.7 - 12.7)	9.3 (8.7 - 10.7)	n.s.
DI 30 ml (mm2/mm Hg)	1.4 (0.9 - 2.4)	2.3 (1.7 - 3.0)	n.s.
DI 50 ml (mm2/mm Hg)	2.1 (1.5 - 2.7)	1.3 (0.9 - 1.6)	n.s.
Distensibility Index Quotient (DI 50 ml/DI 30 ml)	1.4 (1.0 - 2.0)	0.6 (0.5 - 0.9)	0.001

CONCLUSION: In patients with neuromuscular disorders DI remained constant or increased with filling volume, whereas a decrease was encountered in patients with fibrosis. In this study we have shown that a new parameter, the distensibility index quotient (DI 50 ml/DI 30 ml), can be used to distinguish neuromuscular disease from fibrotic lesions at the EGJ. This might have implications for the choice of treatment.
Disclosure of Interest: None declared

P1597 CLINICAL OUTCOME OF PATIENTS UNDERGOING ESOPHAGEAL HIGH-RESOLUTION MANOMETRY (HRM) IS ASSOCIATED WITH MANOMETRIC FINDINGS

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INTRODUCTION: Esophageal manometry is the reference method for diagnosis of achalasia and other esophageal motility disorders. It is also frequently recommended for patients with refractory reflux disease, particularly for those scheduled for fundoplication. The association between manometric findings obtained by HRM and clinical outcome parameters is unknown.
AIMS & METHODS: It was our aim to investigate clinical outcome in patients undergoing HRM with special respect to patients with impaired relaxation of the lower esophageal sphincter (IR-LES). Between September 2011 and June 2013 250 patients undergoing HRM were enrolled into a prospective study assessing demographics, manometric findings, pH-data, reflux symptoms (GerdQ) and dysphagia (HODQ, 5 items). Quality of life (QoL, SF-36) was also evaluated at the time of the investigations and 4-6 months later. The kind of treatment was assessed and patients rated overall treatment satisfaction. Data of all subjects with IR-LES and of an identical number of subjects with normal LES relaxation (NR-LES) were analysed.
RESULTS:

	LES basal tone, mmHg	pH < 4, %	GerdQ	HODQ	SF-36 pre	Invasive TX	SF-36 post
Achalasia	32±3 7	4±3.5	11±1	12±2	79±6	70%	100±6
EGJ-OO	31±2	3.4±1.6	9±1	3±1	90±3	14%	97±3
NR-LES	13±1	9.7±1.4	11±1	2±1	96±3	22%	106±3
p-value	< 0.0001	0.017	< 0.0001	< 0.0001	0.026	0.002	NS

Age and BMI were similar for subjects with IR-LES (n = 55) and NR-LES (n = 55). NR-LES patients were more frequently male (53% vs. 26% p < 0.05). 15 patients with IR-LES were diagnosed with achalasia, 40 had signs of EGJ outlet obstruction (EGJ-OO). Only 7 subjects with NR-LES had completely normal manometric findings. Patients with achalasia had similar GERD symptoms compared with NR-LES patients but more severe dysphagia and the lowest QoL (table). They received more invasive treatment (endoscopic or surgical) and had a more profound increase in QoL, although QoL improved significantly in all patient groups (p < 0.05 pre vs. post).
CONCLUSION: HRM has a high diagnostic yield and manometric findings are associated with choice of treatment modalities and posttherapeutic alterations of QoL. Patients identified as having achalasia according to HRM receive more invasive treatment and have the highest increase in QoL.
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P1598 EFFECTS OF PNEUMATIC DILATION ON LES AND UES PARAMETERS AND THEIR CORRELATION WITH SYMPTOMS IMPROVEMENT IN PROSPECTIVELY EVALUATED PATIENTS WITH ESOPHAGEAL ACHALASIA

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INTRODUCTION: An impairment in lower esophageal sphincter (LES) function is recognized as the hallmark feature of idiopathic achalasia; however, it has

become apparent that malfunctioning in upper esophageal sphincter (UES) may also occur in achalasia, but not in other esophageal motor disorders. In a recent study, pneumatic dilation has been retrospectively linked to an improvement in UES function.
AIMS & METHODS: Aim of this study was to prospectively evaluate the impact of pneumatic dilation on HRMI parameters. 27 (14 Males; age 41 ± 12 ys) newly diagnosed achalasia patients were enrolled. All patients underwent to pneumatic dilatation with a 30 mm diameter balloon, inflated for 120 seconds at 12 psi. In all patients a standardized questionnaire assessing the frequency and the intensity of achalasia-related symptoms (dysphagia for solids and liquid graded from 0:absent to 9: at each meal and precluding daily activities) was administered before and 6 months after pneumatic dilation. At the same time points, a HRMI study was performed in all patients. Manometric parameters studied were (i) LES basal pressure (LESbasalP) and 4-second integrated relaxation pressure (IRP4); (ii) UES resting pressure (restP) (iv) UES basal pressure (UESbasalP) and (v) incomplete esophageal clearance. All data are given as mean ± SD.
RESULTS: According to the Chicago Classification, 20 out of 27 were classified as having type-2 achalsia, 2 patients had type-3 achalasia and 5 patients were diagnosed as type 1. Six months after treatment, patients showed a sustained symptomatic improvement in terms of dysphagia for both solids and liquids (1±1.4 vs 6.7±2.2 and 0.6±1.1 vs 5.3±3.2 respectively; all $p<0.001$). After the pneumatic dilation, a significant reduction in LES basal pressure and IRP4 was observed (28±12 vs 46±12 mmHg and 17±9 vs 35±11 mmHg respectively; all $p<0.001$). Similarly, UES resting pressure resulted significantly decreased as compared to pretreatment values (8±5 vs 16±8 mmHg; $p=0.002$); whilst no differences were observed in UES basal pressure or incomplete esophageal clearance (90±32 vs 78±42 mmHg and 75±29 vs 74±29%, respectively; all p = NS). A positive correlation between the severity of dysphagia and LES pressure, IRP4 and UES resting pressure was observed ($r^2=0.305$, $r^2=0.592$ and $r^2=0.419$, respectively, all $p<0.001$), while UES basal pressure or incomplete esophageal clearance were not significantly correlated.
CONCLUSION: Here we demonstrated that pneumatic dilation of LES induced a sustained reduction of UES resting pressure, showing a positive correlation with patients' symptomatic improvement. Although LES pressure remains the main target of pneumatic dilatation; the positive effect of this technique on UES appears to contribute to the symptomatic improvement of these patients, supporting the idea that pneumatic dilatation has an undervalued effect on UES function.
Disclosure of Interest: None declared

P1599 TRAINING IN PER ORAL ENDOSCOPIC MYOTOMY USING PRECLINICAL ANIMAL MODEL: ANALYZING THE LEARNING CURVE

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INTRODUCTION: POEM is a complex and demanding endoscopic procedure with a potential of serious complications. Therefore it requires a set of endoscopic skills. Training requirements and a learning curve for POEM are to be still defined. Increasing experience with POEM leads to an urgent need of defining adequate training program for new trainees to assure the appropiate clinical safety.
AIMS & METHODS: We report results of our training program for experienced endoscopists using a preclinical porcine model. Prospective cohort study from a single center involved 39 patients (24 men, 15 women) undergoing POEM. All procedures were performed by one experienced endoscopist after training on 10 pigs. The first clinical procedure was supervised by an expert in the field. All patients had a diagnosis of esophageal achalasia. We divided patients into 3 consecutive groups (3x n = 13). We set the length of procedure (LOP) divided by length of myotomy (LOM) as an appropriate outcome (LOP/LOM) of skill's progression in time. Analysis of a learning curve was based on LOP/LOM and frequency of complications (e.g. inadvertent mucosotomies).
RESULTS: POEM was successfully completed in all ten pigs. As for complications we reported 5 bleedings, 2 esophageal perforations and 2 inadvertent mucosotomies in animal model. Autopsies revealed safe closures of porcine esophagus (6.1±1.1 clips), LOP/LOM was 5.1±1.8 minutes/cm. All POEM procedures in 39 patients (aged 45.6 ± 13.6 years; BMI 25.2 ± 4.5 kg/m^2) were performed without any serious intraoperative complications. Mean length of hospitalization was 2.5 ±.0.7 days. The mean LOP was 83.6 ± 22.6 minutes and the mean myotomy length was 12.5 ± 2.6 cm. The mean LOP/LOM (7.1 ± 2.7 minutes/cm) decreased with increasing experience (P-value < 0.001): first group (10.1 ± 1.9 minutes/cm); second (5.9 ± 1.5 minutes/cm); and third (5.3 ± 1.6 minutes/cm).
An inadvertent mucosotomy was reported in 3 patients (7.7%), all of them occurred in the first group of patients and were successfully treated endoscopically with clips. The frequency of carbon dioxide extravasation (capnoperitoneum requiring a puncture (41%) and subcutaneous emphysema (23%)) were not influenced by experience (P-value = 1).
Plateau phase of learning curve (based on LOP/LOM) began with the 12th patient and has fully stabilized since the 14th patient (24th procedure including animal training).
CONCLUSION: A significant learning curve of POEM after preclinical animal training was recorded in decreasing LOP, faster myotomy itself and decreasing number of inadvertent mucosotomies. Carbon dioxide extravasation was not influenced by learning. Our results suggest that primary POEM training of experienced endoscopist on at least ten pigs might shorten the achievement of plateau phase to approximately 14 clinical procedures.
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Disclosure of Interest: None declared

P1600 HYDRAULIC DILATION IN IDIOPATHIC ACHALASIA USING THE ESOFLIP DILATION BALLOON: A FEASIBILITY STUDY

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INTRODUCTION: Pneumatic dilation is a commonly used treatment in achalasia. Fluoroscopy enables positioning of the balloon at the oesophagogastric junction (OGJ) but has the disadvantage of radiation exposure. An important element of dilation is oesophageal distensibility, defined as compliance of the wall at a certain point, which can be used to assess the effect of dilation and possibly the risk of perforation. It is currently not possible to measure distensibility during dilation. A new hydraulic dilation balloon, the EsoFLIP, is able to visualise the shape of the balloon in vivo, thereby obviating the need for fluoroscopy, and measures distensibility during dilation.
AIMS & METHODS: The aim of this study was to evaluate technical feasibility and safety of the 30mm EsoFLIP hydraulic dilation balloon in patients with achalasia. Consecutive patients with newly diagnosed achalasia were dilated on two separate days using the EsoFLIP balloon under endoscopic visualisation. Patients were contacted one week, one month and three months after dilation. Technical success (placement at the OGJ and successful dilation while measuring diameter, pressure and distensibility), clinical success and major complications were evaluated.
RESULTS: Ten patients (4 male [40%], median age 50 years, range 27-62) were included between August 2013 and February 2014. Patients were subjectively symptomatic for a median of 9 months (range 3-24) prior to dilation. Technical success was achieved in all cases. Gradual inflation showed that the balloon had a tendency to migrate during inflation but in vivo imaging enabled precise placement at the OGJ. On day one, the median minimal diameter (mm) of the OGJ before and after dilation were 9.5 (range 7.2-12.9) and 16.3 (range 13.4-21.4), respectively. On day two, these diameters were 13.9 (range 8-15.2) and 16.7 (range 14.2-18.6), respectively. Median difference in diameter before the first and after the second dilation was 7.2 (range 3.2-9.2). Median pressures (mmHg) used during the first and second dilation were 551 (range 310-1130) and 603 (range 390-815), respectively. Median oesophageal distensibility (mm^2/mmHg) on the first day before and after dilation were 1.0 (range 0.2-2.2) and 8.2 (range 0.8-20.1), respectively, while on the second day this was 1.7 (range 1-4.3) and 5.9 (range 3.3-29.3). Median difference in distensibility before the first and after the second dilation was 5.7 (range 2.1-28.3). No major complications were seen. Three patients (30%) reported recurrent dysphagia and laparoscopic Heller myotomy was performed in two (66.7%).
CONCLUSION: Dilation with the 30mm EsoFLIP balloon in achalasia is feasible and safe. In vivo imaging of the balloon shape facilitates placement of the balloon while oesophageal distensibility and diameter measurements allow for a patient-specific dilation regimen, which may improve effectiveness and safety of the procedure.
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P1601 PATTERNS OF PERISTALSIS RECOVERY AFTER PERORAL ENDOSCOPIC MYOTOMY IN ACHALASIA PATIENTS

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INTRODUCTION: A detailed analysis of whether impaired esophageal peristalsis in achalasia patients can recover after peroral endoscopic myotomy (POEM) has not been performed. We tested the hypothesis that the normalization of esophagogastric junction outflow obstruction after POEM is associated with a partial recovery of esophageal peristalsis.
AIMS & METHODS: We performed an analysis of prospectively collected high resolution manometry (HRM) data of patients undergoing POEM at a single institution (IKEM). 27 patients (8 women, 19 men) underwent HRM before and 3 months after POEM. Twenty-six patients were diagnosed with achalasia (type I- 2 patients, type II- 22 patients, type III-2 patients) and one patient had Jackhammer esophagus. Detailed HRM analysis according to the Chicago classification was performed. The main outcome measurements were: changes in integrated relaxation pressure (IRP) and changes in esophageal peristalsis pattern related to the symptomatic response after POEM.
RESULTS: Before POEM, peristaltic fragments were present in 3 patients only (2 with type III achalasia and 1 with Jackhammer esophagus). After POEM, 15 patients (55%) were classified according to the Chicago classification as either frequent failed peristalsis (n = 6) or weak peristalsis with large breaks (n = 9). Nine patients (33%) persisted in having absent peristalsis and three patients (11%) were still meeting the criteria of achalasia (type II). In 17 patients out of 22 with type II achalasia (77%), the panesophageal pressurization completely disappeared or has been reduced to compartmentalized pressurization after POEM. The mean IRP decreased from 24.7 (± 11) mmHg before to 12.0 (±5) mmHg after POEM. All patients with IRP normalization (IRP < 15 mmHg) had an excellent symptomatic response. Among 4 patients with post-POEM IRP > 15

mmHg, three had only partial symptomatic improvement (Eckhard score 2, 3 and 5), which corresponded with persistence of panesophageal pressurization.
CONCLUSION: More than half of achalasia patients with IRP normalization after POEM have signs of partial recovery of esophageal peristalsis. Successful POEM is associated with a disappearance of panesophageal pressurization in type II achalasia. Patients with abnormal IRP after POEM have partial symptomatic improvement without signs of peristaltic recovery.
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Disclosure of Interest: None declared

P1602 CORRELATION BETWEEN GERD AND BMI: IT'S TIME TO THINK ABOUT HYPOSENSITIVITY IN OBESITY

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INTRODUCTION: The positive correlation between GERD symptoms and weight gain is well defined. However, we previously demonstrated that severe upper-GI symptoms may negatively affect body weight by limiting food intake. The aim of our study is to evaluate the correlation between BMI and GERD features and symptoms severity in a large cohort of GERD patients.
AIMS & METHODS: 201 (119 F, mean age: 46.2±15.6 ys, BMI: 25.9±6) outpatients referring for GERD symptoms (heartburn, regurgitation, chest pain, epigastric pain, dysphagia, odynophagia, respiratory symptoms) were enrolled. All patients underwent careful history taking, physical examination and upper-GI endoscopy. Upper-GI symptoms were scored according to standardized questionnaire, assessing the type and the severity of symptoms and their impact on quality of life (PAGY-SYM/QoL). A pH-impedance monitoring was performed in 198 patients, with 89 and 109 of them being off and on-therapy (68 F, mean age: 45.2±13.7 ys; BMI 25.3±5.3 and 67 F, mean age 47.4±14.7 ys; BMI 26.2±5.9, respectively). BMI was recorded and patients were divided, according to internationally accepted criteria, in normal- and overweight. Patients with history of diabetes mellitus were excluded.
RESULTS: Among all the investigated parameters, acid exposition and number of proximal refluxes were significantly higher in over- than in normal-weight patients (3±4.4 vs 1.8±2.6 %pH < 4 and 40.6±22.5 vs 31.9±22.2; all $p < 0.05$). This finding was confirmed in both off- and on-therapy patients' subgroups (4.5±5.5 vs 2.3±1.9 and 1.8±2.9 vs 0.6±0.9 %pH < 4, all $p < 0.05$); while the number of proximal refluxes resulted significantly higher only in off-therapy subgroup (39.7±20 vs 28.6±16.7; $p < 0.05$). The analysis of symptoms' severity yields no significant differences in terms of cumulative symptoms score between over- and normal-weight patients (12.7±9.9 vs 13.9±10). However, a significant correlation between GERD-symptoms score and BMI values was overall observed ($r^2 = 0.03$, CI:-0.3 to -0; $p < 0.01$), with a significant correlation being present in the subgroup of off-therapy ($r^2 = 0.01$, CI:-0.4 to 0; $p < 0.05$), but not in those on therapy ($r^2 = 0.01$, CI: -0.3 to 0.1; p = n.s.). The reduced symptoms' severity in overweight patients did not reflect a significantly different quality of life.
CONCLUSION: In this study we observed that despite a higher esophageal acid exposition and increased number of proximal refluxes, overweight GERD-patients had less severe symptoms and this did not significantly affect their quality of life. Although the underlying mechanisms are unknown, if confirmed by mechanistic studies, our results suggest that the reduced sensitivity in overweight GERD, by limiting patients complaining, may explain the increased risk of GERD-complications frequently observed in this subset of patients.
Disclosure of Interest: None declared

P1603 SYNDROMIC ACHALASIA IN ALGERIA: ABOUT A NOVEL SERIES

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INTRODUCTION: non-syndromic or isolated achalasia represents the most commonly found form in adults. It is most often observed in sporadic cases. In rare cases, achalasia can occur in genetic syndromes or be associated with isolated abnormalities.
AIMS & METHODS: To identify the conditions associated with achalasia and study the clinical profile in these syndromes.
This is a prospective study of 86 consecutive patients (M: 41, F: 45, mean age 18.23 + / - 10.4 (3 months - 42 years) enrolled over a period of 21 years (Jan1992 - Oct 2013). There were 52 children (60%) and 34 adults (40%). All patients underwent a standardized symptoms questionnaire, a complete clinical check up, an ophthalmologic check up with a Schirmer test, an adrenal hormone balance, an esophageal barium swallow, upper endoscopy and an esophageal manometry.
RESULTS: Down syndrome (mental retardation, particular facies.) was observed in 6 isolated cases from 6 families. Allgrove syndrome was noticed in 80 cases. It was familial (siblings) in 35 cases (16 families). Consanguineous parents were found in 71% of cases. All patients had alacrima at birth, they all developed achalasia later (100%). Whereas, adrenal insufficiency was found in 43 cases (54%) and autonomic dysautonomia/ neurological abnormalities (thenar and hypothenar muscle atrophy, reduced force of abduction and adduction of fingers, mental retardation, optic atrophy, ataxia, ...) in 19 cases (24%). It was a 3A syndrome (achalasia, alacrima, Addison) in 46 cases and a 4A syndrome in eight cases. The syndrome was incomplete or called syndrome 2A (alacrima, achalasia) in the other cases. In familial 3A (08 families), 17 cases of probable Allgrove syndrome who had at least alacrima were identified, they died probably after an acute adrenal insufficiency.
CONCLUSION: Allgrove and Down syndrome are the two most common conditions associated with achalasia. They are more frequent in children than in adults. Every achalasia or alacrima of children should lead to look for the others components of the syndrome.
Disclosure of Interest: None declared

P1604 THE TRINITY OF GASTRIC EMPTYING SCINTIGRAPHY, 13C ACETATE GASTRIC EMPTYING BREATH TESTING, AND REAL TIME GASTRIC ULTRASONOGRAPHY INDICATES HIGH PREVALENCE OF GASTRIC MOTOR DYSFUNCTION IN FUNCTIONAL DYSPEPSIA

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INTRODUCTION: Gastric motor physiology can be assessed by gastric emptying scintigraphy (GES), ^{13}C breath testing (GEBT) and real time gastric ultrasound (GUS). The aim of this study was to evaluate how commonly these tests are abnormal in patients with functional dyspepsia (FD).
AIMS & METHODS: Twenty-seven patients fulfilling the Rome III criteria for FD were enrolled in the study. All patients had a normal upper GI endoscopy and underwent standard GES using ^{131}I-technetium labeled mashed potato. On a separate day, these patients underwent a combined liquid GEBT (four hour breath test protocol using 170ml chocolate Ensure liquid substrate + 50mg ^{13}C-acetate) and GUS (calculating antral area at the time of ingestion and 15 minutes after ingestion of the GEBT liquid test meal).
RESULTS: Eight of the 27 patients had one abnormal test, six had two and in five, all three tests were abnormal. In fifteen of the 27 patients with a normal GES (56%), eight had normal GEBT and GUS studies. Of the remaining seven patients, four had a normal GEBT and an abnormal GUS, two had normal GUS with an abnormal GEBT, and in one, both the GEBT and GUS were abnormal. GES was delayed in ten of the 27 patients (37%). In four of these, both GEBT and GUS were abnormal, three had delayed gastric emptying on GEBT with a normal GUS, two had delayed gastric emptying on GUS with normal GEBT, and in one patient, both GUS and GEBT were normal. GES was abnormally rapid in two patients (7%). In one patient, both GEBT and GUS indicated rapid gastric emptying and in the other, GUS revealed rapid gastric emptying with a normal GEBT. Assuming GES as the gold standard for diagnosing abnormal gastric emptying, GUS has a sensitivity and specificity for detecting a motor disorder of 66% and GEBT has a sensitivity of 66% and a specificity of 80%.
CONCLUSION: In this group of FD patients, 70% had at least one abnormal test of gastric motor function. Whilst GES is regarded as the gold standard test, in seven patients with normal GES, the GEBT, GUS, or both, were abnormal. This discrepancy might reflect the day-to-day variability of gastric motor function testing or that each investigation measures a different component of gastric motor physiology. We conclude that in FD, adding GEBT and GUS to GES substantially increases the positive diagnostic yield and the heterogeneous patterns might indicate a variety of FD subtypes.
Disclosure of Interest: None declared

P1605 SCREENING OF GASTRITIS IN A POPULATION OF DYSPEPTIC PATIENTS: ROLE OF STOMACH SPECIFIC PLASMA BIOMARKERS

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INTRODUCTION: A no invasive screening procedure able to identify subjects at high or low risk for gastritis should allow to limit unnecessary endoscopy and histology. The role of specific stomach plasma biomarkers in diagnosis and screening for chronic atrophic gastritis (CAG) is emerging as useful tool in provide informations about gastric mucosa function.
AIMS & METHODS: To evaluate the utility of a serological stomach panel as screening method for identifying patients with high or low risk for gastritis with respect to those with normal gastric function or gastro esophageal reflux disease. 652 dyspeptic patients (M = 223, F = 429, mean age = 42.4±15.3 years, range = 18-87 years) without any alarm symptom (dysphagia, anemia, weight loss and vomiting) were selected from General Practitioners for fasting blood collection and stomach markers assays (Biohit Plc, Finland).
For each of them a standard questionnaire was requested including upper gastrointestinal symptoms, thyroiditis history and PPI therapy. For the study 429 patients were examinated; 223 patients were excluded because of PPI therapy.
Patients affected by CAG were submitted to EGDS and histology and to parietal cell antibodies (PCA) assay (IFA method).
RESULTS: The table reports four groups of patients subdivided according to the stomach marker results.

	Normal (N)	Gastroesophageal reflux Disease (GERD)	*H. pylori* Gastritis (HPG)	CA Gastritis (CAG)
Patients (n°)	132	163	114	20
Age (years)	40.8±22.2	39.6±11.1	42.4±12.4	58.0±15.8
Thyroiditis (%)	6.1	11.7	12.3	50
PG1 (ug/L)	79.4±26.8	84.8±37.7	130.4±11.7	15.2±11.5
PG2 (ug/L)	5.8±2.4	6.2±2.9	14.1±8.2	7.3±3.6
PG1/PG2	14.5±4.3	14.5±4.6	10.0±3.9	2.5±2.5
G17 (pmol/L)	5.4±13.2	0.6±0.3	12.6±15.2	47.4±42.9
Hp Abs (EIU)	5.8±5.9	4.9±5.1	83.9±31.8	29.8±32.8

GERD patients showed significantly lower G17 values with respect to the other groups ($p<0.0001$). HPG subjects had higher Hp Abs and PG2 values ($p<0.0001$). 3.3% were identified as CAG and presented significant lower PG1 and PG1/PG2 values and higher G17 levels ($p<0.0001$). CAG subjects were older than the other patients. 65% of CAG patients showed PCA positivity.
CONCLUSION: A no invasive serological stomach panel allows to distinguish Normal and GERD from HPG and CAG groups in a general population of dyspeptic patients; particularly, patients showing CAG serological findings are also characterized by histological alterations and PCA positivity. Considering these findings, it is necessary to identify as early as possible patients at risk of developing precancerous gastric lesions.
Disclosure of Interest: None declared

P1606 THE IMPACT OF PERCEIVED JOB STRESS, ANXIETY, DEPRESSION, COPING AND SOCIAL SUPPORT ON FUNCTIONAL GASTROINTESTINAL DISORDERS: A CROSS-SECTIONAL STUDY OF FIREFIGHTERS

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INTRODUCTION: Psychological factors play a role in the development of functional gastrointestinal disorders (FGIDs). The work of firefighters is characterized by its danger, urgency, unique work environment, and by its considerable high level of job stress.
AIMS & METHODS: The purpose of this study was to determine the effect of job stress and other psychosocial factors on FGIDs in this high risk population. Within a cross-sectional survey, 1140 firefighters completed validated questionnaires regarding FGIDs including gastroesophageal reflux disease (GERD), functional dyspepsia (FD), irritable bowel syndrome (IBS) and functional constipation (FC) by at least once a week of typical reflux symptoms and Rome III criteria. Self-reported questionnaires for perceived job stress (KOSS-26), anxiety (GAD-7), depression (PHQ-9), coping styles (WCC), social support and quality of life (WHOQOL-BREF) was also completed. Odds ratio with 95% confidence intervals were estimated using unconditional logistic regression in adjusted models.
RESULTS: A total of 425 (37.3%) subjects reported to be bothered by at least one FGIDs and the proportions of GERD, FD, IBS, FC was 362 (31.8%), 132 (11.6%), 101 (8.9%) and 124 (10.8%), respectively. Perceived job stress significantly associated with GERD (OR = 6.4, 95% CI: 2.2-18.3, $p<.001$) and FD (OR = 8.2, 95% CI: 1.1-38.0, $p=.007$), modestly associated with IBS (OR = 4.2, 95% CI: 0.8-20.8, $p=.070$), but not in FC (OR = 1.2, 95% CI: 0.4-4.1, $p=.697$). Subjects reporting anxiety had a 4.1, 3.7, 3.1-fold (95% CI: 2.7-3.8, 2.5-5.4, 2.0-4.8) increased risk of GERD, FD and IBS, respectively ($p<.001$), and with depression had a 5.4, 4.3, 4.3-fold (95% CI: 4.1-7.1, 2.8-6.5, 2.7-6.9) increased risk compared to subjects without depression ($p<.001$). We observed a weak inverse association between measures of emotional support and GERD (OR = 0.3, 95% CI: 0.1-0.8, $p=.020$); esteem, informative support and FD (OR = 0.2, 0.2; 95% CI: 0.4-1.0, 0.0-0.8; $p=.032$, .024). Among the subdomain of job stress, physical environment, job demand and lack of reward were related to the occurrence of FGIDs. Impaired quality of life was found in all FGIDs. The overlap syndrome was observed in 134 (11.8%) and highly associated with perceived job stress (OR = 10.6, 95% CI: 2.3-49.3, $p=.002$) compared to non-overlap FGIDs (OR = 5.3, 95% CI: 1.6-17.3, $p=.005$). We also observed a weak inverse association between informative support and overlap syndrome (OR = 0.1, 95% CI: 0.0-0.9, $p=.043$). Among the subdomain of job stress, all domains were related to the overlap syndrome.
CONCLUSION: Perceived job stress is strongly associated with FGIDs in firefighters. Anxiety and depression was related to FGIDs and weak inverse association between social support while no consistent association regarding coping styles was found. The psychosocial factors such as high level of job stress and lack of social support could affect the development of FGIDs. Recognition and management of these psychosocial factors may aid in the management of FGIDs.
Disclosure of Interest: None declared

P1607 SAFETY AND EFFICACY OF PNEUMATIC BALLOON DILATION AFTER HELLER'S MYOTOMY

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INTRODUCTION: Although Heller's myotomy is one of the most effective treatments for achalasia, symptoms of disease relapse after that in some patients.
AIMS & METHODS: Aim: To evaluate the safety and efficacy of pneumatic balloon dilation (PBD) in cases of symptoms relapse after Heller's myotomy (HM).
Method: 36 patients with achalasia in whom symptoms had relapsed after HM referred to our center from 1993 to 2013. Nine patients who had comorbid diseases or epiphrenic diverticula were treated by botulinum toxin injection and excluded from the study. 27 patients were treated with PBD and followed up prospectively. A good initial response was defined as a decrease in symptom score to 4 or less and a reduction greater than 80% from the baseline in the height and volume of barium in timed barium esophagogram at 1.5 months after the first PBD (with 3 cm rigiflex balloon). Achalasia symptom score (ASS) was assessed every six months in all patients and when symptoms relapsed (ASS > 4), PBD was repeated.
RESULTS: The Mean age of the patients was 47.48±13.91 years (range: 21-73). Good initial response was seen in seventeen patients and five others revealed good response after second PBD with 3.5 cm rigiflex balloon. The mean ASS of patients dropped from 6.88 before treatment to 3.18 at the end of the study ($p=0.003$). The mean duration of follow up was 11.81±5.97 years. At the end of the study sustained good response was reported by twenty two patients (81%). No major complications like perforation or gross bleeding were seen after PBD sessions.
CONCLUSION: We conclude that PBD is effective and safe treatment option of achalasia patients in whom symptoms relapse after Heller's myotomy.
Disclosure of Interest: None declared

P1608 DISTINCT ETIOPATHOGENESIS IN SUBGROUPS OF FUNCTIONAL DYSPEPSIA ACCORDING TO ROME III CRITERIA

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INTRODUCTION: Whether there are distinct pathogenesis in subgroups of functional dyspepsia (FD), the postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), remain controversial.
AIMS & METHODS: Aims: We aimed to identify the risk factors of FD and its subgroups in Chinese.
Methods: Patients with dyspepsia and health subjects who underwent gastric cancer screening were enrolled in this multicenter study from 2010 to 2012. All patients were evaluated by questionnaire, esophagoduodenoscopy, histological examination, and *Helicobacter pylori* tests. Subgroups of FD were classified according to Rome III criteria. Psychiatric stress was assessed by short form Brief Symptom Rating Scale.
RESULTS: Of the 2378 patients with dyspepsia, 818 and 512 fulfilled the diagnostic criteria of uninvestigated dyspepsia and FD, respectively. Of them, 310 (60.6%) and 368 (71.9%) subjects fulfilled the diagnosis of EPS and PDS, respectively, whereas 176 (34.4%) had overlap syndromes. As compared to 1033 healthy controls, we found that PDS and EPS shared some common risk factors, including females (Odd ratio [OR] 1.91, 95% confidence interval [CI] 1.36~2.68), younger age (OR 0.96, 95%CI 0.94~0.97), nonsteroidal anti-inflammatory drugs (OR: 6.70, 95%CI 4.17~10.77), and anxiety (OR 3.30, 95%CI 2.35~4.63). In contrast, *Helicobacter pylori* (OR 1.83, 95%CI 1.21-2.79), unmarried status (OR 4.06, 95%CI 2.45-6.72), sleep disturbance (OR 2.57, 95%CI 1.61-4.1), and depression (OR 2.12, 95%CI 1.22-3.69) were independently associated with PDS, but not with EPS. Betel nut chewing (OR 5.32, 95% CI 1.42-20) and psychological inferiority (OR 0.38, 95% CI 0.19-1.78) were independently associated with EPS, but not with PDS.
CONCLUSION: Different risk factors exist for subgroups of FD based on Rome III criteria, supporting the distinct etiopathogenesis of the subdivisions that might necessitate different therapeutic strategies.
Disclosure of Interest: None declared

P1609 SUPRAGASTRIC BELCHING: PREVALENCE AND ASSOCIATION WITH GASTRO-OESOPHAGEAL REFLUX DISEASE AND OESOPHAGEAL HYPOMOTILITY

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INTRODUCTION: Supragastring belching (SGB) is a phenomenon during which air is sucked into the oesophagus and then rapidly expelled through the mouth without reaching the stomach. Patients often complain of excessive belching with a severe impact on quality of life. SGB is considered to be a behavioral disorder, and in some cases a response to an unpleasant sensation originating from the oesophagus or the abdomen. Furthermore, SGB has been shown in itself to induce gastro-oesophageal reflux.

AIMS & METHODS: We aimed to investigate the prevalence of pathological SGB and its association with gastro-oesophageal reflux and motility disorders. We established normal values for SGB by analyzing 24h pH-impedance in 20 healthy asymptomatic volunteers. We interrogated the database of the Upper GI Physiology Unit of the Royal London Hospital (total number of patients referred for assessment of GORD, dysphagia, chest pain) between 2010-2013 n = 2950). We identified all patients with diagnosis of SGB in their final report and reviewed predominant symptoms, 24h pH-impedance and high resolution oesophageal manometry (HRM).
RESULTS: Asymptomatic controls had between 0 and 15 SGB episodes per 24h. The 95th percentile was 12 episodes. 100/2950 patients showed excessive SGB (54 females), mean age 48 (range 12 – 84 years). The median number of SGB in this group was 69/24h (range 17-510). The 25th percentile was 37 and the 75th 125 SGB episodes. 15 patients had undergone prior Nissen fundoplication.
86 of the patients complained of excessive belching, with 50 feeling that belching was their predominant symptom. 95 patients complained of typical reflux symptoms (heartburn and/or regurgitation). 65 patients complained of dysphagia, 51 had excessive bloating, 16 chest pain and 15 epigastric pain. On 24h pH-impedance, 41 patients had pathological oesophageal acid exposure. In these patients, 27% of oesophageal acid exposure was due to reflux occurring immediately after a SGB. On HRM, 44/100 patients had oesophageal hypomotility (frequent failed peristalsis and weak peristalsis with defects). 31 of these patients referred dysphagia.
CONCLUSION: Increased SGB was identified in 100/2950 patients investigated at the GI physiology Unit over a 4 years period. Increased belching is rarely a symptom in isolation and almost always coexists with other oesophageal symptoms, most commonly dysphagia (65%) and heartburn/regurgitation (95%). Whether SGB is a disordered response to other oesophageal symptoms or their cause is still unclear. Behavioral therapy and baclofen have shown promising results in patients with predominant belching. The role of SGB reduction in patients with SGB-associated reflux symptoms or dysphagia is under current investigation.
Disclosure of Interest: None declared

P1610 THE FUNCTIONAL DYSPEPSIA TREATMENT TRIAL (FDTT): ANTIDEPRESSANT EFFECT ON GASTRIC ACCOMMODATION

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INTRODUCTION: A large, multicenter trial of antidepressants in individuals with functional dyspepsia (FD) was conducted and the primary outcome of adequate relief was presented at DDW 2013. In addition to symptom data, physiologic data was collected including gastric accommodation. The effect of antidepressants on gastric accommodation in FD patients is not known.
AIMS & METHODS: Aims: To determine whether antidepressant use affects gastric accommodation in individuals with FD. **Methods:** This NIH-funded study (DK065713) is a prospective, randomized, double-blind, placebo-controlled 12-week treatment trial conducted at 8 sites in North America that recruited 292 subjects with FD to 3 arms: 50 mg amitriptyline (AMI), 10 mg escitalopram (ESC), placebo (PLA). Gastric accommodation data was collected at baseline in 162 participants at three sites (MCR, MCJ, MCS). Gastric volume was measured using single photon emission computed tomography (SPECT) gastric imaging after administration of intravenous 99 mTc pertechnetate. The ANALYZE^{TM} program was used for volume rendering, three-dimensional reconstruction, and estimation of volumes. The Kruskal-Wallis test was used to assess treatment differences.
RESULTS: Data was analyzed from 59 individuals with post-treatment gastric accommodation data, 46 (78%) female, median age 43 (IQR: 35-52). 46 (78%) were dysmotility-type FD; 13 (22%) were ulcer-like FD. At baseline, 3 (5%) had impaired gastric accommodation, defined by a change in gastric volume $<$428 mls). Post-meal gastric volume changes at baseline were similar among treatment arms (517±23 ml PLA (n = 18), 542±21 ml AMI (n = 21), 591±23 ml ESC (n = 20). At followup after 12 weeks of treatment, no differences in fasting volumes or fed volumes between treatment arms ($p = 0.71$ and $p = 0.09$). Changes in gastric volume from fasting to fed were modestly different between arms (565±22 ml PLA [n = 18], 494±27 ml AMI [n = 21], 508±16ml ESC [n = 20], $p = 0.08$).
CONCLUSION: Data from this small sample suggests that both tricyclic and SSRI antidepressants may decrease gastric accommodation in individuals with FD. Additional studies are warranted to evaluate whether this finding is real and correlates with FD symptoms.
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Disclosure of Interest: None declared

P1611 SYMPTOMS DON'T REFLECT MUCOSAL HEALING IN PATIENT WITH REFLUX ESOPHAGITIS DURING MAINTENANCE THERAPY

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INTRODUCTION: During the maintenance therapy for reflux esophagitis (RE), patients take PPIs regardless presence of symptoms. Many studies are carried out about endoscopic finding or symptom relief in maintenance therapy, however there has been few studies investigating correlation among endoscopic healing, symptom and dosing schedule.
AIMS & METHODS: The aim of this study is to reveal correlation among endoscopic healing, symptom and dosing schedule during maintenance therapy. Among patients with RE who enrolled randomized prospective study for 24 weeks PPI maintenance therapy (continuous arm (Omeprazole 20mg od) or on-demand arm (Omeprazole 20mg on-demand)), we extracted patients data who undertook EGD at 24 week. Patients were divided to healing group and non-healing group by LA classification at 24week EGD. Symptom relief was defined as percentage of patients who achieved no or minimal symptom at 24week visit by Global Overall Symptom questionnaires. Difference of symptom relief and endoscopic findings was analyzed between continuous group and on-demand group.
RESULTS: Seventy patients (M/F:48/22, mean60.9 (range 29-89)yr) were extracted. Patients with LA classification Grade A:B:C:D were 35:29:5:1 before initial therapy and healing group/ non-healing group were 49/21 (Grade A:14, B:5, C:2, D:0) at 24week, respectively. Regarding patients characteristics between healing and non-healing group, age, gender, BMI, presence of hiatal hernia, drinking and smoking had no significant difference but prevalence of recurrent RE was significantly higher in non-healing group ($p < 0.01$). Although there was no significant difference in symptom relief between healing (70.8%) and non-healing group (80.0%) at 24 week, number of non-healing patient was significantly higher in on-demand group (44.4%) than in continuous group (14.7%) ($p < 0.01$).
CONCLUSION: Symptoms were well controlled regardless endoscopic mucosal healing and on-demand therapy was insufficient to maintain mucosal healing during maintenance therapy. These results suggest that PPI should be taken continuously regardless presence of symptoms in patients with reflux esophagitis to prevent recurrence especially recurrent reflux esophagitis.
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P1612 IMPROVED CONTROL OF GASTROESOPHAGEAL REFLUX ON FODMAP-RESTRICTED DIET

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INTRODUCTION: Diet is recommended as first-line treatment for gastroesophageal reflux disease (GERD), but its role is debated. Refractory disease is often due to residual reflux and proximal extent of reflux.
AIMS & METHODS: Colonic fermentation may affect gastroesophageal motility in GERD and we therefore aimed to evaluate the effect of a diet with less fermentable carbohydrates, the FODMAP-restricted diet, on gastroesophageal reflux. 12 patients with symptoms of GERD and/or reflux esophagitis (6M/6F, age 36.8±12.3y) underwent 24h multichannel intraluminal impedance and pH (MII-pH) before and after diet intervention lasting 7.3±2.2 weeks. 8 patients were on stable medication with a proton pump inhibitor (PPI) during the intervention. The patients were instructed in the diet and followed by a dietitian. Symptoms (GerdQ and ReQuest) and health related quality of life (SF36) were recorded before and after the diet intervention. Results (median [IQR] or mean±SD) were compared with Wilcoxon signed rank test or paired t-test ($p < 0.05$).
RESULTS: Intake of FODMAPs was significantly reduced from 19±7 to 2±2 g/day ($p < 0.0001$). The total number of reflux episodes decreased on FODMAP-restricted diet compared to a normal diet (115±135 vs. 152±164, $p = 0.0305$), and particularly the number of proximal refluxes (22±24 vs. 42±37, $p = 0.0076$). Fewer symptom episodes were recorded during the MII-pH on FODMAP-restricted diet compared to a normal diet (12 [16] vs. 24 [46], $p = 0.0278$). For GerdQ there was a decrease in total score on FODMAP-restricted diet compared to a normal diet (8±3 vs. 9±2, $p = 0.0679$). Less frequent heartburn and regurgitation (3±2 vs. 5±1, $p = 0.0028$), less impact of GERD (1±2 vs. 2±2, $p = 0.0311$) and more nausea and epigastric pain (5±1 vs. 3±2, $p = 0.0039$) was reported. However the patients did not experience any differences by nausea (from 0.0 [2.1] to 0.0 [0.0], $p = 0.3125$) and epigastric pain (from 1.8 [4.6] to 0.4 [4.1], $p = 0.5703$) while engaged in daily life activities as recorded on ReQuest.
CONCLUSION: FODMAP-restricted diet improved symptoms of GERD and reduced total and proximal gastroesophageal reflux. This may be effective both as a first-line treatment and in patients refractory to PPI treatment.
Disclosure of Interest: None declared

P1613 DURABILITY OF EFFECT AND LACK OF REBOUND SYMPTOMS FOLLOWING A 14-DAY REGIMEN OF ESOMEPRAZOLE 20 MG TREATMENT IN SUBJECTS WITH FREQUENT HEARTBURN

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INTRODUCTION: Durability of effect and lack of rebound symptoms following a 14-day regimen of esomeprazole 20 mg were evaluated in 2 identical randomized, double-blind, placebo-controlled studies (study one: NCT01370525; study two: NCT01370538) in subjects with frequent heartburn (HB) who are likely to self-treat with over-the-counter (OTC) medications.
AIMS & METHODS: Adults without a confirmed diagnosis of gastro-oesophageal reflux disease who were experiencing HB ≥2 days per week in the past 4 weeks were eligible for study inclusion. Following HB medication washout and a 7-day placebo run-in period, subjects continuing to meet inclusion criteria were randomly assigned to double-blind treatment with esomeprazole 20 mg (administered as esomeprazole magnesium trihydrate 22.3 mg) once daily or placebo for 14 days. All subjects entered a 1-week single-blind placebo follow-up period after the 14-day treatment period. Episodes of HB were documented by daily patient diary via interactive voice response system during the placebo run-in period, treatment period, and placebo follow-up. The primary efficacy outcome was the percentage of HB-free 24-hour days (defined as days when the subject had no HB episodes) during 14 days of treatment. Primary and secondary outcomes from the treatment period have been reported separately elsewhere. The current report presents data collected during the placebo follow-up period.
RESULTS: In study one, 331 subjects were treated in the double-blind treatment phase and 321 entered the placebo follow-up period; study two included 326 and 303 subjects, respectively. The percentage of HB-free 24-hour days achieved during the treatment period for esomeprazole 20 mg was greater than with placebo and remained consistent in the placebo follow-up period (**Table**). The percentage of HB-free 24-hour days in the placebo follow-up for study one was 43% for those who had been treated with esomeprazole 20 mg compared to 35% for placebo. Similarly, in study two, the percentages of HB-free 24-hour days were 43% and 39% in the esomeprazole 20 mg and placebo groups, respectively.
Table: Percentage of 24-Hour Heartburn-Free Days During the 3 Study Phases.

