

ORIGINAL ARTICLE

Laparoscopic surgery as a treatment option for elderly patients with colon cancer

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Summary

Purpose: With the increase in life expectancy, the use of laparoscopic surgery in elderly patients with colon cancer is gaining interest. The aim of this study was to identify the impact of laparoscopic surgery on elderly patients with colon cancer in comparison with open surgery. In addition, we evaluated the role of surgery in elderly patients with colon cancer by assessing long-term outcomes.

Methods: We retrospectively reviewed clinical data of 203 colon cancer patients aged ≥ 75 years who underwent radical surgery by either laparoscopy or open surgery from January 2009 to January 2015. Patient characteristics, short-term outcomes, and follow-up data were compared. Radical laparoscopic surgery was performed in 109 patients and 94 patients underwent open surgery.

Results: Laparoscopic surgery was accompanied with significantly less blood loss, lower analgesic consumption, shorter time to first flatus and soft diet, and shorter postoperative hospital stay compared with open surgery. The 5-year overall survival (OS) and disease-free survival (DFS) rates were similar between the two groups. Multivariate analysis revealed that OS and DFS were influenced only by TNM stage.

Conclusion: Laparoscopic surgery in older patients for colon cancer can be safely performed and maintains the advantage of being minimally invasive.

Key words: colectomy, colon cancer, elderly, laparoscopy, minimally invasive surgery, prognosis

Introduction

In China, life expectancy has consistently increased and more people are expected to live beyond 75 years of age [1-3]. According to reports, even 75-year-old individuals are expected to survive for more than 7 years [1-3]. Similarly, the likelihood of developing colon cancer increases with advanced age [4-6]. Radical surgery is the only treatment modality for curing colon cancer [7-10]. This is applicable to all colon cancer patients. However, elderly patients with colon cancer are often regarded as high risks for radical surgery because of several medical co-morbidities and reduced functional reserves [11]. Nevertheless, several studies have demonstrat-

ed that radical surgery for elderly patients with gastrointestinal cancers was feasible [12-17]; in fact, recently, laparoscopic surgery has been increasingly used in this population [13,14]. Some reports on the outcomes of laparoscopic surgery for elderly patients with colon cancer included only individuals between 65 and 75 years of age [18-21]. Moreover, only a few studies have compared laparoscopic and open surgery for elderly patients. The aim of this study was to review the role of laparoscopic surgery in patients with colon cancer aged ≥ 75 years by comparing short-term and long-term outcomes with those observed after open surgery.

Methods

This retrospective study complied with the Declaration of Helsinki and was approved by the Ethics Committee of our institution. The need for informed consent from all patients was waived because of the retrospective study design.

From January 2009 to January 2015, patients who were at least 75 years old and who had undergone radical surgery for histologically-proven colon cancer at our institution were included in this study. In all patients, colon cancer was verified using colonoscopy and pathologic examination. Patients who underwent palliative resection were excluded from this study. Palliative resection was defined as resection of the primary tumor to manage symptoms, such as obstruction, perforation, and bleeding. Rectal surgery was also excluded from this study. Data on patient characteristics, short-term outcomes and long-term survival outcomes were retrospectively collected. Cancer stage was based on the 7th edition of the TNM classification for colon cancer, as proposed by the Union for International Cancer Control and American Joint Committee on Cancer [22-25].

Complications within the 30-day postoperative period were classified using the Clavien–Dindo classification. Grades 3, 4, and 5 were considered as major complications, whereas grades 1 and 2 were considered as minor complications. Mortality was defined as death from any cause within 30 postoperative days [26-34].

Follow-up data were collected from the outpatient database. Patients were seen at the outpatient department every 3 months for the first postoperative year, every 4 months for the next 2 years, and annually thereafter. OS was calculated from the date of radical resection until the last follow-up or death from any cause. DFS was calculated from the date of radical resection until the date of cancer recurrence or death from any cause. The follow-up period ended in January 2016. Follow-up was completed in 193 patients (193/203), so the follow-up rate was 95.1%.

The type of colon resection was determined based on tumor location. Our institutional indication for laparoscopic surgery was colon cancer without serosal invasion or less than 4 metastatic lymph nodes on preoperative imaging studies. Open surgery was mostly reserved for cases with more advanced disease. However, some patients could chose open surgery despite having tumors operable by laparoscopic surgery due to financial concerns as the mechanical stapler used for laparoscopic surgery, was not covered by the medical insurance system in China.

Statistics

For variables following normal distribution, data were presented as mean with standard deviation and were analyzed using the Student's *t*-test. For data following non-normal distribution, results were expressed as median and range and were compared using Wilcox-

on test. Differences in semi-quantitative results were analyzed using Mann–Whitney *U* test. Differences in qualitative results were analyzed using χ^2 test or Fisher exact test, as appropriate. The Kaplan–Meier method was used to analyze OS and DFS and log-rank test was used to compare survival between the two groups. Univariate and multivariate analyses using logistic regression model were performed to identify the predictive factors of OS and DFS. A *p* value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA).

