18-Fluorodeoxyglucose Positron Emission Tomography Enhances Computed Tomography Diagnosis of Malignant Intraductal Papillary Mucinous Neoplasms of the Pancreas

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Objective: To assess the reliability of 18-fluorodeoxyglucose positron emission tomography (18-FDG PET) in distinguishing benign from malignant intraductal papillary mucinous neoplasms (IPMNs) of the pancreas and its contribution to surgical decision making.

Summary Background Data: Pancreatic IPMNs are increasingly recognized, often as incidental findings, especially in people over age 70 and 80. Computed tomography (CT) and magnetic resonance (MR) are unreliable in discriminating a benign from a malignant neoplasm. 18-FDG PET as imaging procedure based on the increased glucose uptake by tumor cells has been suggested for diagnosis and staging of pancreatic cancer.

Methods: From January 1998 to December 2005, 64 patients with suspected IPMNs were prospectively investigated with 18-FDG PET in addition to conventional imaging techniques [helical-CT in all and MR and magnetic resonance cholangiopancreatography (MRCP) in 60]. 18-FDG PET was analyzed visually and semiquantitatively using the standard uptake value (SUV). The validation of the diagnosis was made by a surgical procedure (n = 44), a percutaneous biopsy (n = 2), main duct cytology (n = 1), or follow-up (n = 17). Mean and median follow-up times were 25 and 27.5 months, respectively (range, 12–90 months).

Results: Twenty-seven patients (42%) were asymptomatic. Forty-two patients underwent pancreatic resection, 2 palliative surgery, and 20 did not undergo surgery. An adenoma was diagnosed in 13 patients, a borderline tumor in 8, a carcinoma in situ in 5, and an invasive cancer in 21; in 17 patients a tumor sampling was not performed and therefore the histology remained undetermined. Positive criteria of increased uptake on 18-FDG PET was absent in 13 of 13 adenomas and 7 of 8 borderline IPMNs, but was present in 4 of 5 carcinoma in situ (80%) and in 20 of 21 invasive cancers (95%). Conventional imaging technique was strongly suggestive of malignancy in 2 of 5 carcinomas in situ and in 13 of 21 invasive carcinomas (62%). Furthermore, conventional imaging had findings that would be considered falsely positive in 1 of 13 adenomas (8%) and in 3 of 8 borderline neoplasms (37.5%). Therefore, positive 18-FDG PET influenced surgical decision making in 10 patients with malignant IPMN. Furthermore, negative findings on 18-FDG PET prompted us to use a more limited resection in 15 patients, and offered a follow-up strategy in 18 patients (3 positive at CT scan) for the future development of a malignancy.

Conclusions: 18-FDG PET is more accurate than conventional imaging techniques (CT and MR) in distinguishing benign from malignant (invasive and noninvasive) IPMNs. 18-FDG PET seems to be much better than conventional imaging techniques in selecting IPMNs patients, especially when old and asymptomatic, for surgical treatment or follow-up.

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Intraductal papillary-mucinous neoplasms (IPMNs) of the pancreas have been characterized by intraductal papillary epithelial neoplasm with mucin hyper-secretion. The first case of IPMN was reported by Ohashi et al[1] in 1982. Since then, several reports appeared in the English literature on the diagnosis and treatment of these neoplasms, characterized by peculiar pathologic and biologic features. In 1988, Kuroda[2] proposed a classification based on the ductal location of the tumor: main pancreatic duct (MPD) type, branch duct type, and combined type. These intraductal lesions with malignant potential are graded by pathologist according to the World Health Organization (WHO) classification as adenoma, borderline, carcinoma in situ, and invasive carcinoma.[3] Despite increasing experience with these neoplasms, whose incidence is estimated between 0.5% and 10% of pancreatic exocrine neoplasms,[4] the most appropriate diagnostic approach and treatment, especially for the branch duct type, is still debated. Appropriate management of IPMNs requires the differentiation between the premalignant and malignant lesions, but preoperative assessment fails to predict neoplasm extension in up to 40% of patients.[5] Differential diagnosis among the types of IPMN is crucial, because treatment should be different in accordance with histologic progression. Particularly,

