Efficacy and safety of laparoscopic surgery in elderly patients with colorectal cancer

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Received January 26, 2015; Accepted February 26, 2015

DOI: 10.3892/mco.2015.530

Abstract. Colorectal cancer (CRC) is predominantly a disease of the elderly. Elderly patients may also exhibit poorer outcomes due to the increased burden of comorbidities, functional dependency and limited life expectancy. The aim of this study was to evaluate the outcome of laparoscopic surgery in elderly patients with CRC. A total of 148 patients who underwent laparoscopic surgery at our institution between January, 2000 and December, 2011 were enrolled. We compared the differences between elderly patients (aged >75 years, n=48) and non-elderly patients (aged <75 years, n=100) and evaluated the demographics and disease-related operative and prognostic data. Postoperative complications occurred in 24 (16.2%) of the 148 patients. The American Society of Anesthesiologists score and comorbidity were found to be significantly correlated with complications and the multivariate analysis demonstrated that pulmonary disease, but not age, was an independent factor affecting postoperative complications (odds ratio = 3.21, 95% confidence interval: 1.02-10.14, P=0.0470). Patients with pulmonary comorbidities also exhibited similar rates of postoperative complications compared with 259 matched patients who underwent open surgery during same period (41.2 vs. 46.7%, respectively; P=0.7547). In conclusion, chronological age alone should not be considered a contraindication for laparoscopic surgery for CRC in elderly patients. In addition, selection criteria for laparoscopic CRC surgery in elderly as well as non-elderly patients should include pulmonary comorbidities.

Introduction

Colorectal cancer (CRC), the most common malignancy worldwide, affects mainly the elderly. The mean age at diagnosis is <72 years, with 40% of the cases occurring in patients aged >75 years (1-4). The geriatric CRC population is a heterogeneous group, including patients in excellent health and those with comorbid conditions, functional dependency and limited life expectancy (5), all of which may considerably affect the outcome of CRC treatment. Surgery is currently the mainstay of treatment and laparoscopic surgery for CRC is generally a feasible and safe alternative to open surgery, with potential benefits such as early postoperative recovery, decreased postoperative pain and shorter hospitalization (6-8). Although laparoscopic surgery for CRC is now widely accepted as the treatment of choice for CRC, its appropriateness for the treatment of elderly patients or those with coexisting high operative risk has not been well established. Elderly patients are more likely to present with comorbidities and age-specific deterioration of organ function, which may reduce their tolerance of surgery.

The published results of surgical morbidity and mortality rates for CRC surgery in elderly patients are contradictory. A systematic review of 28 independent studies demonstrated that the incidence of postoperative morbidity and mortality increased progressively with advancing age (9). The benefits of laparoscopic surgery, less surgical stress and shorter recovery times, make it an attractive choice for elderly patients; however, there remain concerns regarding the longer operative times and the potential cardiopulmonary changes induced by pneumoperitoneum. Several studies have reported the safety and benefits of laparoscopic surgery for elderly patients with CRC (10-14). However, the number of randomized controlled trials is limited and the literature lacks adequate information on the outcomes of elderly and/or high-risk patients who have undergone laparoscopic surgery. The aim of this study was to evaluate the feasibility and efficacy of laparoscopic surgery in elderly CRC patients aged >75 years.

Patients and methods

Patients and preoperative assessment. Between January, 2000 and December, 2011, 616 patients with primary CRC who underwent surgical treatment at the Department of Gastrointestinal Surgery, Mie University Hospital (Tsu, Mie, Japan) were enrolled in this study. Among these prospectively enrolled patients, 468 underwent open colorectal surgery and

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Key words: colorectal cancer, elderly patients, laparoscopic surgery, cormobidity, complication

Table I. Clinical backgrounds of the subjects by age group.