	Study One		Study Two	
	ESO-20mg	Placebo	ESO-20mg	Placebo
7-day single-blind placebo run-in period, mean (%)	18	19	22	21
14-day double-blind treatment period, mean (%)	43	29	47	31
7-day single-blind placebo follow-up period, mean (%)	43	35	43	39

CONCLUSION: In frequent HB sufferers who are likely to self-treat with OTC medications, the rate of HB control during the 14-day double-blind treatment period with esomeprazole 20 mg was maintained for the 7-day placebo follow-up after cessation of study medication. No evidence of rebound symptoms was observed following 14-day treatment with esomeprazole 20 mg.
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P1614 IMPACT OF SHORT-TERM ESOMEPRAZOLE TREATMENT ON PERFORMANCE OF DAILY ACTIVITIES AND ANTACID USE IN SUBJECTS WITH NONEROSIVE SYMPTOMATIC GASTRO-OESOPHAGEAL REFLUX DISEASE AND FREQUENT HEARTBURN

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INTRODUCTION: Symptomatic gastro-eosophageal reflux disease (GORD) can impair performance of daily activities, and self-treatment of reflux symptoms (e.g., heartburn [HB] and acid regurgitation) with antacids is common. We evaluated subject-reported outcomes and antacid use in 2 studies of short-term esomeprazole (ESO) in a population likely to seek self-treatment in an over-the-counter setting.
AIMS & METHODS: Study 1 (N = 368) and study 2 (N = 349) were similarly designed randomized, double-blind, placebo-controlled trials conducted at 26 and 27 gastroenterology centres, respectively, in the US. Subjects with frequent HB for ≥6 months without endoscopic erosive oesophagitis were randomized to ESO 20 mg, ESO 40 mg, or placebo once daily. Antacid tablets (≤6/day) were permitted as rescue for breakthrough symptoms. Week 4 data were previously published (Katz et al. *Aliment Pharmacol Ther*. 2003;18[9]:875-82). The current report includes data from a subject-reported overall treatment evaluation questionnaire and use of rescue medication in the first 2 weeks.
RESULTS: At end of week 2, significantly more subjects (all $P \leq .001$) taking ESO 20 mg and 40 mg vs placebo had relief of HB (≤1 mild HB episode for 7 consecutive days) and rated themselves as "better" than baseline. The majority of those who improved rated it as at least "important" in performing daily activities (ESO 20 mg, 79%–86%; ESO 40 mg, 78%–82%; placebo, 65% > 79%). Mean antacid use in weeks 1 and 2 was lower with ESO (0.9-1.0 tablets/day) vs placebo (1.7 tablets/day).
CONCLUSION: ESO 20 mg for 2 weeks (typical over-the-counter dose/duration) was associated with improvement deemed by subjects as important for daily functioning and lower rates of rescue antacid use.
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The studies were sponsored by AstraZeneca, which entered into an agreement with Pfizer for the over-the-counter (OTC) rights for NEXIUM® (esomeprazole magnesium).
Medical writing support was provided by Diane M. Sloan, PharmD, of Peloton Advantage, LLC, and was funded by Pfizer.
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P1615 CLINICAL AND IMPEDANCE-PH FEATURES PREDICT RESPONSE TO PROTON PUMP INHIBITORS IN PATIENTS WITH NON-CARDIAC CHEST PAIN

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INTRODUCTION: Non cardiac chest-pain (NCCP) is defined as recurrent angina-like retrosternal chest-pain diagnosed after a negative cardiac workup. Gastroesophageal reflux disease (GERD) is by far the most common cause of NCCP. Previous studies showed that proton pump inhibitors (PPIs) are less effective in relieving NCCP than heartburn, but predictors of PPI response in NCCP patients have not been yet investigated.
AIMS & METHODS: We aimed to determine whether any symptom profile or reflux pattern at impedance-pH monitoring was associated with refractoriness to PPI therapy. Consecutive patients with NCCP lasting more than 6 months and with at least three episodes per week, were prospectively enrolled. Demographics, clinical data and symptoms of functional diseases (i.e. functional dyspepsia and irritable bowel syndrome) were collected by means of previously validated questionnaires based on Rome III criteria for functional gastrointestinal disorders. All patients underwent upper endoscopy and, within 3 days, conventional manometry and 24-hour impedance-pH testing while off-PPI therapy. During impedance-pH tracings analysis we measured distal esophageal acid exposure time (AET), characteristics of reflux episodes (acid/weakly acidic) and symptom-reflux association using both symptom association probability (SAP+ if ≥95%) and symptom index (SI+ if ≥50%). Patients were classified as PPI-non responders (PPI-NR), if they had a symptom relief > 50% from baseline or if they had fewer than 1 day of mild NCCP per week while receiving a double dose of PPI treatment for at least 8 weeks.
RESULTS: One-hundred and twenty-two NCCP patients (56F/66M; mean age 47; 4% erosive esophagitis/ 96% endoscopy negative; 100 PPI-NR/22 PPI-Responders) reporting NCCP during the impedance-pH monitoring were included. At univariate analysis, PPI-R presented more frequently erosive esophagitis and hiatal hernia ($p = 0.057$ and $p = 0.03$, respectively). Moreover, PPI-R complained of NCCP more frequently in association with either typical (heartburn and/or regurgitation) or atypical (cough and/or asthma) reflux symptoms compared to PPI-NR ($p = 0.003$) and reported less often symptoms of dyspepsia ($p = 0.02$). Finally, PPI-R had more frequently an abnormal AET (45% vs. 21%, $p = 0.02$), a greater mean AET (9.9 [2.9-48] vs. 1.15 [0.6-15], $p < 0.01$), an higher mean number of total (80 [16-177] vs. 47 [10-228], $p = 0.0037$), weakly-acidic (34.5 [7-101] vs. 24 [2-145], $p = 0.031$) and acidic (44 [6-91] vs. 24 [8-98], $p = 0.011$) reflux episodes compared to PPI-NR. No differences were found between PPI-r and PPI-NR in terms of SI and SAP positivity for acid, weakly acid or both kind of reflux (data not shown). At multivariate analysis, the factors associated with the absence of response were the lack of concomitant reflux symptoms, functional dyspepsia, normal AET and reduced number of reflux episodes ($p < 0.01$).
CONCLUSION: Our data show that symptom profile (concomitant reflux symptoms and functional dyspepsia) and reflux features detected at impedance-pH (AET and number of reflux episodes) are associated with response to PPI therapy in patients with NCCP. On the other hand, reflux symptom association analysis does not seem useful to predict PPI response.
Disclosure of Interest: None declared

P1616 LAPAROSCOPIC SLEEVE GASTRECTOMY (LSG) VERSUS LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING (BGAL): RESULTS AND EFFECTS ON GASTROESOPHAGEAL REFLUX DISEASE (GERD) AND METABOLIC DISORDER

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INTRODUCTION: Bariatric surgery is the gold-standard treatment for morbid obesity because it has low morbidity rates and generates long term sustaned weight loss.
AIMS & METHODS: The aim of this study was to compare short and midterm results between LSG and BGAL. Weight loss, comorbidity improvement or resolution, effect on reflux disease and post-operative complications were evaluated. An observational retrospective study from a database of patients undergoing LSG and BGAL between 2011 and 2012. Patients were followed at 3, 6 and 12 months.
RESULTS: A total of 52 obese patients who underwent sleeve gastrectomy (26 patients) and gastric banding (26 patients). The first group (LSG) comprised 23 female and 3 males with a median age 44 years and a median preoperative BMI of 45.65 kg/m^2. The second group comprised 24 female and 2 males with a median age 42.8 years and a median preoperative BMI of 43.36 kg/ m^2. In the first group (LSG) the incidence of comorbidity was 42% (incidence of hypertension was 38%, of diabetes 30%); in the second group (BGAL) was 38% (incidence of hypertension was 26%, of diabetes 23%). The incidence of reflux disease was 77% in patients undergoing sleeve gastrectomy and 46% in patients undergoing gastric banding. The excess weight loss at one year was 55% in LSG and 29% in BGAL. The complications rate was 7.6% for LSG (one bleeding treated with conservative therapy and one gastric fistula). Diabetic remission and hypertension at six months and sustained at one year were 100% in the first group and 50% and 80% in the second group. The reflux disease improved in 30% of patients (suspension or reduction of therapy).
CONCLUSION: LSG and BGAL are safe procedures that provide good results in weight loss and resolution of comorbidities at 12 months. Our data confirmed recent studies that LSG may be effective in improving/resolving diabetes in obese patients and confirmed some studies that improved reflux disease.
Disclosure of Interest: None declared

P1617 WEIGHT LOSS PRODUCES SYMPTOMATIC IMPROVEMENT IN PATIENTS WITH GERD: PROSPECTIVE, CONTROLLED AND RANDOMIZED

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INTRODUCTION: Objective: Assess the dietary intervention effect for weight loss, in the improvement of symptoms of gastroesophageal reflux disease in patients with over weight and obesity. The secondary objective was to assess the quality of life through the domain general health (SF-36).
AIMS & METHODS: Prospective, controlled and randomized with individuals in out patient follow-up and who fulfilled the criteria of inclusion (age $\geq$ 18 years, BMI $\geq$ 25 m^2/kg, present typical symptoms: heartburn or regurgitation 1 x per week or more, the presence of confirmed diagnosis through digestive endoscopy and GERD treatment with Omeprazole 20 mg, voluntary acceptance to participate in the study) and exclusion (hospitalized patients, pregnant or lactating women, subjected to surgery of the esophagus and/or stomach, inability of cognitive understanding of the guidelines, with chronic diseases such as: diabetes mellitus and neoplasms, presence of GERD complicated with grade C or D esophagitis, Barrett's esophagus, desire to opt for surgical treatment). All patients underwent evaluation anthropometric (weight, height, BMI) and randomized to receive guidance from individualized, low-calorie diet with out patient follow-up monthly (n = 31) for six months, or to a control group that received general guidelines for healthy eating, but without action oriented (n = 31). Validated questionnaires were applied: QS-GERD for symptoms of GERD and the generic quality of life questionnaire SF-36, addressing the General State of health in both groups in two moments. The comparison between the groups was performed by Student paired t-test. For confounders factors control ANCOVA and was applied to evaluate the association between weight loss and improvement of symptoms by QS-GERD, the Pearson correlation coefficient. considered statistically significant when p value was < 0.05.
RESULTS: The mean age was 59.1 in intervention group and 59.7 years in the control group. Dietary intervention provided a weight loss average of 4.4 ($\pm$ 5.3, $p < 0.001$) kg, representing 5% of the initial weight, an average reduction of IMC 1.7 ($\pm$ 2.9, $p < 0.023$) kg/m and a decrease in symptoms of GERD 6.8 ($\pm$ 5.5, $p < 0.001$). Individuals in the control group had worsening of their symptoms with increase of 3.3 points ($\pm$ 4, $p < 0.001$) and won on average 2 kg ($\pm$ 4.4 $p < 0.001$). The intervention group showed improvement in the General Health State domain, 56.6 vs 64 ($p < 0.001$).
CONCLUSION: The study showed that weight loss through dietary intervention for 6 months with low-calorie diet individualised led to reduction of GERD-related symptoms, as well as improvement in the quality of life as general health status score.
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P1618 EFFECTS OF METOCLOPRAMIDE ON ESOPHAGEAL MOTOR ACTIVITY AND ESOPHAGOGASTRIC JUNCTION COMPLIANCE IN HEALTHY VOLUNTEERS

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INTRODUCTION: Presently, proton pump inhibitors are used as first-line treatment against gastroesophageal reflux disease (GERD). However, approximately 30% of GERD patients fail to respond. Esophageal motor activities and compliance of the esophagogastric junction (EGJ) are important for prevention of GER[1], thus prokinetic agents, such as mosapride and metoclopramide, are often used as second-line therapy for patients with GERD in clinical settings, though their beneficial effects remain unclear. We previously showed that high-dose mosapride not only augmented peristaltic contractions and mean resting lower esophageal sphincter (LES) pressure, but also significantly reduced EGJ compliance[2]. Although metoclopramide has been reported to increase LES pressure, its effects on EGJ compliance have not been evaluated.
AIMS & METHODS: The aim of this study was to investigate the effects of metoclopramide on esophageal motor activities and EGJ compliance. Nine healthy male volunteers without abdominal symptoms were enrolled. Peristaltic esophageal contractions and LES pressure were measured using high resolution esophageal manometry (ManoScan^{360}; Sierra Scientific Instruments), while EGJ compliance was evaluated with an endoluminal functional lumen-imaging probe (EndoFLIP; Crospon Ltd). After obtaining baseline values for esophageal motor activities and EGJ compliance, metoclopramide (10mg) was intravenously administered, then all measurements were repeated at 15 and 30 minutes after administration in each subject.
RESULTS: We successfully analyzed EndoFLIP data in 8 subjects, with 1 excluded because of mechanical trouble. All subjects subjected to ManoScan^{360}measurements completed the protocol. Consistent with previous reports, mean resting LES pressure was significantly increased after administration of metoclopramide (15minutes,26.7mmHg; 30minutes, 27.6mmHg) as compared with the baseline (13.7mmHg) ($p < 0.05$ for both). In addition, metoclopramide significantly augmented peristaltic contractions, especially in the distal esophageal segment ($p < 0.05$). On the other hand, distensibility index (DI) did not change after administration of metoclopramide (5.2 vs. 5.8mm^2/mmHg), suggesting no significant difference in EGJ compliance caused by its administration.
CONCLUSION: This is the first study to evaluate the effects of metoclopramide on esophageal motor activity and EGJcompliance in healthy volunteers using high resolution esophageal manometry and an EndoFLIP device. Although metoclopramide significantly augmented esophageal motor activities, no significant effect on EGJ compliance was seen in healthy volunteers, unlike mosapride. Our findings indicate that the effect on EGJ compliance differs between these prokinetic agents, despite their similar pharmacological characteristics. This difference may be derived from the mechanism between the dopamine D_2receptor antagonist and serotonin 5-HT_4receptor agonist, and may also explain, at least in part, the different effects of these prokinetic agents on GERD.
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Disclosure of Interest: None declared

P1619 INFLUENCE OF URSODEOXYCHOLIC ACID ON PROGRESS OF ATROPHIC GASTRITIS IN COMBINATION WITH DUODENAL GASTRIC REFLUX

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INTRODUCTION: Reflux of biliary acids (BA) in gastric (G) opening favors to epitheliolysis or destruction of protective epithelium and leads to inflaming, atrophic and metaplastic lesions in gastric mucosa (GM). Ursodeoxicholic acid (UDCA) has a binding effect on toxic fractions of GM which gives grounds to apply these for patients with AG in combination with DGR. This give the grounds to make an assumption that application of UDCA will allow neutralizing an aggressive impact of toxic fractions of BA and will promote repair of cell structure of gastric epithelium.
AIMS & METHODS: To determine the influence of UDCA in combination with itoprid on AG progress of DGR patients. Clinical series of 45 Hp – negative patients with AG combined with DGR carried out. Morphological diagnostics of GM lesions have been done based on Sydney – Huston recommendations and OLGA system. Verification of DGR carried out based on endoscopic data, daily intragastric pH-monitoring and biochemical testing of gastric aspirate. All patients were referred to take UDCA with dosage of 10 mg per kg of body weight during 6 months period in combination with standard drug therapy of

pro-kinetic. Assessment of therapy efficiency carried out on the basis of endoscopic, pathogistological examinations data and analysis of proliferation index (IP) (marker Ki 67). Investigation results were processed using analysis of variance.

RESULTS: Dynamics of indicants characterized progress of AG and DGR were assessed at average in 12 months from start of therapy. Disappearance of DGR resulting from therapy referred to daily pH-monitoring recorded for 39 (86.7%) of patients. And reflux load which remained for 6 (13.3%) of patients were minor. Based on endoscopic data minimal symptoms of DGR took place in 8 (18.6%) of 43 cases. Morphological characteristics of inflammation of GM were determined for 41 of patients (17 –II stage, 24 –I stage by criterions of OLGA system). Up to the end of monitoring minimal inflammation remained only for 7 (17.1%) of patients. Regress of MT G atrophy registered for 8 (17.6%), foveolar hyperplasia –20 (55.6%) of 36, full intestinal metaplasia (IM) –10 (40.0 %) of 25, and partial IM – 5 (14.7 %) out of 34 patients. Therapy applied promoted decrease of IP: from 87.34±5.54 points to 51.23±3.22 points ($p<0.01$) in hotbeds of partial IM and from 56.32±4.11 points to 49.41±3.96 points ($p<0.01$) at atrophy areas.

CONCLUSION: UDCA therapy associated with DGR leads to disappearance of reflux in 86.7% of cases, jugulation of chronic inflammation, regress of atrophy and metaplasia of gastric epithelium. Ongoing therapy has contributed to the reduction of proliferation index in the centers of full and partial intestinal metaplasia.

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P1620 LOWER ESOPHAGEAL SPHINCTER (LES) ELECTRICAL STIMULATION IMPROVES SLEEP QUALITY, WORK PRODUCTIVITY, AND QUALITY OF LIFE IN PATIENTS WITH REFRACTORY GERD

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INTRODUCTION: Sleep-Quality and Work-Productivity are commonly affected in refractory GERD patients which in-turn negatively affects patients' quality of life.

AIMS & METHODS: AIM: Evaluate Sleep-Quality, Work-Productivity and QoL in refractory GORD patients undergoing long-term electrical stimulation therapy (EST) using the LOS Stimulation System (EndoStim BV, the Hague, Netherlands).**METHODS** We evaluated GORD patients ($n=37$) partially responsive to PPI with Off-PPI GERD HRQL$\geq$20 and at least 5 point improvement on PPI, % 24 hour esophageal pH<4 for $\geq$5%, hiatal hernia$\leq$ 3cm and esophagitis$\leq$ LA Grade-C. The LOS stimulation system was implanted laparoscopically and EST was initiated at 20Hz, 220usec, 5 mAmp in 12, 30-min sessions. Patients completed the Pittsburgh Sleep Quality Index (PSQI), Work-Productivity and Activity-Impairment Questionnaire: Specific Health Problem V2.0 (WPAI:SHP) and SF-12 QoL instrument both On-PPI and Off-PPI at baseline, and at 6 and 12-mo on LOS-EST

RESULTS: Sleep scores [median (IQR)] at baseline On-PPI were 6.5 (5.2-9.5) and 8 (6.2-10.5) when Off-PPI. At 6mo, sleep scores significantly improved to 5 (3.2-6; $p=0.02$ vs. On-PPI and $p=0.02$ vs. Off-PPI scores) and was sustained at 12months [5 (3.2-7) $p=0.057$ vs On-PPI, $p=0.075$ vs. Off-PPI) on LOS-EST.

Patients' median %time missed from work due to GORD at baseline was 0 (0-6.9)% On-PPI and 3.8 (0-11.2)% Off-PPI. At 6mo, this improved to 0 (0-0)% ($n=15$; $p=0.04$ vs. off-PPI) and was sustained at 12mo 0 (0-0)% ($n=8$; $p=0.10$ vs. off-PPI). Median percent impairment while working due to GERD at baseline was 15 (0-45)% on-PPI and 60 (30-80)% off-PPI. At 6mo, this improved to 0 (0-10) ($n=16$; $p=0.07$ vs. On-PPI and $p=0.002$ vs. Off-PPI) and was 0 (0-10) at 12mo ($n=9$; $p=0.21$ vs. On-PPI, $p=0.15$ vs. Off-PPI) on LOS-EST. Median % overall impairment due to GERD at baseline was 20 (0-55.5)% On-PPI and 63 (33.3-81.8)% Off-PPI. At 6mo, this improved to 0 (0-10)% ($n=16$; $p=0.05$ vs. baseline On-PPI and $p=0.003$ vs. Off-PPI) and was sustained at 0 (0-2.5)%; $n=8$; $p=0.02$ vs. On-PPI, $p=0.06$ vs. Off-PPI] at 12mo on LOS-EST.

Subjects reported a median % activity impairment due to GERD of 25 (10-50)% On-PPI and 60 (30-80)% Off-PPI at baseline. This improved to 0 (0-20)% at 6mo, ($n=27$; $p=0.04$ vs. On-PPI, $p<0.001$ vs. Off-PPI) and remained improved at 5 (0-30)% at 12mo ($n=18$; $p=0.03$ vs. On-PPI, $p=0.02$ vs. Off-PPI) on LOS-EST.

Median SF-12 physical health score was 44 on-PPI, 37 off-PPI at baseline, 52 at 6mo ($p<0.0001$), and 50.5 at 12mo ($p<0.0001$). Median SF-12 mental health score was 49 on-PPI, 46 off-PPI at baseline, 52 at 6mo, and 55 at 12mo ($p=$NS) on LOS-EST. There was improvement in all other GORD specific outcomes.

CONCLUSION: In refractory GERD patients, LES-EST significantly improves sleep-quality, work-productivity and overall impairment in activity resulting in improvement in patient QoL. These results were significantly better than baseline PPI therapy in many of the parameters evaluated.

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P1621 ELECTRICAL STIMULATION THERAPY (EST) OF THE LOWER ESOPHAGEAL SPHINCTER (LES) – AN EFFECTIVE THERAPY FOR REFRACTORY GERD – INTERIM RESULTS OF AN INTERNATIONAL MULTICENTER TRIAL

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INTRODUCTION: A long-term single-center trial previously showed that LOS-EST significantly improves esophageal acid exposure and symptoms in GORD patients (Endoscopy 2013; 45:595-604).

AIMS & METHODS: We studied GORD patients partially responsive to proton pump inhibitors (PPI) with off-PPI GORD-HRQL $\geq$20 and $\geq$5 point improvement on-PPI, LOS end-expiratory pressures of >5 mmHg, % 24 hour oesophageal pH$\leq$4 for >5%, hiatal hernia $\leq$3cm and esophagitis $\leq$LA Grade C. Bipolar stitch electrodes and a pulse generator (EndoStim BV, Hague, Netherlands) were implanted laparoscopically. EST was initiated at 20Hz, 220usec, 5mAmp in 12 30-minute sessions post-implant. Patients' GERD-HRQL, daily symptom diaries, SF-12, oesophageal pH, and manometry were evaluated at regular intervals. Stimulation sessions were optimized based on residual symptoms and oesophageal pH.

RESULTS: Thirty-seven patients (50.1yr, men = 19) were implanted with the LOS stimulator. Twenty-nine subjects completed their 6mo, and 19 their 12mo visits. Median (IQR) GORD-HRQL improved from 33 (25-37) off-PPI and 16 (8-22) on-PPI at baseline to 5 (3-9) and 5 (0.2-16.8) at 6mo and 12mo ($p<0.001$), respectively. Median oesophageal acid exposure (pH<4.0) improved from 9.9 (8-12.9)% at baseline to 5.4 (2.8-10)% and 5.2 (1.8-6.1) at 6 mo and 12mo, respectively ($p<0.01$). Seventy-nine% of patients (15/19) at 12mo were completely off PPI; one patient reported intermittent PPI use (<50% days with PPI) and 3 patients reported regular ($\geq$50% days with PPI) use. There were statistically significant improvement in SF-12 physical health scores and trends towards improvement in SF-12 mental health scores on LOS-EST vs. both on and off-PPI baseline SF-12 scores. There was significant improvement in sleep quality as measured by PSQI ($p=0.02$) and work productivity as measured by WPAI ($p=0.003$) in patients treated with LOS-EST. Subgroup analysis revealed numerically better distal esophageal pH response (normalized or >50% improved) in women (75% vs. 57% in men; $p=0.4$) and comparable response in patients with and without hiatal closure performed at the time of implant (60% vs. 69%; $p=0.7$).

One procedure related serious adverse event; trocar perforation of the small bowel during laparoscopy, successfully repaired and device prophylactically explanted; was reported. Thirty-seven non-serious device or procedure-related events were typical of surgical implant procedures, e.g. post-op nausea and pocket pain. Five instances of dysphagia in 4 patients (all in patients with hiatal closure) resolved without intervention.

CONCLUSION: Our interim results show that LOS-EST is safe and effective in treating refractory GORD. LOS-EST results in significant improvement in oesophageal acid exposure, GORD symptoms, and PPI usage, with no device or therapy-related serious events reported. Subgroup analysis revealed comparable results in patient with a significant hiatal defect requiring a hiatal closure to those without a significant hiatal defect.

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P1622 LONG-LASTING ESOPHAGEAL MUCOSAL PROTCTION WITH ALGINATES: A POTENTIAL FOR TOPICAL MUCOSAL THERAPY IN GASTROESOPHAGEAL REFLUX

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INTRODUCTION: Introduction.
Patients with non-erosive reflux disease (NERD) exhibit impaired esophageal mucosal integrity in the form of dilated intercellular spaces and low transepithelial electrical resistance (TER). Such refluxate-induced changes to the mucosal integrity may underlie increased sensitivity to perception of reflux events, even on PPI, and could potentially be modified by application of topical solutions.
Sodium alginate solutions are used in treatment of GERD, with proposed mechanisms of action including acid buffering, displacement of the gastric acid pocket, and reduction of GER events. We have recently described that in vitro topical application of a sodium alginate solution is able to protect mucosal biopsies against impairment of esophageal mucosal integrity when exposed to acidic solutions shortly after application. The potential durability of this protection is unclear.
We **aimed** to assess the protective effect and physical location of a topically applied sodium alginate solution 1 hour after application.
AIMS & METHODS: Methods.
3 mucosal biopsies were taken from the distal oesophagus (3 cm above the z-line) in 15 patients attending the Royal London Hospital for gastroscopy examination. All biopsies were transferred immediately to Krebs buffer pH 7.4. Biopsies were then each placed in a specially adapted Ussing chamber and bathed in Krebs pH 7.4 (neutral) solution for 20 minutes to equilibrate. The luminal surfaces of 2 biopsies were coated with 200 µl of either a sodium alginate solution (Gaviscon Advance, Reckitt Benckiser, Hull, UK) or a viscous control solution (of same viscosity, but without alginate). The biopsies were mechanically washed with 5 ml Krebs, then returned to the chambers then bathed in neutral solution for a further 1 hour. The luminal aspect of the biopsy was then exposed for 30 min to an acidic solution pH 2 + 1 mg/ml pepsin + 1 mM taurodeoxycholate. Percentage changes in TER from baseline at the end of exposure were recorded. For the 3rd biopsy sodium alginate solution containing fluorescein-labeled alginate was used, and after 1 hour bathing in neutral solution the biopsy was fixed for immunohistological examination of the location of the alginate.
RESULTS: Results.
Our previous experiments have demonstrated that exposure of *unprotected* biopsies to the acidic solution results in a -14.4±2.9% change in TER from baseline. I hour after protection with alginate solution the same exposure caused a -8.3 ± 2.2% change in TER compared to -25.1 ± 4.5% change after protection with the viscous control ($p<0.01$).
Labeled alginate could be seen coating the luminal surface in all cases.
CONCLUSION: Conclusion.
In vitro, alginate solutions can adhere to the esophageal mucosa for up to 1 hour and exert a topical protectant effect against acid, pepsin and bile acids. This suggests that durable topical protectants can be further explored and developed as first-line / add-on therapies for GERD, including refractory disease.
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P1623 SRS PROCEDURE COMBINATED TO POEMS IN THE TREATMENT OF ACHALASIA: A FEASEABILITY STUDY ON ANIMAL MODEL

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INTRODUCTION: Both SAGES and the American Gastroenteroloists Association (AGA) now recommend laparoscopic myotomy combined with anterior fundoplication for the treatment of achalasia. Peroral endoscopic myotomy (POEM TM) is a novel approach to performing esophageal myotomy through a long submucosal tunnel and rapprents a feasible, safe, and effective treatment for achalasia. Recently, FDA approved a method for transoral stapled anterior funduplicatio (SRSTM). SRS TM Endoscopic Stapling System (Medigus, Tel Aviv, Israel) is an advanced endoscope procedure to create an effective reflux barrier, like a laparoscopic anterior funduplicatio, using two or three quintuplets of standard 4.8mm titanium "B" shaped surgical staples.
AIMS & METHODS: The aim of this study was to test the feasibility of combining the two procedures, thereby achieving a completely transoral myotomy with anterior fundoplication, functinally equivalent to the standard laparoscopic operation for achalasia.
The feasibility experiment was performed on a swine model at a laboratory certified according to the Israeli Animal Welfare Act. After induction of general anesthesia. A standard gastroscope was inserted into the stomach, and an overtube was slided into the mid-esophagus. A submucosal tunnel, starting about 5 cm above the GE junction and extending to 2 cm below it, was created, and the circular layer of esophageal muscle was incised using the POEM electrode. Following the myotomy, the SRS stapler was inserted through the overtube, and the fundus of the stomach was stapled over the myotomy, using three quintuplets of staples, in a semi-circle. At the end of the procedure, the animal was sacrificied, and the stomach with the distal esophagus were dissected out carefully, and examined macroscopically.
RESULTS: Macroscopically, the resulting fundoplication covered the distal half of the myotomized muscle, including the gastric part. No perforation was observed. The macroscopic apearance was similar to that of a standard anterior fundoplicatio.
CONCLUSION: CONCLUSIONS / EXPECTATIONS:
It is feasible to combine the two procedures, at least in the swine model, and add a transoral reflux barrier to the submucosal myotomy. If the aganglionic segment is short (<3cm) it is possible to cover all the myotomized esophagus with the fundus, which may reduce the risk of perforation. It is probably easier to to ensure that the myotomy is on the side of the esophagus covered by the fundic flap perform the stapling first, and start the myotomy between the two topmost quintuplets,. Although further experiments are needed to optimize stapling location vis-a-vis the myotomy site, the combined procedure may enable the operator to achieve a result which is similar to the standard laparoscopic operation for achalasia, without violating the abodominal cavity, and without any incisions.
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Disclosure of Interest: None declared

P1624 IN VITRO MODELLING OF THE POST-PRANDIAL ACID POCKET AND TESTING THE INFLUENCE OF ALGINATE ANTI-REFLUX SUSPENSIONS

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INTRODUCTION: The region of unbuffered acidity on top of the gastric contents after a meal, known as the 'acid pocket' was initially reported by Fletcher et al [1] and is well established. The acid pocket exists from 15 to 90 minutes after a meal and has a volume of 50-70ml and length of 2cm [2,3]. Post-prandial reflux is linked to this existence of this acid pocket.
Clinical studies utilise complex and invasive techniques including pH pull-through techniques and as a result only a few centres have the skills necessary to carry out such studies. It has been suggested that acidic gastric juice could partition on top of a homogenised fatty meal [1].
AIMS & METHODS: Aim: The aim was to develop a robust and fully validated in vitro model of the post-prandial acid pocket using physiologically relevant conditions stated in the literature. The in vitro model would then be used to investigate the impact of alginate anti-reflux suspensions and antacids on the acid pocket.
Methods: A standard refluxogenic meal (McDonalds double sausage and egg McMuffin + black coffee) was blended with simulated gastric acid and transferred to the model vessel (equilibrated to 37°C). An acid pocket layer was applied to meet the established clinically measured parameters. pH was recorded 2cm into the meal/acid homogenate and within the acid pocket every 5 min. A pull-through pH measurement was performed at 0.5cm intervals 30 minutes after addition of a test product ($n=6$).
RESULTS: The acid pocket had a volume of 70ml and was 2.5cm in depth with a mean pH of 1.08 (SD 0.04) at 1 cm into the acid pocket. On addition of a placebo product to the acid pocket the pH marginally increased to 1.33 (0.16). The addition of Antacid Liquid Supreme increased the acid pocket to 3.99 (1.99). The addition of raft forming alginate – antacid product Gaviscon Double Action (GDA) neutralised the acid pocket to pH 5.89 (0.30).
CONCLUSION: A robust in vitro model of the post-prandial acid pocket has been developed taking into account all relevant clinical literature. The model using a pH pull-though method, allows the evaluation of alginate raft forming products and antacids. Gaviscon Double Action formed an alginate raft which floated on the top of the acid pocket and significantly changed the pH compared to antacid and placebo ($P<0.001$). Whereas the antacid sank below the acid pocket similar to placebo.
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P1625 COST-UTILITY ANALYSIS OF ENDOSCOPIC SURVEILLANCE OF PATIENTS WITH GASTRIC PREMALIGNANT CONDITIONS SUCH AS EXTENSIVE ATROPHY OR INTESTINAL METAPLASIA

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INTRODUCTION: Progression of gastric premalignant conditions to cancer might warrant surveillance programmes. Recent guidelines suggested an endoscopic surveillance every 3 years for these patients (1).