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preoperative correct prediction of malignancy is important for establishing prognosis and for surgical decision-making. Jaundice and diabetes are associated with malignant tumors, but their accuracy as clinical predictors of malignancy is low.[6] The reported radiologic features useful for the identification of malignant lesions are a dilated MPD ≥6 to 10 mm, a diameter greater than 3 to 4 cm, the presence of nodules and/or irregular septa, and the thickness of the wall of the cyst.[5,7–9] However, the distinction between benign and malignant neoplasms is still difficult,[10–12] even with endoscopic ultrasonography (EUS).[13]

Positron emission tomography with F-18-fluorodeoxyglucose (18-FDG PET) has an expanding role in the diagnosis and staging of several tumors[14] including pancreatic adenocarcinoma.[15,16] We previously reported that 18-FDG PET was very accurate in discriminating between malignant and benign cystic tumors of the pancreas,[17,18] a small subset of IPMNs included.

The purpose of this study was to evaluate the usefulness of 18-FDG PET in detecting malignancy among a large cohort of patients with IPMNs of the pancreas and its relevance on clinical management of these patients.

METHODS

From January 1998 to December 2005, 71 patients with suspected IPMN of the pancreas were observed in our Department at University of Padua. Among them, 64 patients underwent 18-FDG PET in addition to conventional imaging techniques, and were prospectively investigated, whereas for 7 patients PET scan was not available. All patients also underwent physical examination, medical history evaluation, blood tests and serum CA 19-9 tumor marker determination (RIA; Centocor Inc., Malverne, PA; serum reference <37 U/mL), and helical computer tomography scanning (CT; interval, 2.5 mm thick). The preoperative work-up also included magnetic resonance (MR) and magnetic resonance cholangiopancreatography (MRCP) with intravenous injection of secretin (n = 60); MR and MRCP was not performed in 4 patients: 1 for claustrophobia, 1 because performed 1 year before, and 2 because of clear pattern of malignancy on CT scan. Patient characteristics included age, sex, presence or absence of symptoms, and presence or absence of diabetes mellitus. Radiographic and cyst characteristics included the presence of septations, a solid component or mural nodulation, pancreatic duct dilation, cyst size, and the pathologic diagnosis for resected lesions. If multiple cystic lesions were present within the pancreas, the diameter of the largest lesion was recorded. Malignant IPMNs were defined as IPMNs with high-grade dysplasia (carcinoma in situ), or invasive carcinoma; benign IPMNs were considered those with adenoma or borderline features.[3]

18-FDG PET images were obtained using a dedicated tomograph (ECAT EXACT 47; Siemens, Erlangen, Germany) with a field of view of 16.2 cm. After an overnight fast, 444 MBq (12 mCi) of 18-FDG was injected intravenously into each patient. To avoid interferences caused by hyperglycemia, blood glucose levels were checked just before the procedure and were decreased to <120 mg/dL with insulin administration whenever needed. Two transmission scans of the abdomen, 15 minutes each, were obtained by 68 Ge/68 Ga rod sources before the administration of 18-FDG to obtain cross-sections for attenuation correction of the emission images. Then, 2 emission scans, 15 minutes each, were acquired starting 60 minutes after the administration of 18-FDG. The reconstruction was performed in a 128 × 128 matrix with Hanning filter 0.3 cutoff. Transaxial, coronal, and sagittal sections were obtained for visual analysis. To perform a quantitative analysis, the standardized uptake value (SUV) was calculated in the suspected neoplastic foci (SUV = tissue tracer concentration/injected dose/body weight). For the SUV analysis, a circular region of interest was placed over the area of maximal focal 18-FDG uptake, and the mean radioactivity values were obtained. A focal uptake with an SUV of 2.5 or greater was considered positive according to our previous experience and literature reports.[17–19] The reporting of each of the imaging modalities was reported blindly of the other results.

A validation of the diagnosis was based on the pathologic findings of a resected specimen biopsy examination, or follow-up. Follow-up evaluation included clinical examination, laboratory tests, CA 19-9 serum levels, and CT and/or MR and MRCP every 6 months. PET was performed at least 12 months after the first observation or in the case of clinical suspicion, tumor marker increase, or inconclusive results of conventional imaging techniques.