Characteristics	All patients (n=148)	Elderly (>75) (n=48)	Non-elderly (<75) (n=100)	P-value
Age, years (mean ± SD)	68.0±10.0	78.6±3.1	62.9±7.8	-
Gender, male/female	74/74	29/19	45/55	0.0791
BMI, kg/m^2 (mean ± SD)	22.8±3.5	22.4±3.0	23.1±3.7	0.2824
ASA score, no.				0.0163[a]
1/2/3	64/45/39	13/17/18	51/28/21	
Comorbidities, no. (%)				
Overall	73 (49.3)	22 (45.8)	51 (51.0)	0.5562
Diabetes mellitus	22 (14.9)	5 (10.4)	17 (17.0)	0.2919
Cardiovascular disease	34 (23.0)	17 (35.4)	17 (17.0)	0.0127[a]
Pulmonary disease	17 (11.5)	9 (18.8)	8 (8.0)	0.0628
Charlson index, no.				0.2618
0/1/2/3/4	82/43/17/5/1	26/18/4/0/0	56/25/13/5/1	
Prior abdominal surgery, no. (%)	19 (12.8)	9 (18.8)	10 (10.0)	0.1363
Tumor location				0.2331
Right colon	44	19	25	
Transverse colon	61	17	44	
Left colon	16	3	13	
Rectum	27	9	18	
Tumor size, mm (mean ± SD)	31.2±16.4	34.8±19.1	29.5±14.7	0.0707
Pathological UICC stage				0.6518
I/II/III/IV	14/47/47/40/0	6/14/13/15/0	8/33/34/25/0	
pN positive, no. (%)	40 (27.0)	15 (31.2)	25 (25.0)	0.4229
Pretreatment CEA, ng/μl	8.1±17.1	9.6±21.5	7.4±14.7	0.4840
Pretreatment CRP, mg/dl	0.27±0.47	0.11±0.21	0.24±0.55	0.1512
Surgical procedure, no.				0.2567
Ileocecal resection	12	6	6	
Right colectomy	40	15	25	
Transverse colectomy	7	0	7	
Left colectomy	11	2	9	
Sigmoidectomy	34	11	23	
Anterior resection	44	14	30	

[a]Statistically significant differences. SD, standard deviation; BMI, body mass index; UICC, Union for International Cancer Control; ASA, American Society of Anesthesiology; pN, pathological node; CEA, carcinoembryonic antigen; CRP, C-reactive protein.

148 underwent laparoscopic surgery. Data for all the patients, including demographics, comorbidities, operative results, complications, mortality and outcomes at follow-up, were entered into a prospective database. The comorbidity status was objectively evaluated using the American Society of Anesthesiologists (ASA) score and the Charlson Comorbidity Index (CCI) (15), which is a partially modified score, not including cancer or age (16). The body mass index (BMI) was recorded to assess the difficulty of laparoscopic surgery. All the patients underwent bowel preparation on the day prior to surgery by intestinal washout with an isosmotic solution. All the patients received antibiotic prophylaxis with cefmetazole during the introduction of anesthesia and again twice daily for 1 or 2 consecutive days after surgery.

Patient selection. All the laparoscopic surgeries were performed or supervised by the same team of colorectal surgeons. The exclusion criteria for laparoscopic surgery incuded T4 or bulky tumor, extended peritoneal dissemination, preoperative chemotherapy and/or radiotherapy, intestinal obstruction, palliative surgery and emergency surgery. In our study, we also compared the differences between patients undergoing laparoscopic surgery and 259 matched patients with stage I-III CRC who underwent open surgery, using the same exclusion criteria.

Mortality was defined as death occurring during the hospital stay or within 30 days after surgery. An operative complication was defined as an event that prolonged the hospital stay or led to an additional procedure.

Table II. Short-term data and complications.

Characteristics	All patients	Elderly (>75)	Non-elderly (<75)	P-value
Operating time, min (mean ± SD)	242.3±70.6	231.3±65.6	247.6±72.7	0.1947
Blood loss, ml (mean ± SD)	62.3±77.0	53.6±61.3	66.5±83.5	0.3584
Conversion to open laparotomy	0	0	0	-
Lymph node harvest, no. (mean ± SD)	16.1±12.7	17.0±13.8	15.7±12.2	0.5786
Mortality, no. (%)	1 (0.7)	1 (2.1)	0	0.1475
Complications, no. (%)				
Overall	24 (16.2)	10 (20.8)	14 (14.0)	0.2990
Bleeding	1 (0.7)	1 (2.1)	0	0.1475
Surgical site infection	12 (8.1)	3 (7.5)	9 (9.0)	0.5661
Anastomotic leakage	6 (4.1)	1 (2.1)	5 (5.0)	0.3997
Pneumonia	1 (0.7)	1 (2.1)	0	0.1475
Urinary tract infection	1 (0.7)	1 (2.1)	0	0.1475
Small bowel obstruction	4 (2.7)	0	4 (4.0)	0.1601
Respiratory disorders	1 (0.7)	1 (2.1)	0	0.1475
Peripheral vasculitis	1 (0.7)	1 (2.1)	0	0.1475
Paralysis	1 (0.7)	0	1 (1.0)	0.4869
Postoperative hospital stay, days (mean ± SD)	12.1±9.3	13.3±10.2	11.6±8.8	0.2828

SD, standard deviation.

Informed consent was obtained from all the patients who underwent surgical treatment at our institution. Approval from the Institutional Review Board was obtained for the use of patient data in the present study.

Procedures. Conventional laparoscopic surgery was performed as a laparoscopic-assisted procedure, with removal of the resected specimen via a 4-cm horizontal supraumbilical minilaparotomy. Laparoscopic surgery was performed using a 5-trocar technique, with one 12-mm trocar inserted via a paraumbilical incision and three 5-mm trocars and one 12-mm trocar inserted in the right and left lower abdomen. Following removal of the resected specimen and creation of the stapled anastomosis, we closed the minilaparotomy and reintroduced pneumoperitoneum. We also used single-port laparoscopic surgery for certain patients with right-sided colon cancer.