AIMS & METHODS: Our aim was to determine the cost-utility of endoscopic surveillance of patients with extensive gastric premalignant conditions such as extensive atrophy or intestinal metaplasia to the corpus. A cost-utility economic analysis for the Portuguese population was performed from a societal perspective using a Markov model to compare two strategies: surveillance versus no surveillance. Clinical data was collected from a systematic review of the literature, costs from published national data and community utilities derived from a population study by the EuroQol questionnaire in terms of Quality Adjusted Life Years (QALY). Population started the model at the age of 50 and for a time horizon of 25 years. The threshold was set at € 36,575, corresponding to the proposed guideline limit of USD 50,000 (2) and an annual discount rate of 3% was used for both cost and effectiveness. The primary outcome was the incremental cost-effectiveness ratio (ICER) of a 3-yearly endoscopic surveillance versus no surveillance for a base case scenario and in deterministic and probabilistic sensitivity analysis. Secondary outcomes were ICER of 5- and 10-yearly endoscopic surveillance versus no surveillance.
RESULTS: Endoscopic surveillance every 3 years provided an ICER of € 18,336, below the adopted threshold and this strategy dominated surveillance every 5 or 10 years. In deterministic analysis, variables that most influenced the ICER were the proportion of males or females affected by the disease (ICER: 17.857-18.841), proportion of patients progressing to dysplasia (13.684-31.887), utilities for endoscopic treatment (12.326-42.875) and the cost of transportation (17,909-20,044), even more relevant than medical costs such as endoscopy (18,117-18,555), anaesthesia (18,223-18,449), surgery (18,302-18,370), chemotherapy (18,330-18,342) and radiotherapy (18,317-18,355). In probabilistic analysis the model remained cost-effective in 78% of simulations.
CONCLUSION: Endoscopic surveillance every 3 years of patients with extensive premalignant conditions is cost-effective for the Portuguese population.
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Disclosure of Interest: None declared

P1626 CLINICOPATHOLOGICAL CHARACTERISTICS AND PROGNOSTIC FACTORS OF PRIMARY GASTROINTESTINAL LYMPHOMA: A 22-YEAR EXPERIENCE FROM SOUTH CHINA

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INTRODUCTION: Primary gastrointestinal lymphoma (PGIL) is rare, and few studies have addressed it well, especially in China.
AIMS & METHODS: This study was to investigate its clinicopathological features and prognosis, and also to make comparisons between different locations of PGIL in South China. All patients with PGIL confirmed by histopathology between January 1991 and October 2012 in the First Affiliated Hospital, Sun Yat-sen University were included. Clinicopathological data were collected and prognostic factors influencing survival were analyzed.
RESULTS: The cohort included 160 males and 56 females, accounting for 0.02% of all hospitalized patients and 1.5% of hospitalized patients with GI cancers. Abdominal pain (75.9%) was the most frequent symptom. The percentage of tumor in Stomach group, Intestine group, and GI group was 38.5%, 55.1% and 6.4%, respectively. Patients in Stomach and GI group were older than Intestine group (Mean age: 54 and 53 years *vs*. 43 years, $p<0.001$). Histologically, intermediate-grade lymphoma was the most common (53.7%), but high-grade lymphoma almost occurred in Intestine group (82.5%). Five-year overall survival (OS) and event-free survival (EFS) was 56.4% and 49.3%, respectively. Univariate and multivariate analysis revealed that performance status, LDH level and histological type were independent prognostic factors for OS and EFS. Stomach group had better OS and EFS (72.3% and 48.4%) than Intestine group (43.1% and 23.6%), respectively ($p=0.003$ and $p=0.021$), but it lost the significance in the multivariate analysis.
CONCLUSION: PGIL is uncommon and lacks specific symptom in China. Intermediate-grade lymphoma is the most common histological type, while high-grade lymphoma almost occurred in the intestine. Patients with good performance status, normal LDH and non-high-grade phenotype may have better prognosis.
Disclosure of Interest: None declared

P1627 PREVALENCE OF HER-2/NEU OVER EXPRESSION IN GASTRIC CARCINOMA;BY USING TISSUE MICROARRAY (TMA)

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INTRODUCTION: Usually anatomical location and histological phenotype of gastric cancer (GC) is considered for selection of chemotherapy regime against GC. In other hand, genetic factors is also influence on out-come of GC and treatment. During recent years many researchers concentrate on molecular characteristics of cancer cell and it is believed that some molecular elements could have a prognostic value for therapeutic regimes. HER-2/neu over expression has proved to have predictive value in breast cancer patients, responding to Trastuzumab treatment. Some researchers also indicated the importance of this element in GC.
AIMS & METHODS: We investigated the frequency of HER-2/neu over expression in gastric carcinoma and its correlation with clinicopathologic variables.
101 paraffin embedded tissue blocks from the pathology archives of Firoozgar Hospital with established diagnosis of gastric carcinoma were used for the study of HER-2/neu over expression using immunohistochemistry (IHC) staining and using tissue microarray method (TMA).
RESULTS: Mean age of patients was 60.13 ± 11 (32-82) years. Male to female ratio was 2.4:1. HER2/neu over expression was positive in 13 cases (12.9%). The frequency of HER2/neuoverexpression in tumors ≥5cm was significant. There was no statistically significant correlation between HER2/neu over expression and other pathological features such as grade, stage, lymph node involvement, tumor location, histopathological type, as well as age and sex.
CONCLUSION: In conclusion, in our study the over expression rate of Her2/neu was reach to 13% which is same as other studies. We confirm that TMA could allow to determining the paten of biomarkers of GC and consequently can be used in clinical practices. Also this study can not confirm the association between Her2 and GC
Disclosure of Interest: None declared

P1628 FEATURES OF THE GASTRIC CANCER IN PATIENTS WITH SYSTEMIC NOT-DIFFERENTIATED DYSPLASIA OF CONNECTIVE TISSUE

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INTRODUCTION: The problem of gastric carcinogenesis is closely connected with the concept of border epithelia. The structure and operation of border epithelia are based on the epithelial-stromal relations. The violations of the epithelial-stromal relations in gastric cancer (GC) are marked both in the intestinal (IGC) and diffuse (DGC) types. It results in the interest in GC with systemic non-differentiated dysplasia of connective tissue (DCT), that initially determines other character of "substrate" for the epithelium, or other epithelial-stromal relationship.
AIMS & METHODS: The aim is to study the peculiarities of GC in patients with systemic non-differentiated DCT. The analysis of the clinical data and morphological study (light microscopy) of surgical specimens were done in 76 patients with GC aged 29-79 years. Among them 41 (54%) patients with visceral signs of DCT amounted group 1; 35 patients without signs of DCT formed group 2. Comparative statistical analysis was performed by χ^2- criterion and Fisher' s exact test at $p<0.05$.
RESULTS: Groups did not differ in structure of histotypes GC: IGC was respectively diagnosed in 51.2 and 45.7% of cases, DGC - in 26.8 and 22.9%, mixed GC - in 22.0 and 31.4% of cases. The stigmatization of the genitourinary system (51.2%) and the gastrointestinal tract (41.5%) prevailed in group 1 among stigma. The nature of stigma was cysts in different organs (68.3%), but mostly in kidneys (41.5%). Peculiarities of GC with DCT were as following: high frequency of gastritic anamnesis (80.5 and 48.6% respectively, $p<0.05$) and chronic ulcers (41.5% and 17.1%, $p<0.05$) which prevailed in group 1 in IGC (52, 4%), but in general – in DGC (42.1%); localization of the tumor in the body of stomach (61.0%, in group 2 – 34.3%, $p<0.05$), in group 2 – in cardia (31.4%, in group 1 – 9.8%, $p<0.05$); greater (in 2.5 times higher than in group 2) proportion of patients aged under 40 years (14.6% in group 1 and 5.7% - in group 2); high frequency of combined lesion of gastric mucosa (GM) and other border epithelium – mucosa of urinary tract in particular (48.8%, in group 2 – 8.6%, $p<0.05$); combined lesion of GM and colonic mucosa (atrophic colitis, adenomatous polyps and in two cases - meta-and synchronous colorectal cancer) – 14.6 and 8.6% of cases in groups respectively (i.e. 1.7 times more frequently in patients of group 1); combined lesion of GM and bronchial mucosa (obstructive bronchitis, bronchial asthma, lung cancer) - by groups of respectively 24.4 and 14.3 % of cases (1.7 times more often in group 1). The features of epithelial «substrate» or system of connective tissue can be one of the basic mechanisms of combined lesions of the mucous membranes of various localizations.
CONCLUSION: The revealed features (stigmatization of gastrointestinal tract and urinary system, in particular cysts in kidneys, gastritic anamnesis, chronic ulcers) can have a marker value in patients with DCT for inclusion in group of risk of developing GC.
Disclosure of Interest: None declared

P1629 DETECTION RATES OF GASTRIC CANCER AT THE QUEEN ELIZABETH HOSPITAL BIRMINGHAM 2009-2013

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INTRODUCTION: Despite open-access endoscopy, previous series have suggested that between 8-20% of early gastric cancers (GC) are potentially missed at prior endoscopy1,2. Although upper gastrointestinal alarm symptoms are more frequently associated with malignancy, this may represent advanced cancer with poorer survival rates, as patients with early GCs may be asymptomatic. The false-negative rate for the diagnosis of GC may also be a measure of quality for endoscopy services. This is based on a reported median duration of 37

months between endoscopic diagnosis of early GC and progression to advanced GC2,3, so we assessed all oesophagogastroduodenoscopy (OGD) findings to assess detection of GC in a large tertiary hospital in the West Midlands.
AIMS & METHODS: Patients with histologically confirmed GC were identified from histopathology and endoscopy records. Patients who had undergone at least one OGD before the diagnosis were studied. Detection of GC within 3 years of a negative OGD was interpreted as a false negative.
RESULTS: Between September 2009 and September 2013, 16823 OGDs were performed. GC was diagnosed in 75 (0.45%) patients (male/female ratio 1.78; median age 74; 85% Caucasian). Sixty-seven (89%) of the 75 patients with GC presented with alarm symptoms. 33% (25) were done as inpatients, with 43% (at least 32 of 50 outpatients) being referred as urgent outpatients. Five of the 75 (7%) patients had previous OGDs within three years preceding diagnosis. Only one of these was planned because of a suspicious gastric ulcerative lesion at the same site, with other causes being gastric polyps (2); normal (1) and gastritis (1). There were 53 (71%) deaths in total, 47 (89%) of these patients had alarm symptoms at diagnosis of GC.
CONCLUSION: The absolute rates of GC are low (0.1%/OGD/year) and false-negative rates of 5% (within 3 years) for diagnosis of GC are reassuring with only a minority of preceding OGDs in this series demonstrating suspicious lesions. Whilst GC presents with alarm symptoms in the vast majority, the prognosis remains very poor, so continued quality measures in endoscopy will be required to ensure that early gastric cancers are not missed.
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Disclosure of Interest: None declared

P1630 TRENDS AND RESULTS IN TREATMENT OF GASTRIC CANCER OVER LAST TWO DECADES AT SINGLE EAST EUROPEAN CENTRE

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INTRODUCTION: A steady decline in gastric cancer mortality rate over the last few decades is observed in Western Europe. However it is still not clear if this trend applies to Eastern Europe where high incidence rate of gastric cancer is observed.
AIMS & METHODS: This was a retrospective non-randomized, single center, cohort study. During this period 557 consecutive patients diagnosed with gastric cancer in which radical operation was performed and who met the inclusion criteria were included in the study. The study population was divided into two groups according to two equal time periods: 01-01-1994 – 31-12-2000 (Group I – 273 patients) and 01-01-2001 – 31-12-2007 (Group II – 284 patients). Primary (five-year survival rate) and secondary (postoperative complications, 30-day mortality rate and length of hospital stay) endpoints were evaluated and compared.
RESULTS: Rate of postoperative complications was similar between the groups, except Grade III (Clavien-Dindo grading system for the classification of surgical complications) complications, where significantly ($p = 0.02$) less complications were observed in Group II (26 (9.5%) vs. 11 (3.9%)). Length of hospital stay was significantly ($p = 0.001$) shorter (22.6±28.9 vs. 16.2±17.01 days) and 30-day mortality was significantly (0.02) lower (15 (5.5%) vs. 4 (1.4%)) in Group II. In both groups similar number of patients died of cancer (92.3% vs. 90.7%). However survival analysis revealed significantly ($p = 0.02$) better overall 5-year survival rate in Group II (35.6%, 101 of 284) than in Group I (23.4%, 64 of 273). There was no difference in 5-year survival rate when comparing different TNM stages.
CONCLUSION: Despite positive changes in early postoperative mortality rate, hospital stay and overall survival over the time, gastric cancer treatment results in Eastern Europe remain poor. Prognosis of treatment of gastric cancer depends mainly on the stage of the disease. Absence of screening programs and lack of clinical symptoms in early stages of gastric cancer lead to circumstances when most of the patients presenting with advanced stage of the disease can expect a median survival of less than 30 months even after curative intent surgery.
Disclosure of Interest: None declared

P1631 PALLIATION OF INTRACTABLE VOMITING CAUSED BY INOPERABLE GASTROINTESTINAL MALIGNANCY: EFFICACY OF A VENTING GASTROSTOMY

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INTRODUCTION: The insertion of percutaneous endoscopic gastrostomy (PEG) tubes for decompression of gastrointestinal obstruction in patients in whom a surgical option is not possible is well established. There is however, very little information on the safety or success of this intervention, which is usually performed in cohort of patients with poor baseline function and prognosis. The aim of this study is to assess the efficacy of a venting gastrostomy to relieve intractable vomiting in a palliative setting.
AIMS & METHODS: We retrospectively analysed our computer based endoscopy databases to identify all venting gastrostomies inserted over a four year period, between January 2010 and January 2014 in three NHS hospital Trusts within a Network Cancer Group (catchment population 1.4 million). Cases were analysed with respects to indication, complications, success at subsequent hospital discharge and survival.
RESULTS: Within a four year period a total of seven venting gastrostomies were inserted. The median age of this cohort was 68 years old (range 61 – 81 years), with a male to female ratio of 5:2. The most common indication for insertion was malignant obstruction (duodenal cancer $n = 2$, metastatic mesothelioma $n = 1$, colorectal adenocarcinoma $n = 2$, pseudomyxoma peritonei $n = 1$). One patient however, did not have evidence of active cancer, with instead multiple foci of fibrotic small bowel strictures secondary to pelvic radiotherapy from a previously treated gynaecological malignancy. Gastrostomy insertion was a palliative measure in five patients, whilst in two patients it was a temporising measure with concomitant total parenteral nutrition (TPN) support, whilst definitive complex surgery at a tertiary referral centre was considered.
The Corflo gastrostomy tube was used in all cases, with PEG size ranging from 16 fr ($n = 3$) to 20 fr ($n = 4$). At the time of insertion 57% had a American Society of Anesthesiology (ASA) score of 3, whilst 43% had an ASA score of 4. Successful placement was achieved in all patients, with no immediate complications. A single patient had several episodes of heamatemesis 22 days post insertion whilst an inpatient, a gastroscopy revealed gastritis only and confirmed normal appearances of the gastrostomy site. The median hospital stay after gastrostomy insertion was 12.4 days (range 1 – 29 days), with the longest continued hospital stay attributable to a patient awaiting transfer to a tertiary centre for home TPN. There were no PEG related readmissions or deaths, and the median survival after gastrostomy insertion was 37 days.
CONCLUSION: This study demonstrates the safety of venting gastrostomy insertion for gastrointestinal obstruction due to a variety of pathologies. Whilst patients undergoing venting gastrostomies may be expected to have a short post procedural survival, our data shows this procedure can lead to a successful palliation and a subsequent successful discharge home in the majority of cases.
Disclosure of Interest: None declared

P1632 THE ROLE OF RADIOLOGICAL STUDY AND ENDOSCOPIC ULTRASONOGRAPHY FOR PRE-OPERATIVE EVALUATION FOR EARLY GASTRIC CARCINOMA

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is a developed EMR technique for reliable en bloc resection and is rapidly becoming standard of treatment for early gastric carcinoma.
AIMS & METHODS: The aims of this study is to clarify the role of radiological study and endoscopic ultrasonography for pre-operative evaluation for early gastric carcinoma. We investigated the 287 gastric carcinoma cases that had been treated by ESD or surgery. Endoscopic, Radiological, EUS findings that indicated SM2 carcinoma were set beforehand respectively. The accuracy of the diagnosis and the additional diagnostic value of radiological and EUS diagnosis were investigated.
RESULTS: The accuracy rates of endoscopic diagnosis were high enough to decide the indications of ESD in the lesions 30mm or less in size, differentiated type without Ul. However in the lesions larger than 30mm, differentiated type with Ul, the accuracy rates were lower than the lesions without Ul because of over-diagnosis. Even in such lesions, using radiological diagnosis, the accuracy rates rose enough to decide the indication of ESD. The accuracy rates of endoscopic diagnosis in the lesions larger than 30mm, differentiated type without Ul were lower than the lesions equal or less than 30mm because of under-diagnosis. The accuracy rates rose using radiological diagnosis in such lesions. In the lesions equal or less than 20mm, undifferentiated type without Ul, the accuracy rates of endoscopic diagnosis were high enough to decide the indications of ESD. EUS was useful in the upper gastric lesions that compression methods could not be used in radiological examinations.
CONCLUSION: Radiological examinations were useful in large lesions that were under-diagnosed in endoscopy to avoid unnecessary ESD and the lesions without Ul that were over-diagnosed in endoscopy to avoid unnecessary surgery. Even in ESD age, it is important to use endoscopy, radiological examination, EUS complementarily according to the lesions to get neither too much nor too little information for deciding treatment strategy.
Disclosure of Interest: None declared

P1633 SERUM C-REACTIVE PROTEIN CAN BE A PREDICTIVE MARKER FOR DELAYED BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has become a promising procedure as a therapeutic tool for early gastric cancer (EGC). However, delayed bleeding occasionally occurs and it sometimes leads to severe hemorrhage or shock. There has been no useful indicator to predict the risk of bleeding after ESD for EGC.
AIMS & METHODS: The aim of this study is to clarify the usefulness of the parameters of blood examination in addition to clinico-pathological factors for the prediction of delayed bleeding after ESD for EGC. A total of 548 subjects with EGC who underwent gastric ESD in Osaka University Hospital and Osaka Rosai Hospital between April 2007 and December 2013 were enrolled. Cases having intraoperative perforation (n = 16) or more than two lesions treated on the same day (n = 45) were excluded. Delayed bleeding was defined as bleeding from post-ESD ulcer with hematemesis, melena or massive blood retention in the stomach at an emergent endoscopy or planned follow-up endoscopy. Cases with bleeding before planned blood examination test on a day after ESD were excluded. We analyzed associations between delayed bleeding and the parameter of blood examination including white blood cell count, hemoglobin level, C-reactive protein (CRP) level (mg/dL), and blood urea nitrogen-to-creatinine ratio. In addition, we also analyzed the following clinico-pathological factors; age, sex, gross-morphology, location, size, presence of the ulceration, and the invasion depth of the tumor, procedure time, comorbidity (hypertension, cardiac disorder, liver cirrhosis, diabetes mellitus and dialysis) and the use of anticoagulants and/or antiplatelet drugs.
RESULTS: Of 26 (5.3%) post-ESD bleeding cases, 23 cases fulfilled the criteria of delayed bleeding and were included in the study. Univariate analysis revealed that presence of the ulceration in tumor, upper third location of the stomach, and the elevations of the serum CRP levels on post-ESD 1day (CRP-DAY1), were significantly associated with bleeding (p = 0.009, p = 0.04 and p = 0.007, respectively). Multivariate logistic regression analysis revealed that the presence of ulceration in tumor (OR, 4.1; 95%CI: 1.2-13.0, p = 0.02) and the elevation of the serum CRP-DAY1 (OR, 3.2; 95%CI: 1.1-9.9, p = 0.04) were independent risk factor for delayed bleeding. When classified the patients into 4 subgroups based on CRP-DAY1, the prevalence of the post-ESD bleeding gradually increased as CRP-DAY1 increased (p = 0.03, for trend, **table 1**).

	CRP level (mg/dL)	The rate of post-ESD bleeding
Q1	0.03-0.33	1.7% (2/117)
Q2	0.34-0.74	5.0% (6/121)
Q3	0.75-1.49	4.2% (5/118)
Q4	1.5-10.09	8.3% (10/120)

Table 1
CONCLUSION: A higher level of serum CRP on the next day of gastric ESD may serve as a predictor for delayed bleeding.
Disclosure of Interest: None declared

P1634 DISCRIMINATION OF EARLY GASTRIC CANCER FROM GASTRIC ADENOMA, BASED ON THE CHARACTERISTICS OF GASTRIC NEOPLASIA

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INTRODUCTION: Background and Aim: Chronic atrophic gastritis has received increased attention, in Japan, because the observed gastric mucosa characteristics have been reported to be associated with gastric neoplasia. However, chronic atrophic gastritis is caused by a *Helicobacter pylori* infection. In the present study, we aimed to discriminate between early gastric cancer (EGC) and gastric adenoma (GA) by analyzing the characteristics of gastric neoplasia.
AIMS & METHODS: Methods: We retrospectively examined the records of 211 patients who underwent endoscopic submucosal dissection for gastric neoplasia at the Miyazaki University Hospital between October 2009 and March 2014. Of these, 78 patients who had not previously undergone *H. pylori* eradication treatment were evaluated and assessed for the presence of pepsinogen and the degree of gastric atrophy. If the border of the atrophy was on the lesser curvature of the stomach, it was defined as a closed-type (C-type). These were subdivided into C0, Cl, C2, and C3 patterns. If the border was shifted orally and did not exist on the lesser curvature, it was defined as an open-type (0-type), subdivided into 01, 02, O3, and 0p patterns. Therefore, gastric atrophy was graded as C0-l, C2-3, 01-2, and 03-p, based on its severity. Statistical analyses were conducted using a chi-squared test, with $P < 0.05$ indicating statistical significance.
RESULTS: Results: In total, 78 patients had gastric neoplasia; of these, 64 were graded as having the 0-type (82%), and 14 with the C-type. EGC was diagnosed in 57 patients, including 13 patients were graded as C2-3, 37 as 01-2, and 7 as 03-p. Moreover, 21 patients had GA, including 1 graded as C2-3, 11 as 01-2, and 9 as 03-p. The degree of atrophy associated with GA was significantly higher than that associated with EGC ($P < 0.05$).
CONCLUSION: Conclusion: The current findings showed that gastric neoplasia was well correlated with severe atrophic gastritis. Based on the current findings, the degree of atrophy appears to be useful for discriminating between EGC and GA.
Disclosure of Interest: None declared

P1635 SIGNET RING CELL EXISTENCE CAN BE A NEGATIVE PREDICTOR OF PACLITAXEL CHEMOTHERAPY EFFICACY FOR PATIENTS WITH UNRESECTABLE GASTRIC CANCER

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INTRODUCTION: The efficacy of chemotherapy is critical for quality of life (QOL) and prognosis of patients with unresectable gastric cancer. Cisplatin/fluoropyrimidine-based chemotherapy is commonly considered first line chemotherapy for gastric cancer, whereas taxian as well as CPT-11 is accepted for second line chemotherapy. However, clinicopathological parameters or biomarkers to decide second line chemotherapy regimen for gastric cancer remain to be elucidated.
AIMS & METHODS: We evaluated efficacy of weekly paclitaxel systemic chemotherapy (wPTX) for patients with unresectable gastric cancer using progress free survival (PFS) retrospectively. From 2008 to 2013, 32 unresectable gastric cancer patients were treated with wPTX as second line chemotherapy in two hospitals, a university hospital and a general hospital.
RESULTS: The mean PFS of all patients was 21.6 weeks (2 to 108 weeks). Three was no significant differences in sex (male; female, 9 cases; 23 cases), age (mean 69.4 years old, 16 cases are younger than 70, others are 70 or older), location of lesion (Upper 9 cases; Middle 16 cases; Lower 7 cases), peritoneal dissemination (18 cases), and clinical stage (IIIb 1 case, IV 31 cases). Microscopic morphology was classified into 4 groups (tubular 13 cases; poorly differentiated 16 cases; signet ring cell 8 cases; mucinous 2 cases). The cases consist of 2 or more types of cancer cell were counted in all their cell type groups. The mean PFS of tubular, poorly differenciated, signet ring cell (SRC), and mucinous were 28.1, 17.6, 8.5, and 12.0 weeks, respectively. There was signifincant difference of PFS only between SRC positive group (mean PFS 8.5 weeks) and negative (26.0 weeks) group (p = 0.006).
CONCLUSION: These results suggest that SRC existence can be a negative predictor of PTX efficacy for unresectable gastric cancer. Further investigation is needed to reveal the precise mechanism and development effective chemotherapies, including CPT-11, for SRC positive gastric cancer.
Disclosure of Interest: None declared

P1636 PRELIMINARY RESULTS OF ENDOSCOPIC SUBMUCOSAL TUNNEL DISSECTION FOR GASTROINTESTINAL SUBEPITHELIAL TUMORS ORIGINATED FROM MUSCULARIS PROPRIA LAYER; A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Although the majority of gastrointestinal subepithelial tumors (SETs) are benign, some do have a malignant potential. Resection of SETs would aid in establishing the diagnosis and may be curative. So, we aim to present the feasibility and safety of a novel endoscopic submucosal tunnel dissection (ESTD) method for resection of upper gastrointestinal SMTs originating from the muscularis propria (MP).
AIMS & METHODS: In 8 patients who presented with an upper gastrointestinal SMT located in the stomach, we underwent submucosal tunnel endoscopic resection between August 2011 and February 2013. A submucosal tunnel was endoscopically created by starting approximately 4cm distant to the lesion. After careful submucosal dissection of the tumor from the surrounding submucosal tissue and the unaffected MP layer with making the tunnel, the SETs were completely removed by the technique of endoscopic submucosal dissection. Finally, the mucosal entrance of the tunnel was closed using endoclips after the tumor was removed.
RESULTS: SETs had a mean size of 21.5mm (range 17–25mm); 4 were located in the antrum,3 in the body and 1 in the cardia. SET resection was successful in all patients with en bloc resection 88% rate. 6 lesions affected the deep MP, so Full thickness resection including MP layer was performed; except ectopic pancreas partialy resected for the purpose of diagnosis. 2 lesions affected the superficial MP for a partial MP resection. The mean procedure time was 66.1 minutes (range 40–80 minutes). The endoscopic procedure was converted into laparoscopic surgery in three patients. Two patients had lost the full thickness resected samples in the peritoneal space. One patient had sustained abdomen pain and fever after successful procedure. The other five patients had no any complications such as delayed hemorrhage and chronic fistula after then. No residual tumor or tumor recurrence were detected during the follow-up period (mean: 4.5 months, range: 3–9 months). Pathological diagnoses of these tumors were low risk gastrointestinal stromal tumors (6/8), a schwannoma (1/8), and a etopic pancreas (1/8).
CONCLUSION: In this study, endoscopic submucosal tunnel dissection (ESTD) was appeared to be feasible endoscopic procedure to remove tumors originating from the muscularis propria layer in the stomach.
Disclosure of Interest: None declared

P1637 COLLAGEN TYPE XI A1 IS ASSOCIATED WITH T STAGE OF GASTRIC CANCER AND REGULATES THE MIGRATION, INVASION AND PROLIFERATION OF HUMAN GASTRIC CANCER HGC-27 CELLS

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INTRODUCTION: Collagen type XI α1 (COL11A1) which plays important roles in carcinogenesis is increasingly recognized, including ovarian cancer and head and neck squamous cell cancer. However, the relation between COL11A1 and gastric cancer is still unclear.
AIMS & METHODS: The main purpose of this study is to investigate the expression levels and potential roles of COL11A1 in gastric cancer.
We examined the COL11A1 mRNA expression levels in fifty-three gastric cancer lesions and twenty normal gastric mucosa from endoscopy or surgery by qualitative real-time PCR. We also evaluated its expression level in seven gastric cancer cell lines by qualitative real-time PCR and western blotting. Furthermore, we established a stable cell line HGC-27 with COL11A1 gene knock-down to study its functional role in regulating cell proliferation, migration and invasion. To identify target candidates of COL11A1, we performed cDNA microarray.
RESULTS: Our qualitative real-time PCR results demonstrated that COL11A1 expression was significantly increased in tumor samples ($n = 53$) compared with that in normal tissues ($n = 20$) ($p < 0.01$). The up-regulation of COL11A1 was associated with T stage ($p < 0.01$). In addition, COL11A1 was highly expressed in the gastric cancer cell line HGC-27 as compared with other gastric cancer cells (SGC-7901, MGC-803, BGC-823, AGS, MKN-28, MKN-45) and a normal immortalized epithelial cells GES-1. We found that knockdown of COL11A1 significantly inhibited the migration ($p < 0.01$), invasion ($p < 0.01$) and proliferation ($p < 0.01$) of HGC-27 cells. Knockdown of COL11A1 also induced cell apoptosis ($p < 0.01$) and impaired cell cycles ($p < 0.01$). HGC-27 cells cDNA microarray showed that COL11A1 regulated multiple tumor metastasis-related genes such as CXCR4, CTSK, SET, KRAS, TPBG, MGAT5 and so on.
CONCLUSION: Our findings suggest that COL11A1 is overexpressed in gastric cancer, which may contribute to tumorigenesis and tumor aggressiveness. These results encourage the exploration of COL11A1 as a potential therapeutic target for gastric cancer.
Disclosure of Interest: None declared

P1638 ALBUMIN AS A MEDIATOR CONJUGATES DOXORUBICIN WITH GOLD NANOPARTICLES TO IMPROVE DELIVERED AND THERAPEUTIC EFFICACY OF DOXORUBICIN IN GASTRIC MKN45-INDUCED TUMOR XENOGRAFTS

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INTRODUCTION: Doxorubicin (DOX) is a drug used in cancer treatment in wide ranges of tumors. More effectively DOX targeting into tumor foci can benefit a better therapeutic efficacy coupled with a lower drug dosage and minimized side effects. With the goal of improving the therapeutic utility of DOX, several forms of drug delivery vehicles to target cancer has been developed and characterized such as liposomes.
AIMS & METHODS: In our current work, we used gold nanoparticles (GNPs) as our drug carrier vehicles loaded with DOX to target MNK45-derived tumors in xenograft nude mice. To avoid the forming of GNPs aggregations and provide the bridges on GNPs to DOX, we formulated bovine serum albumin (BSA) to coat the surface of GNPs and then evaluate the therapeutic effects of DOX-GNPs in animals.
RESULTS: The results demonstrated that our synthesized GNPs after BSA modification with size ranged from 15 to 300nm and the average diameters is near to 76.1±57.6 nm. The peak absorbance of these BSA-decorated GNPs was measured at 534 nm wavelength of light. To determine the cytotoxicity of BSA-decorated GNPs, gastric cancer cells, MNK45, were cultured with medium containing GNPs from concentration of 10 to 100 μM and no cytotoxicity was measured. To evaluate the specificity in tumor targeting of BSA-decorated GNPs in animals, the fluorescein isothiocyanate (FITC) molecules were also directly tagged onto the BSA layers of GNPs for later in vivo real time detection and imaging. The results demonstrated that our BSA-decorated GNPs were more effectively targeting to tumors than other organs. To assess the therapeutic efficacy, DOX were covalently bound to the BSA-decorated GNPs and then was characterized *in vitro* and *in vivo* by intravenously administration into xenograft animals. It revealed that GNP vehicle-driven DOX uptaked by tumor cells *in vitro* was higher and also impact more severe cytotoxicity to tumors. We also observed a better therapeutic outcome *in vivo* therapy in the xenograft nude mice with intravenously injection of DOX driven by BSA-decorated GNPs by displaying the lower tumor volume after 24 days therapeutic period time.
CONCLUSION: It suggests that BSA is a good mediator to bridge chemotherapeutic drugs such as doxorubicin to GNPs for improving tumor targeting and therapeutic outcome with lower cytotoxicity, indicating that GNPs display as a good and safer vehicles for delivering antitumor drugs to tumors.
Disclosure of Interest: None declared

P1639 EPIGENETIC SILENCING OF MIR-137 IS A FREQUENT AND EARLY EVENT IN GASTRIC CARCINOGENESIS

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INTRODUCTION: microRNAs (miRNA) are functional molecules that control gene expression and are frequently dysregulated during carcinogenesis, in particular in gastric cancer (GC). miR-137 functions as a tumor-suppressor-miRNA through silencing various oncogenes. CpG island methylation of miR-137 is a common event in glioblastoma and colorectal cancer (CRC). In this study, we systematically characterize the miR-137 promoter methylation and miR-137 expression in gastric carcinogenesis and correlate these results with overall survival of gastric cancer patients.
AIMS & METHODS: Tissue specimens were prospectively collected in Kaunas, Lithuania and in Magdeburg, Germany. Overall, 287 tissues were included to the study. We analyzed 81 pairs of primary gastric cancer tissues (T-GC) with corresponding adjacent normal gastric mucosa (N-GC), 25 normal gastric tissues from controls (N), 44 tissues from patients with chronic/atrophic gastritis ± intestinal metaplasia (CG) and 28 pairs of primary CRC tissues (T-CRC) with corresponding adjacent normal colonic mucosa (N-CRC). We determined the methylation status of miR-137 using bisulfite pyrosequencing. TaqMan RT-PCR was used to analyze miR-137 expression. Survival differences were evaluated using Kaplan-Meier analyses.
RESULTS: Defined by the distribution of miR-137 methylation in normal mucosa (mean±2SD), methylation of miR-137 is rare in normal mucosa (5%, mean methylation ± SD: 7.47±0.89%), however, increased in CG patients (10.68±0.97%). In correlation, miR-137 methylation was more frequent in tumorous compared to non-tumorous conditions both in CRC and GC (T-CRC 75% vs. N-CRC 15.8% and T-GC 46.8% vs N-GC 42.3%). Quantitative miR-137 methylation analyses revealed higher methylation in T-CRC compared to N-CRC (30.12±17.37% vs. 11.12±9.07%, $p = 0.0009$) and in similar fashion in T-GC to N-GC (21.08±13.88% to 16.92±11.55%, $p = 0.015$). miR-137 expression is inversely correlated with miR-137 CpG methylation as tumors with low methylation level showed higher expression compared to tumors with intermediate or high miR-137 methylation ($p = 0.0006$). In subgroup analyses, miR-137 methylation was higher in GC with intestinal type compared to diffuse one and higher in antrum compared to cardia and corpus, while no association existed to *H. pylori* infection or TNM stages. Overall survival analyses revealed an association between miR-137 methylation and worse prognosis in diffuse type gastric cancer, but not in intestinal type.
CONCLUSION: miR-137 is frequently methylated in gastrointestinal cancers. Increasing methylation of miR-137 from normal mucosa, chronic gastritis to cancerous tissues suggests it is an early event in gastric carcinogenesis. The alterations of miR-137 may play probably a more considerable role in development of intestinal type GC; but also worse prognosis of patients with miR-137 methylation in diffuse type GC supports the need of further functional analyses in both types of GC.
Disclosure of Interest: None declared

P1640 IMMUNOFLUOROMETRIC ANALYSIS OF THE EXPRESSION AND CLINICAL SIGNIFICANCE OF KALLIKREIN-RELATED PEPTIDASES 5 AND 7 (KLK5 & KLK7) IN COLON CANCER

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INTRODUCTION: Existing, colon cancer (CC) markers lack sensitivity and specificity. KLKs present a new class of cancer biomarkers under investigation. KLKs are concomitantly expressed in various tissues participating in proteolytic cascades. KLK5 and KLK7 in human tumors facilitate metastasis by directly degrading components of the extracellular matrix in the area surrounding KLK5 or KLK7-producing cells. KLK5 activates its own pro-enzyme as well as proKLK7. Also, KLK5 promotes tumorigenesis by activating proteinase-activated receptors (PAR_2).
AIMS & METHODS: The aim of this study was to analyse the expression of KLKs 5 & 7 in colon cancer and to find out their clinical significance. In the present study we examined the concomitant expression of KLK5 and KLK7 in the cytosols of 121 CC tissues as well as their paired normal mucosa. We used a non-competitive ELISA methodology (monoclonal–monoclonal for both KLKs).
RESULTS: It was shown that whereas KLK7 protein of CC tissue is up-regulated in comparison to normal mucosa the same does not hold for KLK5. Both KLKs were significantly associated with overall survival in univariate analysis. Also, in multivariate analysis, after adjusting for age, TNM and differentiation stage, both proteins were shown to be significantly associated with overall survival ($p = 0.032$, $p = 0.015$ respectively).