Sensitivity, specificity, positive (PPV) and negative predictive value (NPV), and accuracy of 18-FDG PET and CT/MR and MRCP in differentiating malignant from benign lesions were evaluated, according to the following formulas: sensitivity = TP/TP + FN; specificity= TN/TN + FP; PPV = TP/TP + FP; NPV = TN/TN + FN; accuracy = TP + TN/TP + TN + FP + FN, in which TP indicates true positive; TN, true negative; FP, false positive; and FN, false negative. Our policy in the management of patients with IPMNs was to perform resection, whenever possible, in all the symptomatic or PET positive lesions. For PET negative IPMNs, surgery was performed only when clinical and radiologic features suggested malignancy or the patients were young. A lesion >3 cm, the presence of mural nodules and thick wall, the dilation of MPD >1 cm, high serum levels of CA 19-9, recent-onset of diabetes and jaundice were considered related to potential malignancy, as previously reported.[4,20] Standard resection was the operation of choice for malignancies, whereas type 3 duodenum preserving pancreatic head resection,[21] median pancreatectomy, enucleation, or spleen preserving surgery was reserved for benign or borderline lesions. The pancreatic surgical margins were analyzed intraoperatively by frozen section; negative resection margins were needed for conservative surgery. Follow-up was planned for PET negative patients when old and asymptomatic, or high surgical risk, or with lesions located in the head or in the entire gland.

RESULTS

The clinicopathologic features of the 64 patients enrolled in this study are detailed in Table 1. There were 33 males and 31 females with a mean age of 64 years (range,

TABLE 1. Clinical and Pathologic Characteristics of the 64 Patients Investigated

	Total	Malignant	Benign
Sex			
Male	33	15	18
Female	31	11	20
Age (yr)			
Mean	63.6	65.0	62.3
Range	37–84	41–81	37–80
Treatment			
Resection	42	22	20
Bypass	2	2	0
Observation	20	2	18
Symptoms			
Yes	37	21	16
No	27	5	22
Diabetes			
Yes	13	8	5
No	51	18	33
Ca 19-9 (>37 U/mL)	16	11	5
Subtype			
Main duct	28	19	9
Branch duct	36	6	30
Mural nodules	15	10	5
Pancreatic duct dilation	36	21	15
Mean size (cm)	2.8	3.2	2.6

37–84 years). Twenty-seven patients (42%) were asymptomatic and the pancreatic lesion was incidentally discovered during investigations for unrelated disease. Thirty-seven patients were symptomatic: the most common symptoms were abdominal pain (n = 27) with one or more attacks of acute pancreatitis (n = 15), jaundice (n = 7), malabsorption (n = 1), gastrointestinal hemorrhage (n = 1), and cholangitis (n = 1). A total of 13 patients were diabetic [6 Insulin Dependent Diabetes (IDD)]. The final pathologic diagnosis was obtained by pathologic review of the surgical specimen in 44 patients, percutaneous biopsy in 2, and brush cytology during endoscopic retrograde cholangiopancreatography in 1. Twenty-six patients had malignant neoplasms: 5 carcinoma in situ, 21 invasive carcinoma. Twenty-one patients had a benign neoplasm proven by histology. One of them and 17 patients considered to have benign disease without histology were put on follow-up. Mean tumor diameter was 2.8 cm (range, 1.0–10.0 cm). Forty-one patients had multiple pancreatic cystic lesions. The main tumor arose from a branch duct in 36 patients, and from the MPD in 28 patients.