Results

Among 203 elderly patients with colon cancer who were included in this study, 94 patients underwent radical open surgery and 109 underwent radical laparoscopic surgery. Patient data are presented in Table 1. The median age of both groups was similar, but a higher proportion of medical co-morbidities was observed in the laparoscopy group than in the open group. The median age was 77 years (range 75-81) and 76 years (range 75-82) in the laparoscopy and open group, respectively.

The type of resection was similar between the two groups (Table 2). In our series, there were 8 patients converted to open surgery due to more extensive disease, and they were also included in the laparoscopy group as “intent-to-treat” analysis. The conversion rate was 7.3% (Table 2). Although the pathologic TNM stage did not differ significantly between the two groups, advanced colon cancer was present in a higher proportion of patients in the open group. Compared with the open group, the laparoscopy group had significantly longer operative time, less estimated blood loss, lower median number of analgesic injections, shorter time to first flatus and time to soft diet, and earlier hospital discharge.

The rate of postoperative 30-day complications was similar between the two groups. The rate of severe complications was also similar between the two groups. The most frequent complication was ileus followed by anastomotic leakage. Adjuvant chemotherapy was administered in 7 cases. The most common chemotherapy regimen was oxaliplatin, 5-fluorouracil and folinic acid (FOLF-OX). There was no postoperative 30-day mortality.

The overall median follow-up period was 40 months. There were 70 deaths from any cause during the follow-up period; of these, 64 patients died from colon cancer recurrence, and 6 patients died from causes unrelated to colon cancer. The most common type of cancer metastasis was peri-

Table 1. Patient characteristics

Characteristics	Laparoscopic surgery (n=109) n (%)	Open surgery (n=94) n (%)	p value
Age, years (range)	77 (75-81)	76 (75-82)	0.350
Sex (male: female)	58 (53.2):51 (46.8)	52 (55.3):42 (44.7)	0.764
No. of co-morbidities			0.037
0	66 (60.6)	70	
1	30 (27.5)	17	
2	8 (7.3)	5	
>2	5 (4.6)	2	
Kinds of co-morbidities			0.582
Hypertension	20 (18.3)	9	
Diabetes mellitus	9 (8.3)	6	
Coronary heart disease	8 (7.3)	5	
Liver cirrhosis	1 (0.9)	2	
Chronic atrial fibrillation	3 (2.8)	1	
Chronic obstructive pulmonary disease	2 (1.8)	1	
ASA score			0.056
I	66 (60.6)	70	
II	33 (30.3)	16	
III	10 (9.2)	8	
Clinical TNM stage (cTNM)			0.914
I	18 (16.5)	19 (20.2)	
II	68 (62.4)	51 (54.2)	
III	23 (21.1)	24 (25.5)	

ASA: American Society of Anesthesiologists

Table 2. Perioperative data

Data	Laparoscopic surgery (n=109) n (%)	Open surgery (n=94) n (%)	p value
Operative time (min), median (range)	170 (150-220)	150 (110-230)	0.015
Blood loss (ml), median (range)	110 (80-220)	220 (170-320)	0.019
Postoperative stay, days, median (range)	10 (7-20)	14 (10-32)	0.020
Conversion	8 (7.3)	-	-
Type of resection			
Right hemicolectomy	51 (46.8)	42 (44.7)	
Left hemicolectomy	37 (33.9)	32 (34.0)	
Sigmoidectomy	12 (11.0)	10 (10.6)	
Transverse colectomy	3 (2.75)	4 (4.3)	
Ileocecal resection	6 (5.5)	5 (5.3)	
Number of analgesic injections, median (range)	3 (2-6)	4 (3-9)	0.029
Time to first flatus, day (range)	3 (2-5)	5 (3-6)	0.028
Time to soft diet, day (range)	4 (3-6)	6 (4-8)	0.020
Pathological stage (pTNM)			0.830
I	13 (11.9)	9 (9.6)	
II	54 (49.5)	52 (55.3)	
III	42 (38.5)	33 (35.1)	
Histologic differentiation			0.850
Good	54 (49.5)	49 (52.1)	
Moderate	32 (29.4)	24 (25.5)	
Poor	23 (21.1)	21 (22.3)	
Retrieved lymph nodes, median (range)	14 (11-18)	16 (12-20)	0.759
Residual tumor (R0/R1/R2)	109/0/0	94/0/0	1.000

