Advantage of Laparoscopy Surgery for Elderly Colorectal Cancer Patients without Compromising Oncologic Outcome

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Abstract

Backgrounds: Laparoscopic surgery has achieved good results in elderly patients with colorectal cancer (CRC). In this study, we compared the short-term and long-term outcomes of open surgery and laparoscopic surgery in CRC patients aged above 75 years at a single tertiary medical center.

Methods: Between January 2009 and December 2015, we studied 967 patients who underwent curative resection for primary colorectal adenocarcinoma without distant metastasis in a single institution. Of the enrolled subjects, 305 underwent laparoscopic surgery, and 662 received open laparotomy surgery.

Results: Compared to the patients who received open surgery, those received laparoscopic surgery had prominent shorter postoperative stay (10.3 vs. 13.5 days $p < 0.001$) and similar postoperative mortality ($p = 0.082$) and morbidity ($p = 0.354$). In the laparoscopy cohort, 6 of 305 patients were converted to open surgery and 1 died. The long-term overall survival, cancer-specific survival and recurrence rate were all similar between both cohorts in each stage.

Conclusions: Laparoscopic surgery is suitable for elderly patients due to shorter postoperative stay, similar long-term outcomes with open surgery and acceptably low conversion rates. For long-term overall and oncological outcome, the results of laparoscopic surgery were similar to that of open surgery in each TNM stage.

Introduction

Colorectal cancer (CRC) is a common and deadly disease worldwide. In Taiwan, it is the most commonly diagnosed cancer annually and the third leading cause of cancer death. The incidence of CRC increases dramatically with age. Many population data presented that about 40% of the CRC cases occur in patients over the age of 75 years [1–4]. In 2009, about 31.5% of all CRC patients aged over 75 years in Taiwan, and the figure has been increasing with the aging of the population. Surgery remains the mainstay to cure CRC. However, some studies reported high mortality and morbidity in elderly patients undergoing open colorectal surgery [5, 6]. A systematic review of 28 studies also presented that postoperative morbidity and mortality increased with age [7].

It is a known fact that increasing age is associated with increasing comorbidities like diabetes mellitus, chronic kidney disease, cardiovascular or pulmonary disease, which increase surgical morbidity and mortality. Fortunately, laparoscopic surgery has made progress in the past two decades and has become an attractive option for elderly patients. Randomized control trials like COST, CLASICC, COLOR and COREAN have demonstrated that compared to open surgery, laparoscopic surgery has similar long-term outcomes and morbidity/mortality but better short-term outcomes [8–11]. Less operative pain, less blood loss, shorter hospital stay and recovery time are the benefits of laparoscopic surgery [12]. However, longer operation time and the potential cardiopulmonary change induced by pneumoperitoneum are our concerns.

The major randomized control trials mentioned above compared laparoscopic surgery with open surgery but did not focus on elderly patients. Zeng et al. reported that elderly patients in the laparoscopic group had longer median operation time, less blood loss, shorter postoperative hospital stay and lower overall complication rate than the open surgery group [13]. Nishikawa et al. reported good results of less blood loss, shorter days to resume oral intake, shorter hospital stay and similar mortality and morbidity rate in the laparoscopic group [12]. Another systematic review and meta-analysis also had better short-term outcomes in the laparoscopic group [14]. The good short-term outcomes and morbidity/mortality rate may enable the elderly patients who received laparoscopic surgery return to normal life in a short period of time. However, prospective studies comparing laparoscopic surgery with open surgery on long-term outcomes in elderly patients were rare. In this study, we aimed to identify whether these good short-term outcomes could also improve the long-term oncologic benefits of elderly patients in the laparoscopic group. Our study compared the short-term and long-term survival outcomes between the open surgery group and the laparoscopic surgery group in CRC patients aged over or equal to 75 years at a single academic medical center.

Materials And Methods

Patients and variables

Detailed information regarding clinicopathological variables was retrieved from the Colorectal Section Tumor Registry of Chang Gung Memorial Hospital. This study was approved by the Institutional Review Board. This project was reviewed and approved by our institutional ethics committee (No. 201801090B0). The patient-related variables included age, sex, body weight, body height, body mass index (BMI), and the presence of illness. Patients' health information such as incidences of hypertension, cardiac disease, cerebrovascular accident, asthma, diabetes mellitus, and liver cirrhosis was also collected. Blood analysis including carcinoembryonic antigen (CEA), hemoglobin (Hb), albumin, aspartate aminotransferase (AST), total bilirubin, and creatinine (Cr) was performed before operation. The tumor-related variables included tumor invasion depth (T stage), lymph node involvement (N stage), histologic subtype, histologic grade, tumor location, operation types, and the number of sampled lymph nodes.