Patient classification by age. The patients were categorized into two groups based on age, namely an elderly group, aged >75 years and a non-elderly group, aged <75 years. The cut-off of 75 years was selected as ~40% of the CRC cases are patients aged >75 years and the incidence of CRC increases with advancing age (1-4).

Statistical analysis. JMP version 7 software (SAS Institute Inc., Cary, NC, USA) was used to perform the statistical analyses. Data are presented as mean ± standard deviation. Contingency tables were analyzed using the Fisher's exact test or the χ^2 test with Yates' correction. The correlations between continuous and categorical variables were evaluated using the Mann-Whitney U test. Kaplan-Meier survival curves were constructed and the differences were analyzed using the log-rank test. Each significant predictor identified was assessed by multivariate analysis using a logistic regression model. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 148 consecutive patients [74 men and 74 women; mean age, 68 years (range, 37-89 years)] who underwent laparoscopic surgery for CRC between January, 2000 and December, 2011 were included in this analysis. Of the 148 patients, 48 were classified as elderly (mean age ± SD, 78.6±3.1 years; range, 75-89 years) and 100 as non-elderly (62.9±7.8 years; range, 37-74 years). The background characteristics of the 148 patients by age group are summarized in Table I. There were no significant differences in gender, BMI, tumor characteristics and type of surgical procedure between the elderly and non-elderly groups. There were significant correlations between age and ASA score (P=0.0163). Of the 148 patients, 34 (23.0%) had cardiovascular disease, which was the most common comorbidity. The two groups exhibited similar rates of comorbidities and the CCI did not significantly differ between the elderly (0.54±0.42) and non-elderly (0.70±0.90) groups. However, the elderly group exhibited a higher incidence of cardiovascular disease (35.4 vs. 17.0%, respectively; P=0.0127) and pulmonary disease (18.8 vs. 8.0%, respectively; P=0.0628) when compared to the non-elderly group.

Short-term outcomes. The short-term outcomes for all the patients are summarized in Table II. There were no significant differences between the two groups regarding surgical

Table III. Univariate and multivariate analysis of risk factors for postoperative complications.

	Univariate			Multivariate		
Variables	OR	95% CI	P-value	OR	95% CI	P-value
Age, >75 vs. <75 years	1.62	0.66-3.96	0.2939	-	-	-
Gender, male/female	1.22	0.51-2.93	0.6559	-	-	-
Body mass index >25 vs. <25 kg/m^2	1.55	0.58-4.16	0.3865	-	-	-
ASA score, 2-3 vs. 1	3.45	1.21-9.82	0.0204[a]	2.58	0.85-7.78	0.0938
Cardiovascular disease	1.48	0.56-3.93	0.4326	-	-	-
Pulmonary disease	4.69	1.58-14.00	0.0055[a]	3.21	1.02-10.14	0.0470[a]
Prior abdominal surgery, yes vs. no	0.572	0.12-2.66	0.4760	-	-	-
Tumor location, rectum vs. colon	1.22	0.411-3.62	0.7200	-	-	-
Bleeding, >43 vs. <43 g	1.697	0.68-4.23	0.2567	-	-	-
Operative time, >230 vs. 230 min	0.668	0.28-1.62	0.3730	-	-	-

[a]Statistically significant differences. ASA, American Society of Anesthesiology; OR, odds ratio; CI, confidence interval.

outcomes, including operating time, intraoperative blood loss, lymph node harvest, complications and duration of hospital stay. Postoperative major and minor complications occurred in 24 (16.2%) of the 148 patients. A comparison between patients with and those without postoperative complications, performed to determine the potential effects of patient-, tumor- and treatment-related factors on complications, identified significant correlations with ASA 2-3 (P=0.0204) and pulmonary disease (P=0.0055). The multivariate analysis revealed that pulmonary disease, but not age, was an independent factor affecting postoperative complications (odds ratio = 3.21, 95% confidence interval: 1.02-10.14; P=0.0470) (Table III). In our study, pulmonary comorbidities included chronic obstructive pulmonary disease, pneumonia, bronchiolitis, bronchiectasis, bronchial asthma and history of major surgery for lung cancer. A total of 17 patients had preoperative pulmonary disease, including 9 elderly (18.8%) and 8 non-elderly (8%) patients (Table I). Of these patients, 7 (41.2%) had postoperative complications covering a wide range of conditions, including 1 case of pneumonia, 1 case of respiratory disorder, 2 surgical site infections, 1 case of persistent bleeding, 1 urinary tract infection and 1 case of paralysis. There was 1 reported case of mortality in our study: An 85-year-old man with both pulmonary and cardiovascular disease succumbed to pneumonia 2 weeks following surgery.

