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Risk Factors for Postoperative Complications in Elderly After Colorectal Cancer Resection

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This study aimed to assess perioperative morbidity and mortality in elderly patients following colorectal cancer resection and to investigate risk factors for postoperative complications. This study reviewed 697 consecutive patients who underwent elective colorectal cancer resection between 2005 and 2013 at our institution. Patients were divided into 3 groups according to their age: $\leq$74 (n = 420), 75 to 89 (n = 261), and $\geq$90 years (n = 16). Clinical findings, morbidity, and mortality were compared among these groups. Univariate and multivariate logistic regression analyses were performed with clinically relevant variables for the complications that increased with aging. Postoperative delirium and pneumonia showed significant increases with aging. There were no significant differences in mortality and morbidity among the 3 groups, except for the 2 aforementioned diseases. Multiple logistic regression analysis showed that dementia and laparoscopic surgery were independent determinants of postoperative delirium and that age and American Society of Anesthesiologists (ASA) score were independent risk factors for postoperative pneumonia. Dementia, high ASA score, and age were the risk factors for higher postoperative morbidity in elderly patients. Our results demonstrated the effectiveness of laparoscopic surgery for the prevention of postoperative delirium after colorectal resection.

Key words: Elderly – Colorectal cancer resection – Postoperative complications – Laparoscopic surgery – Delirium – Pneumonia

Surgical resection is the most effective treatment for colorectal cancer.[1] Because of increased life expectancy and aging of the population in several countries,[2–4] the number of operations for elderly

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patients with colorectal cancer has been increasing.[5] Aging may alter the body's antitumor defenses, causing the elderly to be more vulnerable to malignancies.[6] Thus, age is a major risk factor for the development of cancer, and the incidence of carcinomas increases with aging.[4] The incidence of colorectal carcinoma peaks in the seventh and eighth decades of life, with only 5% of cases recorded in those aged <40 years.[7] Because of the improving life expectancy, physicians are likely to treat elderly patients with colorectal cancer. The management of elderly patients with colorectal cancer is an important clinical issue.[8]

Elderly patients have more comorbidities and reduced physiologic reserves compared with younger patients.[9] Therefore, they are often deemed to be high-risk surgical candidates with higher morbidity and mortality rates. Therefore, colorectal cancer resection has been affected by age.[10] It has been reported that postoperative morbidity and mortality were greater in elderly patients with colorectal cancer.[1,11] However, recent reports have recommended applying the standard surgical approach for elderly patients,[8,12] and they suggested that old age itself was not a prognostic factor of short- and long-term outcomes for colorectal cancer resection.[8,13,14] The elderly are a heterogeneous group of patients, ranging from very fit to very frail individuals. Thus, the indications for colorectal cancer surgery in the elderly are debatable.[1] Whether elderly patients are harmed by major colorectal cancer surgery and whether patient age is associated with postoperative complications are unclear.

This study aimed to assess perioperative morbidity and mortality in elderly patients following colorectal cancer resection among different age groups and to investigate risk factors for postoperative complications in elderly patients. We analyzed clinical differences among the oldest patients (aged ≥90 years) versus older patients (aged 75–89 years) versus younger patients (aged ≤74 years) who underwent oncological resection for colorectal cancer at a single institution.

Materials and Methods

This retrospective study involved 697 consecutive patients who underwent elective colorectal cancer resection between April 2005 and December 2013 at the Otaru Ekisaikai Hospital. Informed consent was obtained from all patients at the time of admission to use their clinical information in various studies as required. There were 2 inclusion criteria of our study. Patients were eligible for our study if they had the following characteristics: (1) elective colorectal cancer resection at the Otaru Ekisaikai Hospital and (2) consented to allow us to use their clinical information in this study. Exclusion criteria were as follows: (1) if the procedure was an emergency operation or (2) if colorectal resection was performed for a benign disease. The groups consisted of 420 patients aged ≤74 years (group A), 261 patients aged 75 to 89 years (group B), and 16 patients aged ≥90 years (group C). All patients were operated by the same surgeon or by surgeons trained under him.