Between January 2009 and December 2015, patients above or equal to the age of 75 who underwent curative radical resection for primary colorectal adenocarcinoma were included in this study. Patients who received local tumor excision, were diagnosed with stage IV disease, or acquired emergency operation were excluded from this study. A total of 967 were enrolled for the analysis. Of the enrolled subjects, 305 underwent laparoscopic surgery, and 662 received open laparotomy surgery. The decision of laparoscopic surgery or open surgery depended on the physician's and patient's preferences.

Follow-up and end points

Physicians in the same department of this institute adopted similar follow-up routines and adjuvant treatment protocols. All patients participated in a follow-up program that included outpatient visits every 3 to 6 months for physical examination and CEA tests, as well as chest X-ray, abdominal sonography or abdominal computed tomography, and colonoscopy every 1 to 3 years postoperatively. The endpoint was death from any cause for overall survival (OS) and cancer-related death for cancer-specific survival (CSS). The recurrence of cancer was confirmed by using histology of biopsy specimens, re-operation, or radiological studies. The time to recurrence was defined as the duration between the date of initial surgery and the date of recurrence confirmation. Cumulative recurrence rate (CRR) was referred to as the cumulative probability of colorectal cancer recurrence occurring during follow-up. The prognosis was evaluated by OS, CSS and CRR.

Statistics

All analyses were performed using the Statistical Package for the Social Sciences, release 24.0 (IBM SPSS v.24). Clinicopathologic characteristics were compared using the chi-squared method and Student's t-test for continuous data. OS, CSS and CRR were computed using the Kaplan-Meier method. Differences were estimated using the log-rank test. Statistical significance was set at $P < 0.05$.

Results

A total number of 967 elderly patients were included in this study, with a median follow-up time of 42.1 months. Of the enrolled subjects, 662 patients (68.5%) received open surgery and 305 patients (31.5%) received laparoscopy surgery.

The demographic data were presented in Table 1. There was no difference in age and sex ratio between the open surgery group and the laparoscopy group. The laparoscopy group showed a higher rate of BMI increase (open vs. laparoscopy, overweight: 25.7% vs. 32.1%, obesity: 4.0% vs. 6.9%, $p = 0.014$) and comorbidities of hypertension (open vs. laparoscopy, 57.8% vs. 67.2%, $p = 0.006$). The presence of other comorbidities such as cardiac disease, cerebrovascular event, asthma, diabetes mellitus, and liver cirrhosis showed no difference between the two groups. The open group showed significantly advanced Tumor-Node-Metastasis (TNM) stage (stage 0, I, II and III in open vs. laparoscopy: 1.2%, 12.5%, 44.4%, 41.8% vs. 2.6%, 20.3%, 42.3%, 34.8%, $p = 0.003$), higher rate of abnormal preoperative serum CEA level (open vs. laparoscopy, 36% vs. 24%, $p < 0.001$) and higher rate of hypoalbuminemia (open vs. laparoscopy, 23.4% vs. 14.8%, $p = 0.002$). For other preoperative laboratory examinations, including preoperative anemia (Hb < 10 g/dL), abnormal AST or total bilirubin level, and elevated serum creatinine level (> 1.27 mg/dL) were all similar between the two groups.