Postoperative complications occurred in 81 (31.3%) of the 259 matched patients who underwent open colorectal surgery during the same period. The incidence of complications was significantly higher with open surgery compared with laparoscopic surgery (31.3 vs. 16.2%, respectively; P=0.0008). Of the 259 patients, 128 (49.8%) exhibited comorbidities, including pulmonary comorbidity in 15 patients who underwent open surgery. Of note, the pulmonary comorbidity did not affect the postoperative complications in the open surgery group, unlike in the laparoscopic surgery group. The rates of postoperative complications in patients with pulmonary comorbidities were similar between the laparoscopic and open surgery groups (41.2 vs. 46.7%, respectively; P=0.7547) (data not shown).

Follow-up. After a median follow-up of 51.2 months, we assessed overall survival using Kaplan-Meier survival analysis. There were no significant differences in recurrence rates between the elderly and non-elderly groups (4.2 vs. 5.0%, respectively; P=0.7637). The 5-year overall survival also did not differ between the elderly and non-elderly groups (97.9 vs. 96.7%, respectively; P=0.4955) (data not shown). There was no correlation of preoperative comorbidities or postoperative complications with oncological outcome in our study.

Discussion

In our study, although elderly patients were more likely to have a poor ASA and comorbidities, such as cardiovascular and pulmonary disease, there were no significant differences in clinical outcome compared with non-elderly patients. Our results revealed that only pulmonary disease, and not chronological age, adversely affected short-term outcomes in patients with CRC who underwent laparoscopic surgery.

Laparoscopic surgery has recently become widely accepted as a therapeutic option for CRC due to its superiority to open surgery, including decreased blood loss, reduced pain, fewer postoperative complications and shorter hospital stay (6-8). The long-term outcomes of laparoscopic surgery have also been confirmed as comparable or superior to those of open surgery (15,16). The superiority of laparoscopic surgery to open surgery, clinically as well as physiologically, has been reported. The degree of the postoperative inflammatory response is smaller following laparoscopic surgery compared with open surgery (17,18). In addition, a significantly better preservation of cell-mediated immunity has been reported following laparoscopic compared with open colorectal surgery (19,20). Although pneumoperitoneum with carbon dioxide is known to be potentially associated with adverse pathophysiological changes, including hypercapnia, reduced venous return, increased peak airway pressure and decreased pulmonary compliance (21), clinical evidence provided by a number of previous studies on laparoscopic surgery

demonstrated that, even among the elderly population, the disadvantages are outweighed by its advantages. In fact, a meta-analysis intended for elderly patients also revealed that laparoscopic surgery reduced the rates of postoperative pneumonia, cardiac complications and surgical site infection (22). However, the potential hazards resulting from pneumoperitoneum and longer operative times may put high-risk patients with cardiovascular and/or pulmonary comorbidities at higher risk of postoperative complications.

The mortality case in our study, an 85-year-old man with pulmonary as well as cardiovascular disease, succumbed to pneumonia 2 weeks after surgery, although he had undergone an anterior resection, which is associated with less surgical stress, i.e., short operative duration (165 min) and low blood loss (19 ml). Our results also demonstrated that preoperative pulmonary comorbidity did not necessarily cause postoperative respiratory complications alone, but rather that the complications covered a wide range of conditions. The reason for pulmonary comorbidity being an independent factor of postoperative complications in laparoscopic surgery for CRC has not been elucidated. However, it is well known that pulmonary disease as a comorbidity, including chronic obstructive pulmonary disease, or as measured by ASA score, was a reliable risk factor for surgical site infection, which was representative of complications (23-25).

It appears likely that the patients with pulmonary comorbidities may not be eligible for laparoscopic surgery. However, the postoperative complications in patients with pulmonary comorbidities were less frequent with laparoscopic compared with open surgery (41.2 vs. 46.7%, respectively), although the difference was not statistically significant (P=0.7900). Thus, our results suggest that laparoscopic surgery does not necessarily negatively affect outcome in CRC patients with pulmonary comorbidities, but that its advantages may not offset the risk of postoperative complications in such patients.

The limitations of our study included the small patient sample and that it was a single-site study; consequently, the findings may not be applicable to all patients with CRC. However, we were able to identify patterns associated with laparoscopic surgery in CRC patients aged >75 years and to compare the outcomes between elderly and non-elderly patients.

In conclusion, chronological age alone should not be a contraindication for laparoscopic surgery in elderly CRC patients. The selection criteria for laparoscopic CRC surgery in elderly as well as non-elderly patients should include pulmonary comorbidities, although elderly patients are more likely to have this type of comorbidity.

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