The effects of age on perioperative morbidity and mortality within 30 days were evaluated. Complications were defined as follows: delirium, pneumonia, cardiovascular diseases, anastomotic leakage, anastomotic hemorrhage, surgical site infection (SSI: including superficial, deep, organ, and space SSIs), and postoperative ileus. The analyzed risk factors included age, sex, tumor localization (colon or rectum), the presence of distant metastases, surgical procedure (laparotomy or laparoscopic surgery), the extent of lymph node dissection (D-number defined by the Japanese Society for Cancer of the Colon and Rectum[15]), duration of surgery, blood loss, requirement for blood transfusion, comorbidities, American Society of Anesthesiologists (ASA) score, preoperative body mass index (BMI), preoperative biochemical examinations of blood [total protein, albumin, retinol binding protein (RBP), transthyretin (TTR), and transferrin (Tf)], and the Prognostic Nutritional Index (PNI).[16] PNI was used to determine preoperative nutritional status, which was calculated using the albumin concentration and lymphocyte count. Missing data were excluded from the analysis.

This study was approved by the appropriate ethics committee and was therefore performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Statistical analysis was conducted using StatView 5.0 software (SAS Institute Inc, Cary, North Carolina). Fisher's exact test or the χ^2 test was used to compare categorical variables. The *t*-test was used to compare continuous variables after assessing the data for normality. All tests were 2 sided, and $P < 0.05$ was considered significant. Variables that achieved significance at the 5% level on univariate analysis were included in the multivariate analysis to estimate the risk of postoperative complications.

Table 1 Clinical findings of patients with colorectal cancer in different age groups

Clinical findings	Group A, ≤74 years (n = 420)	Group B, 75–89 years (n = 261)	Group C, ≥90 years (n = 16)
Characteristics			
Age (mean ± SD)	64.5 ± 7.2	80.6 ± 4.4	91.9 ± 1.7
Sex (M/F)	251/169	115/146*	5/11*
Tumor location (colon/rectum)	301/119	220/41*	14/2
Distant metastasis	43 (10.2)	20 (7.7)	3 (18.8)
ASA score (1/2/3)	134/137/5	25/135/18*	0/8/4*,**
BMI (kg/m^2, mean ± SD)	23.2 ± 4.1	22.5 ± 3.5	21.0 ± 4.3
Total protein (g/dL)	6.7 ± 0.58	6.5 ± 0.67*	5.9 ± 0.59*,**
Albumin (g/dL)	3.7 ± 0.50	3.3 ± 0.55*	2.8 ± 0.57*,**
PNI	44.4 ± 6.2	40.3 ± 6.4*	33.2 ± 6.7*,**
RBP (mg/dL)	4.1 ± 2.0	3.6 ± 2.2	3.4 ± 1.5
TTR (mg/dL)	25.4 ± 8.0	20.6 ± 8.1*	16.0 ± 6.1*
Tf (mg/dL)	245 ± 47.3	236 ± 55.8	182 ± 34.4*,**
Comorbidities			
Hypertension	163 (38.8)	159 (60.9)*	12 (75.0)*
Dementia	1 (0.2)	48 (18.4)*	8 (50.0) *,**
Ischemic heart disease	11 (2.6)	22 (8.4)*	3 (18.8)*
Diabetes mellitus	65 (15.5)	62 (23.8)*	4 (25.0)
Cerebral infarction	23 (5.5)	32 (12.3)*	1 (6.3)
COPD	3 (0.7)	9 (3.4)*	0 (0)
Surgical parameters			
Operative time (min, mean ± SD)	144 ± 49.2	141 ± 51.6	112 ± 70.3
Blood loss (ml, mean ± SD)	127 ± 205.0	124 ± 324.4	92 ± 111.9
Blood transfusion	5 (1.2)	6 (2.3)	2 (12.5)*
Lymph node dissection (D1/2/3)	5/75/340	3/42/216	2/5/9*,**
Laparoscopic surgery	127 (30.2)	81 (31.0)	2 (12.5)

Figures in parentheses are percentages.