CONCLUSION: KLK7 is up-regulated in colon cancer, whereas the KLK5 is not in comparison to normal mucosa. Both KLKs are associated with overall survival in univariate as well as in multivariate analysis using as parameters the patients age, the TNM and the differentiation stage.
Disclosure of Interest: None declared

P1641 CATHEPSIN-B GENE EXPRESSION IN THE PROGRESSION FROM ADENOMA TO COLON CANCER

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INTRODUCTION: Colon cancer (CC) remains the third leading cause of worldwide cancer-related death in men and women. Currently, available prognostic and/or predictive markers for colon cancer lack specificity and sensitivity. Developing new biomarker for early detection, accurate diagnosis and therapeutic treatment for CC is of great importance in improving the clinical outcome of the disease. Cathepsin B (CB), a lysosomal cysteine protease, is expressed constitutively in lysosomes, however its expression and localization change in cancer. High levels of expression of CB at both gene and protein levels have been observed in different types of cancer.
AIMS & METHODS: The aim of this study was to analyze the CB expression in different stages of CC progression and to evaluate its clinical relevance. We examined for first time, using quantitative real time PCR, the expression of CB in 185 colonic tissue specimens from 130 patients; 50 were pairs of cancerous-normal tissues, 17 were cancerous tissues and 63 were adenomas for 5 of which normal paired mucosa were also available.
RESULTS: We proved that CB was up regulated in the cancer specimens in comparison to their normal paired mucosa ($p < 0.001$), as well as in the adenomas in comparison to normal tissue ($p < 0.001$). CB expression was found to be associated with histological grade ($p = 0.037$). Cox proportional hazard regression model using univariate and multivariate analysis revealed that high status CB expression is a significant factor for disease-free survival (DFS) ($p = 0.037$ and 0.0038, respectively) and overall survival (OS)($p = 0.003$ and $p = 0.0037$, respectively) of patients. Receiver-operating characteristic (ROC) analysis of our results showed that CB has discriminatory value between CC and adenomas tissues (area under the curve [AUC] = 0.711). Kaplan-Meier survival curves demonstrated that CB expression of low status is significantly associated with longer DFS ($p = 0.023$) as well as OS ($p = 0.002$).
CONCLUSION: Present results suggest that CB gene expression may represent a useful marker of unfavorable prognosis for CC patients with discriminatory power between CC and adenoma patients.
Disclosure of Interest: None declared

P1642 OVEREXPRESSION OF LASP1 IS ASSOCIATED WITH PROLIFERATION, MIGRATION AND INVASION IN GASTRIC CANCER

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INTRODUCTION: LIM and SH3 protein 1 (Lasp1) is an actin-binding protein involved in numerous biological and pathological processes. The overexpression of Lasp1 has been described in many types of cancers[1-4]. But the role of Lasp1 in gastric cancer (GC) remains unclear. We sought to analyze the expression level of Lasp1 in GC, and the role of Lasp1 in the development of GC.
AIMS & METHODS: The mRNA level and protein expression of Lasp1 in 82 cases of gastric cancer tissues and the paired normal gastric tissues were detected by real-time RT-PCR, Western blots and immunohistochemistry (IHC) respectively. The relationship between the Lasp1 expression level and the various clinicopathological parameters were analyzed. Using gene transfection and RNA interference (RNAi) stratage, we investigated the effects of Lasp1 overexpression and depletion on tumor cellular behavior respectively.
RESULTS: The Lasp1 mRNA and protein expressionin cancerous tissues were both increased significantly as compared to the normal gastric tissues ($p < 0.05$). Though there was no significant correlation was found between Lasp1 expression and tumor size and pathological differential degree, Lasp1mRNA level was significantly higher in patients with lymph node metastasis (N1-3) ($P < 0.05$) and those with more advanced clinical stages ($P < 0.05$) respectively. Consistently, IHC revealed that patients with lymph node metastasis ($P < 0.05$) and those with more advanced clinical stages ($P < 0.05$) were prone to show higher Lasp1 protein level. Overexpression of Lasp1 was found in metastatic GC tissues ($p < 0.01$), and its expression level was closely correlated with overall survival of patients with GC ($p < 0.01$). RNA interference mediated silencing of the Lasp1 gene in BGC823 GC cells inhibited cell proliferation and migration significantly. Furthermore, gene transfection-mediated overexpression of Lasp1 in SGC7901 GC cells resulted in aggressive phenotypes of GC cancer cells and promoted cancer growth and metastasis.
CONCLUSION: Above results suggested that Lasp1 was overexpressed in gastric cancer tissues, and the increased expression of Lasp1 may contribute to cancerous progression and lymph node metastasis.
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Disclosure of Interest: None declared

P1644 EPIGENETIC REGULATION OF SH2-CONTAINING PROTEIN TYROSINE PHOSPHATASE 1 (SHP1) IN GASTRIC CARCINOMA CELL LINES

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INTRODUCTION: The SH2-containing protein tyrosine phosphatase 1 (SHP1) is an important negative regulator in cytokine-mediated signal transduction and cell cycling. Recent studies demonstrated that promoter methylation of *SHP1* is frequently observed in gastric adenocarcinoma tissues. However, the functional effect of epigenetic silencing of SHP1 in gastric carcinogenesis has not been reported yet.
AIMS & METHODS: We tried in this *in vitro* study to reveal promoter hypermethylation of *SHP1* and to investigate the its carcinogenic effects in gastric carcinoma cell lines.
RESULTS: We observed that both gene and protein expression of SHP1 were negative in 8 of 10 gastric cancer cell lines (SNU-1, SNU-5, SNU-16, SNU-638, SNU-719, MKN-28, MKN-45, AGS), whereas KATO-III and NCI-N87 showed weakly positive protein expression by Western blot. Conventional methylation specific PCR (MSP) showed methylation-specific band only in all 10 gastric cancer lines. Bisulfite pyrosequencing revealed 96.5%, 97.3% and 94.8% of methylation frequency in AGS, SNU-719 and MKN-28 cells, respectively, whereas only 5.3% in peripheral blood mononuclear cells. When treating SNU-719, MKN-28 and AGS cells with 5 μM of 5-Aza-2'-deoxycytidine (5-Aza-dc) for 4 days, SHP1 was re-expressed in all three cell lines. SHP1 expression is known to be correlated with Janus kinase (JAK) and signal transducers and activators of transcription (STAT) signaling pathway. When introducing exogenous SHP1 in SNU-719 and MKN-28 cells by transient transfection, protein expression of phospho-JAK2 (Tyr 1007/1008) and phospho-STAT3 (Tyr 705) were substantially down-regulated, which in turn decreased the expression of target genes of phospho-STAT3, including Cyclin D1, MMP-9, VEGF and Survivin. Furthermore, induction of SHP1 significantly reduced cell proliferation and inhibited cell migration and invasion in SNU-719 and MKN-28 cells.
CONCLUSION: Epigenetic silencing of *SHP1* is frequently caused by promoter hypermethylation in gastric carcinoma cell lines. Exogenous expression of SHP1 down-regulates JAK2/STAT3 pathway to modulate various target genes and inhibit cell proliferation, migration and inhibition in gastric carcinoma cell lines, which suppports that epigenetic silencing of *SHP1* contributes various carcinogenic and progressive effects in gastric cancer cell lines.
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J Cell Mol Med 2009; 13: 3668-3679.
Disclosure of Interest: None declared

P1645 THE CLINICOPATHOLOGIC SIGNIFICANCE OF EZRIN EXPRESSION IN GASTRIC CANCER

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INTRODUCTION: Ezrin belongs to the ezrin/radixin/moesin protein family, which acts as membrane organizer and link between the plasma membrane and the cytoskeleton. Recent studies have found that through the regulation of adhesion molecules and signal transduction pathways, the Ezrin protein might play an important role in the process of tumor cell invasion and metastasis. There have been reports on the relationship of Ezrin expression to clinical outcome in solid tumors. However, reports on Ezrin expression in *H. pylori* infection and gastric cancer have been rare.
AIMS & METHODS: In this study, we investigated the relationship of Ezrin expression to clinicopathologic parameters and prognosis in *H. pylori* infection and gastric cancer. 113 gastric cancer tissues and same numbers of adjacent non-tumor tissues were obtained from patients who received gastrectomy for curative resection. Prognosis and clinicopathlogic characteristics of patients according to the grade of Ezrin expression were assessed. Western blot was analyzed to reveal differences of expression according to presence of *H. pylori* infection and duration of infection in AGS and HS3C cell line. Thirty pre-eradication gastric mucosal tissues and the same numbers of post-eradication gastric mucosal tissues were obtained from peptic ulcer patients with *H. pylori* infection and immunohistochemical staining was conducted.
RESULTS: The expression rates and Ezrin score were significantly increased in gastric cancer tissue compared to adjacent normal tissue (81.4% vs 66.4%, $P = 0.015$, 4.51 ± 3.29 vs 3.18 ± 3.11, $p = 0.003$, respectively). The expression of Ezrin was also increased in cases of lymphatic invasion, progression of N and TNM staging. As to the analysis of survival and correlation with Ezrin, Ezrin expression score and rates were significantly correlated with survival. In western blot analysis of AGC and HS3C cell lines, the expression of Ezrin protein increased according to presence of infection and duration of infection. In vivo

study using gastric mucosal tissues, The expression rates and score of Ezrin was not significantly elevated in pre-eradication state.
CONCLUSION: Ezrin expression may be used as a marker of not only cancer progression and metastasis but also as a prognostic indicator in gastric cancer and the effect of *helicobacter pylori* on expression of Ezrin in normal gastric mucosa may be needed further study to conclude.
Disclosure of Interest: None declared

P1646 THE EXPRESSION OF MMPS IN GASTRIC CANCER IS NOT ASSOCIATED WITH THE ACTIVATION OF MTOR

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INTRODUCTION: Degradation of the extracellular matrix by matrix metallo proteinases (MMPs) enables invasive growth of gastric cancer. Regulation of MMP expression by activation of mTOR (mammalian target of rapamycin) and related signalling pathways has been demonstrated, although not thus far in gastric cancer.
AIMS & METHODS: We investigated the expression of MMP2, MMP7 and MMP9 in gastric cancer and their association to mTOR in its activated, phosphorylated form (p-mTOR). The study compromised 130 patients with gastric cancer resections; 72% male, mean age 74+12.4 years, 66.2% intestinal type. Quantitative real-time PCR was performed for MMP2, MMP7 and MMP9 in fresh frozen tissue in a pilot of 43 gastric cancer patients and 30 healthy controls. Following this, immune-histochemical (IHC) staining of the MMPs as well as mTOR and p-mTOR was undertaken in the complete study population (n = 130). A semiquantitative immune-reactivity score (IRS) was applied to assess the staining separately for the tumour centre as well as the invasion front. Groups were compared by Mann-Whitney U and Wilcoxon's signed rank test and expression between sites and targets correlated by Spearman's rank correlation test. mTOR-dependent regulation of MMP expression was furthermore assessed in MKN45 gastric cancer cells by rapamycin specific inhibition of mTOR signalling.
RESULTS: RT-PCR demonstrated an up-regulated expression of all MMPs in gastric cancer compared to both non-malignant tissue and gastric mucosa from non-cancer controls. IHC revealed only for MMP2 a higher expression at the invasion front compared to the tumour centre; MMP7 was more highly expressed in the tumour centre, there was no difference for MMP9 between tumour centre and invasion front (Table). There was a trend for higher expression of mTOR in the tumour centre and the IRS for p-mTOR was higher at the tumour centre when compared with the invasion front (Table). These effects were observed in intestinal type cancers but not in diffuse ones. IRS of tumour centre and invasion front correlated positively for all MMPs, mTOR and p-mTOR ($p < 0.001$). There was no correlation between mTOR or p-mTOR expression with any of the MMPs. However, MMP2 expression correlated with MMP9, and mTOR with p-mTOR staining. By treatment of MKN45 cells with rapamycin a reduction of p-mTOR in the Western blot was achieved; however, expression of MMPs was not affected by this.

Target	Tumorcenter		Invasion Front		p-value
	Positive staining	IRS (mean+SD)	Positive staining	IRS (mean+SD)	
mTOR	96%	10.36±7.34	78%	9.66±8.27	n.s.
p-mTOR	80%	2.98±3.76	50%	2.72±4.59	0.019
MMP2	60%	3.75±4.76	74%	6.75±7.36	<0.001
MMP7	42%	5.49±8.59	43%	4.70±7.77	0.003
MMP9	44%	4.97±7.43	41%	4.23±6.91	n.s.

CONCLUSION: Expression of MMP2, MMP7 and MMP9 in gastric cancer is not associated with mTOR activation.
Disclosure of Interest: None declared

P1647 AUTOIMMUNE ATROPHIC GASTRITIS PRESENTS DISTINCT METAPLASTIC AND INFLAMMATORY PHENOTYPES COMPARED WITH CANCER-ASSOCIATED CHRONIC ATROPHIC GASTRITIS

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INTRODUCTION: Patients with autoimmune atrophic gastritis (AAG) have an increased risk of carcinoid tumors whereas patients with chronic atrophic gastritis (CAG) carry an elevated risk of adenocarcinoma.
AIMS & METHODS: We evaluated whether AAG and CAG have distinct metaplastic and inflammatory phenotypes which might contribute to their different evolution. We studied 20 female patients with AAG (age 56.4 ± 9.8 yrs) and 6 patients with CAG (4M, 2 F, age 66.3 ± 16.5 yrs). Diagnosis of AAG was through histology and positivity to anti-parietal cell antibodies. We evaluated by immunohistochemistry the gastric body expression of TFF2 as a spasmolytic-polypeptide expressing metaplasia (SPEM) marker, MUC2 as an intestinal metaplasia marker, CD68 as a macrophage marker, myeloperoxidase (MPO) as a neutrophil marker, CD44 variant, a marker of SPEM in mice, DMBT1, a marker of IM in humans, and Ki67 as a proliferation activity marker.
RESULTS: 1) All AAG patients showed parietal cell loss and TFF2-staining SPEM; 2) 75% AAG patients (15/20) demonstrated MUC2-positive goblet cell intestinal metaplasia; 3) All CAG samples showed parietal cell loss and both TFF2-staining SPEM and MUC2-positive intestinal metaplasia; 4) CD44 variant was expressed in SPEM in both AAG and CAG patients, with weak or absent expression in IM in both groups. In contrast, DMBT1 labeled IM but not SPEM in both groups, although the intensity of staining for DMBT1 in IM was uniformally weaker in the IM associated with AAG; 5) AAG patients showed significantly fewer MPO-positive neutrophils (2.9/1000 cells) as compared to CAG patients (37.0/1000 cells) and significantly fewer CD68-positive macrophages (10.5/1000 cells) as compared to CAG patients (28.0/1000 cells); 6) AAG patients demonstrated significantly lower rates of proliferation as assessed by Ki67-immunostaining cells (3.8/1000 gland cells compared with 103.7/1000 gland cells in CAG patients).
CONCLUSION: Metaplasia in AAG patients has a low proliferative rate and low macrophage and neutrophil infiltration, suggesting that metaplasia in AAG lacks crucial pro-adenocarcinoma influences. This may explain the lower incidence of gastric adenocarcinoma in AAG as compared to CAG.
Disclosure of Interest: None declared

P1648 GASTRIC SECRETORY CELL DENSITY PROVIDES FURTHER EVIDENCE FOR TWO AETIOLOGIES OF GASTROESOPHAGEAL JUNCTIONAL CANCERS

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INTRODUCTION: Serum pepsinogen I:II ratio, a surrogate marker of atrophic gastritis, suggests that some adenocarcinomas at the gastroesophageal junction (GOJ) develop on a background of atrophic gastritis, similar to non-cardia gastric cancer, while others arise on a background of healthy, non-atrophic gastric mucosa similar to oesophageal adenocarcinoma (OAD). In this study, we compare background gastric body mucosa in patients with junctional adenocarcinomas, oesophageal adenocarcinomas and non-cardia gastric (NCG) cancers.
AIMS & METHODS: A total of 127 gastrectomy and oesophagectomy specimens for adenocarcinoma had clear topographic description allowing assignment to oesophageal, junctional (including cardia) and gastric non-cardia locations. In each case a block of gastric body mucosa was identified well clear of the carcinoma. Parietal and chief cells were immunostained for H+/K+ ATPase and pepsinogen-1, respectively. Secretory cells density was counted in 3 to 5 well-oriented fields (1 mm^2 each) and expressed as mean cell number per 1 mm^2 area in each patient. Reactive atypia (RA) and inflammation indicated by polymorphonuclear (PMN) and mononuclear (MN) cells were also scored. Non-parametric statistics were used to compare distributions.
RESULTS: Ten (8%) cases lacked well-orientated blocks of body mucosa. The remaining 117 patients included 34 oesophageal, 52 GOJ and 31 non-cardia gastric adenocarcinomas. Median (IQR) parietal cell densities were 836 (173), 602 (389) and 411 (334) per mm^2 in gastric mucosa of oesophageal, GOJ and gastric cancers, respectively (all differences $P < 0.001$). Using a parietal cell density of 630/mm2, 85% of oesophageal adenocarcinomas had a higher and 84% of non-cardia gastric cancers had a lower values. Applying the same cut-off, 50% of GOJ adenocarcinomas would be classified as gastric and the remainder oesophageal in origin. Parietal cell density was normally distributed in the non-cardia gastric cancer and oesophageal adenocarcinoma groups. In contrast, the junctional adenocarcinoma group showed a biphasic distribution with one peak corresponding to that of non-cardia gastric cancer and the other to that of oesophageal adenocarcinoma. Chief cells show density distributions closely similar to parietal cells in all samples.
Chronic inflammatory score expressed as median (IQR) was higher in non-cardia gastric cancer than in oesophageal adenocarcinoma [0 (IQR:1) vs. 3 (IQR:2), $p < 0.001$], but in junctional cancer [1 (IQR:2)] it was higher than oesophageal adenocarcinoma and lower than non-cardia gastric cancer ($P < 0.001$ for both).
CONCLUSION: This study shows marked differences in gastric mucosal phenotype in the patients with oesophageal versus gastric non-cardia cancer, with the former being healthy and uninflamed, but the latter atrophic and inflamed. The background gastric mucosa of GOJ cancer supports being two distinct aetiologies, one group resembling oesophageal adenocarcinoma and other gastric non-cardia cancer.
Disclosure of Interest: None declared

P1649 ABERRANT AMPLIFICATION OF RECEPTOR TYROSIN-KINASES (RTK) INVOLVED IN CELL CYCLE SIGNALING APPEARS TO DETERMINE PROGNOSIS OF GASTRIC CANCER PATIENTS

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INTRODUCTION: Gastric cancer, which ranks among the top malignancies worldwide, exhibits a notable variety in the course of the disease. Clinical factors, such as tumor stage and localization, are key in patient survival. Lauren histology type is used to discriminate levels of differentiation; however, it is not directly applicable in the anticancer treatment. With the recent rise of molecular targeted therapies, genomic signatures comprising of somatic mutations and gene copy number variations are essential in treatment prediction as well as in prognosis of patient survival. A study by Deng et al. (Gut 2012) has identified molecularly distinct subclones by evaluating aberrant deletions or amplifications of key receptor tyrosin kinases (RTKs).
AIMS & METHODS: In this work we have related survival of gastric cancer patients to molecular classes/clusters derived from comprehensive evaluation of gene amplification with special emphasis on cell cycle signaling. Tumor samples (FFPE or freshly acquired) from a total of 76 patients (all caucasians/Europeans) with clinically confirmed gastric cancer were included in this study along with relevant clinical data including disease stage, Lauren type and tumor localization. The panel of gene amplifications included multiple receptor tyrosin-kinases families as well as other genes involved in cell cycle and proliferation. A hierarchical clustering using Wards method was applied to cluster patients according to molecular profiles. Kaplan-Meyer survival analysis was then applied to test survival of the subgroups.
RESULTS: There was a significant difference in survival for tumor localization (210 days for cardia vs. 563 days for body+antrum, $p = 0.0154$). Amplifications were frequent at 5q, 8q, 10q, 17q and 20q chromosomal locations. Several transmembrane RTKs exhibited importance when related to the patient survival, including PDGFRB, EGFR, HER2 and RET along with of CCND1 (Cyclin D1), and important cell cycle regulator. A subgroup of patients whose tumors revealed amplification of at least one of the prior genes exhibited a significantly shorter survival compared to a group with none of the amplifications detected (904 days vs. 205 days, $p = 0.029$).
CONCLUSION: As reported previously receptor tyrosin kinases play a dominant role in initialization of gastric cancer and its subsequent progression. By using a panel of RTKs along with Cyclin D1 we have observed an effect of gene amplifications on patients prognosis. An independent validation on a separat patient cohort is now in progress. Supported by the Czech Ministry of Health grant no. 13640.
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Disclosure of Interest: None declared

P1650 ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKER SUPPRESS THE FIBROSIS AND PROGRESSION OF GASTRIC CANCER

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INTRODUCTION: Peritoneal dissemination is the most frequent metastatic pattern of gastric cancer. The clinical outcome was poor prognosis because of the presence of rich stromal fibrosis and acquired drug resistance. Our previous study demonstrated that the epithelial-mesenchymal transition (EMT) of human peritoneal mesothelial cells (HPMCs) drives tumor fibrosis. In recent study, Angiotensin II type I (AT1) receptor blocker (ARB) has been attracted attention as drug with direct anti-fibrotic activity.
AIMS & METHODS: In this study, we examined whether ARB attenuates tumor proliferation and fibrosis, and explores the interaction between HPMCs and gastric cancer cells through the Angiotensin II / AT1 receptor / TGF-β1. The effects of ARB in vivo were evaluated in our established fibrotic tumor model, and the expression of fibrosis, E-cadherin and α-SMA was assessed by immunohistochemical staining. The effects of Angiotensin II and ARB on the proliferation of MKN45 were assessed by MTT assay. The AT1 receptor expression of gastric cancer cells was evaluated by western blotting. TGF-β1 expressions by the influence of Angiotensin II and ARB were evaluated by ELISA and western blotting. In addition, the effects of serum-free conditioned media (SF-CM) of MKN45 cells in HPMCs were examined by western blotting and immunofluorescence examination.
RESULTS: In fibrotic tumor model, the mean tumor volume of ARB treatment group was significantly reduced compared with that of absence of ARB. ARB treatment group was increased E-cadherin expression and decreased α-SMA expression and fibrotic area compared with absence of ARB. All gastric cancer cell lines showed AT1 receptor expression. The cell proliferation and TGF-β1 expression was significantly increased with 100nM of Angiotensin II compared with absence of Angiotensin II, and pretreatment with 1000nM of ARB showed significantly decreased compared with treatment of Angiotensin II. SF-CM of treatment with Angiotensin II caused the progression of EMT-like change. On the other hand, SF-CM of pretreatment with ARB suppressed this change.
CONCLUSION: ARB can significantly reduce TGF-β1 expression and EMT-like change, and suppress the tumor proliferation and stromal fibrosis. Targeting the Angiotensin II signaling pathway may be a novel, efficient strategy for treating the tumor proliferation and tissue fibrosis.
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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
H. PYLORI III – POSTER EXHIBITION – HALL XL

P1651 ROLE OF CAGA-POSITIVE STRAINS OF *H. PYLORI* IN ACUTE MYOCARDIAL INFARCTION WITH ST-SEGMENT ELEVATION

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INTRODUCTION: We have previously shown a significant epidemiological association between CagA-positive strains of *H. pylori* and unstable angina or non ST-elevation myocardial infarction (n-STEMI).
AIMS & METHODS: Therefore, we have designed a study aimed at assessing the prevalence of CagA-positive strains in patients with ST-elevation myocardial infarction (STEMI) and of recurring acute coronary syndromes (ACS) as well as the usefulness of the assessment of serum levels of anti-CagA IgG as a predictor of the clinical outcome in patients with STEMI.
Methods: We enrolled 181 patients (155 males, mean age 64±13 years) with STEMI and 50 controls (38 males, mean age 63±10 years) without any history of coronary artery disease and matched for sex, age and socioeconomical status. In all patients, serum levels of IgG anti-CagA were assessed. Moreover, levels of IgG anti-HAV were also evaluated in all patients in order to exclude the presence of a bystander activation of the immune system. Finally, a previous history of ACS and the rate of major adverse cardiovascular events (MACEs) were evaluated in all STEMI patients with a 2 years follow-up.
RESULTS: Prevalence of CagA-positive strains was significantly higher in patients with STEMI compared to controls (33.1% vs 9%, $p = 0.026$). Moreover, anti-CagA antibody titer was significantly increased in patients with STEMI compared to controls (62.7±39 vs 25.6±42.7, $p = 0.02$). Interestingly, patients with STEMI and a previous history of ACS had an higher prevalence of CagA-positive strains (50% vs 29.3%, $p = 0.019$) and higher antibody serum levels (97.5±50.4 vs 55.2±25.3, $p = 0.001$) as compared with patients without previous history of ACS. Furthermore, MACEs rate was significantly higher in patients infected by CagA-positive strains compared to CagA-negative (LogPrank = 0.014). Finally, there was a negative correlation between levels of anti-HAV and anti-CagA IgG ($R = 0.271$, $p = 0.11$) thus excluding the presence of an aspecific bystander activation of the immune system.
CONCLUSION: CagA-positive strains of *H. pylori* may be involved in the pathogenesis of STEMI and in the recurrence of ACS. Moreover, serum assessment of IgG anti-CagA may be an useful tool for risk stratification in patients with STEMI as they may positively predict MACEs rate.
Disclosure of Interest: None declared

P1652 A NOVEL STRATEGY OF PPI-PRETREATMENT IMPROVE ERADICATION RATE IN TRIPLE THERAPY

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INTRODUCTION: A proton pump inhibitor (PPI), amoxicillin (AMPC), and clarithromycin (CAM) are recommended widely used as first-line therapy for *Helicobacter pylori* (*H. pylori*) eradication in Japan. The guideline of Japan Helicobacter Association recommends eradication about all patients infected by *H. pylori.* From 2013, national health insurance covered eradication therapy about all patients who were infected with *H. pylori.* Yet, a decline in eradication rate associated with an increase in the prevalence of CAM resistance is increasingly problematic.
AIMS & METHODS: To improve the outcome, we retrospectively analyzed the factors which influence the failure in eradication conducted multicenter from 1997 to 2013 (n = 2582).
RESULTS: By univariate analysis, young subjects (under 35 years), non-peptic ulcer history, non-PPI therapy before eradication, and CAM-resistance were detected as risk factors of eradication failure. Gastric mucosal atrophy, dose of CAM, and types of PPI had no influence on outcome of triple therapy. By multivariate analysis, young subjects (under 35 years), non-peptic ulcer history, non-PPI therapy before eradication, and CAM-resistance were risk factor of eradication resistance ([OR: 0.63, 95%CI: 0.481–0.944], [OR: 0.78, 95%CI: 0.641–0.948], [OR: 0.78, 95%CI: 0.0.626–0.977], and [OR: 0.16, 95%CI: 0.081–0.306], respectively).

CONCLUSION: Pretreatment of PPI may be a novel strategy improving eradication rate in triple therapy. Further prospective study is necessary to clarify about this.
Disclosure of Interest: None declared

P1653 HELICOBACTER PYLORI IN CHRONIC GASTRITIS: WHAT IS THE RELATIONSHIP BETWEEN THE GASTRIC COLONIZATION AND THE HISTOLOGICAL LESIONS?

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INTRODUCTION: Infection with Helicobacter Pyroli (Hp) is acquired in childhood and the prevalence increases with age. Hp is now recognized as the main etiologic factor of chronic gastritis. Indeed, this infection is responsible for the majority of inflammatory gastric lesions. The aim of our study was to analyze the relationship between the density of gastric colonization by Hp and different gastric histological lesions (inflammation activity, atrophy, intestinal metaplasia and dysplasia).
AIMS & METHODS: From January 2010 to March 2014, were included 336 patients infected with Hp histologically proven on gastric biopsies according to the Sydney system. Statistical analysis of data was performed by SPSS 20.0. The association between the density of Hp and the lesions of chronic gastritis was studied by the chi-square test of Pearson, $p < 0.05$ was considered statistically significant.
RESULTS: The mean age of patients was 44.5 years ± 15.34 with female predominance in 54.8%. The chronic gastritis was mild in 13.1 %, moderate in 44.9%, severe in 7.7% and follicular in 34.2%. The density of the Hp colonization was minimal (+) in 24.1 %, moderate (++) in 56% and high (+ + +) in 19.9 %. Gastritis was antrofundic in 80 % of cases and only antral in 20 % of cases. There is a statistically positive association between the density of Hp and activity of gastritis with ($P < 0.001$). In patients with a minimal density of Hp, chronic gastritis was slightly active in 43.2 % of cases. In patients with a moderate density Hp, gastritis was moderately active in 58.5 % of cases. In patients with a high density of Hp, gastritis was moderately to severely active in 98.8 % of cases. Patients with moderate density of Hp had moderate atrophy gastritis in 8.5 % of cases and patients with significant density of Hp, gastric atrophy was severe in 16.4%, but these differences were not statistically significant. Intestinal metaplasia was present in 3% of our patients, including patients with mild density HP and intestinal metaplasia in 4.93%, and those with a moderate density HP and intestinal metaplasia in 3.14% of cases, but these results were not statistically significant. There were no cases of dysplasia in our series.
CONCLUSION: The activity of gastritis was significantly correlated to the density of Hp. However, the relationship between gastric atrophy, intestinal metaplasia and the density of Hp was no statistically significant in this study.
Disclosure of Interest: None declared

P1654 IRON DEFICIENCY ANEMIA DUE TO HELICOBACTER PYLORI INFECTION IS RELATED TO HYPOCHLORHYDRIA IN THE PATIENTS WITH GASTRIC HYPERPLASTIC POLYP, AND RELATED TO THE SERUM PROHEPCIDIN IN THE PATIENTS WITH NODULAR GASTRITIS

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INTRODUCTION: *Helicobacter pylori* (*H. pylori*) is recognized as a causative agent for unexplained iron deficiency anemia (IDA). However, the mechanism by which *H. pylori* infection contributes to IDA remains unclear.
AIMS & METHODS: To clarify the association between *H. pylori* infection and IDA, we evaluated many background factors influencing an iron deficiency state in adult patients with various *H. pylori* infection-positive upper gastrointestinal tract diseases. **Study 1** *H. pylori*-infected 121 patients (those with nodular gastritis (NG) (n = 19), duodenal ulcer (DU) (n = 30), or gastric ulcer (GU) (n = 47), or gastric hyperplastic polyp (GHP) (n = 25)) were enrolled in the study. The red blood cell count and hemoglobin, serum ferritin, serum iron, serum pepsinogen (PG) I, PGII, serum gastrin, and anti-*H. pylori* antibody (Ab) levels were measured. **Study 2** *H. pylori*-infected 105 patients (NG, n = 19; DU, n = 43; GU, n = 32; GHP, n = 11) and non-*H. pylori* infected individuals (n = 35) were examined for the levels of prohepcidin, ferritin, and iron in the serum. We evaluated the relationship between the prohepcidin and ferritin or iron levels. In addition, we measured the data before and after the *H. pylori* eradication.
RESULTS: In the patients with GHP and NG, hypoferritinemia was observed in comparison to the GU and DU patients ($p < 0.05$). In the GHP patients, low levels of PG I (26.4 ± 5.1 ng/ml, $p < 0.01$ vs DU, GU, and NG) and a decreased PG I/ II ratio (1.6 ± 0.2, $p < 0.01$ vs DU, GU and NG) in the serum were observed, in addition to hypergastrinemia (469.5 ±78.4 pg/ml, $p < 0.01$ vs DU, GU and NG). The levels of serum prohepcidin in the patients with *H. pylori*-associated disease were higher than those in the uninfected adults ($p < 0.01$ vs NG, GU and GHP, $p < 0.05$ vs DU). In the patients with NG, the serum prohepcidin levels were higher than those in the other *H. pylori*–infected patient groups ($p < 0.01$ vs GU, DU), and decreased after the eradication. Moreover, there was a negative correlation ($p < 0.01$, $r = -0.59$) between the serum levels of prohepcidin and the serum iron levels in the NG patients.
CONCLUSION: There were differences the iron status among the patients with different *H. pylori*-associated diseases. Hypochlorhydria due to *H. pylori*-associated gastric mucosal atrophy would affect the hypoferritinemia in the GHP patients. While the production of prohepcidin is induced by *H. pylori* infection, the iron deficiency state in the NG patients appears to be strongly associated with the prohepcidin production.
Disclosure of Interest: None declared

P1655 EXPRESSION OF BH3 ONLY PROTEIN BIM IS ASSOCIATED WITH MUCOSAL INFLAMMATION IN GASTRITIS PATIENTS

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INTRODUCTION: *H. Pylori* is a major cause of gastroduodenal diseases including gastritis, peptic ulcer, and gastric adenocarcinoma. Mechanisms by which *H. pylori* infection leads to persistent inflammatory responses are not completely understood. BH3-only protein Bim is known as a pro-apoptotic protein which participates in mitochondrial cell death (1, 2). Of note, recent study also indicated a paradoxical role of Bim in activating inflammatory cells (3). We have recently shown that Bim was up-regulated in *H. pylori*-infected mucosa (4). However, role of Bim in human gastritis remains unclear.
AIMS & METHODS: Our aim was to examine if Bim is associated with mucosal inflammation in gastritis patients. Patients who underwent upper gastrointestinal endoscopy from June 2007 to May 2013 were enrolled in the study (Total number; 36, *H. pylori* negative: n = 14, positive: n = 22). Biopsy specimens were obtained from the gastric antrum along the lesser curvature during endoscopic examinations, and samples were subjected to real time PCR to assess Bim mRNA expression. Localization of Bim was examined by immunohistochemistry. Correlation of Bim mRNA expression with the degree of gastritis was evaluated according to the updated Sydney system.
RESULTS: Expression of Bim mRNA was significantly elevated in *H. pylori*-infected mucosa compared to uninfected controls ($p < 0.01$). Immunohistochemistry revealed the localization of Bim in inflammatory cells at both lamina propria and submucosa. Double-staining confirmed co-localization of Bim and myeloperoxidase, but not with either B cell marker (CD20) or T cell marker (CD3), indicating that Bim was predominantly expressed by neutrophils. In accordance with the updated Sydney system, levels of Bim mRNA expression were positively correlated with degree of infiltrating neutrophils and monocytes. In contrast, Bim negatively correlated with degree of intestinal metaplasia. Other factors, such as degree of *H. pylori* colonization and atrophy, did not correlate with expression of Bim.
CONCLUSION: Bim is expressed by neutrophils and correlates with activity of gastritis. This study implied a possible link between Bim and pathogenesis of human gastritis. Further studies are awaited to determine the detailed role of BH3-only proteins in *H. pylori* infection.
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Disclosure of Interest: None declared

P1656 HEPCIDIN WAS EXPRESSED NOT ONLY IN THE CYTOPLASM BUT ALSO IN INTRACELLULAR CANALICULI OF GASTRIC PARIETAL CELLS AND EXPRESSED IN LYMPHOCYTES IN THE DEEP LAYER OF THE LAMINA PROPRIA

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INTRODUCTION: Hepcidin is an antimicrobial peptide and the key hormone in iron homeostasis. In the stomach, hepcidin is located in parietal cells and is related to acid secretion. Moreover, serum hepcidin levels are upregulated by *Helicobactor pylori* infection; therefore, hepcidin is an important factor in iron deficiency anemia (IDA) during the course of *H. pylori* infection. However, the localization of hepcidin in the parietal cell and the distribution of hepcidin in the gastric mucosa are unclear. In addition, it is unclear whether *H. pylori* infection influences gastric hepcidin expression in the gastric mucosa.
AIMS & METHODS: We evaluated hepcidin expression and its distribution in the gastric mucosa of *H. pylori*-infected and non-infected patients by immunohistochemistry. We enrolled 20 patients with *H. pylori* infection (mean age 55.6 ± 7.2 years, M:F = 1:1.5) and 20 patients without *H. pylori* infection (mean age 51.6 ± 9.8 years, M:F = 1:1.5). All patients underwent esophagogastroduodenoscopy (EGD). During EGD, biopsy specimens were obtained from the greater curvature of the gastric antrum and corpus. Biopsy specimens were fixed in 10% formalin and embedded in paraffin. Immunohistochemical staining was performed using these sections using monoclonal antibodies against hepcidin (Abnova, Taiwan). The present study was approved by the ethics committee of our institution. Written informed consent was obtained from all patients.
RESULTS: Hepcidin was expressed not only in the cytoplasm but also in intracellular canaliculi of gastric parietal cells in the both groups. Hepcidin was not expressed in other cell types in gastric epithelia. Hepcidin was also expressed in lymphocytes in the deep layer of the lamina propria, and its expression in the *H. pylori*-infected group was stronger than that in the non-infected group.
CONCLUSION: Our study revealed the expression of hepcidin in intracellular canaliculi of gastric parietal cells. Schwarz et al. have reported that hepcidin was detected in human gastric juice (Gut 2012); therefore, our findings suggest that

gastric hepcidin is released into the gastric lumen with gastric acid concurrently from parietal cells. The strong expression of hepcidin in lymphocytes in the gastric mucosa of *H. pylori*-infected patients suggests its role in inflammation and in the etiology of IDA associated with *H. pylori* infection.
Disclosure of Interest: None declared

P1657 14 DAYS SEQUENTIAL OR HYBRID REGIMEN FOR HELICOBACTER PYLORI ERADICATION IN CLINICAL PRACTICE IN SOUTHERN GREECE. A PROSPECTIVE PILOT STUDY

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INTRODUCTION: First line empirical treatment, non bismuth quadruples either 10-day sequential therapy with omeprazole and amoxicillin 5 days followed by omeprazole clarithromycin, metronidazole for another 5 days or concomitant the same drugs for 10 days, in previous studies, in our area (southern Greece) achieve PP eradication 86% and 92% respectively (1,2)
AIMS & METHODS: Investigation in a prospective, randomized, pilot study whether prolonging the treatment duration of sequential therapy and/or continuing the amoxicillin throughout the 14 days (sequential-concomitant hybrid) could raise the PP eradication rate to >95%. METHODS: 3 years single centre study.130 naïve *H. pylori* infected patients were randomly assigned to receive either: Sequential (omeprazole 20 mg and amoxicillin1gr for 7 days followed by omeprazole 20 mg, clarithromycin 500 mg, and metronidazole 500 mg for 7 days; n = 65) or Sequential-Concomitant hybrid: (Sq-Con hybrid) (omeprazole 20 mg and amoxicillin 1 gr for 7 days followed by omeprazole 20mg, amoxicillin1 gr, clarithromycin 500 mg, and metronidazole 500 mg for 7 days; n = 65). All of them given twice daily. UBT or endoscopy was performed 4-8 weeks post treatment to assess the outcome.
RESULTS: 65% male, mean age 46.25 +/- 14.7 years, 55% endoscopic lesions (ulcer, erosions), 35% smokers. Eradication rate by intention to treat analysis was 84%; (95% CI, 76.7% - 90.9%) for 14 days sequential, 91% (95% CI, 86.5% - 97.3%) for sq-con hybrid therapy. Per-protocol analysis yielded 88% (95% CI, 82, 4% - 93.9%) for 14 days sequential and 93% (95% CI, 90.4% - 97.9%) for sq-con hybrid therapy. Both regimens exhibited similar adverse events (42% vs. 46%) and treatment compliance (95 % vs. 97%).
CONCLUSION: Our pilot study, apart from the number of tablets needed per day, is unable to support that extending the duration of sequential therapy to 14-days, neither adopting the hybrid regimen, as first line empirical treatment, will achieve better results than the obtained by either sequential 10 or concomitant in *H. pylori* eradication in our area.
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Disclosure of Interest: None declared

P1658 DOES TAILORED THERAPY BASED ON ANTIMICROBIAL SUSCEPTIBILITY TESTING OVERCOME THE INCREASING FAILURE OF STANDARD EMPIRICAL THERAPY FOR HELICOBACTER PYLORI INFECTION?

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INTRODUCTION: First-line triple therapy for *H. pylori* involves the use of a PPI with amoxicillin & clarithromycin or clarithromycin & Metronidazole in case of penicillin-allergy for one week. However, due to increased resistance to these commonly employed antibiotics, eradication has fallen considerably short of the 80% intention-to-treat (ITT) rates that are considered the minimal acceptable levels as recommended in the Maastricht guidelines. Despite these worrying trends, there are no centres routinely monitoring Irish resistance rates. Data which could help adapt new first line therapies and improve outcome.
AIMS & METHODS: To compare the efficacy of standard empirical triple therapy with tailored therapy based on antimicrobial susceptibility testing.
A prospective, multicentre, randomised controlled study was conducted after ethical approval in all participating hospitals. Treatment naïve *H. pylori*-infected patients (>18 years old), as assessed by a positive antral CLO-test at endoscopy, were invited to participate and informed consent was obtained. Information on age, gender, previous antibiotic use & smoking history was recorded. A single antral biopsy was processed for antimicrobial susceptibility testing employing both standard culture and E-testing & genotyping for antibiotic resistance associated SNPs. Patients were randomised to receive either standard empirical therapy with Amoxicillin, Clarithromycin & PPI or tailored treatment based on their antibiotic resistance profile which included standard triple therapy or if resistance was detected triple therapy with Amoxicillin, Levofloxacin & PPI or Denoltab, Tetracycline, Metronidazole & PPI based quadruple therapy. A follow up UBT was performed after 6-8 week to assess treatment success.
RESULTS: To date 247 consecutive patients had CLO tests assessed at endoscopy. Of these 52 (21%) were *H. pylori* positive. Infected patients tended to be younger men with a mean age of 47 versus 53 years, $p < 0.05$ and 56% versus 46% were male. In all 47 (90%) patients have been randomised to a treatment arm and 40 (85%) have completed the study. Of those 40, 15 (37.5%) and 25 (62.5%) received tailored and empirical therapy respectively. In the tailored arm 6 (40%) received quadruple and 4 (27%) Levofloxacin and 5 (33%) standard triple therapy. Eradication rates were higher for tailored versus empirical therapy, 87% (13/15) and 68% (17/25). This trend did not reach statistical significance. Only 1 (3%) patient had a severe side effect with mild anaphylaxis to amoxicillin. Overall 42% of strains were clarithromycin resistant and 7 of 8 (88%) patients who failed empirical therapy had resistant strains, $p < 0.001$. Of the 2 (13%) who failed tailored therapy neither treatment type nor resistance profiles were predictive.
CONCLUSION: Resistance levels to clarithromycin are high at 42%. Targeted therapy can enhance eradication rates. Larger numbers will be required before a new first line treatment can be recommended.
Disclosure of Interest: R. Haider: None, S. Smith: None, G. Holleran: None, B. Hall: None, C. O'Morain: None, H. O'Connor: None, D. McNamara: None.