Malignant Neoplasms

There were 15 males and 11 females with a mean age of 65 years (range, 41–81 years) (Table 1). Twenty-one patients (80.77%) were symptomatic: 9 had abdominal pain, 7 had jaundice, 4 had one or more attacks of acute pancreatitis, and 1 was presented with steatorrhea. One of the jaundiced patients with a diagnosis of chronic pancreatitis underwent biliary and pancreatic endoprosthesis before referral to our department. Five patients were asymptomatic and their lesion was incidentally found during investigation or follow-up for other disease (chronic hepatitis 2, prostate cancer 1, trauma of the hip 1, and high serum CA 19–9 levels 1). Eight patients were diabetic (4 IDD) and 11 presented with high serum levels of CA 19–9 tumor marker. Mean tumor diameter was 3.2 cm (range, 1.0–10 cm). The CT scan showed a lobulated cystic mass (n = 9), multiple cysts (n = 10), dilated MPD (n = 19) with mural nodules (n = 10). Clear CT features of malignancy were found in 15 patients (58%). Twenty-four of the 26 patients (92%) showed 18-FDGF PET uptake with an SUV range of 2.5 to 9.0, mean 4.2. A focal uptake was found in 20 patients and a peripheral uptake with central absence of metabolism was found in 4; 18-FDG PET also showed hepatic metastases in 2 of 24 patients, and a lymph node metastasis was not seen by conventional imaging in 1 of 24. Thirteen patients underwent pylorus-preserving pancreaticoduodenectomy (PPPD), 2 total pancreatectomy (TP), 7 distal pancreatectomy (DP) and splenectomy, 2 biliary and gastric bypass. The 2 patients with hepatic metastases demonstrated by 18-FDG PET did not undergo surgery; the diagnosis was confirmed by percutaneous fine-needle biopsy.

Pathologic diagnosis showed 21 invasive cancers (2 metastatic) and 5 noninvasive (in situ) carcinomas. 18-FDG PET showed an increased uptake in 4 of 5 carcinomas in situ (80%) and in 20 of 21 invasive cancers (95%) (Table 2): all the 5 asymptomatic patients showed a pathologic uptake of 18-FDG and were resected. The 2 false negative PET patients were a woman with recurrent attacks of acute pancreatitis with a 2-cm-cyst in the head of the pancreas and a carcinoma in situ (CT and MR features negative for malignancy), and a man with invasive malignant IPMN of the head of the pancreas with solid component at CT examination, suggesting malignancy. Conventional imaging techniques showed clear or equivocal signs of malignancy in 2 of 5 (40%) carcinomas in situ and in 13 of 21 (62%) invasive cancers.

Benign Neoplasms

Among the patients with benign neoplasms, there were 18 males and 20 females with a mean age 62 years (range, 37–80 years) (Table 1). Sixteen patients (42%) were symptomatic: the most common symptoms were abdominal pain (n = 14), one or more bouts of acute pancreatitis (n = 11), gastrointestinal hemorrhage (n = 1),

TABLE 2. Imaging and PET Results According to Pathologic Features

		PET		CT/MR	
Pathology	N	Pos	Neg	Pos	Neg
Adenoma	13	0	13	1	12
Borderline	8	1*	7	3	5
Ca in situ	5	4	1	2	3
Carcinoma	21	20	1	13	8
Undetermined	17	0	17	3†	14
Total	64	25	39	23	41

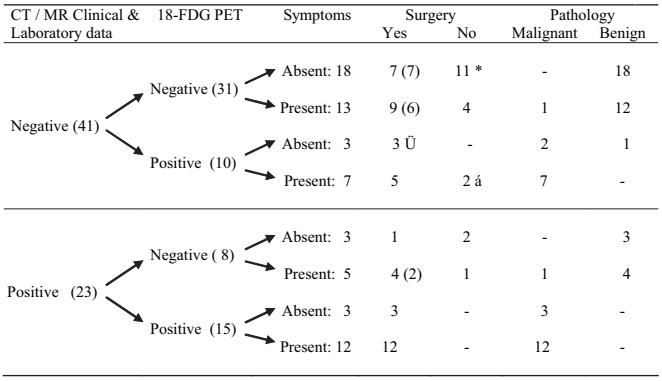
*Patient with associated colon carcinoma.
†Two patients with equivocal radiological features of malignancy.

and cholangitis (n = 1). Five patients were with diabetes (2 IDD) and 5 presented with increased CA 19–9 levels. Twenty-two patients (58%) were asymptomatic and their lesion was incidentally found during investigations for unrelated disease. CT and/or MR showed a lobulated cystic mass in 9 patients, multiple cysts in 23, and a marked dilation of MPD in 6 patients. The dilation of the MPD was associated to cystic lesion in a total of 15 patients. The main tumor diameter was 2.6 cm (range, 1.0–10.0 cm). Seven patients (18%) showed CT or MR features suggesting a malignant tumor (solid component or mural nodules). In 37 of 38 patients (97%) no pathologic uptake of 18-FDG was shown. The remaining patient showed a focal uptake in the head of the pancreas (SUV = 2.5) corresponding to very small mural nodules within cystic lesion and MPD dilation at CT and MR examinations. A focal uptake of 18-FDG was detected also in the right colon: colonscopy showed a polipoid mass. A TP and right colectomy were performed; pathology showed a diffuse borderline IPMN of the pancreas and a carcinoma in situ of the right colon.