Table 1
Demographic data

Characteristic	Open (*n* = 662)	Laparoscopy (*n* = 305)	*P*
Age (y/o)	80.4 ± 4.2	80.4 ± 4.6	0.878
Sex (male)	369 (55.7)	166 (54.4)	0.703
Body mass index (kg/m^2)			0.014
Underweight (< 18.5)	54 (8.3)	16 (5.2)	
Healthy (18.5–25)	406 (62.1)	170 (55.7)	
Overweight (25–30)	168 (25.7)	98 (32.1)	
Obese (> 30)	26 (4.0)	21 (6.9)	
Hypertension	384 (58.0)	205 (67.2)	0.006
Cardiac disease	113 (17.1)	60 (19.7)	0.326
Cerebral vascular disease	53 (8.0)	20 (6.6)	0.428
Asthma	34 (5.1)	14 (4.6)	0.717
Diabetes Mellitus	171 (25.8)	74 (24.3)	0.602
Cirrhosis	11 (1.7)	6 (2.0)	0.737
TNM stage			0.003
0	8 (1.2)	8 (2.6)	
1	83 (12.5)	62 (20.3)	
2	294 (44.4)	129 (42.3)	
3	277 (41.8)	106 (34.8)	
CEA > 5 (ng/ml)	238 (36.0)	75 (24.6)	< 0.001
Hb < 10 (g/dL)	176 (26.6)	76 (24.9)	0.583
Albumin < 3.5 (g/dL)	155 (23.4)	45 (14.8)	0.002
AST > 34 (U/L)	50 (7.6)	26 (8.5)	0.602
Total bilirubin > 1.3 (mg/dL)	16 (2.4)	7 (2.3)	0.908
Cr > 1.27 (mg/dL)	141 (21.3)	79 (25.9)	0.113

Data are presented as n (%) unless otherwise indicated. *CEA*: carcinoembryonic antigen, *Hb*: hemoglobin, *AST*: aspartate transaminase, *Cr*: creatinine

The operative data was shown in Table 2. Although the tumor locations were similar between the two groups, the rate of performing anterior resection was significantly higher in the laparoscopy group (open vs. laparoscopy, 56.6% vs. 60.7%, $p = 0.048$), and the rate of performing segmental resection, subtotal colectomy and Hartmann's procedure were higher in the open surgery group. The open group and the laparoscopy group had similar retrieved lymph nodes (open vs. laparoscopy: 29.8 ± 14.9 vs. 30.3 ± 15.8, $p = 0.636$). The postoperative morbidity rate was 17.8% in the open group and 15.4% in the laparoscopy group ($p = 0.354$). The postoperative mortality rate was 1.7% in the open group and 0.3% in the laparoscopy group ($p = 0.082$). Although the postoperative morbidity and mortality were similar between both cohorts, the postoperative hospital stay was 10.3 ± 8.5 days in the laparoscopy group, which was significantly shorter than that in the open group of 13.5 ± 9.4 days ($p < 0.001$). There were 6 patients out of 305 patients (2.0%) received laparoscopy initially and then converted to open surgery. In Table 3, advanced pathology T stage was shown in the open cohort, but the N stage, histology type, and histology grade between the two cohorts were all similar.

Table 2
Operative data

Characteristic	Open (*n* = 662)	Laparoscopy (*n* = 305)	*P*
Tumor site			0.419
Right colon	196 (20.6)	84 (27.5)	
Left colon	264 (39.9)	115 (37.7)	
Rectum	202 (30.5)	106 (34.8)	
Operation types			0.048
Right hemicolectomy	174 (26.3)	80 (26.2)	
Left hemicolectomy	41 (6.2)	23 (7.5)	
Anterior resection	375 (56.6)	185 (60.7)	
Abdomino-peritoneal resection	16 (2.4)	8 (2.6)	
Segmental resection	13 (2.0)	0 (0)	
Subtotal colectomy	17 (2.6)	2 (0.7)	
Hartmann's procedure	26 (3.9)	7 (2.3)	
No. of resected lymph nodes	30.3 ± 15.8	29.8 ± 14.9	0.636
Duration of hospital stay after surgery (day)	13.5 ± 9.4	10.3 ± 8.5	< 0.001
Postoperative morbidity	118 (17.8)	47 (15.4)	0.354
Postoperative mortality	11 (1.7)	1 (0.3)	0.082
Conversion		6 (2.0)	
Data are presented as n (%) unless otherwise indicated			

Table 3
Pathological data

Characteristic	Open (*n* = 662)	Laparoscopy (*n* = 305)	*P*
T stage			0.009
is	8 (1.2)	8 (2.6)	
1	33 (5.0)	27 (8.9)	
2	78 (11.8)	44 (14.4)	
3	447 (67.5)	198 (64.9)	
4	96 (14.5)	28 (9.2)	
N stage			0.108
0	385 (58.2)	199 (65.2)	
1	184 (27.8)	69 (22.6)	
2	93 (14.0)	37 (12.1)	
Histology			0.886
Adenocarcinoma	618 (93.4)	287 (94.1)	
Signet ring cell	4 (0.6)	1 (0.3)	
Mucinous adenocarcinoma	36 (5.4)	16 (5.2)	
Other	4 (0.6)	1 (0.3)	
Histology grade			0.123
Well	67 (10.1)	38 (12.5)	
Moderate	530 (80.1)	248 (81.3)	
Poor	65 (9.8)	19 (6.2)	
Data are presented as n (%) unless otherwise indicated			