P1659 RANDOMIZED CLINICAL TRIAL: COMPARISON OF 10-DAY CONCOMITANT THERAPY AND HYBRID THERAPY FOR HELICOBACTER PYLORI INFECTION IN KOREA-PRELIMINARY RESULT. (CRIS KCT0000728)

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INTRODUCTION: In the era of increasing resistance of *Helicobacter pylori* against antibiotics, non-bismuth-containing regimens have been validated for the optimal treatment.
AIMS & METHODS: We aimed to identify the superb treatment option comparing concomitant and hybrid regimen as a first-line treatment for *H. pylori* infection. A total of 359 naïve *H. pylori*-infected patients from six hospitals in Korea were randomly assigned to concomitant and hybrid therapy groups. The concomitant regimen consisted of 20 mg of esomeprazole, 1 g of amoxicillin, 500 mg of clarithromycin, and 500mg of metronidazole, twice daily for 10 days. The hybrid regimen consisted of a 5-day dual therapy (20 mg of esomeprazole, and 1 g of amoxicillin, twice daily) followed by a 5-day quadruple therapy (20 mg of esomeprazole, 1 g of amoxicillin, 500 mg of clarithromycin, and 500 mg of metronidazole, twice daily).
RESULTS: Concomitant and hybrid eradication rates were 78.2% (161/206 patients, 95% CI 72.6-83.8) vs. 81.9% (163/199 patients, 95% CI 76.6-87.2) by intention-to-treat ($p = 0.841$) and 89.9% (151/168 patients, 95% CI 85.3-94.5) vs. 90.5% (153/169 patients, 95% CI 86.1-94.9) by per-protocol ($p = 0.841$), respectively. The incidence of adverse events was similar between the two groups.
CONCLUSION: Concomitant and hybrid therapy were proven to be equally efficient regimens as the first line treatment option for *H. pylori* infection.
Disclosure of Interest: None declared

P1660 COMPARATIVE STUDY OF HELICOBACTER PYLORI ERADICATION RATES WITH 10-DAY NON-BISMUTH QUADRUPLE THERAPY AND 10-DAY SEQUENTIAL THERAPY

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INTRODUCTION: Since the efficacy of the standard triple therapies for *Helicobacter pylori* (*H. pylori*) eradication has decreased, novel antibiotic regimens have been introduced.
AIMS & METHODS: The aim of this study was to compare non-bismuth quadruple therapy with sequential therapy for the first-line *H. pylori* eradication.
One hundred and thirty-seven with proven *H. pylori* infection were randomly assigned to one of 2 regimens: amoxicillin 1000mg with clarithromycin 500 mg, metronidazole 500 mg, and pantoprazole 40mg twice daily for 10 days (non-bismuth quadruple therapy) or amoxicillin 1000mg with pantoprazole 40mg twice daily for 5 days followed by clarithromycin 500mg with metronidazole 500mg, and pantoprazole 40mg twice daily for 5 days (sequential therapy). The success of *H. pylori* eradication was evaluated 4-5 weeks after completing treatment.
RESULTS: Eradication rates were 93.4% in the concomitant therapy and 85% in the sequential therapy (per protocol), but the difference was not statistically significant ($P = 0.154$). Compliances were 97.2% in non-bismuth quadruple therapy and 97.1% in sequential therapy. Adverse events were generally mild in both groups.
CONCLUSION: Non-bismuth quadruple therapy led to a non-statistically advantage over sequential therapy, It is well tolerated and could be considered as the first-line empirical therapy for *H. pylori* in Korea.
Disclosure of Interest: None declared

P1661 COMPARISON OF 10-DAY SEQUENTIAL THERAPY WITH BISMUTH BASED QUADRUPLE THERAPY FOR SECOND LINE HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: 10-day sequential therapy has been evaluated as the first line therapy for *Helicobacter pylori* eradication and studies of sequential therapy as a second line therapy has been scarce.
AIMS & METHODS: The aim of our study was to evaluate the efficacy of 10-day sequential therapy as second line treatment after failure of standard triple therapy.
Patients diagnosed as *H. pylori* infection by rapid urease test, giemsa staining, or ^{13}C-urea breath test and who failed from standard triple therapy for *H. pylori* eradication from January, 2010 to June, 2013 in Yeungnam university hospital were included. Post treatment *H. pylori* status was determined by rapid urease test, giemsa staining, or ^{13}C-urea breath test. Eradication rate, side effects were compared.
RESULTS: A total of 123 *H. pylori* infected patients were included and 39 patients were treated by bismuth based quadruple therapy and 84 patients, by 10-day sequential therapy. Age and sex were not significantly different between both groups. The per-protocol eradication rates were 82.1% (32/39) in quadruple group and 60.7% (51/84) in sequential group. Side effects were similar in both groups (quadruple group, 20.5% vs sequential group, 11.9%, p = 0.273).
CONCLUSION: For second line *H. pylori* eradication after failure of standard triple therapy, bismuth based quadruple therapy showed significantly higher *H. pylori* eradication rate than 10-day sequential therapy. Further prospective studies are needed to evaluate efficacy of 10-day sequential therapy as second line *H. pylori* eradication treatment.
Disclosure of Interest: None declared

P1662 2ND LINE LEVOFLOXACIN-BASED TRIPLE THERAPIES PROVIDE SIMILAR HELICOBACTER PYLORI ERADICATION RATES TO BISMUTH-BASED QUADRUPLE THERAPIES

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INTRODUCTION: The eradication rate of 1st line treatment with standard triple therapy in Greece remains persistently under 80% since 2007 and parallels Clarithromycin resistance of > 20%. Quadruple bismuth containing regimens were the standard of care as 2nd line treatments until 2010 when bismuth was withdrawn from the market.
AIMS & METHODS: The aim of our study was to evaluate the efficacy of 2nd line treatments over the periods before and after bismuth withdrawal.
Patients – Methods: Data from patients, who received 2nd line treatment for Helicobacter pylori, were collected retrospectively. Two periods were compared in terms of eradication success: period A (≤2010) and period B (≥2011). During period A patients received: {proton pump inhibitor bid + metronidazole 500mg tid + amoxicillin 1gr bid+ bismuth subcitrate 120mg qid} for 14 days while during period B: {proton pump inhibitor bid + levofloxacin 500mg bid + amoxicillin 1gr bid} for 10 days. Patients tested with urea breath test (UBT) 4-6 weeks after completion of treatment were analyzed. Susceptibility to levofloxacin was evaluated by E-test.
RESULTS: 159 patients (61 men), age (mean±SD = 51.7±12.3 years). Period A: 88 (34 men), and B: 71 (27 men). The 2 groups did not differ neither for age, gender, smoking and other demographic parameters nor for endoscopic lesions. Eradication rates according to UBT results for the 2 periods are shown in table 1. Eradication rates according to UBT results for period B ≥2011 are shown in table 2. For the years 2011-2013 the primary levofloxacin resistance rate as evaluated continuously in samples of our population remained stable (8-9%).
Table1

	UBT (+)	UBT (-)	Chi-square
<2010	13 (15%)	75 (85%)	p = 0.41
>2011	14 (20%)	57 (80%)	

Table2

2011	15	4	Fisher test
2012	19	4	p = 0.80
2013	18	6	
2014	5	0	

CONCLUSION: 1) 2nd line treatment with 10 days of levofloxacin-based treatment is equally effective to 14 days of quadruple bismuth-based treatment, with a levofloxacin resistance of <10% for the studied period. 2) During 4 years of levofloxacin use, the success rate did not change in this group and parallels the stability of levofloxacin resistance rates. However, increase of resistance is probable in the future and it may affect the efficacy of levofloxacin-based treatments.
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P1663 TEN-DAYS CONCOMITANT THERAPY IS SUPERIOR TO SEQUENTIAL THERAPY FOR HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: *Helicobacter pylori* (*H. pylori*) infection is the main cause of gastritis, peptic ulcer disease, gastric MALT lymphoma, and gastric cancer. The first-line international choice for treating *H. pylori* was consists of standard triple therapy, which includes two antibiotics (clarithromycin plus amoxicillin or metronidazole) plus proton-pump inhibitor for 7-14 days. Because the efficacy of the standard triple therapy for *H. pylori* eradication has declined, new regimens such as sequential therapy (ST) and concomitant therapy (CoCTx) have been introduced.
AIMS & METHODS: The aim of this study was to compare the efficacy of 10-days sequential therapy and 10-days CoCTx (non-bismuth quadruple drugs) for *H. pylori* eradication. We retrospectively reviewed the medical records of 316 patients with proven *H. pylori* infection. They were assigned to one of 2 regimens: (a) ST (n = 191): lansoprazole 30mg and amoxacillin 1g for 5 days followed by lansoprazole 30mg, metronidazole 500mg, and clarithromycin 500mg for 5 days; (b) CoCTx (n = 125): lansoprazole 30mg, amoxicillin 1g, metronidazole 500mg, and clarithromycin 500mg for 10 days. All drugs were administered twice a day. Bacterial eradication was checked by using a ^{13}C-urea breath test, at least 4 weeks after treatment. Side effects and compliances were evaluated with interview and more than 90% of drug administration.
RESULTS: The mean age and male to female ratio was 51.74 and 1.03. Baseline characteristics (age, gender, smoking) were not different in both groups. Ten days CoCTx group (94.4%, 118/125) showed better eradication rate than ST group (82.2%, 157/191) ($p = 0.002$). The difference was statistically significant. Drug compliances were not statistically different between both groups (ST: 96.3%, 184/191; CoCTx: 92.8% 116/125) ($p = 0.19$). Side effects were more frequently reported in the CoCTx group (42.4%) than in the ST group (29.8%) ($p = 0.03$). The most common side effect was taste disturbance.
CONCLUSION: Ten-days CoCTx was superior to ST in terms of eradicating *H. pylori* infection. Although the CoCTx was producing more side effects than ST, CoCTx is thought to be a promising alternative to ST as a treatment regimen for *H. pylori* eradication.
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Disclosure of Interest: None declared

P1664 INFLUENCE OF CYP2C19 GENOTYPE AND SERUM PEPSINOGEN LEVEL ON FIRST-LINE ERADICATION THERAPY WITH ESOMEPRAZOLE FOR PATIENTS WITH HELICOBACTER PYLORI-POSITIVE GASTRITIS

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INTRODUCTION: Esomeprazole is the proton pump inhibitor (PPI) that was developed as the S-isomer of omeprazole. Although extensive metabolizer genotype of CYP2C19 metabolizes omeprazole rapidly, it is believed that esomeprazole is not affected by CYP2C19 genotype and is more effective for suppression of gastric acid secretion. However, there is no evidence for clinical advantage of esomeprazole in first-line *Helicobacter pylori* (*H. pylori*) eradication therapy.
AIMS & METHODS: In the present study, we investigated influence of CYP2C19 genotype and serum pepsinogen level on first-line eradication therapy with esomeprazole for patients with *H. pylori*-positive gastritis. Patients with gastritis who were diagnosed as positive for *H. pylori* were included in this study between January and September 2013. They were treated by first-line eradication therapy with esomeprazole 40 mg/day, amoxicillin 1500 mg/day and clarithromycin 400 mg/day for 7 days. Three-months after eradication, *H. pylori* infection was validated by ^{13}C-urea breath test. Correlation between *H. pylori* eradication and CYP2C19 genotype and serum pepsinogen level was analyzed. This study is registered with the UMIN Clinical Trials Registry, number UMIN000009642.

RESULTS: *H. pylori* eradication rate of first-line therapy with esomeprazole was 68.3% (54/79), which was similar to that of first-line therapy with lansoprazole (69%; 80/116). Eradication rates of first-line therapy with esomeprazole in three different CYP2C19 genotypes, extensive metabolizer (EM), intermediate metabolizer (IM) and poor metabolizer (PM) were 50% (11/22), 72.7% (32/44) and 84.6% (11/13), respectively. Eradication rate of EM group was significantly lower than that of PM group ($p = 0.043$) and IM+PM group ($p = 0.03$). Serum pepsinogen I level and pepsinogen I/II ratio were significantly increased after eradication of *H. pylori* ($p = 0.007$), suggesting that gastric atrophy was improved by eradication therapy.
CONCLUSION: These findings suggest that EM genotype of CYP2C19 metabolizes esomeprazole more rapidly, and therefore plasma concentration of esomeprazole become lower, resulting in higher gastric acid secretion and lower *H. pylori* eradication rate. Evaluation of CYP2C19 genotype and serum pepsinogen level is important to develop effective personalized therapy of first-line eradication with esomeprazole for patients with *H. pylori*-positive gastritis.
Disclosure of Interest: None declared

P1665 "MALT OR NOT MALT, THAT'S THE QUESTION" – UPPER GASTROINTESTINAL ENDOSCOPY IN DIAGNOSIS AND FOLLOW-UP OF GASTRIC MALT LYMPHOMA

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INTRODUCTION: Diagnosis of gastric *mucosa-associated lymphoid tissue* (MALT) lymphoma (G-MALT) is frequently established after an upper gastrointestinal endoscopy (UGE) with biopsies, for investigation of nonspecific digestive symptoms. Described endoscopic changes of this rare neoplasia are heterogeneous.
AIMS & METHODS: The aim of this study was to characterize endoscopic findings of G-MALT in diagnosis and follow-up endoscopies.
We performed a retrospective study of all G-MALT cases, in a single tertiary center, over a 14-year period (2000-2013). Data regarding patients' demographics and clinical factors and endoscopic findings were collected.
RESULTS: Sixteen patients were included, with a mean age of 60.8±2.7 years and 9 (56.3%) were male. Indications for UGE were: epigastric pain in 8 (57.1%) patients, postprandial fullness in 6 (26.1%), heartburn in 2 (8.7%), asthenia in 2 (8.7%), hematemesis in 2 (8.7%), anorexia and weight loss in 2 (8.7%) and anaemia in 1 (4.3%). G-MALT was located in the (gastric) body in 9 (56.3%) cases, antrum in 5 (31.3%) and both in 2 (12.4%). According to endoscopic findings, changes were classified as: erosions of gastric folds in 3 (18.8%) patients, gastric ulcer in 3 (18.8%), nonspecific areas of irregular mucosa in 3 (18.8%), structural modifications in gastric folds in 2 (12.5%), hypertrophic gastric folds in 2 (12.5%), erythematous mucosa in 2 (12.5%) and exophytic tumor in a single case (6.3%). The mean follow-up time was 5.6 ± 0.9 years, with no mortality. On follow-up endoscopies in non-gastrectomized patients, gastric ulcers only maintained an area with a scar and there were no gastric folds erosions. The remaining changes persisted similar to the first UGE, regardless disease evolution.
CONCLUSION: Endoscopic findings of G-MALT are nonspecific and, most of the times, apparently benign. Given this, histological characterization of these lesions is preponderant to its diagnosis and follow-up.
Disclosure of Interest: None declared

P1666 PRIMARY GASTRIC LOW-GRADE MALT LYMPHOMA: EVALUATION OF CLINICAL AND LABORATORIAL FACTORS FOR ACHIEVING COMPLETE REMISSION

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INTRODUCTION: Gastric mucosa associated lymphoid tissue (MALT) lymphoma, is an indolent cancer, that occurs in the presence of pre-existing prolonged lymphoid proliferation in mucosal sites. In that instance, the most well established trigger is the gastric *Helicobacter pylori* (Hp) infection.
AIMS & METHODS: Evaluation of clinical and laboratorial factors, and the effect of therapy in achieving Complete Remission (CR) in 1 year of patients with gastric MALT lymphoma. Multicentric study, in which clinical and pathological features of patients with gastric MALT lymphoma, according Dawson criteria for primary gastrointestinal lymphoma, were evaluated retrospectively.
RESULTS: A total of 34 cases were identified, 23 men, and 11 women, with an average age of 59 years. The most common symptom was epigastric pain (74%), six patients presented Gastrointestinal Bleeding and three patients had type B symptoms. The most prevalent localization was gastric body and 18 patients had ulcerative pattern at presentation. At diagnosis, 91% and 94% were classified has limited disease (Lugano I-II and Ann Arbor IE-IIE respectively) and 94% had an International Prognostic Index (IPI) <3. A total of 20 patients (59%) had histologic evidence of Hp infection. One year rate of CR was 77% (70% in the Hp-positive versus 86% in the Hp-negative), with an average remission time of 8.5 months. Using Lugano Staging System, CR was achieved in 77% of patients with limited disease versus 67% in those with advanced disease. In the Hp-positive group, isolated antibiotic therapy led to a CR in 60% of the cases, including a CR in a patient with advanced disease. There was achieved a CR in a patient of the Hp-negative group treated only with isolated antibiotic therapy. The variables Limited Disease, IPI score <3, age, histologic evidence of HP, serum LDH, Albumin and Beta2-microglobuline levels, were not associated with one year rate of CR ($P < 0.05$). At one year there was 1 death (Hp-positive patient).
CONCLUSION: The results confirm the good prognosis and the indolence of MALT lymphoma. The variables studied couldn't predict CR in 1 year, but enhances the idea that patients with early stage Hp-negative MALT lymphoma and with advanced disease, might still benefit from antibiotic treatment.
Disclosure of Interest: None declared

P1667 THE GASTRIC CANCER DEVELOPMENT IN PEPTIC ULCER PATIENTS WITH HELICOBACTER PYLORI INFECTION

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INTRODUCTION: *Helicobacter pylori* (*H. pylori*) is a risk factor for gastric cancer. We investigate the incidence for gastric cancer development in peptic ulcer patients with *H. pylori* infection.
AIMS & METHODS: This was a retrospective study created from chart review for patients who diagnosed by gastric cancer in peptic ulcer patient with *H. pylori* infection between 2003 and 2013. They consisted of 86 gastric ulcer patients and 15 duodenal ulcer patients. Gastric and duodenal ulcer patients were excluded from the analysis because of their limited number.
RESULTS: The prevalence rates of gastric cancer in gastric ulcer with *H. pylori* infection were 3.60% (86/2387) and in duodenal ulcer with *H. pylori* infection were 0.84% (15/1775). Kaplan-Meier analysis showed that the incidence of gastric cancer in duodenal ulcer patients was lower than that in gastric ulcer patients, and the prognosis of gastric cancer in duodenal ulcer patients was poorer than that in gastric ulcer patients (log-rank test, $p = 0.191$). Cox's proportional hazard model denotes the relative risk for duodenal ulcer against gastric ulcer adjusted by pathologic differentiation as 1.71 (95% CI: 1.09-2.70, $p = 0.02$). In univariate and multivariate analysis, pathologic differentiation, stage and cell type were related to gastric cancer in peptic ulcer patients with *H. pylori* infection ($p < 0.05$).
CONCLUSION: In duodenal ulcer patients with *H. pylori* infection, the risk of gastric cancer development was less and the prognosis was poorer than that of gastric ulcer patients with *H. pylori* infection. The prevalence rates of gastric cancer were 3.60% in gastric ulcer with *H. pylori* infection and 0.84% in duodenal ulcer with *H. pylori* infection. The relative risk for duodenal ulcer against gastric ulcer adjusted by pathologic differentiation as 1.71 (95% CI: 1.09-2.70, $p = 0.02$).
Disclosure of Interest: None declared

P1668 THE EFFECT OF *H. PYLORI* ERADICATION ON METACHRONOUS GASTRIC NEOPLASMS AFTER ENDOSCOPIC RESECTION OF GASTRIC DYSPLASIA

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INTRODUCTION: *Helicobater pylori (H. pylori)* infection was closely related in gastric atrophy, intestinal metaplasia (IM), and a progression to dysplasia or cancer. Furthermore, some studies showed that the eradication of *H. pylori* after endoscopic resection (ER) of early gastric cancer (EGC) was helpful to prevent the development of metachronous gastric cancer.(1.2) However, there are no sufficient data about the role of eradication of *H. pylori* after ER for gastric dysplasia.
AIMS & METHODS: The aim of this study was to investigate the effect of *H. pylori* eradication would affect the development of the metachronous gastric neoplasms after ER in patients with gastric dysplasia.
We retrospectively reviewed 1850 patients who underwent endoscopic resection of gastric dysplasia from January 2007 to February 2012 at Severance hospital. We excluded patients with follow-up period of < 2 years and who had not undergone tests for active *H. pylori* infection at the time of endoscopy. Total of 289 patients were enrolled in this study. Then divided them into three groups: those without active *H. pylori* infection (Hp negative group, $n = 131$), those who successfully underwent *H. pylori* eradication (eradicated group, $n = 119$), and those who failed or did not undergo *H. pylori* eradication (non-eradicated group, $n = 39$). The rate of metachronous recurrence after ER was compared.
RESULTS: Metachronous reccurence was diagnosed in 42 patients, including 25 in the Hp negative, 8 in the eradicated, 9 in the non-eradicated group. Median time to metachronous recurrence was 36 months (range, 6-85 months). The incidence of metachronous recurrence was 5.13 cases per 1,000 person-years in the Hp negative group, 1.57 cases per 1,000 person-years in the eradicated group, and 6.07 cases per 1,000 person-years in the noneradicated group. Patients in non-eradicated group had a higher risk of developing metachronous gastric neoplasms than eradicated group (hazard ratio [HR] 3.974, $p = 0.005$).
CONCLUSION: The successful *H. pylori* eradication may reduce the development metachronous gastric neoplasms after ER in patients with gastric dysplasia. Also regular follow-up of test for *H. pylori* infection is important to prevent the metachronous recurrence in those high-risk patients.

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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
SMALL INTESTINAL III – POSTER EXHIBITION – HALL XL

P1669 THE PH IN THE NORMAL GASTROINTESTINAL DECREASE FROM THE TERMINAL ILEUM TO CECUM BY USING "PH CAPSULE" FOR RECORDING SEQUENTIAL IMAGES AND THE PH OF THE GASTROINTESTINAL TRACT

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INTRODUCTION: Before the introduction of capsule endoscopy and double-balloon endoscopy, there were no effective modalities for reliable evaluation of the small bowel. Evans D F reported the measurement of gastrointestinal pH profiles in normal ambulant human subjects by using pH sensitive radiometry capsule in 1988 (Evans D F et al. Gut 1988;29:1035-41). Recently, the SmartPill, a wireless pH, temperature and pressure recording capsule, has been utilized to measure the whole gut transit time. This modality can record gastrointestinal pH, but could not record correct gastrointestinal location, especially ileum into cecum. Evans reported that the pH in the normal gastrointestinal increase in pH from the duodenum to the terminal ileum, decrease in the cecum by using sensitive radiometry capsule. Recently we have designed a new noninvasive modality "pH capsule" for recording sequential images and the pH of the gastrointestinal tract (Iida H, et al. Hepatogastroenterology 2011;59:114).
AIMS & METHODS: The aim of this study was to investigate the pH changes from the terminal ileum to cecum by using the "pH capsule". Ten healthy male volunteers swallowed the "pH capsule" with 50cc water. The "pH capsule" transmitted the acquired images and pH to a recorder unit located outside the body for about ten hours while the subject was fasting.
RESULTS: Ten male subjects completed this study. The intragastric pH was low, and the pH in the small intestine ranged from 7.2 to 8.1 (mean of 7.61). The pH in the terminal ileum (mean of 8.15) significantly decreased in the cecum (mean of 6.60).
CONCLUSION: We could noninvasively monitor sequential images and the pH of the gastrointestinal tract, especially terminal ileum to cecum, with the "pH capsule". Thus, the "pH capsule" is expected to become a valuable tool for the assessment of gastrointestinal pH abnormalities in various kind of diseases with the accurate location and mucosal images of gastrointestinal tract.
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Disclosure of Interest: None declared

P1670 A NOVEL GENE TRANSDUCTION SYSTEM INTO SMALL INTESTINAL ORGANOID ENABLED THE IDENTIFICATION OF THE STEM CELL SUBPOPULATIONS IN A CRYPT

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INTRODUCTION: Recently, two kinds of stem cell population are advocated; +4 quiescent stem cell and Lgr5+ crypt base columnar (CBC) cell by the progress of stem cell research using small intestinal organoids that was generated from a single stem cell by the 3-dimentional culture method. However, single stem cell dynamics in a crypt remains not to be fully elucidated, because plural stem cells exist in a crypt. We therefore hypothesized that the identification of a single stem cell by fluorescent labeling might enable to explore the dynamics and relationship between plural stem cells in a crypt.
AIMS & METHODS: Lentivirus encoding mCherry gene was mixed with matrigel to directly infect the small intestinal organoids. The localization of mCherry positive cells in whole organoids was analyzed by confocal microscope and time-lapse imaging microscope. The cell types of mCherry positive cells were identified by the immunostaining with OLFM4 and Lysozyme.
RESULTS: We have established a lentiviral transduction system into the intestinal organoids to detect mCherry protein expression for a long time, 50 weeks after transduction. Three-dimensional analysis using confocal microscope showed both mCherry -positive and -negative cells in a crypt, which suggested that both mCherry-positive and -negative stem cells might be long lived in the same crypt. Moreover, we found a single mCherry positive cell in a crypt, which was co-localized with stem cell marker: OLFM4. Furthermore, Paneth cells in a crypt were differentiated from both mCherry-positive and -negative stem cells. Time-lapse imaging showed that a single mCherry-positive stem cell in a crypt divided and supplied cells to both crypt base columnar cells and transit amplifying cells. These results suggested that epithelial cells in a crypt might be permanently supplied from independent different stem cells in a crypt but not single stem cell.
CONCLUSION: Our original lentiviral transduction system to mark stem cells might be useful to elucidate the subpopulation of intestinal stem cells in a crypt. Live imaging of single cell in a crypt is useful for the analysis of the stem cell division and maintenance.
Disclosure of Interest: None declared

P1671 NOTCH SIGNALING REGULATES EXPRESSION OF GELSOLIN SUPERFAMILY GENES, GELSOLIN AND SCINDERIN, AND PROMOTES RE-ASSEMBLY OF ACTIN CYTOSKELTON IN HUMAN INTESTINAL EPITHELIAL CELLS

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INTRODUCTION: In our previous study, we have shown that activation of Notch signaling plays an indispensable role in differentiation and proliferation of human intestinal epithelial cells (IECs). Dynamic change of the actin cytoskeleton is regulated by actin-binding proteins, including Gelsolin superfamily proteins, and is critically involved in fundamental cellular processes such as cell adhesion or cell migration. However, the role of Notch signaling in regulation of actin cytoskeleton dynamics remains completely unknown.
AIMS & METHODS: The present study was planned to identify whether Notch signaling may also regulate the dynamic changes or reassembly of actin cytoskeleton in human IECs. To analyze the cellular effect of Notch activation, tetracycline-dependent overexpression of the Notch intracellular domain (NICD) was induced in LS174T or DLD1 cells. Microarray analysis was performed to compare the expression of genes encoding actin-binding proteins, before and after activation of Notch signaling in IECs. Change in gene expression was further confirmed by quantitative PCR or immunoblot analysis. Also, the dynamic change of actin-based cell structures was visualized by phalloidin staining. Finally, assembly of focal adhesion, a cell structure indicating actin- and integrin-mediated cell adhesion to the extracellular matrix, was examined by double staining of phalloidin and paxillin.
RESULTS: Microarray analysis of LS174T cells showed a significant increase in expression of two Gelsolin superfamily genes, Gelsolin and Scinderin, upon Notch activation. Validation of the data by quantitative PCR confirmed significant increase of Gelsolin and Scinderin mRNA expression by Notch activation, in both LS174T and DLD-1 cells. Significant up-regulation of the Gelsolin protein expression was also clearly confirmed by immunoblot analysis. However, in sharp contrast, expression of other Gelsolin family genes, such as Villin or Supervillin remained completely unchanged. Consistent with the up-regulation of Gelsolin and Scinderin expression, phalloidin staining clearly revealed promotion of actin cytoskeleton reassembly by Notch activation, resulting in significant increase of lamellipodia and filopodia formation, but decrease of actin stress fiber formation. Futhermore, double staining of phalloidin and paxillin showed a significant decrease in formation of focal adhesions upon activation of Notch signaling in DLD-1 cells, suggesting decreased cell adhesion, as well as increased cell motility of those cells.
CONCLUSION: Activation of Notch signalling up-regulates expression of Gelsolin superfamily genes, Gelsolin and Scinderin, in human IECs. Such an up-regulation of actin-binding proteins may mediate the promotion of actin reassembly by Notch activation, and subsequently regulate the behavior of IECs, such as cell adhesion or cell migration.
Disclosure of Interest: None declared

P1672 ENTEROHEMORRAGIC ESCHERICHIA COLI TARGET PEYER'S PATCHES VIA LONG POLAR FIMBRIAE

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INTRODUCTION: Enterohemorrhagic *Escherichia coli* (EHEC) are food-borne pathogens associated with diarrhea, hemorrhagic colitis and life-threatening complications such as hemolytic-uremic syndrome. EHEC interact preferentially with the Follicule-Associated Epithelium (FAE) of Peyer's patches (PPs) regions of the distal ileum in humans and translocate across the intestinal epithelium *via* M cells. The Long Polar Fimbriae (LPF), encoded by two *lpf* operons, contribute to epithelial cells adhesion and intestinal colonization.
AIMS & METHODS: To investigate the involvement of LPF in the ability of EHEC strain EDL933 to target PPs, we generated the D*lpfA1,* D*lpfA2,* D*lpfA1*-D*lpfA2* isogenic mutants and trans-complemented them with *lpf*operons.
In vivo interactions with murine PPs were analyzed in ileal loop assays. Mice were infected with a mixture of two bacterial strains, and the numbers of PPs-interacting bacteria were determined using a competitive index analysis. LPF interaction with M-like cells was investigated using the *in vitro* model of specialized M cells.
RESULTS: *Lpf* isogenic mutants (i) were not able to interact with ileal biopsies containing PP compared to the wild type strain in competitive colonization assays, and (ii) did translocate across M cells at levels significantly lower than those observed for the wild type strain. Trans-complementation of the mutants

with the cloned *lpf* operons restored their ability to interact with PPs and M cells, indicating that expression of *lpfA1* or/and *lpfA2* operons is required for interactions with PPs.
CONCLUSION: We conclude that LPF are involved in the interaction of EHEC with murine PPs and are needed for an active translocation across M cell monolayer.
Disclosure of Interest: None declared

P1673 LACTOBACILLUS PARACASEI SUBSPECIES PARACASEI F19 PREVENTS BOWEL SYMPTOMS IN PATIENTS AT LONG-TERM PPI TREATMENT: A RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED CROSS-OVER MULTICENTER STUDY

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INTRODUCTION: Proton pump inhibitors (PPIs) may foster intestinal dysbiosis and related-bowel symptoms.
AIMS & METHODS: Aim of this study was to evaluate the effect of Lactobacillus paracasei subspecies paracasei F19 (LP-F19) on bowel symptoms' onset in patients at long-term PPIs. Patients with typical gastroesophageal reflux disease symptoms were screened. Enrolled patients received pantoprazole 40mg/d for 6 months and were randomly assigned to: 1) LP-F19 for 6 months (LP-F19); 2) placebo for 6 months (PBO); 3) LP-F19 for the first 3 and placebo for the following 3 months (LP-F19→PBO); 4) placebo for the first 3 and LP-F19 for the following 3 months (PBO→LP-F19). Bowel symptoms (bloating, flatulence, abdominal pain) and bowel habit were assessed baseline and monthly.
RESULTS: 100/312 patients were enrolled, 84 of whom completed the study. The percentage of patients who developed at least one bowel symptom at 3-month checkpoint was 4% in the LP-F19 group and 27% in the PBO group ($p = 0.04$). At 6-month checkpoint, the percentage of symptomatic patients increased up to 18% in the LP-F19 and 57% in the PBO group ($p = 0.01$). In details, only the percentage of patients who complained of bloating and flatulence, were significantly higher in PBO group in respect to LP-F19 group. In the LP-F19→PBO group the percentage of patients who developed at least one bowel symptom was 20% during active treatment and increased up to 55% during placebo treatment ($p = 0.05$). Opposite, in the PBO→LP-F19 group, the percentage of symptomatic patients was 48% during placebo treatment and progressively decreased to 14% during active treatment ($p = 0.04$). In details, in the LP-F19→PBO group, the percentage of patients who complained of bloating, flatulence and abdominal pain did not significantly differ in respect to baseline during active treatment. Opposite, during placebo treatment, 40% of patients developed bloating ($p = 0.003$) and 35% flatulence ($p = 0.008$). In the PBO→LP-F19 group, 14% of patients complained of bloating ($p = 0.003$) and 33% of flatulence ($p = 0.008$) during placebo treatment in respect to baseline. Opposite, during active treatment, only 5% of the patients still complained of bloating ($p = 0.02$) and none of flatulence ($p = 0.008$). At multivariate analysis, LP-F19 treatment was the only covariate independently associated with absence of symptoms (OR 0.2; 95%CI 0.09-0.46; $p = 0.0001$). Mean stool frequency/week and stool form significantly changed only during placebo treatment in both standard and cross-over groups.
CONCLUSION: LP-F19 supplementation prevents the onset of bowel symptoms in patients at long-term PPI treatment. In view of the growing number of patients requiring long-term, high-dose PPIs, our results provide evidence for new treatment strategies to reduce the burden of PPI-related intestinal diseases. Further studies to define the best strain, dose, and timing of probiotics are needed.
Disclosure of Interest: None declared

P1674 EVALUATION OF PROBIOTIC AND POSTBIOTIC EFFECTS OF LACTOBACILLUS CASEI DG ON ENTEROGLIAL-DERIVED S100B PROTEIN EXPRESSION AND NITRIC OXIDE PRODUCTION IN HUMAN INTESTINAL BIOPSIES

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INTRODUCTION: Intestinal bacterial translocation is usually increased in inflamed tissues. Postbiotics (probiotic-produced soluble factors) have been proposed to specifically manipulate intestinal functions[1]. We have previously shown that pathogen bacteria-induced release of the enteroglial derived S100B protein plays an active role in nitric oxide (NO)-dependent gut inflammation[2].
AIMS & METHODS: We aim to study the effects, in human intestinal biopsies, of the probiotic *Lactobacillus Casei DG* (LC) and of the postbiotics derived from LC (LC-PB), on *Enteroinvasive Escherichia Coli* (EIEC)-induced NO and S100B secretion and iNOS protein expression. To achieve this goal, rectal biopsies, without macroscopic signs of inflammation, obtained from 7 healthy subjects undergoing screening for colorectal cancer, were stimulated with EIEC and/or with LC or LC-PB, as the following experimental scheme: A) stimulation with EIEC from 0h to 5h (0-5h); B) LC or LC-PB 0-5h; C) [LC or LC-PB] 0-5h + EIEC 2.5-5h; D) EIEC 0-5h + [LC or LC-PB] 2.5-5h; E) EIEC + [LC or LC-PB] 0-5h. After 24 h, S100B release was evaluated by ELISA and NO release and iNOS expression were evaluated by nitrite assays and Western Blot analysis respectively, in stimulated compared to un-stimulated biopsies (control). Data are expressed as mean±SD.
RESULTS: EIEC, but not LC or LC-PB, significantly increased S100B secretion (+3.7±1.1 fold increase vs control; $p < 0.05$). When LC or LC-PB were added to biopsies before, after or together EIEC, S100B secretion was not increased respect to control and, interestingly, LC-PB were significantly more effective in reducing S100B expression (-8.1±0.6, -3.7 ±0.4, -19.1±1.1 fold decrease vs viable LC; $p < 0.05$). In parallel, incubation with EIEC led to a significant increase of iNOS protein expression (+5.6±1.6 fold increase vs control; $p < 0.05$) and of NO secretion (+2.4±0.3 fold increase vs control; $p < 0.05$), that was not observed with LC or LC-PB. When LC or LC-PB were added to biopsy before, after or together EIEC, iNOS expression and NO secretion were similar to control.
CONCLUSION: We showed that both LC and LC-PB are able to decrease EIEC-induced S100B and NO secretion in human biopsies and that LC-PB was more effective in reducing S100B expression than viable LC. Since probiotics may be detrimental in those pathologies where bacterial translocation is increased, with this preliminary report we propose postbiotics as a safer and effective alternative to probiotics.
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Disclosure of Interest: None declared

P1675 XYLOGLUCAN: A NEW AGENT TO PROTECT THE INTESTINAL MUCOSA AND TO PREVENT BACTERIALLY- MEDIATED ALTERATION OF TIGHT JUNCTION PERMEABILITY

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INTRODUCTION: Xyloglucan (XG) is a water-soluble hemicellulose from vascular plants, indigested by digestive enzyme. This polysaccharide has various application areas like drug-delivery technology, food technology and textile industry. It has also been suggested that it may act as a film-forming barrier distributed on the intestinal mucus layer able to protect the mucosa from chemical or bacterial aggression. However until now, no data has yet been published to confirm such hypothesis.
AIMS & METHODS: Aims: Our studies aimed to evaluate both in vitro and in vivo the potency of xyloglucan to prevent the bacterial toxin- induced -increase permeability and the subsequent epithelial cell bacterial invasion.
Methods: A first series of experiments performed *in vitro* on co-cultured CaCo2/ Goblets cells submitted to *E. coli* inoculation, XG was added on the apical site of the bath both preventively and curatively. Changes in tight junction (TJ) permeability was measured by TEER, Lucifer yellow transfer, E. coli adhesion and epithelial cell invasion were counted. In a second series performed in vivo, Wistar rats received orally XG (12.5mg/kg) and 2 h. later were injected IP with LPS from *E. coli*. Jejunal strips were collected 6 hours later for in vitro TJ permeability measurement using FITC-dextran and mucosal myelo-peroxidase (MPO) activity as a marker of inflammation. In a last series, XG was given orally associated or not with gelatin or co-administered with cholera toxin (CT) into isolated jejunal loops in anesthetized rats. Evaluation of CT-induced water secretion was performed 2hours later.
RESULTS: *In vitro,* given preventively XG (2.5mg/200ml), reduced significantly by 78% the degree of *E.coli* mucosal colonization after 30min. Added curatively, 1after *E.coli* inoculation, XG attenuated by 87% the decrease in TEER measured 3h. later. Administered orally 2 hours before LPS, XG (12.5mg/kg) reduced significantly ($P \leq 0.01$) by 81.8% the LPS-triggered increase in permeability and subsequently by 63.2% the increase in mucosal MPO activity. When administered orally 4h earlier (12.5mg/kg) or 12h earlier with gelatin (250mg/kg), XG suppressed CT-induced water secretion. Co-administered locally with CT at dose of 0.75 and 1.25mg/loop, XG reduced (67%) or suppressed respectively, the secretory effects of CT.
CONCLUSION: Both in vitro and in vivo data indicate that xyloglucan has protective effects on intestinal bacterial invasion, alterations of gut permeability and CT-induced intestinal secretion reaching 12h when associated with gelatin. These data support that this compound may be of therapeutic interest in the treatment of infectious diarrhea.
Disclosure of Interest: None declared

P1676 SMALL INTESTINAL BACTERIAL OVERGROWTH MAY INCREASE THE LIKELIHOOD OF LACTOSE, FRUCTOSE AND SORBITOL INTOLERANCE FALSE POSITIVE DIAGNOSIS

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INTRODUCTION: Small intestinal bacterial overgrowth (SIBO) is defined by the presence of an excessive concentration of bacteria in the small intestine. Lactose intolerance (LI), fructose intolerance (FI) and sorbitol intolerance (SI) and SIBO share many gastro-intestinal (GI) symptoms usually attributed to patients diagnosed with irritable bowel syndrome (IBS).
AIMS & METHODS: To evaluate the role and effect of SIBO in the formation of LI, FI and SI symptoms in affected patients. A total of 348 patients with suspected IBS underwent SIBO and LI, FI and SI diagnosis by hydrogen breath test (HBT). 15 gr of lactulose dissolved in 50 ml of water and 50 gr of lactose, 25 grams of fructose and 15 grams of sorbitol dissolved in 250 ml of water were used for SIBO and LI, FI and SI HBT respectively. The test results were considered positive when hydrogen concentration acceded 10 PPM for SIBO and 20 PPM for LI, FI or SI above baseline.