Twenty patients underwent resection: PPPD (3), pylorus-preserving TP (2), type 3 duodenum preserving pancreatic head resection[21] (3), median pancreatectomy (1), enucleation (2), and spleen-preserving DP (9). Eighteen patients considered harboring a benign disease were put on follow-up; only 1 of them underwent brush cytology during endoscopic retrograde cholangiopancreatography with a pattern compatible with adenoma. Three (77, 77, and 78 years old) of the 18 patients were CT scan positive and 18-FDG PET negative; 1 refused surgery and 2 were considered at high risk due to associated diseases. All patients were followed as described (mean and median follow-up 25 and 27.5 months, respectively; range, 12–90 months); none of them showed malignancy or substantial changes in the radiologic appearance of their lesion. The final pathologic diagnosis was adenoma in 13 patients, borderline tumor in 8, and remained undetermined in 17 nonoperated patients (Table 2).

Sensitivity, specificity, PPV, NPV, and accuracy of 18-FDG PET in detecting malignant IPMNs were 92%, 97%, 96%, 95%, and 95%; these figures for CT and/or MR were 58%, 82%, 68%, 74%, and 72%; if only patients with proven histology are considered, the corresponding figures were 92%, 95%, 96%, 91%, and 94% for 18-FDG PET and 58%, 81%, 79%, 61%, and 68% for CT and/or MR. The figures of MR were 1% to 3% lower than the corresponding figures of CT scan.

Treatment strategy based on PET findings is depicted in Figure 1. Positive 18-FDG PET findings influenced surgical decision making in 10 patients (16%): it suggested surgical resection in 7 (2 asymptomatic) without signs of malignancy on conventional imaging, avoided laparotomy in 2 patient with hepatic metastases not seen by CT, allowed resection of a borderline IPMN associated with unsuspected colon cancer in 1 patient. Furthermore, negative 18-FDG PET findings prompted the choice to put 3 CT positive patients on follow-up, allowed more limited resection in 15 patients (23%), and a follow-up strategy in other 16 patients (25%).



( ) Organ sparing surgery
* Brush cytology during ERCP in 1/11
ÜColon cancer discovered by PET in 1/3
á Percutaneous fine-needle biopsy

FIGURE 1. Treatment tree of the 64 IPMNs.

DISCUSSION

This is the largest study performed on the role of 18-FDG PET in IPMNs. The present study demonstrated a better sensitivity (92% vs. 58%), specificity (97% vs. 82%), and accuracy (95% vs. 72%) of 18-FDG PET than CT and MR in detecting malignant IPMNs. If only patients with proven histology are considered, the corresponding figures were 92% versus 58%, 95% versus 81%, and 94% versus 68%. There are few reports dealing with PET imaging and IPMNs of the pancreas. In 2001, we reported a better accuracy of 18-FDG PET than CT in detecting malignancy in 56 cystic tumors of the pancreas, 9 IPMNs included.[17] The results were confirmed in 2005 on further 50 patients, 17 IPMNs included.[18] In 2003, Yoshioka et al[22] reported a high 18-FDG uptake in 2 patients with IPMN and invasive carcinoma. In the same year, McHenry et al[23] reported that EUS fine needle aspiration biopsy was more accurate (71%) than PET scan (50%) in detecting malignant cystic lesions in 13 patients, 8 IPMNs (3 benign and 5 malignant) included. Unfortunately, this study was published only as an abstract, and the procedure of the 18-FDG PET was not clearly described. The authors suggested the need of further experiences to assess the role of 18-FDG PET in pancreatic cystic lesions. More recently, Mansour et al[24] of the Memorial Sloan-Kettering Cancer Center of New York, investigated 68 patients with suspected cystic tumors of the pancreas (5 IPMNs) with PET scan, and reported that the sensitivity (57%) and specificity (85%) of PET for malignancy was much lower than previously reported by our group.[17,18] Unfortunately, only 21 patients (29%) were resected and, among them, only 8 had malignant lesions. Furthermore, only 5 patients had an IPMN (3 benign and 2 malignant), and the 18-FDG PET was performed in only 4 (3 negative and 1 positive). Finally, the procedure of the 18-FDG PET was not reported. We should remember that the results of 18-FDG PET depend on several factors, procedure and instrumentation included.[25]