The median follow-up time was 47.9 months in the open group and 35.9 months in the laparoscopy group. The estimated 5-year-survival rate was 62% in the open group versus 66% in the laparoscopy group (Fig. 1, p = 0.224). The estimated 5-year cancer-specific survival rate was 81% in the open group versus 86% in the laparoscopy group (Fig. 1, p = 0.176). The estimated 5-year recurrence rate was 17% in the open group versus 16% in the laparoscopy group (Fig. 1, p = 0.314). The differences in OS, CSS, and CRR between the two groups were not statistically significant.

The 967 patients were divided into three groups by TNM stage: the stage 0 and I group, the stage II group, and the stage III group. We compared the OS, CSS, and CRR in the three groups after open surgery and

laparoscopy surgery. In the stage 0 and I group, the OS, CSS and CRR were similar between the open group and the laparoscopy group (Fig. 2, open vs. laparoscopy, 5-year OS rate: 75% vs. 67%, $p = 0.909$, 5-year CSS rate: 97% vs. 94%, $p = 0.875$, 5-year CRR: 0% vs. 2%, $p = 0.204$). In the stage II group, the OS, CSS and CRR were similar between the open group and the laparoscopy group (Fig. 3, open vs. laparoscopy, 5-year OS rate: 66% vs. 72%, $p = 0.575$, 5-year CSS rate: 86% vs. 85%, $p = 0.864$, 5-year CRR: 15% vs. 14%, $p = 0.220$). In the stage III group, the OS, CSS and CRR were also similar between the open group and the laparoscopy group (Fig. 4, open vs. laparoscopy, 5-year OS rate: 51% vs. 60%, $p = 0.575$, 5-year CSS rate: 71% vs. 82%, $p = 0.122$, 5-year-CRR: 35% vs. 29%, $p = 0.179$).

Discussion

In our study, although elderly patients with CRC who underwent laparoscopy were prone to develop early T stage cancer, obesity and high serum albumin level, their length of postoperative stay was significantly shorter, their postoperative morbidity and mortality were similar to that of those underwent open surgery, and the rate of conversion was acceptably low (6 out of 305 patients, and 1 died). In each TNM stage, the long-term outcomes including OS rate, CSS rate and CRR between the open surgery group and the laparoscopy group were also similar.

The role of laparoscopic surgery in colorectal cancer treatment is worldwide accepted [8, 15]. However, considering the surgical risks in elderly patients (high risks of anesthesia, operative morbidity and mortality, malnutrition, immunity decline, poor performance status, and having comorbidities) [16] and long operation time, surgeons may hesitate to perform laparoscopic surgery on elderly patients. Seshadri et al. reported that 62 octogenarians who received laparoscopic colorectal procedure (including benign disease) in the 1990s resulted in favorable postoperative outcome [17]. Law et al. compared the groups of open and laparoscopic colorectal resections of malignant or benign colorectal disease in Asians aged over 70 years in early 2000, and the two groups shared similar postoperative morbidity rates [18]. For elderly patients with non-metastatic CRC who underwent surgery, we revealed that the overall postoperative morbidity and mortality rates were similar in the open group and the laparoscopy group. The postoperative morbidity rate was 15.4% and the mortality rate was 0.3% in the laparoscopy group. The operative mortality and morbidity of laparoscopy were in agreement with previous reports [19–24]. Fujii et al. had reported that the postoperative complication rate in the laparoscopy group was lower than that in the open group (23% vs. 36%) for elderly patients, and the postoperative ileus rate in the laparoscopy group was significantly lower [23].

The conversion rate was 2% in our study and it was similar to or even lower than previous studies (6.1%-21%) [12, 25–28, 19]. Of these converted patients, only three patients developed postoperative morbidity and none had tumor recurrence during follow-up. The short-term or long-term outcomes may not be influenced by the conversion if adequate surgical safety is achieved. The retrieved lymph nodes in the two groups were sufficient as suggestions for the guidelines. We agreed that laparoscopic surgery could meet the similar oncological quality as open surgery for CRC treatment through this study. The length of postoperative stay was shorter in the laparoscopic group, and several studies had confirmed the

result [18, 19, 21, 27, 29–31]. The most obvious benefit for elderly patients to receive laparoscopy surgery is a reduction in hospital stay.