RESULTS: Out of the 348 patients tested for SIBO and LI, 101 (29%) were positive for both tests. Out of the 197 patients tested for SIBO and FI, 17 were positive for both tests. And finally, out of the 196 patients tested for SIBO and SI, 45 were positive for both tests. Out of the 101 SIBO and LI, 17 SIBO and FI and 45 SIBO and SI positive patients, 82 (81%), 14 (82%) and 23 (53%) respectively had an increase of hydrogen measurement above threshold between 30-90 minutes during their LI/FI/SI-HBT, implying SIBO.
CONCLUSION: The fermentation of lactose, fructose or sorbitol in the small bowel due to SIBO may increase the likelihood of LI, FI and SI incorrect diagnosis. We suggest that all symptomatic patients will undergo SIBO testing and eradication if diagnosed positive, prior to LI, FI or SI HBT evaluation.
Disclosure of Interest: None declared

P1677 IS A GLUTEN CHALLENGE REQUIRED TO DIAGNOSE ADULT COELIAC DISEASE IN EQUIVOCAL CASES: A SINGLE CENTRE EXPERIENCE OF 'REAL' CLINICAL PRACTICE

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INTRODUCTION: Coeliac disease (CD) is under diagnosed which may result in significant morbidity. The gold standard for diagnosing CD is the demonstration of villous atrophy. However in some cases there is a strong suspicion of CD but histology is normal or equivocal. In these cases the gold standard is a 6 week gluten challenge and repeat duodenal biopsy. To date there is little clinical data reported in the adult literature for outcomes or effectiveness of a gluten challenge outside of research studies. This study aims to determine the clinical utility of gluten challenge and predictive factors that could be used to aid diagnosis.
AIMS & METHODS: We undertook a prospective analysis of all patients who were asked to undertake a gluten challenge over a 5 year period. Data were recorded from referral to outcome. Presenting characteristics, baseline haematinics, tissue transglutaminase (tTG) and endomysial antibody (EMA) and HLA type were recorded prior to gluten challenge. Repeat coeliac serology and biopsy results were then recorded post gluten challenge. CD diagnosis required an appropriate HLA phenotype, positive coeliac serology and deterioration in duodenal histology.
RESULTS: 64 patients (46 female, mean age 48.8, SD 16.5) were reviewed. 4 (6.3%) declined gluten challenge. 42/60 (70.0%) of patients challenged were HLA DQ2 or DQ8 positive (6 homozygous). 21/60 (35.0%) patients were diagnosed with CD and 32/60 (53.3%) had CD excluded. 7/60 (11.7%) patients were diagnosed with potential CD based on an HLA type compatible with CD and positive serology but a normal duodenal biopsy on gluten challenge.
6/60 (10%) were unable to complete the full 6 week challenge (median 14.5 days) due to gluten induced symptoms. A conclusive diagnosis was made in all 6 of these patients.
Gluten challenge caused an increase in tissue tTG of 50.6% ($p = 0.034$) in patients with CD. No cut off for tTG prior to gluten challenge could be used to diagnose CD. Of 30 EMA negative patients prior to endoscopy 6 (20%) became positive on gluten challenge all of whom were diagnosed with CD. A combination of tTG > 20 times the upper limit of normal and a positive EMA prior to challenge ($n = 7$) had a positive predictive value of 85.7%.
There was no difference in presenting characteristics, baseline bloods or demographics between those diagnosed with CD, potential CD or those who had CD ruled out.
CONCLUSION: No presenting characteristics, blood results or genotype could reliably predict a diagnosis of CD. Increased tTG or new EMA positivity on gluten challenge were associated with CD diagnosis. A gluten challenge will ensure the best chance of recognition or exclusion of patients with CD. A 2 week gluten challenge may be sufficient to make conclusive diagnosis. A shortened gluten challenge could reduce the length of distress to patients with significant gluten induced symptoms and ensure prompt diagnosis.
Disclosure of Interest: None declared

P1678 INCREASED PREVALENCE OF CHRONIC LIVER AND PANCREAS ABNORMALITIES IN PATIENTS WITH CELIAC DISEASE

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INTRODUCTION: It was reported that involvement of the pancreas, liver and biliary tract, including the gallbladder is rare in patients with celiac disease (CD).
AIMS & METHODS: Our aim to find the prevalance of these involvements by using transabdominal ultrasound (US). Additionally, we further characterized pancreas parancyhmal changes by echoendoscopy (EUS). We evaluated our CD clinic's records which includes 198 patients. We used US to show pancreas, liver and biliary tract abnormalities. Then, patients with pancreas abnormalities were further examined by EUS. Patients with recent onset dyspepsia were used as a control group.
RESULTS: Of the 198 patients with CD, 102 had documented US results. There were 102 patients without CD as a control group. All of the patients, 25% in CD and 33% in control were male ($p > 0.05$). The prevalence of abnormalities as follows: liver steatosis, 46% in CD vs 48% in controls ($p > 0.05$); gallbladder polip, 3.9% in CD vs 6.9% in controls ($p > 0.05$); gallbladder sludge&stone, 4.9% in CD vs 11.8% in controls ($p > 0.05$); hepatomegaly, 2.9% in CD vs 28.4% in controls ($p < 0.001$); gallbladder operation, 5.9% in CD vs 8.8% in controls ($p < 0.001$); gastric antrum wall tickness, 4.9% in CD vs 2.0% in controls ($p > 0.05$); hepatic simple cyst, 3.9% in CD vs 2.9% in controls ($p > 0.05$); hemangioma, 3.9% in CD vs 2.9% in controls ($p > 0.05$); chronic liver disease findings, 5.9% in CD vs 0% in controls (p: 0.014); hepatoportal sclerosis 1.0% in CD vs 0% in controls ($p > 0.05$); pancreas parancyhmal changes, 5.9% in CD vs 0% in controls ($p = 0.029$). EUS investigation was performed in all of the patients with paranchymal changes that were found by US. EUS showed major B or minor findings according to the Rosemont classification. None was autoimmune pancreatitis (AIP). Echoendoscopy findings as follows: main duct and side branch dilation, small cysts, pancreas atrophy, hyperechogen stria and foci. Further analysis of the 6 patients with chronic liver disease showed that none had autoimmune or viral serology. One of them showed grade 1 eosephageal varices with portal hypertensive gastropathy findings.
CONCLUSION: Our results showed that chronic type involvement of the pancreas and liver is significantly frequent in patients with CD. Even, cirrhosis with varices was seen. So, CD might be a cause of cryptogenic cirrhosis. Thus, we consider that pancreas and liver abnormalities were underestimated in clinical practice and should be followed to detect progression.
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P1679 DEVELOPMENT OF NOVEL T CELL BASED ASSAYS TO IMPROVE THE DETECTION OF COELIAC DISEASE

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INTRODUCTION: Coeliac disease (CD) is an immune disorder characterized by intestinal pathology with systemic manifestations. Accuracy of CD diagnosis is limited by need for continued ingestion of gluten. Unlike antibodies, memory CD4 T cells can be stimulated to proliferate after low levels of antigen exposure *in vivo* (1,2).
AIMS & METHODS: We developed and compared four *in vitro* assays to detect peripheral blood GSTCs in newly diagnosed CD patients. Subjects on a gluten-containing diet had CD diagnosed by positive anti-tissue transglutaminase (tTG) antibody, appropriate histology and expressed HLA alleles DQ2/DQ8. Whole blood (WB) and/or peripheral blood mononuclear cells (PBMCs) were stimulated with coeliac associated antigens (whole gliadin [WG], deamidated gliadin [DG] and tTG) after which cells and supernatants were analysed for: CD4 T cell expression of lymphocyte activation markers (CD134/CD25), soluble Ox40 ligand (sOx40L) by ELISA, Th1, Th2 and Th17 cytokines (IL-6, TNFα, and IL-17α) by Cytokine Bead Array (CBA) and CD antigen specific cytokine secreting cells from cryopreserved PBMCs by TNFα ELISpot assay.
RESULTS: Six patients with CD and three patients without CD were studied. Detection of % CD4+CD134+CD25+ T cell levels above baseline were present to at least one CD antigen (medians: WG 0.09%, DG 0.04%, tTG 0.11%) in four patients with CD and one patient without CD to antigens DG (0.11%) and tTG (0.13%). sOx40L levels were detected in three patients with CD and one patient without CD. The CBA assay showed increased levels of TNFα to DG antigen in four CD patients (baseline 6.9 pg/ml; stimulated median 13.8 pg/ml, range 7.0-24.2 pg/ml), increased levels of IL-6 to WG antigen in three CD patients (baseline 98.5 pg/ml; stimulated median 130.7 pg/ml, range 101.8-226.1 pg/ml), and increased levels of IL-17α to WG antigen in two CD patients (baseline undetectable; stimulated median 26.6 pg/ml, range 23.9-28.6 pg/ml). However in patients without CD, increased IL-6 and IL-17a levels were also detected whereas TNFα was not, suggesting it may be a more suitable cytokine marker for patients with CD. DG stimulated T cell secretion of TNFa was detected in three CD patients by TNFa ELISpot assay (baseline 6.7 SFU/million cells; stimulated median 49.7 SFU/million cells, range 4.7-55.8 SFU/million cells), whilst no patient without CD had detectable responses.
CONCLUSION: GSTCs can be detected in the peripheral blood of patients with CD using methods to measure memory T cell responses to coeliac associated antigens. Such assays have potential for implementation into future CD diagnostics, but will need improved performance characteristics to be clinically useful.
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P1680 BONE MINERAL DENSITY DIFFERS ACCORDING TO DISEASE PHENOTYPE IN CELIAC DISEASE

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INTRODUCTION: Coeliac disease (CD) is a genetically determined autoimmune condition, with an estimated worldwide prevalence of 1%. It is believed to be the result of an abnormal autoimmune response in susceptible individuals to dietary gluten derived from wheat, rye and barley. Disease phenotype can be

mainly classiffied as typical and atypical. Typical CD patients are defined as patients having diarrhea as predominant symptom.
AIMS & METHODS: The evidence for reduced bone mineral density (BMD) in CD is well known although it is not known whether there is a difference between disease phenotypes. This study has aimed to compare bone mineral densities of typical and atypical CD patients.
Between February 2008 and April 2014, 102 patients with CD were prospectively included into the study. After serologic screening of CD by antigliadin antibody (AGA) IgA, AGA IgG and antiendomysium antibody (EMA), duodenal biopsies were obtained once a positive serology has been reported to confirm the diagnosis. Typical CD patients are patients presenting with diarrhea and patients referring with complaints other than diarrhea are classified as having atypical CD. Both groups are evaluated in terms of BMD results and routine biochemistries.
RESULTS: A total of 102 patients with CD were included in this study. Patients were assigned into two groups as atypical and typical form of CD. Comparision of mean biochemistry parameters and bone mineral density in patients with typical and atypical celiac patients are shown in Table 1.
Table 1: Comparision of mean biochemistry parameters and bone mineral density in patients with typical and atypical celiac patients.

	Typical (n = 38)	Atypical (n = 64)	P
Age (years)	35.42±11.31	34.76±12.15	NS
Body Mass *I*ndex kg/m^2	21.36±4.02	23.38±4.64	NS
Hip T score	-1.26±1.04	-0.89±1.05	NS
Vertebral body T score	-1.64±1.34	-0.99±1.17	<0.05
Serum Calcium (mg/dl)	9±0.62	9.09±0.71	NS
Serum Phosphorus (mg/dl)	3.57±0.55	3.39±0.636	NS
25-hydroxyvitamin D (ng /ml)	16.04±11.8	15.96±8.68	NS
Parathyroid Hormone (pg/ml)	100.92±78.6	68.4±46	<0.05

CONCLUSION: Low BMD, osteopenia, and osteoporosis are frequent complications of CD. In this study vertebral T score was found to be significantly lower and parathyroid hormone levels significantly higher in typical CD patients. Calcium malabsorption seems to play an important role in low bone mineral density in CD but the apparent difference between typical and atypical CD patients suggest there should be another mechanism in typical CD.
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P1681 METABOLIC SYNDROME AND HEPATIC STEATOSIS IN COELIAC PATIENTS ON GFD

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INTRODUCTION: BACKGROUND: Several studies have shown that weight changes are common in patients affected by coeliac disease (CD) after the adoption of a gluten-free diet (GFD). However data on the prevalence of metabolic syndrome (MS) and hepatic steatosis (HS) in patients with CD on free diet and after GFD are still scarce.
AIMS & METHODS: 1) to assess the prevalence of MS in CD patients at time of diagnosis and 1 year after starting GFD 2) to evaluate the prevalence of HS in CD patients before and after GFD. Between January 2011 and March 2013, we enrolled all consecutive patients with newly diagnosed CD who were referred to our third-level CD Unit. All patients were investigated about waist circumference with BMI, blood pressure, lipid profile (HDL cholesterol, triglycerides), levels of glucose, aspartate (AST, U/l), alanine aminotransferase (ALT, U/l) and HS. MS diagnosis was made according to International Diabetes Federation criteria (IDF) for European countries. HS diagnosis was performed by ultrasonography (US) in accordance to the current literature. The prevalence of MS and HS was revaluated after 12 months of GFD. Statistical analysis was performed by using X^2, Mann-Whitney U test, Wilcoxon signed-rank test and odd ratio (O. R.) when indicated. The differences were considered significant with a $p < 0.05$.
RESULTS: Finally, 98 CD patients (29 men, 69 women; mean age: 35.7 years) were analysed at diagnosis and after 1 year of GFD. At diagnosis, only 2 CD patients (2%) fulfilled the criteria for MS while 29 patients (29.5%) met the diagnostic criteria of MS after 12 months of GFD ($p<0.01$; O. R. 20). The comparison of MS sub-categories 1 year after GFD respect to the baseline showed that 72 *vs* 48 patients exceeded waist circumference cut-off ($p<0.01$; O. R. 2.8), 18 *vs* 4 patients showed high values of blood pressure ($p<0.01$; O. R. 5.2), 25 *vs* 7 patients exceeded glycemic threshold ($p=0.01$;O. R. 4.4), 34 vs 32 CD patients had reduced levels of HDL cholesterol ($p=0.7$) and 16 *vs* 7 patients had high levels of triglycerides ($p=0.05$). Mean BMI increased after GFD initiation (22.9 kg/m^2 *vs* 24.1 kg/m^2; $p=0.01$). At time of CD diagnosis, 18 out of 98 patients showed HS at US (18%). One year after starting GFD, 28 out of 98 patients showed HS (18% vs 28.5%; $p=0.1$); HS was present in 19 out of 29 patients with MS and 9 of 69 CD patients without MS (65% vs 13%;$p<0.01$;O. R.19).
CONCLUSION: CD patients show a high risk of MS and HS 1 year after starting GFD. We suggest a deep nutritional assessment at diagnosis and during the follow-up of patients affect by CD.
Disclosure of Interest: None declared

P1682 LEVEL OF ANTI-TRANSGLUTAMINASES IN PREDICTING THE MARSH GRADE FOR THE DIAGNOSIS OF ADULT CELIAC DISEASE

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INTRODUCTION: The new ESPGHAN guidelines for diagnosis of pediatric celiac disease (CD) suggest to avoid intestinal biopsy in genetically predisposed and symptomatic individuals with positive anti-endomysial antibodies (EMA)/ anti-tissue transglutaminases (a-tTG). On the other hand, duodenal biopsy (in combination with positive a-tTG and EMA) remains the *gold standard* in adults with suspected CD.
AIMS & METHODS: To assess the cut-off values of a-tTG able 1) to predict the presence of a duodenal histology (Marsh ≥2) diagnostic for CD; 2) to predict the presence of villous atrophy (Marsh 3) in CD. From September 2011 to March 2014 we performed an observational prospective study including all consecutive adult patients referred to our third-level centre for suspected CD. All subjects were tested for EMA (absent/present) and a-tTG (U/ml). All patients with positive antibodies underwent upper endoscopy with duodenal biopsies/histology. CD diagnosis was made in presence of Marsh ≥ 2 histology associated with both a-tTG IgA > 7 U/ml and positive EMA. Furthermore, a ROC curve was constructed in order to detect the best cut-off of specificity of a-tTG level able to predict the presence of Marsh ≥ 2 and Marsh 3 on duodenal histology. Sensitivity, specificity, PPV and NPV of a-tTG level were calculated by using SPSS statistical software. In addition, the presence of any disease other than CD found on upper endoscopy was recorded.
RESULTS: The study included 310 patients with suspected CD (M/F: 35%/ 65%; mean age 33.6 years) in presence of both positive EMA and a-tTG. Final histology showed: Marsh 1 in 27 patients (8.7%), Marsh 2 in 11 subjects (3.5%) and Marsh 3 in 272 cases (87.7%). The best cut-off value of a-tTG in predicting Marsh ≥2 histology was 45 U/ml (sensitivity 70%; specificity 100%; PPV 100%; NPV 79%) while the best cut-off in predicting villous atrophy (Marsh 3) was 62.4 U/ml (sensitivity 69%, specificity 100%; PPV 100%; NPV 31%). In addition, we found other endoscopic findings: reflux-related esophagitis in 38 patients (12%), hiatal hernia in 45 cases (14%), mild/superficial gastritis in 113 subjects (36%), atrophic gastritis in 5 cases (1.6%).
CONCLUSION: CD diagnosis could be performed without biopsy/histology in adult patients with positive EMA and a-tTG levels > 45 U/ml. A a-tTG level > 62.5 is diagnostic for villous atrophy. These results could improve the diagnostic work-up of CD with a significant reduction of diagnosis-related costs.
Disclosure of Interest: None declared

P1683 PERSISTENCE OF VILLOUS ATROPHY AND IRON-DEFICIENCY ANEMIA IS FREQUENTLY OBSERVED IN ADULT PATIENTS WITH CELIAC DISEASE AFTER AT LEAST ONE YEAR OF GLUTEN FREE DIET

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INTRODUCTION: Iron-deficiency anemia is a frequent manifestation of celiac disease (CD), often leading to the diagnosis of the disease. Few studies look at the evolution of anemia after a gluten free diet (GFD). The persistence of villous atrophy (VA) and its connection to the improvement of anemia was also rarely studied.
Goal of our work: to describe the incidence of anemia with hypoferritinemia after at least a year of GFD in patients with CD, depending on the presence or absence of persistent VA.
AIMS & METHODS: In a cohort of 655 patients with a diagnosis of CD, followed at the Hôpital Européen Georges Pompidou in Paris, France between the year 2000 and 2012, we have analyzed 262 patient records, (40% of the cohort), of which 158 had duodenal biopsies after at least a year of GFD (after excluding all patients with refractory celiac disease) and 120 patients had a hemoglobin level before and after a GFD.
RESULTS: Among the 120 patients with available hemoglobin levels before and after GFD (98 women, 22 men, mean age of diagnosis 28 yrs.), 46 (38.3%) had anemia at the time of diagnosis (40.8% of women and 27.27% of men). After a year of GFD, 27 (22.5%) had persistent anemia.
Among the 158 patients with available duodenal biopsies after at least a year of GFD (122 women, 36 men, mean age of diagnosis 28 yrs.), 70 (44%) had persistent VA, varying from partial to subtotal, after GFD, and 88 (56%) showed no more atrophy. Anemia was found in 20 patients (28.57%) with persistent VA, and in 11 patients (12.5%) who had villous regrowth ($p=0.015$; OR: 2.78). Hypoferritinemia was found in 23 patients (33%) with persistent atrophy, and in 21 patients (24%) with villous regrowth ($p=0.217$; OR: 1.55). Consistent observance of GFD was found in 48 patients (69%) with persistent VA, and in 62 patients (71%) without atrophy (NS). Among the 20 patients with residual atrophy and anemia, 9 patients (45%) had inadequate GFD observance.
CONCLUSION: After at least a year of GFD, 22.5% of the patients in our series had iron-deficiency anemia, and 44% had persistence of VA (after excluding refractory CD). Some involuntary errors in GFD might explain this finding in 30% of cases, but there seem to appear a subgroup of patients who have no villous regrowth and have more frequent iron-deficiency anemia in spite of strict

GFD. These patients might beneficiate from intravenous iron therapy. The future and follow-up of these asymptomatic patients, but with no villous regrowth, needs to be evaluated, particularly regarding concerns of lymphomatous complications (1).

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Disclosure of Interest: None declared

P1684 RAISED INTRAEPITHELIAL LYMPHOCYTES IN THE PRESENCE OF NORMAL SMALL BOWEL MUCOSA: CONFIRMATION OF COELIAC DISEASE IN CLINICAL PRACTICE

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INTRODUCTION: Raised intraepithelial lymphocytes (IEL) (>30-40 IEL/100 enterocytes) in small bowel (SB) mucosa is most commonly associated with coeliac disease (CD) when accompanied by distorted villous architecture. In addition to CD, there are various other causes of raised IEL including NSAIDs, autoimmune conditions, tropical sprue, H pylori associated gastritis, parasitic or viral infections and intestinal lymphoma. It is recommended that patients who have raised IEL without distorted villous architecture (Marsh classification Stage 1 criteria) undergo further serological testing along with HLA DQ2/DQ8 genotyping to assist in the diagnosis of CD.

AIMS & METHODS: The aim of the study was to determine the further assessment in clinical practice of patients with raised IEL in otherwise normal SB biopsies to confirm the diagnosis of CD.

A single centre, retrospective analysis of patients with the histological finding of raised IELs on distal duodenal (D2) biopsies in a district general hospital in north London over a two year period between March 2012 and March 2014 was performed. A database of patients with raised IEL was obtained from the hospital histology database and data on the patients coeliac antibody result, symptoms, diagnosis and management was scrutinized using the hospital's electronic patient record system.

RESULTS: 121 patients had raised IEL on D2 biopsy specimens. 58 of these patients had a confirmed diagnosis of CD with villous atrophy. The remainder (63) had raised IEL with preserved villous architecture. 48/63 patients were negative for coeliac antibodies, 1 was positive and 14/63 (22.2%) were not tested. 15/63 (23.8%) were initiated on a gluten free diet and of this, 4 did not report an improvement in their symptoms despite adherence to the diet. Only 2 patients had HLA DQ2/DQ8 testing to aid in the diagnosis of CD. A final diagnosis of CD was made in 11/63 (17.5%) patients meeting Marsh 1 criteria. 32/63 (50.8%) patients had a diagnosis of gastrooesophageal reflux disease (GORD) including 10 patients (15.9%) with H pylori associated gastritis. H pylori was not tested in 13/32 patients with GORD (40.6%). A third of patients (20/63 = 31.7%) with raised IEL and normal SB mucosa did not undergo any further specific investigation to elucidate the cause of the raised IEL.

CONCLUSION: We conclude that there is marked variability in management of patients following the findings of raised IEL with normal SB mucosa. A fifth of patients did not have coeliac antibody tested and only 2 patients had HLA DQ2/DQ8 genotype assessment to affirm or deny association with CD. Latent CD was diagnosed in almost a fifth (17.5%) of patients with raised IEL and preserved villi. GORD and H pylori gastritis were present in half of the patients with this histological finding. We recommend that all patients in whom raised IEL is identified have coeliac serology and HLA DQ2 DQ8 testing to exclude CD prior to entertaining other diagnoses in clinical practice.

Disclosure of Interest: None declared

P1685 PROMOTER REGION IL-16 GENE POLYMORPHISM IN WHIPPLE'S DISEASE

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INTRODUCTION: Whipple's disease (WD) is a rare chronic systemic disorder caused, in genetically predisposed subjects, by *Tropheryma whipplei*, a common bacterium widespread in the environment [1]. The relevance of genetic predisposition in WD is shown by the association with HLA alleles DRB1*13 and DQB1*06 and by the demonstration that in patients with WD the cytokine genetic profile is skewed toward a Th2 and Treg response [2,3]. Since IL-16 is involved in hampering the development of a protective macrophagic response against *Tropheryma whipplei* [4], we investigated whether the genetic background of IL-16 is different between patients with WD and controls.

AIMS & METHODS: Thanks to the European Consortium on WD (QLG1-CT-2002-01049), rs 4778889, a polymorphism of the promoter region of IL-16 gene, was studied in 80 patients with WD and in 74 healthy controls using the PCR-real time technique; the frequencies of alleles and genotypes were then compared. Levels of serum IL-16 protein were also tested by means of an ELISA technique in samples from the same 74 healthy controls; a possible relationship between genotype and levels of serum IL-16 was investigated.

RESULTS: The wild type T allele was found in 138/160 (86%) patients with WD and 114/148 (77%) controls (p = NS for Chi squared test). TT genotype was found in 58/80 (72.5%) patients with WD and 44/74 (59.5%) controls (p = 0.08 for Chi squared test); no relationship was found between levels of serum IL-16 and genotypes.

CONCLUSION: IL-16 gene polymorphisms have already been found associated with different diseases [5]. Despite this, a relationship has not yet been found between types of polymorphism and serum levels of IL-16 protein. Although TT genotype seems to be more frequent in patients with WD than in controls, our results did not reach statistical significance and do not support an association. These very preliminary results need to be expanded to hopefully reach statistical significance.

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P1686 BIOCHEMICAL DIAGNOSIS OF BILE ACID DIARRHOEA USING FGF19

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INTRODUCTION: Bile acid diarrhoea (BAD) is a common and less acknowledged cause of chronic watery diarrhoea. The 7-day radiolabled ^{75}Selenium homocholic acid taurine (SeHCAT) test is not generally available, and it is cumbersome and expensive. Patients suffering from undetected BAD have a poor quality of life and are withheld effective therapy with sequestrants. New insight into the regulation of bile acid physiology have identified fibroblast growth factor FGF19 as one possible marker of BAD and demonstrated a correlation with SeHCAT. FGF19 concentrations are easily measurable but subject to diurnal variation and postprandial increase. Further studies of FGF19 as a test for BAD therefore are warranted.

AIMS & METHODS: To confirm the association between SeHCAT and FGF19 in a prospective patient series, to examine the inter- and intra-individual variation and effect of cholecystectomy on FGF19 levels, and to explore whether the overlap between normal and individuals with BAD could be reduced by measuring the meal induced change in FGF19. FGF19 was measured by commercially available quantitative sandwich enzyme immunoassay technique before and one hour after meals and after 1 week in healthy volunteers, in patients with previous diagnosed BAD or cholecystectomy, and in consecutive patients referred to SeHCAT. The median (range) FGF 19 values are given as pg/mL. No correction for cholesterol values or weight was performed. The interassay variation was 9.6 % in our laboratory.

RESULTS: The results are depicted in the table. The median FGF19 was lower for patients with BAD with a wide overlap. The least squares linear correlation coefficient r = 0.5 for the relation between SeHCAT and FGF19 in the prospective series in which the breakfast induced increase in FGF19 did not differ significantly (Mann-Whitney). Neither single values nor meal induced changes in FGF19 could predict or rule out BAD. The inter-individual variation of fasting FGF19 values in all 56 participants was large.

Median (range)	*Healthy volunteers*	*Previous BAD*	*Cholecystectomy*	***Prospective SeHCAT***	
				≤10%	***> 10%***
N	10	8	12	9	17
Fasting	**94** (50 – 291)	**41** (12 – 130)	**71** (25 – 286)	**62** (14 – 91)	**103** (24 – 287)
Change after breakfast	**17** (-153 – 67)	**8** (3 – 66)	**39** (-94 – 141)	**4** (-30 – 20)	**36** (-136 – 435)
Before lunch	**134** (86 – 236)	**75** (21 – 210)	**108** (69 – 1102)	n.a.	n.a.
Change after lunch	**26** (-15 – 105)	**8** (-71 -51)	**7** (-143 – 76)	n.a.	n.a.
Diff. between fasting values	**44** (-211 – 294)	**13** (183 – 593)	**10** (-150 – 245)	**4** (-21 – 135)	**4** (-220 – 245)

CONCLUSION: While the overall results confirm that FGF19 is lower in patients with BAD, the inter- and intra-individual variation of FGF19 is large. Neither fasting nor single postprandial values of BAD could identify patients with BAD. The utility and timing of FGF19 values as a diagnostic test for BAD using a more powerful and uniform stimulation of the bile acid transporter should be tested. Analysis of area under the curve of FGF19 values following stimulation and combination with other markers such as C4 should be included.

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Disclosure of Interest: None declared

P1687 IN IRRITABLE BOWEL SYNDROME THERE IS NO SIGNIFICANT ASSOCIATION BETWEEN FRUCTOSE MALABSORPTION AND INTOLERANCE AND THE FRUCTOSE TRANSPORTER, GLUT5 AND GLUT2, PROTEIN OR MRNA EXPRESSION LEVELS

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INTRODUCTION: Food intolerances are a major complaint in IBS. Fructose intolerance prevalence in IBS is up to 70%, but the causative mechanism is unknown (1). Fructose is transported across the intestinal epithelia by glucose transporters 5 (GLUT5, Slc2a5) and 2 (GLUT2, Slc2a2) in the apical and basolateral membranes, resp.(2). In mice, deletion of GLUT5 resulted in malabsorption of dietary fructose and typical signs of intolerance (3). Several of the postulated underlying mechanisms in IBS, e.g. inflammation and stress, reduce GLUT5 expression (2) Recently, no group differences in GLUT5 and GLUT2 protein and mRNA expression in IBS patients with fructose intolerance and controls were shown (4).
AIMS & METHODS: To further analyze the relationship between fructose-associated symptoms in IBS patients with malabsorption, a correlative analysis with GLUT5 and GLUT2 protein and mRNA expression levels was performed. Duodenal biopsies were obtained in 11 male or female IBS patients with fructose malabsorption and intolerance, diagnosed by breath testing after 8h fasting and ingestion of 35g fructose. Malabsorption was characterized by an increase of $H2 > 20$ppm or $CH4 > 10$ppm in breath and intolerance was defined by a positive GI-symptom index within 5h of fructose ingestion. 15 matched healthy subjects aged between 18 and 60 years were used as controls. Coeliac's disease and IBD were excluded. mRNA for GLUT5 and GLUT2 was quantified by multiplex RT-qPCR, and expressed as a ratio of β-actin. GLUT5 and GLUT2 protein expression level were determined by Western Blot relative to alpha-tubulin. Analysis was by Spearman Rank correlation and Mann-Whitney test for group comparisons.
RESULTS: The maximum H2 and CH4 concentrations across all individuals did not correlate with either GLUT5 or GLUT2 mRNA or protein expression levels ($r < 0.14$, $p > 0.48$). There were no significant group differences in GLUT5 mRNA expression levels between fructose intolerant IBS patients (median: 0.18 (IQR 0.13-0.21)) and controls (0.17 (0.12-0.19))($p > 0.05$). Respective GLUT2 mRNA expressions were 0.26 (0.20-0.31) and 0.26 (0.19-0.31)($p > 0.05$). There were also no significant group differences in GLUT5 protein expression between patients (0.95 (0.52-1.68) and controls (0.95 (0.59-1.15))($p > 0.05$). Respective GLUT2 protein expression levels were 1.56 (1.06-2.14) and 1.35 (0.96-1.79)($p > 0.05$).
CONCLUSION: Duodenal GLUT5 and GLUT2 mRNA and protein expression did not correlate with fructose malabsorption characterized by classic breath testing, and did not differ significantly between fructose-intolerant IBS patients and healthy controls. Our results suggest that human fructose intolerance or malabsorption may not be associated with marked changes in GLUT5 and GLUT2 mRNA and protein expression.
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Disclosure of Interest: None declared

P1688 HEADACHE DURING LACTOSE BREATH TEST: IS THERE ANY RELATIONSHIP?

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INTRODUCTION: Lactose malabsorption (LM) consists of the incomplete absorption of lactose, mainly due to lactase deficiency on the brush border. While generally well-tolerated, a certain rate of lactose malabsorbers may experience symptoms (diarrhoea, abdominal pain, bloating, and flatulence) characterizing the so-called lactose intolerance (LI). Therefore, LI commonly shows a clinical overlap with Irritable Bowel Syndrome (IBS). Headache affects IBS patients with an estimated OR of 2.66 according to previously published studies, showing a range of similar comorbidities such as fibromyalgia, depression, insomnia. Thus, several authors support the idea that both headache and IBS are central pain-related disorders. We investigate the onset of headache during the LBT, and a possible correlation with lactose malabsorption.
AIMS & METHODS: We enrolled 93 (74 F/19 M; mean age 42±15 yrs) outpatients who perform a LBT in our Gastroenterology Unit according to the guidelines. Patients were asked to report on a Visual Analogue Scale the intensity of usual headache, before lactose administration and after the end of the test. We considered as significant an increase of headache in VAS peak during the test > 10 mm (dVAS). A positive LBT was considered with a peak > 20 ppm in H_2 excretion over baseline. Statistical analysis was performed with Pearson's correlation test and with χ^2 test.
RESULTS: 67 out of 93 (72%) patients result lactose malabsorbers, while 53% (49 out of 93) referred a headache worsening. Within the group of lactose malabsorbers, headache worsened in 50.7% patients compared to 57.7% in non-malabsorber subjects ($p = 0.36$). More interestingly, we observed that in the subgroup of patients with a habitual headache (VAS > 30 mm; 41 subjects) there is a significant worsening of headache during the test compared to the subgroup with a non habitual headache VAS ≤30 mm (70.7% vs 38.5%; $p = 0.003$), regardless of the breath test result. A significant correlation was observed between habitual-headache VAS and headache-during-the-test VAS ($r = 0.313$; $p = 0.02$). No significant correlations were observed between the VAS increase and H_2 nor CH_4 excretion.
CONCLUSION: We did not find any correlation between headache and lactose malabsorption. Although, we observed that the majority of patients undergoing a LBT complain of headache and the rate dramatically increases among the patients usually suffering from headache. We are not able to determine whether the onset of headache or its deterioration are linked to the load of lactose or prolonged fasting. We think that this data should be taken into account, since we suppose that the onset of clinically relevant headache during a LBT could affect compliance in the correct execution of the test and maybe lead to an overestimation of classic LI symptoms. Moreover, the onset of headache might be a cause of premature suspension of LBT.
Disclosure of Interest: None declared

P1689 PERCEPTION OF LACTOSE INTOLERANCE IMPAIRS HEALTH RELATED QUALITY OF LIFE

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INTRODUCTION: Changes in health impacts well-being, which is perceived as an impaired health related quality of life (HRQOL). It is debated whether adult lactose malabsorption is a normal situation or a pathological condition. In any case, the symptoms that people attribute to lactose intolerance or malabsorption have great relevance as they are associated with a lower consumption of calcium/vitamin D and a lower bone density. In addition, it is not known if malabsorption or intolerance to dairy products is associated with a loss of HRQOL.
AIMS & METHODS: Our aim was to determine the HRQOL based on the perception of tolerance to lactose and on the objective determination of the absorption of lactose. METHODS: Prospective, observational, cross-sectional study in a cohort of patients referred to assess absorption of lactose. After signing the informed consent, patients completed a validated questionnaire to determine the perception of symptoms of intolerance during their regular consumption of dairy products at home and a visual analogue scale 0-100 generic measure of quality of life (VAS). Afterwards, a standardized hydrogen breath test with 50 g lactose was performed. At the end of the breath test, the questionnaire was administered again to determine the intensity of symptoms after the lactose overload in the lab.
RESULTS: 173 patients were included (median age 42 y, F/M 132/41). 77 (44 %) of patients considered themselves lactose intolerants and that perception was associated with avoidance of dairy consumption (56 % of self-defined intolerants avoid dairy intake vs only 6 % of self-defined tolerants). Self-perception of intolerance was associated with lower scoring of the VAS (median of 60 vs 70 scored by tolerant, $p < 0.01$). In contrast, lactose malabsorption established by a positive hydrogen lactose test was not associated with dairy avoidance (36 % of malabsorbers avoid dairy vs 32 % of absorbers). However, scoring of VAS was also significantly lower in malabsorbers than in absorbers (60 vs 70 respectively, $p < 0.001$).
CONCLUSION: Subjective perception of lactose intolerance affects the decision to avoid dairy even more than objective malabsorption. However, both the self-perception of lactose intolerance and the objective lactose malabsorption are associated with poorer perceived quality of life.
Disclosure of Interest: None declared

P1690 GALLSTONES, LACTOSE MALABSORPTION AND METHANOGENIC FLORA: A STRANGE TRIO

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INTRODUCTION: Cholelithiasis, is defined as the presence of stones in the gallbladder, is one of the most common digestive diseases, affecting 9-19 % of the general population, with a female prevalence. The most common symptom is postprandial biliary colic, characteristic for localization, duration and intensity. Cholecystectomy, usually laparoscopic, is the definitive treatment of choice. The altered composition and excretion of bile in the duodenum is very irritating to the lining of the intestines, altering the brush border with a possible interference on the lactose absorption.
AIMS & METHODS: The aim of this study was to assess the prevalence of lactose malabsorption through a H2/CH4 lactose breath test (LBT) in subjects affected by gallstones.
Twenty (4M/16F; mean age 55±8 yrs) subjects, which would undergo cholecystectomy in the following month for gallstones, have performed a H2/CH4 LBT in our Gastroenterology Unit according to the guidelines. We have considered a positive LBT when there was a peak > 20 ppm over baseline.
RESULTS: 14 out of 20 (70%) pts resulted lactose malabsorbers with a mean peak value of H2 of 73±23 ppm.

The most interesting data was that 90% (18/20) of these pts produced high levels of CH4, with a mean basal value of 8±5 ppm and a mean peak value of 28 ± 12 ppm.
CONCLUSION: We found a high prevalence of lactose malabsorption in pts affected by gallstones, confirming the hypothesis that an alteration of bile composition could destroy the lactase enzyme on the brush border.
The high prevalence of methanogenic flora observed in these pts could be a cause or a consequence of the formation of gallbladder stones. Further studies are needed to better understand this interesting findings.
Disclosure of Interest: None declared

P1691 THE EFFECT OF GLUTEN ON SOME GASTROINTESTINAL FUNCTIONS IN HEALTHY VOLUNTEERS: A STUDY OF GASTRIC AND GALLBLADDER EMPTYING AND COLONIC FERMENTATION

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INTRODUCTION: Gluten is the main protein complex of wheat and represents a complex substance on both chemical and genetic grounds. The exposure to gluten in genetically predisposed subject determines the onset of celiac disease, a frequent condition characterized by increased comorbidity and mortality. However, gluten exposure may cause a spectrum of disorders, involving different organs and recently it was suggested to be responsible for a condition characterized by a complex clinical presentation involving both the intestinal tract and extraintestinal organs defined non celiac gluten sensitivity (NCGS) (1). Besides un unblinded evaluation of intestinal fermentation (2), in healthy volunteers (HV) the response to a gluten-containing (GCM) in comparison to a gluten-free meal (GFM) was not yet evaluated.
AIMS & METHODS: Therefore, in a group of HV, we analyzed the effect of a GCM and a GFM on gastric and gallbladder emptying time and intestinal fermentation.
In a group of 40 HV a preliminary evaluation of gluten recognition in the meal was performed. Then 18 HV (6 female, median age 25.7±2.4 ys, range 21-29) on separate days at least ten days apart, underwent ultrasonographic measurement of gastric and gallbladder emptying time after a GCM and a GFM. In 16 HV (11 female, median age 24.5±3.2 ys, range 21-30) measurement of breath hydrogen excretion (sampling every 15 min for 7 hours) after a GCM, a GFM and after a GFM added of powdered gluten was performed in order to evaluate intestinal fermentation. All the evaluations were performed in a random order, according to a crossover protocol. Presence and severity of symptoms were monitored during all the tests with VAS (0-10).
RESULTS: The recognition of GCM and GFM was similar (21/40 versus 23/4, p = NS). After GCM, presence and severity of symptoms was similar than after GFM. After both meals, the mean parameters of gastric and gallbladder emptying were similar. Hydrogen peak (12.5±7.3 vs 6.5±5.1 ppm, $p<0.01$) and cumulative breath excretion (2139±1720 vs 989±680 ppm x min, $p<0.01$) was significantly higher after GCM than after GFM. Adding gluten powdered to GFM did not modify intestinal fermentation (peak of breath H2 4.4±1.8 ppm, AUC 984±342 ppm x min).
CONCLUSION: Gluten doesn't modify gastric and gallbladder kinetics, but induces differences in the fermentation process at colonic level even if it didn't increase the symptoms. It is possible that, at least in a subgroup of patient, alterations of visceral sensitivity may represent a co-factor in the pathophysiology of symptoms after gluten ingestion.
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P1692 FOUR CASES OF SEVERE OLMESARTAN SPRUE-LIKE ENTEROPATHY

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INTRODUCTION: Olmesartan is an angiotensin-II antagonists use in the treatment of arterial hypertension. In 2012 it was described the first case of spruelike enteropathy related to this antihypertensive.
AIMS & METHODS: To present 4 cases that are clinical and histological compatible (figure 1) with spruelike enteropathy related to olmesartan. The clinical characteristics and evolution of patients are summarized in table 1.
RESULTS: The 4 cases presented the clinical features of the entity described as olmesartan spruelike enteropathy, with chronic diarrhea, associated clinical manifestations, injury to the duodenal mucosa and especially by clinical and histopathologic improvement after the removal of olmesartan.
Clinicians should be aware of olmesartan as a potential drug than can cause severe chronic diarrhea and severe spruelike enteropathy.
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Disclosure of Interest: None declared

P1693 NEGLECTED PREDISPOSING CONDITIONS IN THE CONTEXT OF BILE ACID DIARRHOEA

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INTRODUCTION: Bile acid diarrhoea (BAD) associated to diseases other than those of the ileum is known as BAD type 3. A variety of diseases are known to be associated with bile acid diarrhoea type 3, though the mechanisms are not always well understood. There is a degree of awareness of BAD in the context of post-cholecystectomy diarrhoea and microscopic colitis, and these predisposing conditions have been included in previous studies. However, where BAD is not idiopathic, there is less information as to the prevalence of reduced bile acid turnover rate (as measured by the ^{75}SeHCAT test) in other diseases.
AIMS & METHODS: Our aim was to study a population with BAD, with special consideration for bile acid turnover rates of those with amyloidosis, pancreatic disease, upper gastrointestinal (GI) resection (not including the ileum) and GI radiotherapy. These represent conditions known or suspected to be associated with BAD, but where the investigation by the ^{75}SeHCAT test is not commonly considered. Medical records in patients investigated with ^{75}SeHCAT for chronic diarrhoea at a large tertiary hospital since 1989 were reviewed, and any patients with the diagnoses above noted. The ^{75}SeHCAT of these patients was compared to 29 previously published healthy controls, both as a unified group and as individual diagnostic groups using Mann-Whitney U. ^{75}SeHCAT retention on day 7 (S7) < 10% was considered abnormal.
RESULTS: Despite the small number of patients referred with the aforementioned diagnoses, all diagnoses showed significantly lower ^{75}SeHCAT retention than controls. Median S7 values were significantly lower in all groups other than amyloidosis. However, the patients with amyloidosis exhibited universally low retention.