In recent years, 18-FDG PET imaging has been increasingly used in the diagnosis, staging, and post-treatment surveillance of many types of malignancies.[19] During the pro-

cess of malignant transformation, the majority of cells become avid glucose scavengers, with increased glucose transport and utilization. The enhanced glucose uptake explains why 18-FDG PET can functionally identify malignant tissue. This principle led us to verify in 2001[17] and 2005[18] a possible role of 18-FDG PET in the differential diagnosis of cystic lesions of the pancreas, particularly in distinguishing malignant from benign pancreatic cystic tumors. In both studies, 18 FDG PET showed a better accuracy in detecting malignant cysts compared with conventional imaging techniques, and the results were confirmed by histology in 55 of 56 patients of the first study[17] and in 35 of 50 of the second study.[18] In the present study, the 26 IPMN patients of the previous studies were also included and histology was confirmed in 47 of 64 patients. The accuracy of the procedure was therefore verified by histology in a total of 116 of 144 patients.

In our hands, 18-FDG PET was able to detect 24 of 26 malignant IPMNs (sensitivity 92%), and, among them 4 of 5 patients with a carcinoma in situ; in 3 of these patients CT and MR did not show any sign of malignancy. Furthermore, 18-FDG PET added new information about tumor extension in 2 of 26 patients, showing hepatic metastases not detected by traditional imaging. The false negative results occurred in a patient with IPMN and carcinoma in situ (not seen also by traditional imaging) and in a jaundiced patient with invasive IPMN carcinoma of the head of the pancreas correctly detected by CT scan. The recent International Association of Pancreatology guidelines for the management of IPMN of the pancreas stated that, at present, it is impossible to diagnose preoperatively the minimal invasion of IPMN as is the case in minimally invasive MCN.[26] If we consider that 18-FDG PET was positive in 4 of 5 of our patients, and in the 80-year-old female with IPMN in situ reported by Mansour et al,[24] it may be considered a promising diagnostic test for minimally invasive IPMNs.

In our study, only 1 of 38 patients with benign lesions was PET positive (specificity, 97%); a simultaneous focal uptake of 18-FDG was shown in the right colon, and the patient underwent a TP and right colectomy. Pathology showed a main duct diffuse borderline IPMN and a carcinoma in situ of the right colon. Considering all the patients with benign lesions who underwent 18-FDG PET for cystic lesions in our department, only 4 of 110 were PET positive (specificity 96%).

Cystic lesions of the pancreas, IPMNs included, are increasingly recognized, often entirely asymptomatic, because of the increasing use of high quality cross-sectional imaging.[27] IPMNs are considered a premalignant precursor to pancreatic adenocarcinoma; so, surgical resection is advocated for these lesions. However, the time and the real incidence of progression from benign to frankly malignant tumor is very difficult to be defined,[28] and a difference in potential malignancy between main duct and branch duct type IPMNs, has been reported.[29,30] Furthermore, an increasing number of asymptomatic patients with IPMN are now detected, and, frequently, these neoplasms are discovered in people over age 70 and 80 with comorbidities that make surgical resection less desirable. Finally, the resection of neoplasms located in the head or diffuse to all pancreas suggests caution even in younger patients, especially if alternative pancreas sparing procedures are available for benign or borderline disease. Such an approach might be applied with more confidence if reliable preoperative indicators of malignant versus benign neoplasms exist. Therefore, we need a simple, reliable, and noninvasive test that is able to differentiate malignant from benign IPMN.