The long-term oncological outcomes including OS, CSS and CRR did not differ between the two groups. In our study, patients in the open group had much advanced TNM stage and abnormal CEA level compared to the laparoscopy group. This finding may be due to the surgeons' preference for patient selection. However, we divided the patients into 3 groups by TNM stage, and the long-term oncological outcomes showed no difference in each group. Several studies had reported that OS and disease-free survival did not differ between patients undergoing open surgery and laparoscopy [13, 30–32]. To our knowledge, there were few studies focusing on the long-term oncological outcomes in elderly patients receiving open surgery and laparoscopy surgery, and we had the largest number of patients enrolled from a single medical among the studies.

We analyzed CSS because elderly patients with CRC passed away not only for malignant reasons but also for multiple causes related to aging, and can result in significant reduction in OS. In this study, the CSS rate for each TNM group was about 15%-30% higher than the OS rate. Hinoi and his colleague reported that the 3-year CSS rates for both colon and rectal cancer patients aged over 80 were about 86.5–93.4%, similar to our result (88%) [31]. For elderly patients, once the recurrence occurred, they may not be able to tolerate recurrence treatment compared to younger patients. Cumulative recurrence was analyzed in this study for evaluating the efficacy and oncological quality of open surgery and laparoscopic surgery. The cumulative recurrence rate was similar in each TNM stage group and few studies had mentioned this. According to our results, laparoscopic surgery for CRC treatment in elderly patients, could be used as a standard method for radical resection of malignancies.

The present study has some potential limitations. First, this is a retrospective study conducted at a single institute while collecting data prospectively and is subject to various biases. Second, the selection bias is an essential issue because the choice of laparoscopy or laparotomy surgery is very subjective to surgeons' preference, although the long-term outcome was compared with each stage. Third, some cases of the laparoscopic group were performed during the surgeon's learning curve period in this institute, which may influence the long-term outcomes.

Conclusion

Laparoscopic CRC resection is suitable for elderly patients with appropriate short-term outcomes including low conversion rate and similar postoperative morbidity and mortality compared to open surgery. For long-term overall and oncological outcome, the results of laparoscopic surgery were similar to that of open surgery in each TNM stage. In addition, elderly patients can even have the benefit of short postoperative hospital stay from laparoscopic surgery. Laparoscopic surgery for elderly patients with CRC can be the standard method for malignant treatment.

Declarations

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Conflicts of interest

We have no conflicts of interest to declare.