*$P < 0.05$ compared with group A.

**$P < 0.05$ compared with group B.

Results

Between 2005 and 2013, a total of 697 patients underwent elective colorectal cancer surgery at our institution. There were 371 men (53.2%) and 326 women (46.8%). Their mean age was 71.1 ± 10.4 years, with the youngest patient being 33 years and the oldest patient being 95 years.

All 697 patients were divided into 3 groups. Group A consisted of patients aged ≤74 years (n = 420; median age, 66 years), group B consisted of patients aged 75 to 89 years (n = 261; median age, 79 years), and group C consisted of patients aged ≥90 years (n = 16; median age, 92 years). Table 1 presents the characteristics, comorbidities, and surgical parameters of the patients in the 3 groups. The ratio of female patients was significantly higher in groups B and C than in group A. The number of patients with a high ASA score showed a significant increase, and preoperative nutritional status (total protein, albumin, and PNI) showed a significant decrease with aging. TTR and Tf, which are types of rapid turnover proteins, were lower in group C than in group A.

The most common comorbid disease was arterial hypertension. The prevalence of hypertension, dementia, and ischemic heart disease increased significantly with aging. The prevalence of diabetes mellitus, cerebral infarction, and chronic obstructive pulmonary disease (COPD) was significantly higher in group B than in group A, but similar in groups A and C.

There were no differences in the operative time, blood loss, and number of patients who underwent laparoscopic surgery among the 3 groups. The number of patients who required blood transfusion was significantly higher in group C, whereas lymph node dissection was lesser in group C than in the other 2 groups.

Postoperative complications are shown according to the group in Table 2. The number of patients who had postoperative complications was significantly higher in group C than in group A, but similar in groups A and B. The incidences of postoperative delirium and pneumonia showed significant increases with aging. There were no significant differences among the 3 groups in cardiovascular disease, anastomotic leakage, anastomotic hemor-

Table 2 Morbidity and mortality of patients with colorectal cancer in different age groups

Morbidity and mortality	Group A, ≤74 years (n = 420)	Group B, 75–89 years (n = 261)	Group C, ≥90 years (n = 16)
Overall complication rate	127 (30.2)	97 (37.2)	9 (56.3)*
Delirium	4 (1.0)	27 (10.3)*	3 (18.8)*
Pneumonia	7 (1.7)	12 (4.6)*	3 (18.8)*,**
Cardiovascular disease	4 (1.0)	1 (0.4)	0 (0)
Anastomotic leakage	33 (7.9)	12 (4.6)	1 (6.3)
Anastomotic hemorrhage	1 (0.2)	2 (0.8)	0 (0)
SSI	51 (12.1)	36 (13.8)	1 (6.3)
Ileus	32 (7.7)	15 (5.7)	2 (12.5)
Deaths	2 (0.5)	0 (0)	1 (6.25)

Figures in parentheses are percentages.

*$P < 0.05$ compared with group A.

**$P < 0.05$ compared with group B.

rhage, SSI, and postoperative ileus. However, there were 2 postoperative deaths in group A and 1 in group C; however, there were no significant differences in the mortality rates within the first 30 days after surgery among the 3 groups.

To investigate whether aging affected the incidences of postoperative delirium and pneumonia, independent risk factors for the 2 complications from among the patient characteristics, including age, comorbidities, and surgical parameters, were assessed.