Despite previous reports of typical clinical and radiologic features, conventional imaging modalities, such as CT and MR do not reliably distinguish between benign and malignant IPMNs.[8,11,12] In our experience, the accuracy of CT and/or MR in detecting malignant IPMNs was 72%, with sensitivity and a specificity of 58% and 82%. It was only slightly lower (accuracy 68%, sensitivity 58%, specificity 81%) if only histologically proven lesions are considered. The sensitivity and specificity of CT and MR for malignant cystic lesions have been reported as 25% to 100% and 40% to 92%.[24]

EUS has an expanding role in the preoperative evaluation of pancreatic neoplasms, including IPMNs,[9,31] but EUS alone seems not to substantially improve CT results in distinguishing malignant from benign lesions.[10,13] Furthermore, EUS is a highly operator dependent procedure, and a large experience is needed before reaching satisfactory results. EUS fine-needle aspiration cytology seems to be a logical adjunctive test to better define a malignant cystic mass of the pancreas.[32] However, cytology often shows false negative or inconclusive results, and only presence of atypia has been suggested as reliable indicator of malignancy.[8,33] Wiesenauer et al[8] emphasized the usefulness of cytologic sources (ductal lavage, brushing, FNA) in detecting malignant IPMNs with a sensitivity of 91%. However, only 40% of noninvasive cancers (ie, carcinoma in situ) were detected by examination of cytologic specimens.

Our surgical policy changed with increasing experience with PET-scan. Although we started resecting with standard procedures (PD, PPPD, TP, and DP) most of our IPMNs, nowadays we perform type 3 duodenum preserving pancreatic head resection,[21] median pancreatectomy, or spleen preserving surgery whenever possible (Fig. 1), and propose a wait and see policy to patients with PET negative branch duct IPMNs, and also for older (>70 or 80 years) or high risk patients with a PET negative main duct IPMN. According to this policy, a negative PET-scan prompted a more conservative pancreatic resection (n = 6) or avoided unnecessary splenectomy (n = 9).

Furthermore, 18 patients underwent follow-up. All nonoperated patients were checked at 6 months, and thereafter once a year. None showed changes in cyst diameter or appearance. Although the follow-up is relatively short (mean and median follow-up 25 and 27.5 months, respectively; range, 12–90 months) it is in the range of that reported by others.[4,12,24]

Finally, positive 18-FDG PET findings influenced surgical decision making in 10 patients (16%) suggesting surgical resection in 7 patients (2 asymptomatic) without signs of malignancy on conventional imaging, allowing resection of a borderline IPMN associated with an unsuspected colon can-

cer in 1 patient, and avoiding laparotomy in 2 patients with hepatic metastases not seen by CT. Negative 18-FDG PET allowed planning follow-up strategy for 3 patients with CT-positive lesion.

CONCLUSIONS

18-FDG PET is a very useful technique for the preoperative work-up of patients with suspected IPMNs of the pancreas. It is much more accurate than conventional imaging in distinguishing benign from malignant lesions, including noninvasive carcinomas. 18-FDG PET is better than other imaging techniques in selecting IPMNs patients, especially asymptomatic, for surgical treatment or for long-term follow-up.

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Discussions

PROFESSOR K. CONLON: We have heard from this presentation and the previous presentation that the diagnosis of intraductal papillary mucinous tumors is problematic and the treatment is somewhat controversial. In addition, a significant proportion of patients, up to 50%, irrespective of whether or

not main or branch ducts are involved will either harbor invasive cancer or in situ disease. I have a number of specific questions.

First, I would like you to expand on your criteria for CT assessment of these patients. I am somewhat unclear from your presentation as to what would make you, on the basis of the CT alone, adopt a conservative approach. For the 2 examples you showed in this presentation, if I saw them in my clinic, I would take them to the operating theater.

My second question relates to the actual CT technology used in your study. You have shown us 2 types of CT technology – the helical scanner before 2004 and the multisliced integrated PET scanner from 2004 onward. Was there any difference in the results from these differing technologies?

My third question addresses the role of PET scanning in the follow-up of this group of patients. Do you have any experience using PET scanning in follow-up?

PROFESSOR S. PEDRAZZOLI: Perhaps the images that were chosen are not the best, but our criteria were tumor diameter <3 cm mural nodules less than 10 mm. There is a debate as to whether the lower limit of the size of mural nodules should be considered potentially malignant; several limits have been proposed: 6, 7, 8, 9, and 10 mm. So we used the criteria defined by previous authors. I admit that we saw referred patients coming from several places, and the CT scan was not always of good quality, so the result may not be as good as if performing them following the same procedure and using the same scanner. But I believe that it is important for general surgeons to understand that accuracy is not higher than 60% to 75%, and that is quite a bit lower than >90% with the 18-FDG PET.

