

Analysis of Factors Affecting Short-term Results in Elderly Patients Undergoing Elective Surgical Resection for Stage I-II Colon Cancer

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Abstract. *Aim:* The aim of this study was to analyze the influence of comorbidities and to compare the short-term results of elective surgical resection of stage I-II colon adenocarcinoma in elderly (≥ 65 years) versus younger patients. *Patients and Methods:* Two groups of sex-matched younger and older patients were compared: Group A: N=36, median age 58 (range=43-65) years; and group B: N=67, median age 73 (range=66-86) years. *Results:* Overall, 71 out of 103 (68.9%) patients had one or more comorbidities. A greater number of older patients had an American Society of Anesthesiologists (ASA) score >2 ($p=0.004$) and were on multiple medications (polypharmacy) ($p=0.016$), but the distribution of the other parameters was similar ($p\geq 0.05$). Intra- and postoperative complications in group A vs. B occurred in 25.0% vs. 26.9%, and 47.2% vs. 64.2%, respectively ($p\geq 0.05$). *Conclusion:* Elderly patients with colon cancer scheduled to elective surgical resection should not be considered at increased risk of intra- or short-term postoperative complications with respect to younger patients. However, they require careful individual preoperative evaluation because they are usually polypharmacy users and have a higher ASA score.

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Colorectal cancer (CRC) is one of the most common types of cancer in the world, with more than 1.4 million new cases diagnosed yearly (1). In the USA and in the European Union, the estimated CRC incidence is approximately 41 and 44 cases per 100,000 people per year, respectively (2, 3). CRC primarily affects the elderly (≥ 65 years), who usually have several comorbidities, potentially leading to several short- and long-term operative complications (4). Unfortunately, since CRC is quite uncommon in young people, most patients are usually considered at increased risk compared to those with other types of cancers. However, it is still unclear whether the incidence of perioperative complications differs between elderly and younger patients (5). The aim of this study was to analyze the influence of comorbidities and to compare the short-term results of curative surgery in older versus younger patients with colon adenocarcinoma, which accounts for approximately 95% of cases of colon cancer (6).

Patients and Methods

Design and study population. Our Institution's database was searched for medical records of patients with stage I-II (Dukes' A-B) colon adenocarcinoma, according to the American Cancer Society staging system (7), diagnosed and treated between 2013 and 2014. Patients with advanced (stage III-IV) cancer, other histological type of tumor, who required emergency surgery or had rectal cancer, were excluded from the study. All selected patients (N=103) had undergone elective surgical resection with curative intent at the same Institution. The data collected included age, gender, comorbidities, intra- and postoperative short-term (during the hospital stay) complications, operative time, intraoperative bleeding and duration of the hospital stay. There were 71 (68.9%) men and 32 (31.1%) women, with an overall median age of 66 years (range=43-86 years). The study population was divided into two groups of sex-matched patients according to their age: Group A: younger (≤ 65 years), N=36 (34.9%), median age=58 (range=43-65) years; and group B: older (>65 years), N=67 (65.1%), median age=73 (range=66-86) years.

Table I. Definitions and source of definition of comorbidities.

| Comorbidity | Definition and source |
|---|--|
| American Society of Anesthesiologists (ASA) score | ASA Physical Status Classification System. Available at: https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system |
| Anticoagulation therapy | The use of drugs (<i>i.e.</i> warfarin) to reduce clot formation in the blood and to maintain the International Normalized Ratio within the individual therapeutic range, usually from 2 to 3 |
| Cardiovascular disorders | Arterial hypertension, coronary artery diseases, silent ischemia, angina, heart failure, arrhythmia, and peripheral arterial diseases |
| Chronic neurological disorders | Cerebrovascular diseases, senile dementia, Alzheimer's and Parkinson's diseases, amyotrophic lateral sclerosis, Huntington's disease, and multiple sclerosis |
| Chronic obstructive pulmonary diseases | Chronic bronchitis, emphysema, refractory asthma, and some forms of bronchiectasis |
| Diabetes mellitus | The American Diabetes Association (8) |
| Liver failure | Child-Pugh score B or C. According to Albers <i>et al.</i> (9) |
| Renal failure | Stage ≥ 2 chronic renal failure (glomerular filtration rate ≤ 60 ml/min/1.73 m ²) according to The Renal Association. Available at: http://www.renal.org/information-resources/ |
| Smokers | Patients smoking more than 1-2 cigarettes per day |
| Polypharmacy | The use of multiple medications not all necessary. According to Maher <i>et al.</i> (10) |

The conditions that patients had before surgery potentially affecting results were considered comorbidities and are reported in Table I.