Table 3 summarizes the results for the risk of postoperative delirium on univariate and multivariate analyses. Age, ASA score, total protein, albumin, PNI, RBP, TTR, Tf, dementia, and laparoscopic surgery were significant. Multiple logistic regression analysis using these factors identified dementia and laparoscopic surgery to be independent determi-

Table 3 Univariate and multivariate logistic regression analyses of postoperative delirium

	Univariate analysis			Multivariate analysis		
Variables	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Characteristics						
Age	1.145	1.093–1.199	<0.001	1.100	0.998–1.212	0.054
Male sex	0.873	0.438–1.739	0.699			
Tumor location rectum	0.426	0.148–1.228	0.114			
Distant metastasis	0.938	0.279–3.157	0.918			
ASA score	5.101	2.271–11.461	<0.001	0.846	0.202–3.548	0.819
BMI	0.948	0.846–1.063	0.360			
Total protein	0.543	0.325–0.906	0.019	0.890	0.276–2.873	0.846
Albumin	0.331	0.187–0.585	<0.001	17.962	0.551–585.673	0.104
PNI	0.902	0.858–0.948	<0.001	0.822	0.612–1.104	0.193
RBP	0.468	0.289–0.759	0.002	1.265	0.674–2.374	0.464
TTR	0.841	0.775–0.912	<0.001	0.855	0.712–1.026	0.093
Tf	0.992	0.983–1.002	0.128			
Comorbidities						
Hypertension	1.588	0.789–3.197	0.195			
Dementia	20.833	9.821–44.193	<0.001	6.887	1.431–33.137	0.016
Ischemic heart disease	1.156	0.266–5.027	0.846			
Diabetes mellitus	1.866	0.870–4.005	0.109			
Cerebral infarction	2.069	0.768–5.574	0.151			
COPD	1.796	0.225–14.331	0.580			
Surgical parameters						
Operative time	0.999	0.992–1.006	0.825			
Blood loss	1.000	0.998–1.001	0.918			
Blood transfusion	1.644	0.207–13.025	0.638			
Lymph node dissection	1.217	0.521–2.839	0.650			
Laparoscopic surgery	0.213	0.064–0.705	0.011	0.104	0.011–0.980	0.048

CI, confidence interval.

Table 4 Incidence of postoperative delirium in patients over 75 years old who underwent laparoscopic surgery and laparotomy

Diagnosis	Laparoscopic surgery (n = 83)	Laparotomy (n = 194)	*P* value
Delirium	2 (2.4)	28 (14.4)	0.003
Dementia	12 (14.5)	44 (22.7)	0.142

Figures in parentheses are percentages.

nants of postoperative delirium ($P = 0.016$ and $P = 0.048$, respectively). The incidence of postoperative delirium in elderly patients aged ≥75 years was significantly lower in those who underwent laparoscopic surgery than in those who underwent laparotomy ($P = 0.003$); however, there was no significant difference in the incidence of dementia between the 2 groups ($P = 0.142$; Table 4).

Table 5 shows the results for the risk of postoperative pneumonia on univariate and multivariate analyses. Age, ASA score, total protein, albumin, PNI, dementia, cerebral infarction, blood loss, and requirement for blood transfusion were significant. No patients with COPD developed postoperative pneumonia. Multiple logistic regression analysis using these factors identified age and ASA score to be independent determinants of postoperative pneumonia ($P = 0.036$ and $P = 0.026$, respectively).

Discussion

Recently, the elderly is the largest group of patients with colorectal cancer.[17] Because the aging population is growing and numerous geriatric patients are developing colorectal cancer, physicians and surgeons are faced with difficult treatment decisions. However, recent advances in cancer screening, anesthesia, surgical techniques, and understanding of the physiology of aging have caused improved results and the safe performance of surgery for appropriately selected elderly patients.[18] Therefore, it is important to analyze the risk factors for mortality and morbidity, including not only patient age but also general condition, comorbidity, and surgical factors using recent data.