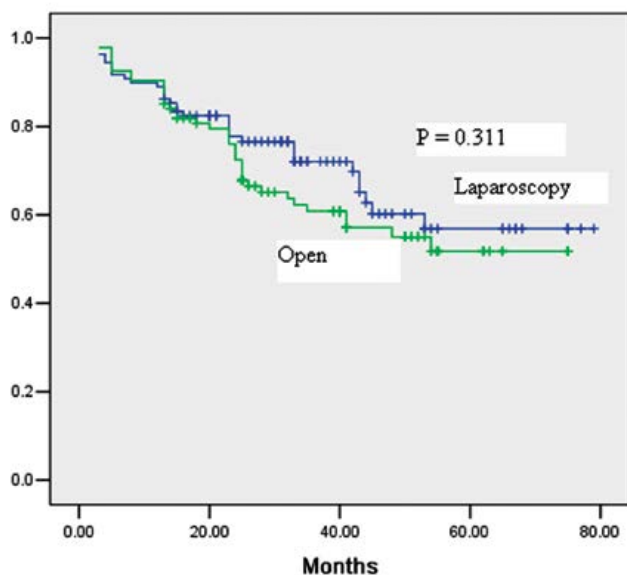


Figure 1. Kaplan–Meier estimates of overall survival for the laparoscopy and open groups.

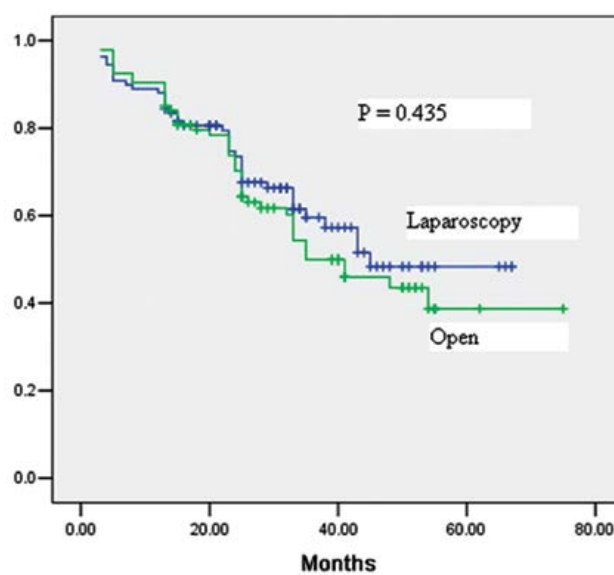


Figure 2. Kaplan–Meier estimates of disease-free survival for the laparoscopy and open groups.

Table 3. Postoperative course

	Laparoscopic surgery (n=109) n (%)	Open surgery (n=94) n (%)	p value
Postoperative 30-day complications	26 (23.8)	27 (28.7)	0.834
Ileus	9 (8.3)	8 (8.5)	
Pneumonia	4 (3.7)	6 (6.4)	
Anastomotic leakage	5 (4.6)	6 (6.4)	
Heart failure	3 (2.8)	1 (1.1)	
Intra-abdominal bleeding	2 (1.8)	1 (1.1)	
Intra-abdominal abscess	1 (0.9)	1 (1.1)	
Acute coronary syndrome	2 (1.8)	3 (3.2)	
Multiple organ failure	0 (0.0)	1 (1.1)	
Severity of complications			0.954
Major (3, 4 and 5)	4 (3.7)	4 (4.3)	
Minor (1 and 2)	22 (20.2)	23 (24.5)	

toneal seeding. The 5-year OS rate was 54% for the whole cohort and did not differ significantly between the two groups ($p=0.311$) (Figure 1). The 5-year DFS rate also did not differ significantly between the two groups ($p=0.435$) (Figure 2). Multivariate analysis revealed that OS was influenced by TNM stage, but not by old age (≥ 80 years), presence of co-morbidity, or tumor size. Furthermore, DFS was influenced by TNM stage, but not by the presence of co-morbidity, tumor laterality, or lymphovascular invasion.

Discussion

Laparoscopic surgery is a potential alternative to open surgery in terms of better short-term outcomes [35–37]. Reduced postoperative pain, earlier functional recovery, reduced stress response,

and shorter length of hospitalization with laparoscopic surgery are particularly appealing for elderly patients who are high risks for radical surgery [35–39]. However, laparoscopic surgery in these patients has the potential to cause cardiopulmonary dysfunction from pneumoperitoneum. Therefore, the impact of laparoscopic surgery in elderly patients with colon cancer has been controversial.

This study demonstrated that laparoscopic surgery had better short-term outcomes than open surgery without increasing postoperative morbidity and mortality in elderly patients with colon cancer. Laparoscopic surgery did not adversely affect the long-term survival of these elderly patients. In addition, we observed more deaths from colon cancer than deaths from other causes, even in patients aged ≥ 75 years and with several medical co-morbidities.