Statistical analysis. The comparisons of distributions of dichotomous variables between groups were evaluated using the chi-squared (χ^2) test and contingency tables, or the Fisher exact probability test when expected cell frequencies were 5 or less. Assuming that the data were not normally distributed, the Mann-Whitney *U*-test was used to compare continuous variables. A *p*-value of less than 0.05 was considered statistically significant.

Results

The gender distribution between groups was the same ($p=0.718$). Overall, 71 (68.9%) patients had one or more comorbidities, as reported in Table II. A significantly greater ($p<0.05$) number of older patients had an American Society of Anesthesiologists (ASA) score >2 , and were on multiple medications (polypharmacy). A weak non-significantly increased incidence of both cardiovascular ($p=0.088$) and chronic neurological ($p=0.058$) disorders was observed in patients of group B, but the distribution of the other parameters was similar ($p\geq 0.05$). Thus, the two groups were homogeneous with regard to the majority of comorbidities, excluding ASA score and polypharmacy. Overall, intraoperative complications occurred in 25.0% of group A and 26.9% of group B patients, while postoperative complications occurred in 47.2% and 64.2% patients, respectively (Figure 1). The single complication rates did not differ significantly ($p\geq 0.05$) between younger and older patients (Table III). Both operative time (151 ± 35 vs. 166 ± 41 min, $p=0.066$) and postoperative hospital stay (7.2 ± 1.8 vs. 8.1 ± 2.6 , $p=0.067$) were shorter in group A, but the difference was not significant ($p\geq 0.05$). Similarly, intraoperative bleeding (81 ± 27 vs. 95 ± 42 mL, $p=0.074$) was slightly reduced but without statistical significance.

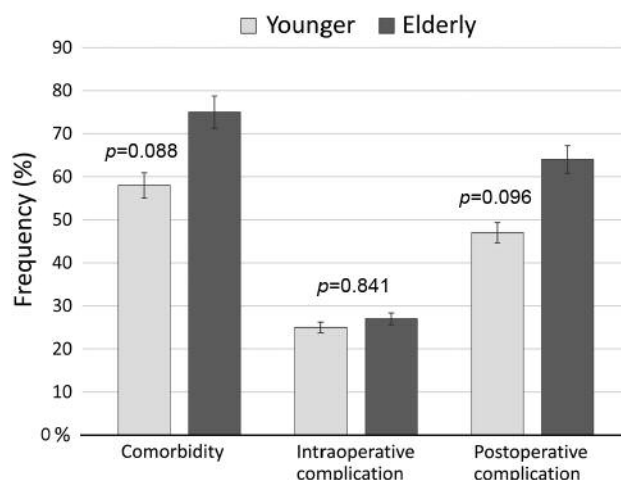


Figure 1. Rates of comorbidities and complications in the two groups of patients.

Discussion

In patients with CRC undergoing elective surgery, the rate of postoperative complications ranges widely, approximately from 33% to 57% (11-14). According to a cumulative review, the most frequent complications were prolonged ileus, pneumonia, and urinary tract infections, while the main risk factors were age, male gender, ASA score, and malnutrition (15). In patients taking anticoagulants, including vitamin K antagonists, several concomitant factors may lead to an increased risk for major hemorrhage (16). More recent studies report other predictors, including cancer stage, operative time, and blood loss (13, 14). The presence of

Table II. Comorbidity rates in the overall study population and in the two groups of patients.