Table to abstract P1692
Table 1 Clinical characteristics and evolution. VA, villous atrophy; CH, crypt hyperplasia; IEL, intraepithelial lymphocytes

Age	Sex	Weight loss (kg)	Doses (mg)	Years of treamtent	Evolution after drug withdrawal	HLA	Duodenal histology at diagnosis	Duodenal histology after drug withdrawal	Colon histology
78	F	22	40	2	Improvement	DQ2 DQ8	Total VA total and IEL	Partial VA and few IEL	Nonspecific inflammation
59	M	20	40	5	Improvement	DQA1 DQB1	Total VA, IEl, CH, eosinophilia and lymphoid follicular hyperplasia	Remission of atrophy	Collagenous colitis
69	M	15	40	3	Improvement	DQA1 DQB1	Partial VA	Histological improvement	Not performed
53	F	12	40	1,5	Improvement	DQA1 DQB1	Partial VA, IEL, CH	Pending outcome	Pending outcome

Diagnosis	Number of patients with 75SeHCAT < 10%	Median 75SeHCAT (10th, 90th percentile)	Mann-Whitney U	Median age at investigation (years)	RR (95% CI)
Upper GI surgery (n = 41)	14	15.0* (3.6, 48.2)	266 (Z = -3.917)**	53	5.0 (1.2-20.1)
GI radiotherapy (n = 29)	17	7.0* (0.1, 30.0)	82.5 (Z = -5.258)**	69	8.5 (2.2-33.5)
Pancreatic disease (n = 25)	14	9.0* (0.6, 43.8)	102 (Z = -4.520)**	54	8.1 (2.0-31.3)
Amyloidosis (n = 6)	5	1.7 (0.01, n/a)	172 (Z = 3.722)**	54	12.1 (3.0-48.2)

CONCLUSION: Patients with amyloidosis, chronic pancreatitis, upper GI surgery and GI radiotherapy showed significantly lower ^{75}SeHCAT retention than healthy controls. These predisposing conditions remain rare causes of referral for the ^{75}SeHCAT test, and bile acid diarrhoea may be underdiagnosed in the context of these diseases.
Disclosure of Interest: None declared

P1694 LACTOSE INTOLERANCE. URINE GAXILOSE TEST, DIAGNOSTIC PERFORMANCE AND TOLERANCE IN CLINICAL PRACTICE

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INTRODUCTION: Recently, a new test has been integrated for the noninvasive diagnosis of hypolactasia disease. This test analyze urine D-xylose after lactase cleavage of a lactose analogue 4-galactosylxylose (Gaxilose).
AIMS & METHODS: Evaluate the diagnostic performance of the method compared to the most widely accepted, hydrogen breath test with lactose. Genetic testing of hypolactasia was also assessed. Determinate the clinical tolerance of these methods and the patient acceptance.
A prospective study of patients with clinical symptoms suggesting lactose intolerance was performed. Hydrogen breath test was carried out after 50 g of oral lactose. Malabsorption was considered as an increase of 20 ppm over the basal level. A Gaxilose test was performed by the measure of five hours urine D-xylose after 0.45 g of oral Gaxilose. Hypolactasia was considered when the level of D-xylosa was lower than 37.87 mgr. The study was completed with the analysis of the polymorphism of the gene 13910 (CC associated with hypolactasia).
Furthermore, every patient fulfilled a previously validated symptom score, that consist of a 5 items-scale from 0 to 10, in relation with milk intake and analyzed by both diagnostic tests. Finally, each patient chooses their preferred test.
RESULTS: In our study, 31 patients were included (24 women, average age: 34.5 years). Twenty-eight patients who meet all the requirements were analyzed. According to the hydrogen test, 50% of the patients (14/28) were diagnosed of malabsorption. The rest of them were negative for the test, five patients were non-hydrogen producers. A lower percentage of hypolactasia was achieved with Gaxilose test, 35.7% of the patients (10/28). The same conclusion was obtained in 22 patients (78.6%) using both tests. Gaxilose test could detect hypolactasia in one of the five non-hydrogen producer patients and it excluded this possibility in the other. The results were different in the other five patients (17.9%): two of them were probably a false positive of the hydrogen test. The other three patients were false negative of Gaxilose test, with urine D-xylosa level above and close to the cut-off (39.2-40.2 and 41.9 mg). In our experience the cut-off 41.9 mg improves the result (100% Sensitivity, 87% Specificity, 87% PPV and 100% NPV). All the patients who had the 13910 CC genotype, showed malabsorption in the hydrogen test except one, non-hydrogen producer.
In terms of the clinical expression, every patient had symptoms after drink milk (average 24 points), 90% while performing the hydrogen test (average 14 points) and only 33% during Gaxilose test (average 10 points). Gaxilose test was selected by 89% of patients.
CONCLUSION: Urine Gaxilose test offers an efficient tool for hypolactasia diagnosis, as well as the hydrogen test. However, this test is inaccurate when urine xylose level is near over the cut off. In our experience increase the cut-off would improve the efficacy of the test. Furthermore, the Gaxilose test allows diagnosis of the non-hydrogen producing patients. It is a well-tolerated test and the most accepted by the patients.
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Disclosure of Interest: None declared

P1695 THE ROLE OF WATCH AND WAIT STRATEGY IN THE TREATMENT OF INTESTINAL FOLLICULAR LYMPHOMA IN RITUXIMAB ERA: A RETROSPECTIVE STUDY OF 33 CASES COMPARED WITH 70 CASES OF NODAL FOLLICULAR LYMPHOMA

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INTRODUCTION: The majority of intestinal follicular lymphomas (intestinal FL) have some distinct clinical features different from those of nodal follicular lymphomas.
AIMS & METHODS: In this study we compared the clinical course of 33 cases of FL-GI patients with 70 cases of nodal FL patients both treated by watch and wait (W&W) strategy in order to evaluate W&W strategy in the era of rituximab being introduced as a treatment option for intestinal FL. Thirty-three cases of intestinal FL diagnosed as low-tumour-burden follicular lymphoma (LTB-FL) according to GELF criteria for LTB, M/F = 18/15, age 49-82, clinical stage (CS), Ann Arbor staging system I: 16, II: 7, IV: 9, WHO grade 1: 32, 2: 1, 3: 0, were followed for over 12 months by W&W, median time period of 46 months. Seventy cases of nodal FL, M/F = 36/34, age 36-92, CS (Ann Arbor) I: 6, II: 10, III: 21, IV: 30, WHO grade 1: 32, 2: 30, 3: 4, followed by watch and wait strategy for median period of 57 months were compared. The clinical stage at diagnosis was confirmed by blood test, bone marrow (BM) aspiration, positron emission tomography (PET), contrast-enhanced CT scan (from neck to pelvis), esophagogastroduodenoscopy (EGD), colonoscopy, double balloon enteroscopy. During the period of W&W, EGD and blood test were performed every four months and PET, colonoscopy and capsule endoscopy were performed every year.
RESULTS: There was no difference in the age and sex in the patients between intestinal FL and nodal FL. CS, WHO grade, follicular lymphoma international prognostic index (FLIPI) grade and the value of sIL-2R were significantly lower in intestinal FL. The proportion of BM involvement was significantly low in the patients of intestinal FL. No patient died of disease in intestinal FL while 2 patients of nodal FL died after treatment. The overall survival showed no difference between intestinal FL and nodal FL. The discussion of progression free survival (PFS) showed significantly better result in intestinal FL compared with nodal FL. The factors causing the difference in PFS were considered to be BM involvement, the existence of bulky mass and FLIPI. In all the 28 nodal FL patients with the progression of the disease, LTB turned into high-tumor-burden and they were treated by chemotherapy, rituximab-chemotherapy combinations or peripheral blood stem cell transplantation. Only 6 patients of intestinal FL showed progression of the disease. Out of these six patients, 2 patients deviated from the category of LTB-FL and received rituximab-chemotherapy combinations and 4 patients, although the CS progressed (I to II in 3 patients and II to IV in one), remained in the category of LTB-FL and were followed by 'W&W'.
CONCLUSION: The treatment modality of LTB-FL comprising large proportion of intestinal FL is 'watch and wait' in the era of rituximab as a choice of treatment.
Disclosure of Interest: None declared

P1696 USEFULNESS OF ULTRASONOGRAPHY FOR DIAGNOSIS OF SMALL BOWEL TUMORS; A COMPARISON BETWEEN ULTRASONOGRAPHY AND ENDOSCOPIC MODALITIES

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INTRODUCTION: Recently, many papers showed that ultrasonography (US) is a conventional and non-invasive modality for the examination of abdominal cavity. The aim of this study was to evaluate the usefulness of US for the detection of small bowel tumors (SBTs).
AIMS & METHODS: The aim of this study was to evaluate the usefulness of US for the detection of SBTs. Five hundred and fifty eight consecutive patients (295 male, 263 female, mean age 71.1) who underwent capsule endoscopy (CE) and/or balloon assisted endoscopy (BAE) were enrolled in this study. All patients underwent US prior to CE and BAE. The sensitivity and specificity of US in detecting SBTs, size of detected SMTs, detection rate of SBTs by US were evaluated.
RESULTS: Ninety three tumors (benign 48, malignant 45) detected by CE and/or BAE were retrospectively analyzed. The sensitivity and specificity of US in the detection of SBTs were 50.5% (47/93) and 100% (465/465). Tumor size in patients with SBTs detected by US (mean 33.2 mm) were significant larger than those undetected by US (mean 8.7 mm). The ratio of SBTs located in the ileum was significantly higher in SBTs detected by US (12/17) compared to those undetected by US (5/17). Body mass index was irrelevant to the detection rate. Of all patients with SBTs undetected by US, 91.3% (42/46) were benign tumors with good clinical prognosis.
CONCLUSION: US examination is considered to be a useful modality for detecting small bowel lesions. We consider that US examination is the first choice modality for examining SBTs because it is a conventional and non-invasive procedure.

Disclosure of Interest: None declared

P1697 FAMILIAL AND MULTIPLE GASTROINTESTINAL STROMAL TUMORS WITH FAIR RESPONSE TO HALF DOSE OF IMATINIB

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INTRODUCTION: GISTs are known as the most common tumor originated from gastrointestinal (GI) mesenchyme. In 1998, we firstly reported gain-of-function mutations of the c-*kit* gene in GISTs which appear to originate from interstitial cells of Cajal (ICC)[1]. As we and others have already reported, some families with multiple GISTs carry a germline gain-of-function mutation of the c-*kit* gene. The c-*kit* gene mutations are reported in approximately 90% of all sporadic GISTs, and are located most frequently in exon 11. In patients with familial GISTs, most of the mutations are located in exon 11 as well. We have experienced a family who has a germline gain-of-function mutation of the c-*kit* gene in exon 11 (Del-Val560). Notably, one of the patients has shown fair response to imatinib. To our knowledge, there are few reports describing the response to imatinib in familial GISTs. We report here the clinicopathological features of the patients together with a review of literature.
AIMS & METHODS: A 40-year-old female (case 1) with a history of rheumatoid arthritis treated with infliximab, complained right lower abdominal dull pain and underwent contrast enhanced abdominal computed tomography (CT). It revealed a large mass lesion with the size of 50 x 30 mm at the small intestine. Single balloon enteroscopy showed a jejunal protruding submucosal tumor with ulceration on the surface. Partial resection of the jejunum was performed. Immunohistocheical analysis revealed the tumor was positive for KIT and CD34 and was diagnosed as GIST. The father of this patient (case 2) had a previous history of small bowel operation for small bowel perforation due to mass lesion. He underwent an abdominal CT which revealed multiple mass lesions at the duodenum and small intestine. EUS-guided fine needle aspiration (EUS-FNA) biopsy was performed. The tumor showed positivity for KIT and CD34 and was diagnosed as GIST. To identify germline gain-of-function mutation of the c-*kit* gene, blood samples were obtained and analyzed for c-*kit* gene sequencing.
RESULTS: After obtaining informed consent, blood samples from case 1 and 2 were analyzed. In case 1 and 2, germline c-*kit* gene mutation was identified in exon 11, resulting in deletion of codon 560 valine, and they were diagnosed as familial GIST patients. Imatinib treatment for GISTs was considered in case 2 because of previous history of intestinal perforation. Considering his age, the dose of imatinib was reduced in half. All GISTs were markedly reduced in size in one year.
CONCLUSION: Multiple GISTs were more frequently observed in patients with type 1 neurofibromatosis (NF-1) than in familial GISTs with germline c-*kit* gene mutation. Patients who have multiple GISTs without classical symptoms of NF-1 have the possibility of such familial GISTs. Therefore, detailed familial history should be taken. In patients with sporadic GISTs harboring exon 11 KIT mutations, the partial response rate of imatinib was 83.5%[2]. In our case, half dose of imatinib was effective. Even in the patients with familial GISTs, imatinib can become an encouraging therapeutic option.
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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00
NUTRITION III – POSTER EXHIBITION – HALL XL

P1698 RAPID GASTRIC AND INTESTINAL TRANSIT IS A MAJOR DETERMINANT OF CHANGES IN BLOOD GLUCOSE, INTESTINAL HORMONES, GLUCOSE ABSORPTION AND POST-PRANDIAL SYMPTOMS AFTER GASTRIC BYPASS

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INTRODUCTION: Gastric emptying usually regulates the rate of small intestinal (SI) nutrient entry to 1-4 kcal/min. It is hypothesized that Roux-en-Y gastric bypass (RYGB) augments distal gut hormone release and modifies glycaemia by uncontrolled transit of liquid nutrients, which should be normalized if nutrient delivery were controlled.
AIMS & METHODS: To determine the contribution of rapid gastrointestinal transit of nutrient liquid on blood glucose, incretin hormones, glucose absorption and gastrointestinal (GI) symptoms after RYGB. 10 RYGB patients were studied twice in random order, separated by at least a week, with either: (i) an oral glucose drink (50g glucose/ 150ml water with 3g 3-O-methyl-D-glucopyranose (3-OMG) and 20MBq 99mTc-sulfur colloid) over 3 min or (ii) the same solution (without 99mTc-sulfur colloid) infused via an endoscope into the proximal Roux-limb over 50 min (4kcal/min). 10 healthy control subjects were studied with the latter solution infused into the duodenum (4kcal/min). GI transit of the glucose drink was assessed by scintigraphy. On each study, blood glucose, and plasma 3-OMG, insulin, glucose-dependent insulinotropic polypeptide (GIP), and glucagon-like peptide-1 (GLP-1) concentrations, and GI symptoms, were measured over 270 min.
RESULTS: In RYGB subjects, the glucose drink emptied rapidly into the distal SI (pouch emptying (PE), $t50 = 3 \pm 1$min; caecal arrival time (CAT) $= 26 \pm 10$min). CAT, but not PE, was inversely correlated with peak plasma GLP-1 ($r = -0.73$, $p = 0.01$). Compared to oral glucose, 4kcal/min SI glucose infusion in RYGB subjects was associated with substantially lower plasma GLP-1, GIP, insulin and GI symptoms, similar to those observed in healthy subjects. Both plasma 3-OMG and blood glucose were higher in RYGB subjects during SI glucose infusion than after oral glucose, and higher than in healthy subjects. Peak plasma 3-OMG correlated closely with peak blood glucose ($r = 0.94$, $P < 0.0001$) in RYGB subjects during SI infusion, but not after oral glucose or in healthy subjects.
CONCLUSION: After RYGB, reducing intestinal glucose delivery to 4kcal/min is associated with higher blood glucose, greater glucose absorption, lower incretin responses and less GI symptoms, supporting rapid transit contribution to the exaggerated incretin responses and "dumping symptoms".
Disclosure of Interest: None declared

P1699 VEGETAL VERSUS ANIMAL FOOD PROTEINS: A DIFFERENT IMPACT IN 1-H POST-PRANDIAL IMPEDANCE AND PH ANALYSIS IN GERD PATIENTS

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INTRODUCTION: Gastroesophageal reflux disease (GERD), affecting up to 20% of the general population in Western countries, develops when the reflux of gastric contents causes troublesome symptoms and/or complications. Behaviors changes and lifestyle modifications are considered the first line treatment for GERD with the least possibility of side effects.
Although few data are available on eating habits, in clinical practice different foods (i.e., chocolate, peppermint, wine, tomato, spicy food, coffee) and, generally, high-fat diet are indicated as triggering reflux symptoms. However, the role of dietary behavior, mainly in terms of specific dietary components, in influencing GERD clinical manifestations remains controversial.
AIMS & METHODS: By means of impedance and pH monitoring, we aimed to evaluate the effect of two meals with a bromatological-balanced composition: one with a prevailing component of animal food protein and the other with vegetable food protein.
We enrolled 30 consecutive patients with typical reflux symptoms and negative endoscopy, who had been proposed for esophageal manometry and 24-h impedance and pH monitoring (MII-pH) (OFF-therapy) during their scheduled diagnostic program.
All patients were allocated to receive a scheduled diet with a caloric intake of about 1200 Kcal, divided into two meals of 600 Kcal: one with a prevailing component of animal protein and the other with vegetable protein. Breakfast was free and not considered during the 1-h postprandial analysis.
According to MII-pH analysis, we evaluated total reflux number, acid exposure time (AET) and symptom-reflux association. Moreover, during the first postprandial hour (both lunch and dinner), we evaluated: total reflux number, number of acid and weakly-acidic refluxes, AET, presence of symptoms.
A student t-test for paired data was performed and the differences were considered significant when p values were < 0.05.
RESULTS: Male/female ratio was 0.5 (10/20). Mean age was 53.4 ± 12.7 yrs. All patients had heartburn. Twenty-four hour MII-pH analysis showed that 14/30 patients had pathological AET (non-erosive reflux disease, NERD), and 16/30 had normal AET but positive symptom-reflux association (hypersensitive esophagus, HE). The comparison between the first postprandial hour analysis showed a higher total reflux number (7.6 ± 3.9 vs 4.7 ± 3.1) and acid reflux number (4 ± 2.7 vs 1.9 ± 2.2), and greater AET (3 ± 3 vs 0.7 ± 1.3) after the animal protein meal than after the vegetable protein meal. Moreover, more symptoms were reported after the animal protein meal (2.3 ± 1.8 vs 0.8 ± 0.7) ($p < 0.05$).
CONCLUSION: Vegetable proteins are associated with a lower number of refluxes, particularly acid refluxes, and thus with a reduced number of symptoms during the first postprandial hour. This is a pilot study and future investigations are warranted to confirm these results.
Disclosure of Interest: None declared

P1700 IRON, B12, AND FOLIC ACID. HAVE WE FORGOTTEN ABC?

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INTRODUCTION: Micronutrient deficiency including B12, Folic Acid (FA) and Iron (Fe) are frequent in Inflammatory Bowel Diseases (IBD). Laboratory manifestations of these deficiencies are evident on blood count. B12 and/or FA may present as macrocytosis, and Fe as microcytosis. Combined deficiencies can present as normo/macro or micro-cytosis with a large Red Cell Distribution Width (RDW). These laboratory abnormalities should lead to investigation of these deficiencies.
AIMS & METHODS: The aim of this study is to check the awareness for investigation of these deficiencies.
Data regarding all IBD patients hospitalized for exacerbation during 2010-3.2014 with mean corpuscular volume (MCV) ≤ 75 fL; MCV ≥ 100 fL; RDW $\geq 17\%$

was retrieved from the electronic files. Deficiencies were defined in accordance to our local laboratory values.
RESULTS: Three hundred and seventy-three patients; 46% males; age 38.9+/-17.7 years. Relevant abnormal laboratory results were found in 90 (24%) patients. 28 and 22 of 56 patients with low MCV had high and normal RDW respectively. Four and three of ten patients with high MCV had normal and high RDW respectively. 41/56, 4/7 and 11/27 of patients with laboratory findings mandating investigation for Fe, B12 and Folic acid, and combined deficiencies according to the above criteria had complete evaluation. A stratified tendency towards higher awareness for investigation was noted as highest for Fe, and lowest for combined deficiencies (p = NS). 55/59; 2/7 of patients who underwent investigation for Fe and B12 and FA, were found to be deficient. Almost 40% did not undergo full evaluation. 86% of investigated patients were found to be deficient. 56% of patients diagnosed with Fe deficiency were prescribed treatment.
CONCLUSION: Deficiency of Fe and/or B12 and/or FA is suggested in almost a quarter of hospitalized IBD patients, but is far too often overlooked. Untreated deficiencies can cause significant morbidity. Measures to increase awareness are needed.
Disclosure of Interest: None declared

P1701 DIETARY MANIPULATION OF GASTROINTESTINAL FUNCTION CAN MODIFY POSTPRANDIAL ENDOTHELIAL DYSFUNCTION IN HEALTHY HUMANS

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INTRODUCTION: Endothelial function, measured by flow-mediated dilatation (FMD), predicts cardiovascular events, and is known to be impaired after meals. The rate of gastric emptying and nutrient delivery to the small intestine has a substantial influence on postprandial glycaemic excursions in health and type 2 diabetes, but its impact on endothelial function is unclear.
AIMS & METHODS: Our aim was to evaluate the effects of dietary modifications designed to slow gastric emptying and/or small intestinal nutrient exposure on postprandial endothelial function in healthy humans.12 healthy subjects (6 male, 6 female: 33 ± 5.6 years) were studied on 3 occasions each, in a randomised, crossover design. After an overnight fast, subjects consumed a mashed potato meal (meal 1) or the same meal mixed with 9 g guar (meal 2) within 10 min, or the mashed potato meal divided into 12 equal portions over 60 min (meal 3), each labelled with ^{13}C-octanoic acid. Brachial artery FMD was measured every 30 min for 120 min. Blood glucose and serum insulin concentrations, and gastric emptying (breath test), were evaluated for 240 min. Data are means ± SE.
RESULTS: Addition of guar to the meal ('meal 2' vs 'meal 1') slowed gastric emptying (half-emptying time 285 ± 27 vs. 208 ± 15 min, $p < 0.05$), lowered postprandial glycaemia and insulin ($P < 0.001$ for each), and was associated with a delayed but sustained suppression of FMD ($P < 0.005$). With 'meal 3', the glycaemic excursion was modestly suppressed ($P < 0.001$), but the insulin response was more marked after the first 30 min ($P < 0.001$) compared with 'meal 1', while the reduction in FMD was markedly attenuated ($P < 0.05$). The magnitude of reduction in FMD at t = 30 min was inversely related to the cumulative $^{13}CO_2$:$^{12}CO_2$ ratio ($r = -0.53$ $P < 0.01$), suggesting a relationship to small intestinal nutrient delivery, but FMD did not correlate with postprandial glycaemia.
CONCLUSION: These observations indicate that gastrointestinal function can be manipulated by dietary means to regulate postprandial endothelial function. The underlying physiology potentially reflects interplay of multiple factors including gastric volume, rate of small intestinal nutrient exposure, and insulin secretion. Further studies are warranted to develop therapeutic strategies to reduce postprandial endothelial dysfunction in high-risk populations (eg. type 2 diabetes).
Disclosure of Interest: None declared

P1702 THE EFFECT OF CONSUMING SMALL VOLUMES OF BEER ON GASTRIC MOTILITY AND SMALL INTESTINAL FUNCTION AND THE INVOLVEMENT OF GENE POLYMORPHISMS

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INTRODUCTION: The effects of alcoholic beverages such as small amount of wine have been proposed for keeping healthy conditions.
AIMS & METHODS: The aim of this study was to investigate the effect of consuming small amounts of beer or a non-alcoholic beer taste beverage (non-beer) on internal organ functions, including gastric motility.
The subjects included 20 male healthy volunteers. All subjects were questioned regarding their alcohol consumption status. Blood was collected for DNA extraction prior to the test, and the genetic polymorphisms in ADH1B (rs1229984, Arg47His) and ALDH2 (rs671 Glu487Lys) was analyzed using the TaqMan assay method. The subjects consumed 150 ml of beer (5.0 % v/v contain ethanol) or non-beer once per week, followed by the ingestion of 200 ml of the test nutrient containing 13C-acetate 15 min later, after which the subjects' exhalations were collected in a breathing bag at 0, 5, 10, 15, 20, 30, 40, 50, 60, 90, and 120 min. The concentration peak of 13C was measured as Tmax. The volunteers was measured their body weight, height, body mass index (BMI), body surface area (BSA), basal metabolic rate. Diamine oxidase activity (DAO) for the marker of small intestinal function activity was measured in a fasting blood sample collected the day after the test. Statistical analyses were performed with Wilcoxon signed-rank test, and F-test.
RESULTS: Gastric motility was significantly slower in the group that consumed a small amount of beer (Tmax = 49.0 vs. 38.3, respectively, $p = 0.00137$). Similar results were found in the ADH1B *2/*2, ALDH2 *1/*2, and daily beer consumption groups. BMI, BSA were not related with gastric empting time. DAO values were significantly variable in beer drinking group compared with non-alcoholic beer drinking group ($P < 0.0001$).
CONCLUSION: The consumption of even a small amount of beer affects gastric motility and small intestinal function. And the polymorphisms in alcohol metabolism-related enzyme-encoding genes are related to gastric motility and small intestinal function.
Disclosure of Interest: None declared

P1703 THE ROLE OF PROPHYLACTIC PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE PLACEMENT IN PATIENTS WITH HEAD-AND-NECK CANCER TREATED WITH DEFINITIVE CHEMORADIATION THERAPY

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INTRODUCTION: Head-and-neck cancer (HNC) patients have a high-risk of malnutrition and swallowing dysfunction, particularly during chemoradiation therapy (CRT) that justifies prophylactic percutaneous endoscopic gastrostomy (PEG) placement for nutritional support.
AIMS & METHODS: Evaluate the utility, duration of use and nutritional outcome of prophylactic PEG tube placement in patients with HNC undergoing definitive CRT, with a follow-up longer than 1 year.
Prospective analysis of consecutive patients with HNC refered for prophylactic PEG placement in a 6-month period, between July/2012-December/2012, in a single center. Demographic data, tumor location and stage, body mass index (BMI), duration of PEG usage (exclusive and complementary) and weight evaluation before, during and after treatment were assessed.
RESULTS: PEGs were placed in 47 patients with HNC (41M/6W), mean age = 58 year old (40-76). TNM: T1/2 = 11, T3/4 = 36 N0/1 = 20, N2/3 = 27. BMI = 24kg/m^2 (15-33). Of the 47 PEGs placed, only 2 were not used. Average length of PEG usage: 7 months (0.1-20 months). After one-year of follow-up, of the 45 patients who used PEG: 27 were in remission, 3 had persistent disease, 15 died (13 of disease progression; 2 of respiratory infection). Of the 27 in remission: 22 removed PEG on average after 7 months (3-15) and 5 still use PEG on average after 17 months (14-20). Of the 15 deceased patients only 2 removed PEG. Average length of exclusive use of PEG: 3 months (0-18). Use of PEG (exclusive/partial/null): during treatment (15/29/2); after treatment (6/26/9); six months after treatment (7/5/23). Mean weight (before/during/after treatment): 65/62/60Kg. Weight reduction occurred in 31 patients during treatment and in 24 after treatment even using PEG for nutritional support.
CONCLUSION: Enteral nutritional support is essential in patients with HNC during and after treatment with definitive CRT. Prophylactic PEG placement allowed enteral intake but did not prevent weight loss. Almost all patients required PEG not only during but also after treatment. One fifth of the patients in remission required long-term PEG usage for nutritional support.
Disclosure of Interest: None declared

P1704 TRANSNASAL PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (TN-PEG) IN HEAD AND NECK CANCER PATIENTS: COMBINED APROACH WITH GASTROENTEROLOGY AND PNEUMOLOGY

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INTRODUCTION: Head and neck cancer patients (HNCP) are prone to malnutrition due to malignancy and side efects of treatment. The placement of a percutaneous endoscopic gastrostomy (PEG) is necessary for most of these patients. In some situations, oropharyngeal obstruction or trismus preclude a transoral aproach and a transnasal (TN) route with a thin scope is the available option. Adaptation of a bronchofiberoscope for PEG placement in this context has been previously described.
AIMS & METHODS: Retrospective analysis of all TN-PEG tubes placed in HNCP in a single institution, over a 5-year period, using the "pull" method, in a combined aproach by a gastroenterologist in the abdominal side and a pneumologist in the head side, employing an adapted bronchofiberscope.
Demography, indication (prophylatic versus palliative), TN-PEG procedure outcome, complications and treatment, and overall survival were reviewed.
RESULTS: Between 2009-201, 23/649 (3,5%) consecutive HNCP patients referred for PEG placement, underwent a TN-PEG procedure. TN-PEGs were successfully placed in 22/23 patients, 17 men and 6 women, with a mean age of 56 years old (26-74) and a mean BMI = 20 (15-27). Only one TN-PEG technical failure due to missing transillumination. Palliative TN-PEGs in 14/23 and

prophylatic in 9/23 patients. TN-PEG route due to trismus (22/23) and oropharyngeal obstruction (1/23), in patients with tumors of oropharynx (8), oral cavity (7), tongue (5) e maxillary sinus (3). TN-PEG was the only way of nutrition in the 22 patients for a mean time of 242 days (31-1115). On follow-up, 15 patients died of disease progression, 2 died of other causes and 5 are alive in remission. None of the patients removed TN-PEG. The 5 patients in remission were using TN-PEG for exclusive enteral nutrition for a mean time of 378 days (110-730). Minor complications ocurred in 8/22: 1 burried bumper syndrome; 1 PEG extrusion; and 6 infections, 3 early ($<=7$ days after TN-PEG placement) and 5 late (>7 days after TN-PEG placement). Neither immediate, major complications ocurred nor mortality associated with the procedure.

CONCLUSION: Combined TN-PEG placement by a Gastroenterologist and a Pneumologist using an adapted bronchofiberoscope is a safe and useful option for HNCP in witch transoral PEG placement is not possible.

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Disclosure of Interest: None declared

P1705 HEPATOPATHY IN CHRONIC INTESTINAL FAILURE AND PARENTERAL NUTRITION: OUTCOME AND PROGNOSTIC FACTORS

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INTRODUCTION: Chronic intestinal failure (CIF), mostly caused by short bowel syndrome (SBS), frequently - through malabsorption - leads to malnutrition which requires parenteral nutrition (PN). PN, particularly long-term PN, is frequently complicated by a form of hepatopathy (intestinal failure associated liver disease, IFALD), which is not well understood in pathogenesis, diagnosis and consequences for CIF-patient-management.

AIMS & METHODS: The incidence, severity and outcome of IFALD were studied in a retrospective fashion in a cohort of 142 patients with CIF from an interdisciplinary team at an acedemic referral center. Statistical analysis was performed using SPSS 19.0.

RESULTS: 142 patients from 2004 - 2013 with CIF due to SBS were analyzed; 88 (62%) of them had a non-malignant cause of CIF due to venous (11%) or arterial (28%) mesenteric ischemia, Crohn's disease (14%), adhesions or volvlus (23%), radiation enteritis (2%) or other causes. 80 (91%) patients of non-malignant CIF required PN. 52% had a type I (end-jejunostomy), 24% a type II (jejunocolostomy) and 24% a type III (ileocolostomy) SBS-anatomy. Elevated liver enzymes were detected in all patients during the initial 24 months (hypersecretive and adaptive period) of SBS and in 90% beyond 24 months (during stabilization period). After stabilization period was reached, an elevation of ASAT, ALAT and total bilirubin (but not AP or GGT) indicated a significantly worse prognosis by Cox regression analysis. A combined score considering a more than 2-fold elevation of at least two of these 3 parameters indicated a statistically worse long-term outcome as indicated by decreases overall survival by Kaplan-Meier analysis ($p<0.001$); this was idependent from other statistically significant prognostic factors such as type of SBS or presence and number of catheter-related blood stream infections.

CONCLUSION: In CIF-patients IFALD as defined by elevated liver enzymes ASAT, ALAT and elevated total bilirubin is highly prevalent even after intestinal stabilization has been achieved independently from type of SBS and other complications. A simple assessment score based on these lab values may indicate poorer long-term outcome and should thus direct medical and surgical CIF- and PN-management.

Disclosure of Interest: None declared

P1706 A MULTICENTRE, RANDOMISED CLINICAL TRIAL COMPARING OUTCOMES OF GASTROSTOMY TUBES PLACED USING THE MIC INTRODUCER KIT OR THE TRADITIONAL PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PUSH/PULL TECHNIQUE

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INTRODUCTION: Different techniques for direct insertion of a gastric feeding tube (g-tube), are reported. Advantages are:easy and safe positioning in upper tract stenosis;reduced incidence of peristomal infections;possibility to place, as first choice, a balloon type g-tube, which is easy to be changed at bed-side.

AIMS & METHODS: To compare the push/pull endoscopic method (PEG) to the MIC introducer kit (KIT; Kimberly-Clark Corporation, Roswell, GA, USA) for placing g-tubes. From September 2010 to April 2013,206 consecutive patients (age:18-85) without upper tract stenosis randomly received a 20 French g-tube by push/pull PEG method (106), or by direct insertion using the KIT (100). Primary enpoints were complication rates during tube placement and at 30-days and Jain score-based[1] peristomal infection severity. Secondary endpoints were time necessary for the placement, longevity of the g-tube until first change and the need of endoscopic substitution. Patients were planned to be followed for 13 months. Data were analysed using the Mann-Whitney test, while frequencies were analysed by the Chi-squared test with Yate's correction or Fisher exact test, when appropriate. Significant differences between means were indicated by $p \leq 0.05$.

RESULTS: Placement was successful in 106/106 PEG and in 99/100 KIT patients. Complication rates were not significantly different in the two arms. Major complications were 2 fistulas and 1 death in PEG,1 respiratory arrest in KIT. Minor complications were only in KIT patients (2 superficial lesion of gastric mucosa;2 pneumoperitoneum;1 deformation of dilator device). Complications at 30-days included infection (4 cases in both groups), death (PEG:10;KIT:11) minor bleeding (PEG:2;KIT:1), leakage (PEG:1), and ab-ingestis pneumonia (KIT:1). Peristomal infection severity scores were similar at 30-days (0.28 vs 0.31). G-tube substitutions occurred in 62% and 95% ($p<0.01$) of PEG and KIT patients, with a greater incidence of these procedures occurring in endoscopy unit for PEG (58% vs. KIT:22%; $p<0.01$). The mean time required to place tube was shorter by PEG (10.4 ± 4.5 min vs. KIT: 14.8 ± 5.2; $p<0.001$). Time prior to first change exceeded 90-days (PEG:230 vs KIT:124).

CONCLUSION: These results suggest that KIT is a feasible and safe alternative to PEG. Furthermore, patients with g-tubes placed using the KIT were significantly less likely to require a second endoscopic procedure to have their g-tubes removed, whith a reduction of endoscopic suite costs.

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Disclosure of Interest: V. Iori Other: The KITs were obtained free of charge from Innova Medica Ltd. Innova Medica is the official Italian importer., C. Guatti Zuliani Other: The KITs were obtained free of charge from Innova Medica Ltd. Innova Medica is the official Italian importer., V. Mirante Other: The KITs were obtained free of charge from Innova Medica Ltd. Innova Medica is the official Italian importer., D. Vasta: None declared, G. Iori: None declared, L. Casoni: None declared, A. Mazzocchi: None declared, L. Rossi: None declared, R. Conigliaro: None declared, R. Sacchero: None declared, R. Sassatelli: None declared, L. Camellini: None declared

P1707 ARE NUTRITION ASSESSMENT TOOLS OF ANY USE IN THE MANAGEMENT OF THE SURGICAL PATIENT?

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INTRODUCTION: Nutrition is an important biological factor in the holistic approach towards management of the surgical patient. The MUST (Malnutrition Universal Scoring Tool) is a tool used in many studies to assess the nutritional status of patients. In 2012, we performed an audit of the MUST scoring tool, comparing it with with a trust devised tool. In 2013, we repeated the audit to complete the audit cycle, following recommendations implemented from the previous audit.

AIMS & METHODS: Aims: We aimed to assess the accuracy of these assessment tools, and the value of the concerted education of our nursing staff regarding the use of these tools.

Methods: Data was prospectively collected over a 2 month period, including both elective and acute admissions to surgical wards. The same audit tool was used this year, as was used in the previous year, to allow for comparative analysis. Education was given to the nurses on how best to implement the MUST tool.

RESULTS: The 2013 cohort included 140 patients (32 elective and 108 acute admissions) as compared with 120 patients in the 2012 cohort (24 elective and 96 acute admissions). In 2012 86% of patients had nutrition assessment completed on admission, compared to 94% in 2013. 52% of patients assessed by MUST were deemed to have low, 12% had moderate and 36% had high risk of malnutrition in 2012, compared to 54% low, 13% moderate and 40% high respectively in 2013. 56% of these were reviewed by dietitian/ had appropriate nutritional support started by their medical team in 2012, compared to 76% in 2013. Higher re-admittance rates were also reflected in different MUST score groups. Low risk group readmission rates were 7.9% (8.6% in 2013), moderate 33.3% (33.3% in 2013) and 14.2% (14.8% in 2013) in high risk MUST groups. Wound infections occurred in 8.6% of patients in 2012, and 7.2% of patients in 2013.

CONCLUSION: Conclusions: Both years audits reveals a direct correlation between MUST scores and the length of stay in hospital, readmission rate, risk of wound infection and risk of death. Promisingly, after the education of nursing staff on the wards, there appears to have been an increase in the number of surgical patients receiving adequate care in regards to nutrition/ nutrition assessment.