As for your second question about PET scan and the PET CT scan, we did not see any difference between the two. Here is an example of a more recent case regarding follow-up. A female patient of 82 years was put on follow-up because of a negative PET. One year later the PET scan became positive. I was convinced, it was cancer although no criteria for the CT scan were positive for cancer, and I successfully resected a malignant tumor. I have more cases like that so I believe that having a method that allows you to have >90% confidence that it is malignant or benign is important. I am not sure but I believe that it is much better than 70%.

PROFESSOR K. CONLON: I have just 1 additional question. In your study, if I read the data from your slides correctly, you had 16 patients with a negative CT scan and a negative PET scan and yet they were taken to the operating theater, and 9 of those patients turned out to have malignant disease.

PROFESSOR S. PEDRAZZOLI: Thirty-one were CT and PET negative. Fifty-six percent of the 16 resected patients were symptomatic. Only 1 was malignant.

PROFESSOR K. CONLON: So it is symptoms, then?

PROFESSOR S. PEDRAZZOLI: Yes, for 56%.

PROFESSOR P.-A. CLAVIEN: This is a clinically significant topic with the aim of identifying the timing and maybe the type of surgery for this difficult population of patients. I have, however, a concern regarding the design of the study, which is reflected in the title of your presentation: "18-FDG PET is much better than CT in distinguishing benign from malignant IPMN of the pancreas". Currently, we do not want to compare PET scanning with CT, but rather the combined PET/CT versus CT alone. I understand that many patients in your study had a PET scan alone followed by a CT scan, but today the PET machine without a combined CT is no longer available. The industry is producing only PET/CT, in which CT can be performed with or without IV contrast.

PROFESSOR S. PEDRAZZOLI: Are you speaking about PET CT with or without contrast?

PROFESSOR P.-A. CLAVIEN: Most of us today will get a PET/CT using IV contrast. With this tool we have the full information from the CT scanning plus the exact anatomic information of the positive PET lesions. But I would formulate my question as follows: "Today would you do just a PET scan on these patients without CT at all?"

PROFESSOR S. PEDRAZZOLI: No.

PROFESSOR P.-A. CLAVIEN: Therefore, the relevant question that needs to be addressed using your important data is whether PET plus a CT scan is superior to the CT scan alone. In other words, does the addition of the PET enable the detection of more tumors and their dignity? We want to be better in detecting malignant versus benign lesions in IPMN patients.

PROFESSOR S. PEDRAZZOLI: The diagnosis of IPMN does not need PET scan, but certainly PET scan is much better than CT alone to identify a malignant IPMN. The main problem in premalignant IPMNs is to be able to detect malignant changes when they occur. Malignant IPMN needs a pancreatic resection even if the surgical risk is increased, while the same patient with still benign, although premalignant, lesion may be put on follow-up. The addition of PET, with its very high accuracy, is of great aid in the decision making process.

PROFESSOR M. BÜCHLER: Regarding clinical reliability and relevance, Helmut Friess, my coworker, has already published, in 1990, about PET and pancreatic cancer. This is now 17 years ago. Then, we had a sensitivity and specificity of the PET for pancreatic cancer that was around 85%. And then there were multiple trials after and, more or less, the sensitivity and specificity for the malignancy is

around 80% but not better. So it is hard to believe that, in the IPMN situation, it should be better than 80%. Our experience is that you still have many cases where you see a false positive or a false negative and we will not rely on it.

PROFESSOR S. PEDRAZZOLI: You remember that there are 2 ways for pancreatic cancer to present. One is IPMN, the other is PANIN, and perhaps, there is a difference in their glucose uptake. We can have an uptake in route 1 (IPMN) that is much higher than in route 2 (PANIN and pancreatic cancer) and this may be an explanation as to why, because we now have 144 cystic lesions with an accuracy that remains over 90%. It has remained so for 7 years. One hundred sixteen of 144 have histology. It may be by chance, but I do not believe so with such a number.