| Comorbidity | Overall | Group A (≤ 65 years) | Group B (>65 years) | RR (95% CI) | p-Value [‡] |
|--|---------|----------------------------|------------------------|------------------|----------------------|
| Anticoagulation therapy | 26.2% | 16.7% | 31.3% | 1.21 (0.97-1.51) | 0.106 |
| ASA score >2 | 34.9% | 20.0% | 44.8% | 1.51 (1.16-1.96) | 0.004 |
| BMI >25 kg/cm ² | 14.6% | 16.7% | 13.4% | 0.96 (0.81-1.14) | 0.654 |
| Body weight loss $>10\%$ | 12.6% | 11.1% | 13.4% | 1.03 (0.88-1.19) | 0.770 |
| Cardiovascular disorders | 33.0% | 22.2% | 38.8% | 1.27 (0.98-1.65) | 0.088 |
| Type 1 or 2 diabetes mellitus | 16.5% | 13.9% | 17.9% | 1.05 (0.88-1.25) | 0.603 |
| Liver/renal failure | 15.5% | 13.9% | 16.4% | 1.03 (0.87-1.22) | 0.740 |
| Chronic neurological disorders | 14.6% | 5.6% | 19.4% | 1.18 (1.02-1.35) | 0.058 |
| Chronic obstructive pulmonary diseases | 15.5% | 11.1% | 17.9% | 1.08 (0.92-1.27) | 0.362 |
| Smokers | 18.4% | 22.2% | 16.4% | 0.93 (0.76-1.14) | 0.473 |
| Polypharmacy | 49.5% | 33.3% | 58.2% | 1.59 (1.11-2.30) | 0.016 |
| None | 31.1% | 41.7% | 25.4% | 0.78 (0.57-1.06) | 0.088 |

BMI: Body mass index, RR: relative risk, CI: confidence interval. [‡]Between groups.

Table III. Intra- and postoperative short-term complications (%) in the overall population and in the two groups of patients.

| Complication | Overall | Group A (≤ 65 years) | Group B (>65 years) | RR (95% CI) | p-Value [‡] |
|----------------------------|---------|----------------------------|------------------------|------------------|----------------------|
| Intraoperative | | | | | |
| Bowel injury | 2.9% | 2.8% | 3.0% | 1.00 (0.93-1.07) | 0.720 |
| Splenic injury | 4.9% | 5.6% | 4.5% | 0.99 (0.90-1.07) | 0.598 |
| Ureter/bladder injury | 1.9% | 2.8% | 1.5% | 0.98 (0.93-1.05) | 0.579 |
| Serious bleeding* | 2.9% | 5.6% | 3.0% | 1.00 (0.93-1.07) | 0.720 |
| Other complication | 6.8% | 5.6% | 7.5% | 1.02 (0.92-1.13) | 0.532 |
| None | 73.8% | 75.0% | 73.1% | 0.93 (0.47-1.85) | 0.841 |
| Postoperative | | | | | |
| Anastomotic leak | 9.7% | 8.3% | 10.4% | 1.02 (0.90-1.16) | 0.513 |
| Pneumonia/pleural effusion | 27.2% | 11.1% | 20.9% | 1.12 (0.95-1.33) | 0.213 |
| Sub-ileus | 7.8% | 5.6% | 8.9% | 1.04 (0.94-1.16) | 0.423 |
| Sepsis | 2.9% | 2.8% | 3.0% | 1.00 (0.93-1.07) | 0.720 |
| Surgical site infection | 9.7% | 11.1% | 11.9% | 1.01 (0.87-1.17) | 0.587 |
| Urinary tract infection | 18.4 | 13.9 | 20.9 | 1.09 (0.91-1.30) | 0.383 |
| Other complication | 12.6 | 8.3 | 14.9 | 1.08 (0.94-1.24) | 0.376 |
| Reoperation | 3.9 | 2.8 | 4.5 | 1.02 (0.94-1.10) | 0.563 |
| None | 41.7 | 52.8 | 35.8 | 0.74 (0.50-1.09) | 0.096 |

RR: Relative risk, CI: confidence interval. *Requiring intraoperative blood transfusion. [‡]Between groups.

chronic pulmonary diseases is a risk factor for intraoperative complication but does not affect postoperative results, although usually prolonging hospital stay (17). In this study, the main intraoperative complication occurring in patients with rectal cancer was spleen injury. In elderly patients with CRC, a lack of cardiovascular comorbidities does not reduce the occurrence of postoperative complications, but a higher ASA grade significantly affects their recovery rate and mortality (18, 19). Older patients may have more infective complications with respect to younger ones, but laparoscopic

surgery significantly reduces the morbidity rate and amount of blood loss (13, 14, 20).

Conclusion

We conclude that older patients (>65 years) with colon cancer scheduled for elective surgical resection should not be considered at increased risk of intra- or short-term postoperative complications with respect to younger patients. However, the elderly require careful individual preoperative

evaluation when they have more than one comorbidity because they are usually users of multiple medications, and may more frequently have a higher ASA score.