Disclosure of Interest: None declared

P1708 SAFETY OF UNSEDATED PEG PLACEMENT USING TRANSORAL ULTRATHIN ENDOSCOPY IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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INTRODUCTION: In patients with amyotrophic lateral sclerosis (ALS), percutaneous endoscopic gastrostomy (PEG) placement under sedition often causes apnea or hypoventilation. To prevent complications of sedation, unsedated transnasal PEG placement using small diameter endoscopy (SDE) has been

performed. However, even with SDE, transnasal intubation sometimes fails due to the impossibility of crossing the nasal cavity or results in epistaxis and/or nasomucosal injury. Moreover, a recent study revealed that transoral insertion using SDE is superior to transnasal insertion using SDE in endoscopy procedures.
AIMS & METHODS: The aim of the present study was to assess whether unsedated PEG placement in ALS patients using ultrathin endoscopy (UTE) via the transoral route can improve safety. Between 2003 and 2012, PEG placement was identified and reviewed in 42 patients with ALS. PEG was performed in 11 patients using transoral UTE without sedation (UTE group), 17 patients using conventional normal-diameter esophagogastroduodenoscopy (C-EGD) without sedation (unsedated C-EGD group) and 14 patients using C-EGD with sedation (sedated C-EGD group). We compared the clinical features, cardiopulmonary data before and during PEG placement, and complications related to PEG placement among the three groups.
RESULTS: There were no significant differences in age, M/F ratio, forced vital capacity (FVC), blood pressure, oxygen saturation before and during PEG or major complications among the three groups. With regard to complications, no major complications such as adverse events requiring surgery, permanent adverse sequelae or death, were observed in any patient. However, among the three groups, there were differences in the incidence of minor complications, including apnea and/or hypoventilation, aspiration pneumonia and peristomal infection. No minor complications were observed in the UTE group, whereas, aspiration pneumonia was observed in the unsedated C-EGD group (3/17, 7.6%) and apnea and/or hypoventilation were observed in the sedated C-EGD group (3/14, 21.4%). The proportion of patients whose BP was elevated by more than 20% compared with that observed before the PEG procedure was 7.1% (1/14) in the UTE group, 23.5% (4/17) in the unsedated C-EGD group and 14.2% (2/14) in the sedated C-EGD group. In the UTE group, PEG placement was successfully performed in all patients, and no patients required sedation during the procedure. However, among the three patients complicated with apnea and/or hypoventilation due to sedation in the sedated C-EGD group, PEG placement could not be successfully performed due to apnea and/or hypoventilation in two patients.
CONCLUSION: Unsedated PEG placement using transoral UTE in ALS patients is a safe method.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 22, 2014 9:00–14:00

THE IMMUNE SYSTEM: A DRIVING FORCE IN DIGESTIVE HEALTH AND DISEASE III – POSTER EXHIBITION – HALL XL

P1709 COLITIS-ASSOCIATED COLORECTAL CANCER INDUCES PHENOTYPE INSTABILITY AND EFFECTOR FUNCTIONS IN TUMOR-INFILTRATING REGULATORY T CELLS

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INTRODUCTION: Regulatory T cells are critical to maintain the immune system homeostasis in the gut and Treg malfunctioning is associated with chronic colitis. At the same time, accumulating evidence indicates that proinflammatory stimuli can downregulate the Treg lineage commitment transcription FoxP3 leading to Treg phenotype instability. Although Tregs have been shown to accumulate in the stroma of sporadic colorectal cancers suppressing the intratumoral immune response, the role and functional stability of Tregs in colitis associated colorectal cancer is unknown.
AIMS & METHODS: Aim of the study was to characterize Treg phenotype and stability in a model of colitis-associated colorectal cancer. To address this issue a Tregs fate mapping reporter mouse was generated where Tregs and ''ex-Tregs'', which have lost FoxP3 expression are identified by the emission of specific combinations of green and red fluorescences. Treg fate mapping reporter mice underwent the Azoxymethane/Dextrane Sulphate Sodium model of colitis-associated colorectal cancer. At the end of the experiment, the expression of Th1- and Th17-specific markers (i.e. Tbet and IFN-gamma for Th1 and RORgamma-t and IL17A for Th17) were analyzed by flow cytometry in Treg and ''ex Treg'' cells isolated from tumors and tumor-surrounding lamina propria.
RESULTS: The frequency of both Tregs but not ''ex-Tregs'' among CD4+ T cells isolated from the lamina propria of treated mice was higher as compared to untreated mice (45% vs 28% Tregs treated vs untreated respectively) while the absolute number of both Tregs and ex-Tregs was increased in treated as compared to untreated mice. In inflammatory conditions, in the peritumoral areas, both Tregs and ex-Tregs upregulated the transcription factors Tbet and RORgamma-t and expressed the proinflammatory cytokines IL17A and IFN-gamma. However in the tumor Tregs and ex-Tregs were characterized by the expression of Th17- but not Th1-related markers.
CONCLUSION: Tregs and ex-Tregs characterized by the expression of Th1 and Th17 effector molecules represent a sizable fraction of CD4+ T cells accumulating in the peritumoral lamina propria and in the tumor stroma. The exclusive expression of Th17 markers by Tregs and ex-Tregs infiltrating the tumor stroma suggest that Tregs phenotypic plasticity might enhance rather than suppress the intratumoral Th17 immune response.
Disclosure of Interest: None declared

P1710 ACRYLAMIDE, A DIETARY GLYCATED PRODUCT IMPLICATED IN INTESTINAL INFLAMMATION

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INTRODUCTION: A strong body of evidence supports the role of environmental influence in the development of Inflammatory Bowel Diseases (IBD). The increase in incidence of IBD during the 50's in Europe and United States and since about 10 years in developing countries parallel the modification of alimentary habits and in particular, the consumption of refined food.
Acrylamide is a chemical compound considered a potential carcinogen in humans. Acrylamide is produced naturally in food as a result of cooking starch rich food at high temperature (>120°C, baking, frying or grilling). High amounts of acrylamide are present in Western diet (in potato chips, pizza, French fries or pastries) with unknown effects on intestinal inflammation.
AIMS & METHODS: The aim of our study was to determine the effects of acrylamide on intestinal homeostasis in mice. C57bl6 mice were given increasing doses of acrylamide in their drinking water (25; 50 et 100µg/kg of body weight/day) for 9 months, control mice receiving water only. Colon was then harvested and assessed for macroscopic, structural and histological modifications. Markers of intestinal barrier, inflammatory and immune responses were also quantified.
RESULTS: No macroscopic lesions were observed in mice receiving acrylamide. However, the 3 doses of acrylamide induced structural abnormalities of the colon with a modification of the intestinal permeability compared to control mice. Crypts depth (148µm for control mice, 215µm for 25µg of acrylamide, and 211µm for 50µg, $p=0.0317$), number of goblet cells per crypt (respectively x3 for 25µg and 50µg, and x2 for 100µg, $p=0.0195$) and Muc 2 expression (+75% for 100µg, $p=0$ .04) were higher in mice receiving acrylamide. Acrylamide also induced expression of inflammatory markers; a significant increase of myeloperoxidase activity (+48%, $p=0.03$ for 50µg, and +50%, $p=0.04$ for 100µg), and of oxidative stress (+103% for 50µg, $p=0.03$ and +52% for 100µg, $p=0.009$ for iNOS expression, and +32% for 25µg, $p=0.04$ and +37% for 100µg, $p=0.009$ for NADPH oxydase expression) were observed in mice receiving acrylamide compared to control mice. The immune response was also disturbed; with an increased expression of Th1 cytokines (+57% for 50µg, $p=0.02$, for TNF expression, and +477%, $p=0.009$, +443%, $p=0.01$, and +408%, $p=0.009$, for 25µg, 50µg and 100µg of acrylamide respectively for IFNg expression), Th2 cytokines (+291%, $p=0.02$, +81%, $p=0.03$, and +82%, $p=0.03$ for 25µg, 50µg et 100µg respectively for IL-4 expression) and a decreased expression of Th17 cytokines (-24% for 100µg, $p=0.02$ for IL17f) in mice receiving acrylamide compared to control mice.
CONCLUSION: At low doses, acrylamide disturbed intestinal homeostasis with architectural modifications, altered permeability, increased inflammation and mucosal immune response. More studies are now needed to evaluate the role of acrylamide in IBD.
Disclosure of Interest: None declared

P1711 LIVING WITH CROHN'S DISEASE: EXPECTATIONS, EXPERIENCES AND DECISION-MAKING IN RELATION TO BEST CONVENTIONAL AND AUTOLOGOUS STEM CELL TREATMENT-THE DECIDES STUDY

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INTRODUCTION: The DECIDES study involved an in-depth qualitative investigation into experiences of living with severe Crohn's Disease (CD), exploring expectations, decision-making and perceived risk within the context of the Autologous Stem Cell Transplantation International Crohn's Disease (ASTIC) trial. The ASTIC trial examines the role of haematopoietic stem cell treatment (HSCT) for Crohn's sufferers. Although the study examines quality of life and disease-specific measures of patient response, feedback from participants indicated other important issues impacting on their experiences of CD and specifically on decision-making and experience of trial participation.
AIMS & METHODS: The DECIDES study used semi-structured interviews to investigate the experiences, expectations, decision-making and perceptions of risk taking of participants who, a) took part in the ASTIC trial, b) considered participation by did not take part, and c) patients with matched severity of CD. Research questions investigated the impact of CD on life, attitudes towards current best conventional treatment, expectations, risk taking, perceived decision making towards radical treatments, and information needs. Interviews were analysed using thematic analysis informed by a framework analysis approach.
RESULTS: 1. **'Running out of options and time'**. The majority of participants described having exhausted all available treatment options prior to considering ASTIC, often stating they had 'nowhere else to go'. This decision making process was driven by a sense of limited time and options, but with the knowledge of possible randomisation to delayed or early treatment arms.
2. **Fertility**- Decision-making about fertility emerged as an important and emotive factor to consider for participants. Perceptions varied on how this issue was initially mentioned in consultations. Regardless, a number of participants reported that fertility and family planning was an unexpected, unconsidered, yet important issue to consider during the decision making process.
3. **Shared decision-making and control-** Participants described the relationship with their specialist IBD consultant and research nurse as essential factors in their decision making process, valuing expert opinion and advice. The majority of participants stated that the recommendation to participate in the trial by their

IBD Consultant strongly influenced their decision, in addition to media/internet resources.
4. **Balancing risks and benefits-** Perceived benefits of the ASTIC trial such as 'buying more time' or being a 'potential lifeline' outweighed the risks of the trial. With the understanding that the treatment procedure was very severe and there was a realistic risk of death, the risks were negated by the potential enhancement of their quality of life.
CONCLUSION: This research provides new insights into the decision making processes of patients with severe Crohn's disease faced with potential participation in a trial of a radical treatment option. The research indicates a variety of external influences and critical moments or 'touch points' in the decision making journey, providing opportunities for additional support, information and a suite of decision making support tools.
Disclosure of Interest: None declared

P1712 IMPROVEMENT OF ULCERATIVE-COLITIS-ASSOCIATED MICROBIOTA DIYSBIOSIS AFTER TREATMENT WITH MESALAZINE-MMX (MEZAVANT™) USING MUCOSAL F. PRAUSNITZII/E. COLI INDEX AS A MARKER

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INTRODUCTION: Microbiota (MI) in Cohn's disease's (CD) and Ulcerative Colitis (UC) are structurally different from healthy ones. We assume that the inflammation on colon mucosa may disrupt the normal MI ecosystem. Thus, any treatment given to curb the inflammation process has to be expressed by a recovery of the lost healthy equilibrium. In this study, our research group has developed a bacterial marker to evaluate treatment effectiveness on UC. We designed a specific index of Fp/Ec (FEI), based on the disappearance of *Faecalobacterium prausnitzi (Fp)* and the different abundance of *E.coli* (Ec). In previous studies, it has been established that the lower the value the more disturbed is the MI ecosystem.
We designed a study to assess Mesalazine-MMX (MZX) clinical response on mild/moderate UC and how that correlates on MI dysbiosis changes by examining FEI, previous (T0) and after (T1) treatment (TM).
AIMS & METHODS: We obtained rectal biopsy from mild/moderate UC patients on MZX (4,8 gr once daily) given with intention to treat and re-sample them 4 wks after. We included 8 patients in total. Biopsies are obtained from first 5 cm of rectum by flexible gastroscope with standard procedures.
Inclusion criteria were: Patient >18yo. UC diagnosed histologically, naïve to treatment, with a mild/moderate flare (Mayo index ≤ 5) and histological criteria; and signed informed consent. We excluded patients with previous antibiotic and/or any concomitant drugs aimed to IBD TM given in the previous 6 months. All samples were analyzed using DNA real-time PCR methods.
RESULTS: All patients but one (number 5) in this study showed an improvement on disease activity as measured by Mayo Index. At T0, patients showed an FEI under 2,6 (previously established cut-off point, COP, for major dysbiosis) and in T1 the median was 3,150. That increase on value is related to the improvement on MI dysbiosis. In T1, the number of EC was reduced (in average 55%) of patients. There were no differences in the total number of Fp after TM. MZX is able to significantly ($p = 0.035$) change the FEI above the COP. The FEI detects, with 83% of accuracy, the MI dysbiosis improvement. Coefficient of variation after TM of the FEI is 0.34%.
CONCLUSION: TM on mild/moderate UC flare with MZX contributes to an improvement on dysbiosis situation as shown by a clear increase in the FEI. FEI looks as a good marker to measure MI dysbiosis and thus, it is a promising new tool to assess response to TM on UC. *This study has been supported by Shire, Inc.*
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Disclosure of Interest: None declared

P1713 USE OF MELATONIN IN THE TREATMENT OF EXPERIMENTAL DSS-DEPENDENT COLITIS IN RATS

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INTRODUCTION: Melatonin is known as a factor regulating daily activity, but it is also a powerful antioxidant and a substance with an anti-inflammatory properties. Significant amounts of melatonin is produced in the mucous membrane of the digestive tract and liver. Melatonin has a protective effect on oxidative stress dependent damage of proteins, lipids and DNA. Melatonin reduces the inflammatory response by blocking the NF-κB signal pathway which is responsible for the expression of proinflammatory cytokines. These mechanisms are involved in the pathogenesis of ulcerative colitis.
AIMS & METHODS: Evaluation of Melatonin possible influence on severity and the course of rats' large intestine inflammation induced DSS.
Methods: The study was performed on 40 Wistar rats. Animals were divided into 4 groups. Group 1 received saline intraperitoneally (1ml/kg), group 2 - received saline and Melatonin 100mg/kg/day, groups 3 and 4 were given 1% DSS in the drinking water for 14 days. In group 3 during last seven days of DSS administration rats were receiving saline intraperitoneally. Group 4 during last seven days of DSS administration were receiving saline intraperitoneally and melatonin in dose of 100mg/kg/day. Histological changes in all goups were evaluated. Level of Il-1β, Il-6, Il-10, TNF-α, paraoxonase (PON-1), reduced glutathione (GSH) and oxidized glutathione (GSSG) in intestinal homogenate was determined in enzyme – linked immunosorbent (ELISA) assay.
RESULTS: Melatonin administration to rats with DSS-dependent colitis significantly reduced the severity of histopathological inflammation features. The use of melatonin resulted in a reduction in the level of IL-1β (7.53 in group 1) from (17.86 pg/mg in the group 3) to the (9.24 pg/mg group 4), IL-6 (8.39 in group 1) from (16.92 pg/mg in the group 3) to the (8.66 pg/mg in the group 4) and TNF-α, (7.21 in the group 1) from (14.57 pg/mg in the group 3) to the (6.76 pg/mg group 4), and had no significant effect on the level of anti-inflammatory IL-10 ($p > 0.05$). Experimental colitis resulted in reduced levels of antioxidant agents (GSH and PON-1), melatonin reversed this adverse event ($p < 0.05$).
CONCLUSION: Melatonin by anti-inflammatory and antioxidant effect reduces the severity of experimental colitis in rats.
Disclosure of Interest: None declared

P1714 REMISSION IN CROHN'S DISEASE AND THE MANAGEMENT OF RELAPSES: A REVIEW OF REAL WORLD PATIENT CASES

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INTRODUCTION: Biologic agents have improved the outlook for many patients with moderate to severe Crohn's disease (CD). However, clinical data suggest that many patients may still not be attaining remission.
AIMS & METHODS: Our aim was to better understand disease remission in CD by reviewing "real-world" patient cases and assessing the management of relapses. We used patient data collected as part of an online treatment survey conducted among a panel of gastroenterologists between November 2012 and December 2013 across the five largest EU countries (France, Germany, Italy, Spain and the UK) and analysed the treatment history of 4284 patients (2879 bio pts and 1405 pts receiving immunosuppressants). We then analysed the characteristics of 1229 patients who at their most recent visit were not experiencing any flares in their disease. We also examined the records of 1064 biologic experienced patients who were currently in remission or had experienced it in the past.
RESULTS: 29% of patients were said to be experiencing no flares in their CD at the time of their visit, with the highest levels seen in France and Spain where 37% and 35% of patients were free from flares, respectively. There were no statistically significant differences in the age or gender of these patients compared to all "other" patients (pts with an increase, decrease or stabilisation of flares) though they were more likely to have a CDAI < 150 (97% vs. 45% for "other" pts). Patients in remission were also less likely to have fistulising disease (19% vs. 28% for all "other" pts) although the proportion of patients with mucosal lesions remained similar in all groups (55% - 57%). Patients in remission were less commonly treated with steroids and biologics although use of the latter stayed high. 3% of patients received a steroid (22% for "other" pts) and 60% received a biologic (70% for "other" pts). Among current biologic patients, 41% had experienced remission in the past with an average of 3 episodes and 36% experiencing remission for > 12 months. At relapse doctors immediately initiated biologic therapy in 57% of patients and in 71% of cases elected to re-start the biologic the patient had been receiving prior to remission. There was little correlation between these decisions and the number or duration of remission episodes. However, 90% of patients who had experienced ≤ 3 remissions had undergone 0-1 surgical interventions for their disease vs. 76% for those who had experienced ≥ 4. 9% of all patients cases reviewed had discontinued biologic therapy and disease remission was the most common reason for this change (52%, no statistically significant differences between bios). However, while 66% of patients had been in remission for > 12 months, 57% had experienced remission before (average of 3 episodes).
CONCLUSION: Our data show that both the induction and maintenance of remission are common but also highlight that while patients may see a reduction in the number of drugs they receive and an improvement in their CDAI and fistulae, drug-free remission and deep-remission with mucosal healing are not guaranteed. Additional analysis is required to assess how treatment strategies may optimise outcomes by maximising the duration of remission and minimising relapses, delaying or halting the progression of CD to increasing damage and disability.
Disclosure of Interest: L. Chanroux: None to report, J. Casellas: None declared

P1715 REDUCED MONOCYTE ACTIVATION AND RECRUITMENT TWO WEEKS AFTER TREATMENT START REFLECT EARLY INFLIXIMAB THERAPY RESPONSE IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: The cellular mechanisms leading to infliximab therapy response in patients with ulcerative colitis (UC) are still incompletely known. Also, it is difficult to assess early therapy response during treatment.
AIMS & METHODS: The aim was to determine effects of infliximab therapy on monocytes and monocyte related chemokines in UC patients during their first 4 months of therapy, and to evaluate early immunological effects linked to therapy response.
Blood, biopsies and stool samples were obtained before treatment (baseline), 2 weeks and 4 months after infliximab therapy start from 42 previously anti-TNF therapy-naïve UC patients. Therapy response was defined as decreased Mayo score ≥ 3 after 4 months (20 responders and 22 non-responders). The expression of CD86 and CD14 on monocytes in serum and in lysed biopsies was measured by FACS and ELISA, respectively. Expression of the chemokines CCL2, CCL3, CCL4, CX3CL1 and CXCL10 in serum and biopsies was determined by cytokine bead array. Data are presented as median (range).
RESULTS: At baseline there were no differences in monocyte phenotype, chemokine secretion, CRP levels, fecal calprotectin or Mayo score between therapy responders and non-responders. However, in therapy responders, infliximab reduced blood monocyte expression (median fluorescent intensity) of CD86 (2904 (2043-9862) *vs*. 2826 (1351-5618), $p = 0.02$) and CD14 (4004 (1492-23164) *vs*. 3008 (798-9872), $p = 0.02$), 2 weeks after therapy start, relative to baseline. In contrast, therapy non-responders showed increased levels of CD86 (2628 (1420-4848) vs. 3828 (1527-7568), $p = 0.01$) and similar levels of CD14 (3518 (1151-11631) vs. 5312 (3530-17163), $p = 0.1$) at 2 weeks post therapy start, relative to baseline. In intestinal tissue, CD14 (0.36 ng/ml (0.14-0.57) *vs*. 0.63 ng/ml (0.54-0.85), $p = 0.006$) and CD86 (0.43 ng/ml (0.23-0.89) *vs*. 1.35 ng/ml (1-3.09), $p = 0.01$) was lower in therapy responders compared to non-responders 4 months after therapy start.
Two weeks after therapy start, serum CCL2 decreased in therapy responders (169 pg/ml (69-663) vs. 132 pg/ml (43-241), $p = 0.03$) but not in non-responders (118 pg/ml (34-637) vs. 133 pg/ml (44-364), $p = 0.22$), relative to baseline. At 4 months after therapy start, serum CCL2 was still decreased in therapy responders (169 pg/ml (69-663) vs. 126 pg/ml (49-403), $p = 0.009$) but not in non-responders (118 pg/ml (34-637) vs. 128 pg/ml (60-174), $p = 0.16$) relative to baseline. This correlated with lower levels of CCL2 in intestinal tissue in responders as compared to non-responders after 4 months of treatment (12.6 pg/ml (1.4-56.9) vs. 755 pg/ml (465-862), $p = 0.006$). Serum CCL3, CCL4 and CX3CL1 were not linked to therapy response while CXCL10 was only decreased in therapy responders after 4 months (241 pg/ml (75-552) vs. 157 pg/ml (68-608), $p < 0.05$), relative to non-responders.
CONCLUSION: Infliximab therapy response in UC patients is associated with reduced monocyte expression of CD86 and CD14 and serum levels of CCL2 two weeks after therapy start. A similar pattern was observed in intestinal tissue 4 months after therapy start. Thus, reduced monocyte activation and recruitment two weeks after treatment start may reflect early infliximab therapy response in UC patients.
Disclosure of Interest: None declared

P1716 THE INTESTINAL ENVIRONMENT OF PATIENTS WITH ULCERATIVE COLITIS IMPAIRS THE ABILITY OF MACROPHAGE AND DENDRITIC CELL SUBSETS TO PRODUCE RETINOIC ACID

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INTRODUCTION: Intestinal dendritic cells (DCs) and macrophages (MQs) have pivotal roles in intestinal homeostasis, and disruption of this balance can culminate in ulcerative colitis (UC). Relatively little is known about human DC and MQ subsets in the intestinal mucosa in health versus disease. Also, not much is known about retinoic acid, a vitamin A metabolite that can influence the generation of tolerance, and its role in UC.
AIMS & METHODS: Our aim was to study the population dynamics and retinoic acid production of DC and MQ subsets in UC patients with active inflammation and in clinical remission compared to non-inflamed control tissue. Colonic biopsies and surgical samples were collected from patients with active UC (inflamed tissue, $n = 28$), UC in remission (non-inflamed tissue, $n = 6$) and non-inflamed control subjects (non-inflamed tissue, $n = 28$). Blood samples were collected from UC patients in remission ($n = 6$) and non-inflamed control subjects ($n = 7$). Characterization of DCs and MQs was performed by flow cytometry. Lamina propria DCs were grouped into lin-HLADR+CD14-CD1c+ cells (CD1c+DCs) and lin-HLADR+CD14-CD141+ cells (CD141+DCs) and studied for their expression of CD103. Lamina propria MQs were grouped into lin-HLADR+CD14+HLADRint MQs (DRintMQs) and lin-HLADR+CD14+HLADRhi MQs (DRhiMQs). Blood monocytes were grouped into classical (CD14++CD16-), intermediate (CD14++CD16+) and non-classical (CD14+CD16++) monocytes. The ability of cells to produce retinoic acid was analyzed using the Aldefluor assay, which measures aldehyde dehydrogenase (ALDH) activity. Data are presented as median (range).
RESULTS: The inflamed intestinal mucosa of UC patients is characterized by an increased number per 10^5 lamina propria cells of DR^{int}MQs (1472 (160-4066) *vs*. 138 (1-1947), $p < 0.0001$) and a decrease in CD103+$CD1c^+$DCs (4 (1-26) *vs*. 19 (2-59), $p = 0.002$) and $CD103^+CD141^+$DCs (7 (1-38) *vs*. 24 (4-54) $p = 0.0009$) compared to non-inflamed controls. The frequency of $ALDH^+$ cells was reduced in $CD1c^+$DCs (13 % (6-28) *vs*. 47 % (18-61), $p = 0.003$), $CD141^+$DCs (16 % (7-29) *vs*. 33 % (14-64), $p = 0.006$), DR^{int}MQs (8 % (7-24) *vs*. 24 % (21-33), $p = 0.002$) and DR^{hi}MQs (18 % (9-33) *vs*. 56 % (47-69), $p = 0.0002$) from the inflamed lamina propria of UC patients compared to healthy controls. Interestingly, when studying ALDH activity in lamina propria of UC patients in remission, the frequency of $ALDH^+$ cells was also lower among $CD1c^+$DCs (18 % (8-30) *vs*. 47 % (21-61), $p = 0.005$), $CD141^+$DCs (18 % (13-26) *vs*. 41 % (17-64), $p = 0.003$) and DR^{hi}MQs (33 % (19-56) *vs*. 57 % (45-69), $p = 0.01$), compared to controls. In contrast, no difference in the frequency of $ALDH^+$ cells among classical, intermediate or non-classical blood monocytes was detected between UC patients and controls.
CONCLUSION: The inflamed intestinal mucosa in UC is characterized by an influx of DR^{int}MQs and reduced numbers of $CD103^+CD1c^+$DCs and $CD103^+CD141^+$DCs. Colonic myeloid cells of UC patients are imprinted by the intestinal environment to display low ALDH activity, regardless of disease activity, which may influence the delicate balance between inflammation and tolerance.
Disclosure of Interest: None declared

P1717 OSTEOPATHY IMPROVES THE SEVERITY OF IBS-LIKE SYMPTOMS ASSOCIATED WITH CROHN DISEASE IN REMISSION

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INTRODUCTION: Osteopathy may improve the severity of the irritable bowel syndrome (IBS) (1). About 35% of patients with quiescent Crohn Disease (CD) continue to suffer from IBS-like symptoms (2).
AIMS & METHODS: We aimed to evaluate the effect of osteopathy on the severity of IBS-like symptoms in CD patients on remission. We prospectively assigned 38 patients with CD on remission over 12 months while receiving infliximab every 8 weeks. Twenty-five patients received 3 sessions of standardized osteopathy 15, 30 and 45 days after the last infusion of infliximab. Ten patients were followed at same interval for clinical interview. IBS-like symptoms were evaluated according to Rome III criteria. The impact of IBS-like and abdominal pain associated with CD on quality of life was evaluated using the Francis score and the Inflammatory Bowel Disease Questionnaire (IBDq). The severity of psychological factors was appreciated by evaluating anxiety, depression and fatigue with HAD, Beck and Fatigue Impact scale questionnaires. All patients were evaluated at day 0, 30, 45 and 60. Comparisons from baseline values were performed between groups and during time in each group.
RESULTS: Compared with baseline, the severity of IBS-like symptoms was significantly reduced in patients receiving osteopathy. Compared with controls, this decrease was significantly more pronounced in patients treated with osteopathy at day 30 (-38.4±43.9 vs 37.7±49.1, $p = 0.005$) and day 45 (-38.4±43.9 vs 37.7±49.1). Compared with controls, the clinical benefit of osteopathy was not sustained at day 60 (-30 ±43.3 vs -13±36.8, $p = 0.4$). The quality of life was significantly greater during osteopathy ($p = 0.09$ at day 30, $p = 0.02$ at day 45), being not significantly different at day 60 ($p = 0.3$). The severity of fatigue was significantly improved in patients receiving osteopathy with a persisting effect at the end of the study. The effect of osteopathy on depression scores was less marked, being statistically significant only at day 30. However, anxiety was not affected by osteopathy.
CONCLUSION: Three sessions of osteopathy improve the severity of IBS-like symptoms and quality of life associated with CD in remission, with no sustained clinical benefit after stopping treatment. Osteopathy improves fatigue and depression traits whereas anxiety is not changed. Osteopathy should therefore be considered in future clinical trials aimed at reducing the severity of abdominal pain and discomfort in patients with CD considered in remission.
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Disclosure of Interest: None declared

P1718 ANTI-TNF THERAPY RESPONSE IS ASSOCIATED WITH LOWER MUCOSAL EXPRESSION OF INFLAMMATORY CYTOKINES BEFORE THERAPY START IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The mechanisms of action of therapy response to anti-TNF treatment in IBD patients are currently not completely known. Therefore, we aimed to determine the mucosal immunopathology in IBD patients before anti-TNF treatment and four months after therapy start, in therapy responders and non-responders, respectively.
AIMS & METHODS: Mucosal biopsies from 37 IBD patients (UC = 27, CD = 7, unclassified = 3), (28 males, median age 36) were collected before anti-TNF antibody (infliximab or adalimumab) treatment start and at evaluation of therapy response, four months after therapy start. Therapy response was evaluated by comparing one or several of the following parameters before treatment start and after four months of therapy; CRP, fecal calprotectin, partial or complete Mayo score (UC) and HBI (CD). Biopsies were obtained from 24 therapy responders (UC = 17, CD = 5, unclassified = 2) before therapy start, and at four months post therapy start from 11 of these patients. Among non-responders, biopsies were obtained from 13 patients (UC = 10, CD = 2, unclassified = 1) at baseline, and at four months post treatment start from five of these patients. Total mRNA from biopsies was analyzed with real-time PCR. Expression of TNF, IL-1b, IL-17A, IFN-γ, IL-6, IL-13, FOXP3, TNFR1, and TNFR2 was determined. Results were normalized to the expression level of GAPDH and expressed as $2^{\text{-Target-GAPDH}}$. Data are shown as median arbitrary units, 25-75 percentile.
RESULTS: At baseline, there was no difference between UC and CD patients in any of the targets analyzed; therefore patients were not subdivided according to UC or CD-phenotype in subsequent analyses. At baseline, patients responding to therapy had lower levels of TNF (responders $36*10^{-5}$($24*10^{-5}$-$56*10^{-5}$) vs. non-responders $59*10^{-5}$ ($45*10^{-5}$-$76*10^{-5}$); p = 0.046)), and IL-1β ($200*10^{-5}$ ($110*10^{-5}$-$510*10^{-5}$) vs. $510*10^{-5}$ ($370*10^{-5}$-$800*10^{-5}$); p = 0.03) as compared to non-responders. Similar trends were seen for the expression of IL-17A, IFN-g and FOXP3. Among anti-TNF therapy responders, a reduced expression of TNF, IL-1b, IL-6 and FOXP3 was demonstrated, comparing baseline to four months post treatment start (Table 1). Among the patients not responding to the therapy, four out of five patients had reduced expression of IL-17A, IFN-g and IL-1b (p = n.s.) at baseline as compared to after four months of therapy.
Table 1. Mucosal RNA expression in therapy responders at baseline and four months after therapy start.

Target gene	Baseline (x10-5)	4 months post treatment start (x10-5)	p-value
TNF	54 (33-91)	19 (11-72)	0.03
IL-1β	360 (180-1200)	93 (49-180)	0.006
IL-6	130 (66-240)	11 (4.7-40)	0.03
FOXP3	37 (19-70)	18 (8.7-40)	0.007

CONCLUSION: The expression of several mucosal cytokine RNA decreases after four months of anti-TNF therapy among both responders and non-responders, although the cytokines regulated by the therapy may differ between the two groups. Before therapy start, therapy responders have lower mucosal cytokine expression of TNF and IL-1b than non-responders, indicating that non-responding patients might have a more severe immunopathology than responders.
Disclosure of Interest: None declared

P1719 CHARACTERIZATION OF APPENDICEAL LYMPHOCYTES IN ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: An increasing body of literature reported on the negative correlation between an appendicectomy and the development of ulcerative colitis (UC). Extensive infiltration of CD4+ T cells has been observed in the inflamed mucosa of UC patients, and it has been suggested that aberrant activation of T-lymphocytes in the appendix could serve as a priming site. Furthermore, appendiceal mucosal tissue of UC patients showed an increased CD4/CD8 ratio that correlated with the disease activity in the colon. However, which T helper subsets accumulated in the appendix that might account for the enhanced susceptibility to develop UC, remains to be investigated.
AIMS & METHODS: In this study we aimed to characterize the T cell populations in appendiceal mucosal tissues of UC patients with inactive and active disease and compared them to Crohn's disease (CD) and acute appendicitis (AA).
Surgical samples of the appendix were obtained from UC patients and compared to patients with Crohn's disease (CD) and acute appendicitis (AA). UC patients were either in remission (inactive, median mayo score 1) or therapy refractory (active, median mayo score 3). The appendix was histologically evaluated by assessing the degree of inflammation and compared to a retrospective cohort of patients with unaffected appendices (operated upon for cancer). In order to determine the T-cell composition of the appendix in these patients, we took the advantage of multicolour flow cytometric analysis. Both freshly isolated mucosal appendix resection specimens and peripheral blood were stained with a cocktail of antibodies to discriminate between the cytotoxic T cells and T helper subsets.
RESULTS: In contrast to the transmural infection seen in appendices of CD and AA patients, resection specimens of UC patients appeared macroscopically normal. However, histological evaluation showed increased mucosal lymphocyte infiltration, which was not significantly different between inactive and active disease.
We observed in the appendix of UC patients a significantly lower proportion of pro-inflammatory CCR6+ CD4+ T helper cells when compared to CD.
Furthermore, although no significant difference was observed in CCR6+ CD4+ T helper cells between inactive and active UC resection specimens, the proportion of CCR6+ CD4+ T helper cells in peripheral blood of UC patients was significantly higher for inactive disease when compared to active disease.
CONCLUSION: Our results demonstrate that despite a macroscopically normal appearing appendix, there is an increased infiltration of T lymphocytes in appendices of UC patients, irrespective of disease activity. Although no difference was seen between inactive and active UC, the lower frequency of pro-inflammatory CD4+ CCR6+ T cells in the appendix of UC patients compared to CD patients is possibly a result of enhanced efflux of these cells to the affected colon.
Disclosure of Interest: None declared

P1720 NARROW SPECTRUM KINASE INHIBITORS (NSKI) TARGET KINASES INVOLVED IN BOTH INNATE AND ADAPTIVE IMMUNE RESPONSES LEADING TO POTENT AND HIGHLY EFFICACIOUS EFFECTS IN EXPERIMENTAL MODELS OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is a complex disease involving both the adaptive and innate immune responses. Here we demonstrate that NSKI TOP1210 can modulate kinases (P38α & Lck) leading to inhibition of pro-inflammatory cytokine release from cells involved in both arms of the immune response. Furthermore, in vitro, in vivo, and patient explants demonstrate the potent and efficacious effects of NSKIs and their superiority to corticosteroids in these models.
AIMS & METHODS: Inhibition of phospho- P38α (pP38α) & phospho-Lck (pLck) were assessed *in vitro* in either an ATP-based biochemical assay or in human T cells and macrophages by flow cytometry or spectrophotometry methods. *In vivo* efficacy and target engagement of TOP1210 was investigated in an adoptive T cell transfer colitis model with modulation of pP38 and pLck in the mucosal tissue assessed by immunohistochemistry (IHC). Biopsies and cells isolated from IBD patients were cultured *ex-vivo* in the presence or absence of TOP1210 or Budesonide and assessed for pro-inflammatory cytokine release. Cytokine release for all models was assessed by ELISA.
RESULTS: In the *in vitro* assays, TOP1210 exhibited sub-100nM IC_{50} against both pP38α and pLck. Inhibition of pP38α was linked to a reduction of IL-8 release from stimulated human macrophages and inhibition of pLck correlated with a similar inhibition profile of IFNγ release from stimulated human T cells. Oral administration of TOP1210 (5 mg/kg) in an adoptive transfer T cell colitis model led to down modulation of pP38α and pLck in the mucosa of these animals and linked to a reduction in IL-8 and IFNγ release in colon homogenates. Furthermore, TOP1210 was superior compared to a maximum tolerated dose of Budesonide (1 mg/kg) in efficacy end points in the model (histopathology scores). Consistent with the *in vitro* and *in vivo* data, TOP1210 was also found to be a highly efficacious and a potent inhibitor of pro-inflammatory cytokine release from IBD patient biopsies and isolated cells (LPMC and myofibroblasts) with effects comparable, and in some cases superior, to Budesonide.
CONCLUSION: TOP1210 targets key kinases involved in the inflammatory signalling cascades of IBD pathogenesis. Down-modulation of these kinases in both a mouse *in vivo* colitis model and UC patient explants led to a significant reduction in pro-inflammatory cytokine release. TOP1210's efficacy, relative to budesonide, suggests NSKIs may provide an important alternative to corticosteroids in the treatment of IBD.
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P1721 GENETIC POLYMORPHISM IN TRAF3IP2 GENE COULD BE PREDICTIVE FACTOR OF LONG-TERM EFFECT OF INFLIXIMAB AGAINST CROHN'S DISEASE

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INTRODUCTION: Infliximab (IFX) is a TNF-α monoclonal antibody which have substantial effects for remission induction and maintenance for Crohn's disease (CD). However, there are primary failure patients who could not get remission and secondary failure patients who once got remission but the effect of IFX was lost later. In this regard, the identification of biomarkers to predict the therapeutic effect is important. The present study was conducted to elucidate the association of genetic polymorphisms in IL17RA, IL17RC, TRAF3IP2, IL17A, and IL17F in interleukin-17 signaling pathway with therapeutic effects of IFX against CD.

AIMS & METHODS: CD patients who were treated with infliximab in Oita Red Cross Hospital, Nagasaki University Hospital and Nagasaki Harbor Medical Center City Hospital were enrolled in this study. The study was approved by each ethics committee and informed consent was obtained from each subject. For correlation analysis of the short-term treatment effect, we extracted 112 patients who have been assessed treatment effect of 10 weeks after infliximab administration, and for analysis of long-term effect, extracted 104 patients assessed 1 year after, and 93 patients assessed 2 years after administration, and in each treatment period, the patients were divided into two groups whether the treatment was effective or not. In each period, significance tests were performed between sensitive group and resistance group about the frequency of occurrence of genetic polymorphism of IL17RA, IL17RC, TRAF3IP2, IL17A and IL17F.

RESULTS: There were significant differences in the frequency of occurrence of rs10872070 which is single nucleotide polymorphism (SNP) in TRAF3IP2 between the sensitive group and the resistance group two years after IFX administration ($p = 0.022$, $OR = 0.068$). Sensitivity as a biomarker to predict the treatment-resistance was 16.7%, and the specificity was 98.7%. In addition, the positive predictive value was 75.0%, and negative predictive value was 83.1%.

CONCLUSION: We for the first time found that TRPF3IP2 could be the treatment-resistant gene in IFX therapy for CD. This gene polymorphism could be a biomarker to predict the treatment-resistance and secondary failure of IFX. Moreover, IL-17 signaling pathway suggested that participating in the treatment-resistance of IFX would involve the pathogenesis of CD, and it could be a target molecule for novel therapeutics combined with a TNF-α monoclonal antibody.

Disclosure of Interest: None declared