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Figures

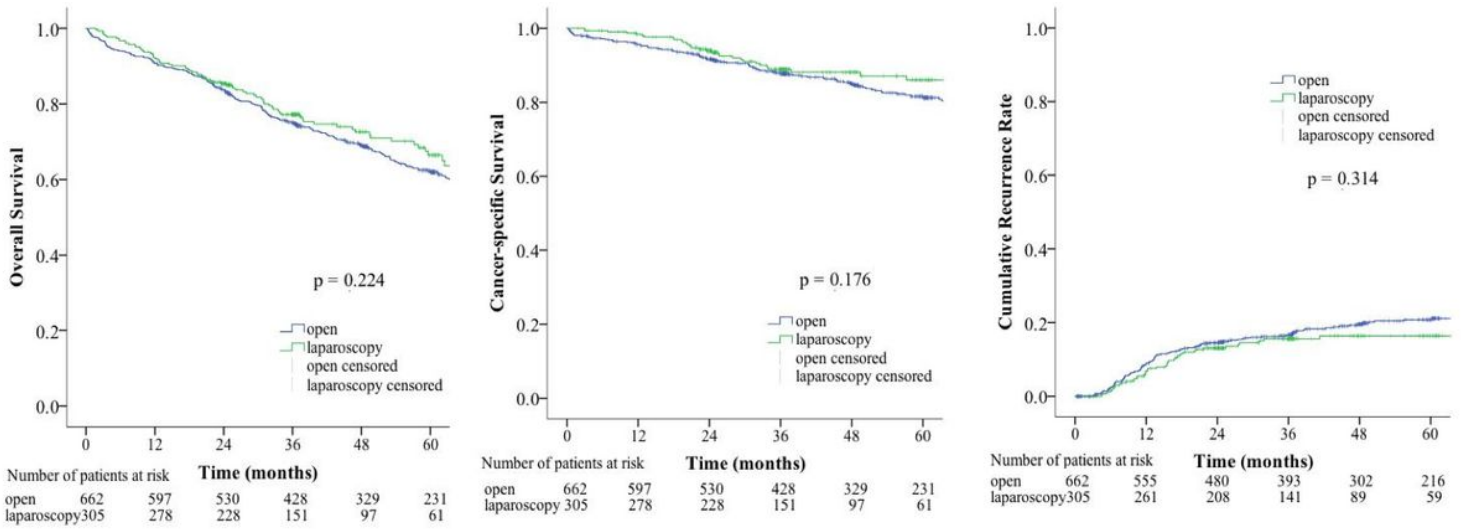

Figure 1

Survival rate and recurrence rates in open and laparoscopic groups for stage 0-III colorectal cancer in elderly patients

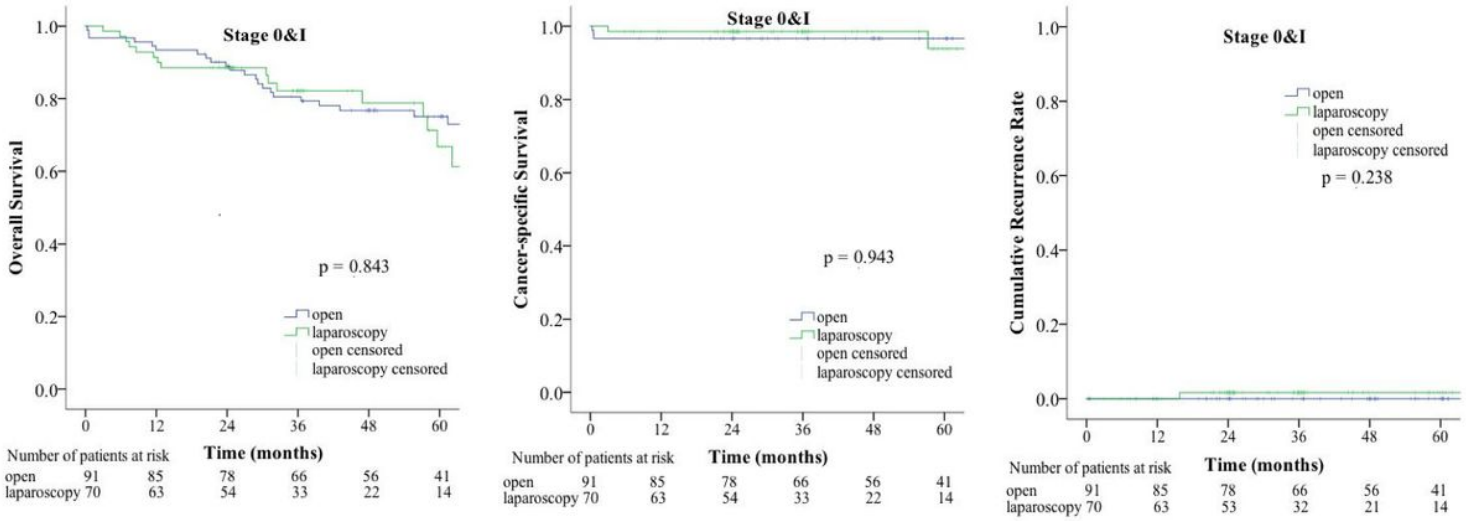

Figure 2

Survival rate and recurrence rates in open and laparoscopic groups for stage 0 and I colorectal cancer in elderly patients