References

- 1 World Research Cancer Fund International. Colorectal cancer statistics. Available at: <http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/colorectal-cancer-statistics>
- 2 National Cancer Institute. Surveillance, Epidemiology, and End Results Program (SEER). Cancer Stat Facts: Colon and Rectum Cancer. Available at: <https://seer.cancer.gov/statfacts/html/colorect.html>
- 3 Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, Forman D and Bray F: Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur J Cancer* 49: 1374-1403, 2013.
- 4 Kvasnovsky CL, Adams K, Sideris M, Laycock J, Haji AK, Haq A, Nunoo-Mensah J and Papagrigroriadis S: Elderly patients have more infectious complications following laparoscopic colorectal cancer surgery. *Colorectal Dis* 18: 94-100, 2016.
- 5 Deiner S, Westlake B and Dutton RP: Patterns of surgical care and complications in the elderly. *J Am Geriatr Soc* 62: 829-835, 2014.
- 6 Fleming M, Ravula S, Tatishchev SF and Wangcorresponding HL: Colorectal carcinoma: Pathologic aspects. *J Gastrointest Oncol* 3: 153-173, 2012.
- 7 American Cancer Society. Colorectal cancer stages. Available at: <https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/staged.html>
- 8 American Diabetes Association: Diagnosis and classification of diabetes mellitus. *Diabetes Care* 37(Suppl 1): S81-90, 2014.
- 9 Albers I, Hartmann H, Bircher J and Creutzfeldt W: Superiority of the Child-Pugh classification to quantitative liver function tests for assessing prognosis of liver cirrhosis. *Scand J Gastroenterol* 24: 269-276, 1989.
- 10 Maher RL, Hanlon J and Hajjar ER: Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf* 13: 57-65, 2014.
- 11 Tominaga T, Takeshita H, Takagi K, Kunizaki M, To K, Abo T, Hidaka S, Nanashima A, Nagayasu T and Sawai T: E-PASS score as a useful predictor of postoperative complications and mortality after colorectal surgery in elderly patients. *Int J Colorectal Dis* 31: 217-225, 2016.
- 12 Mokutani Y, Mizushima T, Yamasaki M, Rakugi H, Doki Y and Mori M: Prediction of postoperative complications following elective surgery in elderly patients with colorectal cancer using the Comprehensive Geriatric Assessment. *Dig Surg* 33: 470-477, 2016.
- 13 Kvasnovsky CL, Adams K, Sideris M, Laycock J, Haji AK, Haq A, Nunoo-Mensah J and Papagrigroriadis S: Elderly patients have more infectious complications following laparoscopic colorectal cancer surgery. *Colorectal Dis* 18: 94-100, 2016.
- 14 Tei M, Ikeda M, Haraguchi N, Takemasa I, Mizushima T, Ishii H, Yamamoto H, Sekimoto M, Doki Y and Mori M: Postoperative complications in elderly patients with colorectal cancer: comparison of open and laparoscopic surgical procedures. *Surg Laparosc Endosc Percutan Tech* 19: 488-492, 2009.
- 15 Kirchhoff P, Clavien PA and Hahnloser D: Complications in colorectal surgery: risk factors and preventive strategies. *Patient Saf Surg* 4: 5, 2010.
- 16 Shoeb M and Fang MC: Assessing bleeding risk in patients taking anticoagulants. *J Thromb Thrombolysis* 35: 312-319, 2013.
- 17 Riss S, Mittlböck M, Riss K, Chitsabesan P and Stift A: Intraoperative complications have a negative impact on postoperative outcomes after rectal cancer surgery. *Int J Surg* 12: 833-836, 2014.
- 18 Arenal-Vera JJ, Tinoco-Carrasco C, del-Villar-Negro A, Labarga-Rodríguez F, Delgado-Mucientes A and Cítores MA: Colorectal cancer in the elderly: characteristics and short term results. *Rev Esp Enferm Dig* 103: 408-415, 2011.
- 19 An Q, Yu T, Cao X, Yang H, Zhao G, Wu G, Jia W and Xiao G: Comparative analysis of postoperative complications on elderly colorectal cancer patients over 65 years with and without comorbid cardiovascular diseases. *Zhonghua Wei Chang Wai Ke Za Zhi* 19: 1035-1039, 2016.
- 20 Fujii S, Ishibe A, Ota M, Yamagishi S, Watanabe K, Watanabe J, Kanazawa A, Ichikawa Y, Oba M, Morita S, Hashiguchi Y, Kunisaki C and Endo I: Short-term results of a randomized study between laparoscopic and open surgery in elderly colorectal cancer patients. *Surg Endosc* 28: 466-476, 2014.

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