Examining the present patients' characteristics, elderly patients were predominantly female and had higher ASA scores and lower nutritional status. More female patients among the elderly reflect the difference in life expectancy between men and

Table 5 Univariate and multivariate logistic regression analyses of postoperative pneumonia

Variables	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Characteristics						
Age	1.073	1.023–1.125	0.004	1.107	1.007–1.217	0.036
Male sex	0.793	0.332–1.893	0.602			
Tumor location rectum	1.333	0.509–3.495	0.558			
Distant metastasis	1.024	0.233–4.499	0.975			
ASA score	7.704	3.011–19.712	<0.001	5.066	1.216–21.103	0.026
BMI	1.049	0.952–1.156	0.335			
Total protein	0.422	0.230–0.774	0.005	0.820	0.297–2.259	0.700
Albumin	0.247	0.124–0.496	<0.001	0.464	0.032–6.808	0.575
PNI	0.889	0.837–0.945	<0.001	1.090	0.866–1.373	0.462
RBP	0.789	0.509–1.223	0.289			
TTR	0.943	0.880–1.011	0.101			
Tf	0.999	0.988–1.009	0.798			
Comorbidities						
Hypertension	1.797	0.735–4.392	0.199			
Dementia	6.260	2.416–16.218	<0.001	1.469	0.315–6.847	0.624
Ischemic heart disease	0.916	0.119–7.021	0.932			
Diabetes mellitus	2.226	0.880–5.630	0.091			
Cerebral infarction	3.830	1.348–10.878	0.012	2.891	0.619–13.489	0.177
COPD	—	—	—			
Surgical parameters						
Operative time	1.007	0.999–1.015	0.071			
Blood loss	1.001	1.000–1.002	0.005	1.002	0.999–1.004	0.169
Blood transfusion	6.036	1.255–29.042	0.025	2.834	0.085–93.998	0.560
Lymph node dissection	0.531	0.245–1.154	0.110			
Laparoscopic surgery	1.165	0.463–2.929	0.745			

women.[11] In addition, there were more comorbid conditions among elderly patients, and this resulted in significantly higher ASA scores in the elderly patient group. This result was in accordance with previous studies.[11,12,14] Malnutrition increases the rate of wound infection and anastomotic leakage after colorectal cancer resection.[19] The PNI score is a predictor of postoperative complications and overall survival.[20] In the present study, with regard to postoperative delirium and pneumonia, nutritional status was not an independent risk factor on multivariate analysis.

Although perioperative mortality was higher in the group with patients aged ≥90 years than in the younger group, the rates were not significantly different. The mortality rate in elderly patients was similar to or slightly better compared with patients in other studies.[1,11,14] In recent studies, postoperative mortality was not significantly higher in the elderly than in younger patients.[1,13] There has been a mean decrease in mortality rates of elderly patients who underwent colorectal cancer resection during the last decades.[5]

The morbidity rate in younger patients in the present study was similar to that in previous studies[1,11]; however, the rate increased with aging. The incidence of postoperative complications in elderly patients varied among studies because there were differences in the definition of the elderly patient population, documented morbidities, assessment of preoperative patient status, and surgical procedure (elective or emergent, laparotomy or laparoscopic surgery, and palliative or radical). Thus, it is controversial whether age is a significant risk factor for postoperative complications.[8,12,13] However, various studies have reported that morbidity increased with increased age.[1,11,21] Some reports have demonstrated that postoperative complications in elderly patients were related to increased comorbidities[12,13,22] and the ASA score,[12,22] rather than age.

In agreement with the literature,[1,12,14] elderly patients had a similar incidence of surgical complications compared with younger patients; however, they developed more general complications. Significant differences were observed for postoperative delirium and pneumonia among the age groups. This result demonstrates that the higher postoperative morbidity rate in elderly patients is because of the significant increase in general postoperative complications and that age is not associated with surgical complications.