Table 4. Univariate and multivariate analyses for predictive factors of overall survival

Factors	Univariate analysis		Multivariate analysis		
	Favorable vs unfavorable	p value	OR	95% CI	p value
Age	<80 vs ≥ 80	0.032	1.366	0.605 - 2.110	0.109
Sex	Male vs female	0.215	-	-	-
Co-morbidities	No vs yes	0.038	1.588	0.514 - 1.718	0.190
Tumor laterality	Left vs right	0.329	-	-	-
Tumor size,cm	<3 vs ≥ 3	0.025	1.694	0.589 - 1.890	0.203
Tumor differentiation	Well/moderate vs poor	0.540	-	-	-
Lymphovascular invasion	No vs yes	0.280	-	-	-
Pathologic stage	I/II vs III	0.005	3.584	1.894 - 5.481	0.012

OR: odds ratio, 95% CI: 95% confidence interval

Table 5. Univariate and multivariate analyses for predictive factors of disease-free survival

Factors	Univariate analysis		Multivariate analysis		
	Favorable vs unfavorable	p value	OR	95% CI	p value
Age, years	<80 vs ≥ 80	0.263	-	-	-
Sex	Male vs female	0.385	-	-	-
Co-morbidities	No vs yes				
Tumor laterality	Left vs right	0.038	1.320	0.459-1.639	0.209
Tumor size (cm)	<3 vs ≥ 3	0.098	-	-	-
Tumor differentiation	Well/moderate vs poor	0.399	-	-	-
Lymphovascular invasion	No vs yes	0.029	1.258	0.651-1.981	0.090
Pathologic stage	I/II vs III	0.002	2.894	1.589-4.023	0.007

OR: odds ratio, 95% CI: 95% confidence interval

Elderly patients are considered to be high risks for radical surgery because of decreasing functional reserves and increasing medical co-morbidities [11]. However, the positive experience of elderly patients who undergo laparoscopy for other types of cancer led us to expect that laparoscopic surgery for elderly patients with colon cancer would also be feasible [12-17]. This study confirmed that laparoscopic surgery for elderly patients with colon cancer was technically feasible and led to better short-term outcomes than did open surgery, without compromising long-term outcomes.

One of the main concerns regarding laparoscopic surgery in elderly patients is the possibility of cardiopulmonary dysfunction due to pneumoperitoneum during operation. However, similar to several studies [12-17], our data showed that the incidence of cardiopulmonary dysfunction after laparoscopic surgery was similar to that after open surgery. The decreased blood loss during laparoscopic surgery may have augmented cardiopulmonary stability in these patients.

Adjuvant chemotherapy plays an important role in the treatment of advanced colon cancer [40,41]; however, its applicability and optimal regimen for elderly patients with colon cancer have been controversial. In this series, adjuvant

chemotherapy was administered to 7 cases only. A number of factors have been associated with no administration of adjuvant chemotherapy. These factors can be classified as non-recommendation by clinicians and patient refusal. Medical condition(s) diagnosed prior to cancer surgery and perceived to be a contradiction for chemotherapy, elderly patient where age is perceived to be a contradiction for chemotherapy and cardiac condition which may be a contradiction for chemotherapy have been associated with non-recommendation by clinicians [40,41]. Postoperative complications have also been associated with no administration of adjuvant chemotherapy in colon cancer patients [40,41]. Previous bad experience with chemotherapy (relative/friend), and treatment benefit not considered significant enough to accept chemotherapy are common reasons associated with patient refusal of chemotherapy [40,41].

Data on long-term survival in elderly patients with colon cancer have been limited because most retrospective and prospective studies excluded >75-year old patients [11,13,14]. Moreover, the natural course of colon cancer in elderly patients is still unclear. Contrary to the common belief that elderly patients may die of non-cancer diseases, we found that a greater proportion of these patients died of colon cancer than of non-cancer

diseases. The number of deaths from other causes was only half the number of deaths due to colon cancer during the follow-up period. In this study population, the 5-year OS rate was 54%. If these elderly patients had not undergone radical surgery, they may not have survived for >3 years. This study showed similar prognosis between the laparoscopy and open groups. Previous studies on the general colon cancer population have revealed comparable survival outcomes for laparoscopic and open surgery [42-45].

The present study has some limitations. First, our results were based on a single-center retrospective analysis; therefore, we cannot exclude selection bias of patients and surgical approach. Second, this was a single-center study on Asian population; therefore, our results may not be directly applicable to Western patients. However, considering the cost of randomized clinical trials,

more investigators are now conducting observational studies as alternative research. We believe that this study could serve as useful background research for future trials on laparoscopic surgery in elderly patients with colon cancer.

Conclusion

In summary, in terms of peri-operative morbidity and long term outcomes, there is no difference between laparoscopic and open approaches.

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Conflict of interests

The authors declare no conflict of interests.

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