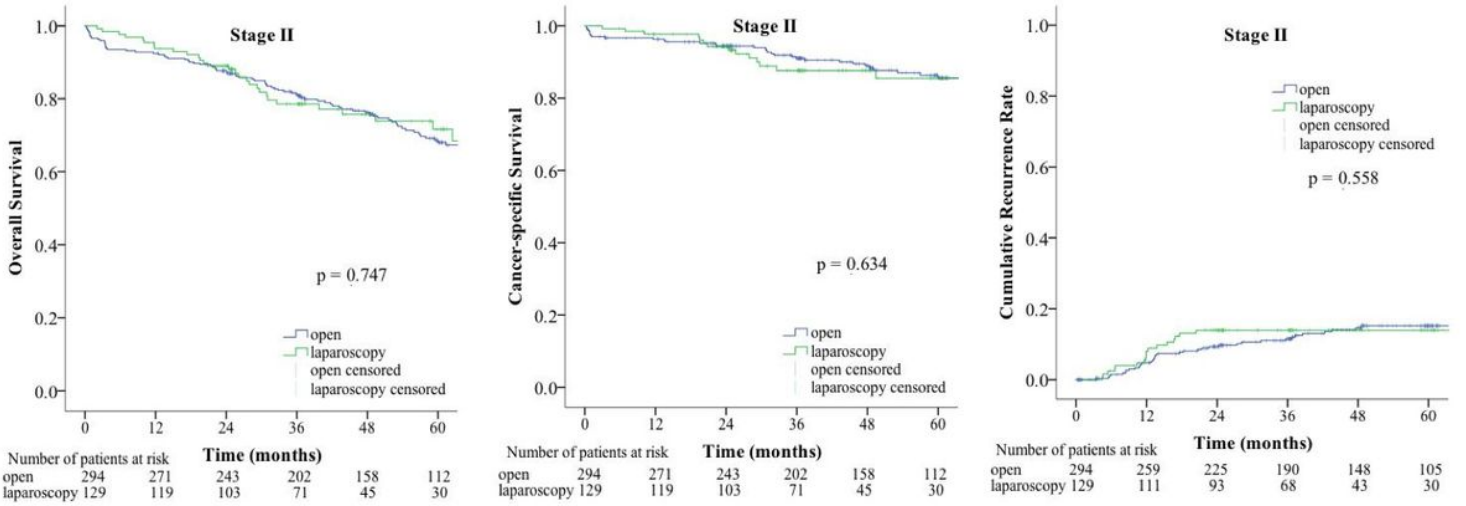

Figure 3

Survival rate and recurrence rates in open and laparoscopic groups for stage II colorectal cancer in elderly patients

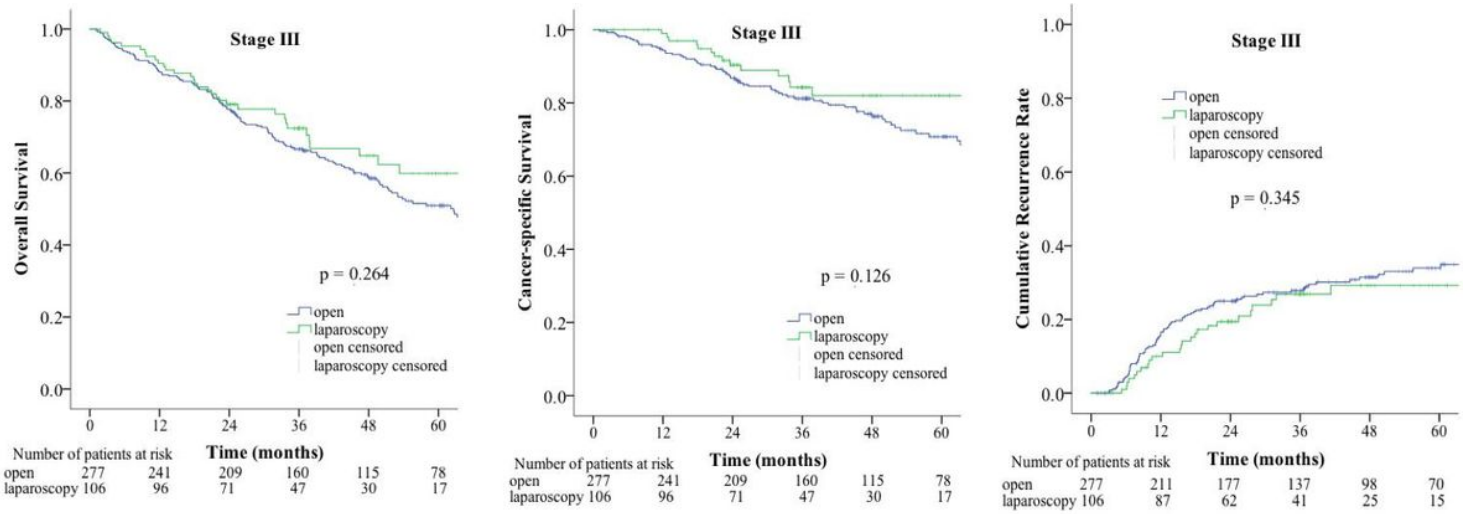

Figure 4

Survival rate and recurrence rates in open and laparoscopic groups for stage III colorectal cancer in elderly patients