One of the morbidities that increased with aging was postoperative delirium. Delirium is a transient fluctuating disturbance of consciousness, attention, cognition, and perception. Postoperative delirium develops in 36.8% (range, 0%–73.5%) of surgical patients.[23] Limited data are available regarding the actual pathophysiologic mechanism of postoperative delirium; however, it is believed to be associated with inflammation, altered neurotransmission, and postoperative stress.[24] However, postoperative delirium usually resolves within hours to days,[25] although patients in this state can be very difficult to manage and frequently require additional sedation. Furthermore, postoperative delirium is often associated with higher rates of major complications, prolonged hospital stay, postoperative cognitive dysfunction, newly diagnosed dementia, and increased mortality.[25,26] Prevention of delirium can have a significant impact on good outcomes for surgical patients.

In the present study, dementia was the independent risk factor for postoperative delirium. Postoperative delirium increases with aging because elderly patients have a higher probability of dementia than younger patients. This result is comparable to previous studies that reported aging and poor preoperative cognitive status as risk factors for postoperative delirium.[25,26]

Furthermore, the present study demonstrated that the incidence of delirium was lower in patients who underwent laparoscopic surgery than in those who underwent laparotomy. To the best of our knowledge, this study is the first to demonstrate a significant correlation between delirium and laparoscopic colorectal cancer resection. A number of surgical features, including intraoperative bleeding, operative time, and crystalloid infusion, have previously been reported to be associated with postoperative delirium in the literature.[27] However, heterogeneity in study designs in the previous studies hindered the identification of common surgical risk factors among the elderly who underwent colorectal resection. The recruitment of 697 patients from one facility in our study produced a sample with little variability in the target diseases, surgical team, surgical procedure, pre- and postoperative medical management, and nursing care. Therefore, our results support the conclusion that the lower incidence of postoperative delirium among elderly patients in our study is attributable to the laparoscopic surgical procedure. Reasons for the lower rate of postoperative delirium among patients who underwent laparoscopic surgery than

among those who underwent conventional open surgery include less destruction of the abdominal wall, pain, and stress. Patients experience lesser pain and fatigue after laparoscopic than after conventional colorectal cancer resection.[28] The stress response from surgery is known to cause an increase in sympathetic activity and the release of cortisol, which may play a role in the genesis of delirium.[29] We could not collect data on the type and amount of postoperative analgesics, pain scale or score, or the length of the wound. Further studies are required to determine the correlation between these factors and postoperative delirium. We believe that this result suggests that laparoscopic colorectal cancer resection is appropriate for elderly patients.

In the present study, another morbidity that increased with aging was postoperative pneumonia. Patient age and ASA scores were independent risk factors for this complication. Pneumonia accounts for 2.7%–3.4% of complications among surgical patients.[30] Elderly patients are at a higher risk of postoperative pneumonia than their younger counterparts,[1] partly because of their comorbidities and higher ASA grades.[31] The ASA score appears to be appropriate for predicting the risk of perioperative morbidity and mortality,[11,12,14] but not intraoperative or surgical morbidity.[14] Recent evidence suggests that lung expansion therapy (incentive spirometry, deep breathing exercises, and continuous positive airway pressure) reduces postoperative pulmonary risks after abdominal surgery.[32] A few studies reported a pneumonia prevention program in non–intensive care unit settings[33,34] and showed a significant long-term decrease in the incidence of ward-acquired pneumonia.[34,35] Although there are no established guidelines for pneumonia prevention for non–mechanically ventilated patients, postoperative pulmonary rehabilitation would likely reduce the risk of pneumonia.

In conclusion, colorectal cancer resection was safe for elderly patients with respect to surgical complications and mortality. The causes of higher postoperative morbidities in elderly patients were delirium and pneumonia. Dementia, high ASA score, and age were the risk factors for these complications. Furthermore, our results demonstrated the effectiveness of laparoscopic surgery for the prevention of postoperative delirium after colorectal resection. The limitations of this study include its retrospective and single-center design, potential bias in the selection of patients, and potential flaws in the accuracy of documentation in the medical records. Nevertheless, we believe that our data not only supply surgeons with useful information regarding surgical management but also reveal the requirement for future studies to reduce postoperative complications in elderly patients with colorectal cancer.

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