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ORIGINAL ARTICLE

Comparison of long-term outcomes after laparoscopic-assisted and open colectomy for splenic flexure cancer

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Summary

Purpose: *This study aimed to use propensity score matching (PSM) to compare long-term outcomes after laparoscopic-assisted and open colectomy for splenic flexure cancer (SFC).*

Methods: *Clinical and follow-up data from 189 SFC patients undergoing colectomy at our hospital between January 2009 and January 2016 were retrospectively analyzed. According to the surgical approach employed, the patients were categorized into a laparoscopy group and an open group. The patients were matched at a ratio of 1:1 using PSM, with the match variables including gender, body mass index, clinical stage, and American Society of Anesthesiologists (ASA) score. Sixty-two patients in each group were ultimately included in this study and their short- and long-term outcomes were compared.*

Results: *In contrast to the open group, the laparoscopy group had less intraoperative blood loss, faster postoperative recovery, and shorter hospitalization duration. On day 30 after surgery, there was no statistically significant difference in the incidence of minor or major complications between the two groups. The intraoperative mortality and mortality within 30 days after surgery were all 0% in the two groups. There was no statistically significant difference in pathological results between the two groups. There was no statistically significant difference in the tumor recurrence, 5-year overall survival (OS), and 5-year disease-free survival (DFS) rates between the two groups.*

Conclusion: *Laparoscopic-assisted colectomy for SFC had the same long-term outcome as open colectomy.*

Key words: *colectomy, laparoscopy, minimally invasive surgery, prognosis*

Introduction

Colorectal cancer (CRC) is one of the most commonly encountered malignant tumors [1-3]. With the increase in mean life expectancy, the westernization of life style and the decrease in physical activity the incidence of CRC shows an increasing trend [4]. Surgical resection is the primary treatment for CRC [5-7]. However, open abdominal surgery has some limitations, such as requiring a large incision and the slow postoperative recovery. Since the first application of radical laparoscopic resection in CRC in the 1990s, randomized controlled trials (RCTs) have shown that laparoscopic surgery is associated with less blood loss, shorter hospitalization, fewer complications, and similar oncological outcomes (pathological results, tumor recurrence rate during follow-up, OS, and tumor-free survival rate) compared to conventional open abdominal surgery [9-14]. Therefore, laparoscopic surgery has been widely adopted in CRC therapy. SFC is rarely seen in clinical practice, constituting only 5% of CRC cases [15-17]. Since SFC has a low incidence and is difficult to treat laparoscopically, studies on laparoscopic surgery for SFC are limited in number [18-24]. Most of these studies were only concerned with short-term outcomes [19-24] and only one study [18] compared long-term outcomes

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of laparoscopic-assisted and open abdominal surgery but was limited by a small sample size and short follow-up duration [18]. The present study aimed to use PSM to compare the long-term outcomes of laparoscopic-assisted and open colectomy for SFC.

Methods

This study complied with the Declaration of Helsinki and was approved by our local ethics committees. The need for informed consent from patients was waived because of its retrospective nature.

A total of 189 SFC patients treated with radical surgery at our hospital between January 2010 and July 2017 and who met the following inclusion criteria were analyzed: (1) pathological diagnosis of colon adenocarcinoma, (2) preoperative clinical stage of T1-3 N0-2 M0, (3) no other organs were resected, and (4) the data was complete. Patients who underwent emergency surgery or were only examined without radical resection were excluded. The patients were categorized according to the surgical approach into a laparoscopy group (undergoing laparoscopic-assisted colectomy) and an open group (undergoing open colectomy). PSM based on age, gender, body mass index (BMI), clinical stage, and ASA score was performed using R software (The R Foundation, Vienna, Austria). The patients in the laparoscopy group were matched at a 1:1 ratio with those in the open group, forming two groups of 62 patients each. The general preoperative characteristics and the short- and long-term outcomes of the two groups were compared.

All patients underwent standard examinations, such as electronic colonoscopy, pelvic magnetic resonance imaging, chest and abdominal computed tomography, laboratory tests, lung function tests, electrocardiography, and echocardiography to determine their clinical stage and whether they could tolerate surgery [25-29]. Colon cancer staging was performed according to the 7th edition of the TNM classification of CRC, which was proposed by the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC) [30]. The operative technique has been previously published [18]. Postoperative complications, defined as morbidity occurring within 30 postoperative days, were graded according to the Clavien–Dindo classification. Major complications were defined as those of grades 3, 4, and 5. Minor complications were defined as those of grades 1 and 2 [31-36]. Operative death was defined as mortality within 30 days after resection.

All patients were followed up after hospital discharge. Patients were followed up once every 3 months in the first year after surgery, once every 6 months in the second year, and yearly thereafter. The follow-up protocol included regular physical examination, tumor marker testing, and chest and abdominal imaging examination. Electronic colonoscopy was performed once per year [37]. Disease recurrence was defined as locoregional or distant metastasis proven by radiological and/or pathological methods, when available. The last documented follow up visit was in August 2017.

Statistics

All calculations were performed using IBM SPSS Statistics 22®. For variables with normal distribution, data have been presented as mean and standard deviations and were analyzed by Student's *t*-test. For variables with non-normal distribution, data were expressed as median and range and were compared by Mann–Whitney *U* test. Differences of semiquantitative results were analyzed by Mann–Whitney *U* test. Differences of qualitative results were analyzed by chi-square test or Fisher's exact test, where appropriate. Survival rates were analyzed using the Kaplan–Meier method, and differences were analyzed with the log-rank test. Univariate analyses were performed to identify prognostic variables related to OS and DFS. Univariate variables with probability values of <0.10 were selected for inclusion in the multivariate Cox proportional hazard regression model. Hazard ratios (HR) along with the corresponding 95% confidence intervals (CI) were calculated. P<0.05 indicated statistical significance.

Results

There was no statistically significant difference in the general preoperative characteristics, such as age, gender, BMI, clinical stage, and ASA score between the two groups (Table 1).

Most patients underwent subtotal colectomy and only a few underwent an extended left hemicolectomy. Surgery in 8 patients in the laparoscopy group was intraoperatively converted to open surgery because of adhesions and bleeding (Table 2). Compared with the open group, the laparoscopy group had a longer surgical duration (Table 2). However, the laparoscopy group had less intraoperative blood loss, faster postoperative recovery, and shorter hospitalization duration (Table 2). There was no statistically significant difference in the incidence of minor or major complications within 30 days of surgery between both groups (Table 2). Pathological characteristics, such as TNM stage and tumor differentiation state, did not show a statistically significant difference between the two groups (Table 3).

The median follow-up time in the laparoscopy and open groups was 46 months and 41 months, respectively, with no statistically significant difference. During the follow-up, 13 and 20 patients in the laparoscopy and open groups died, respectively, with most deaths caused by tumor recurrence and a small fraction due to non-tumor factors. The 5-year OS rates were 65.5% and 61.4% in the laparoscopy and open groups, respectively, with no statistically significant difference (p=0.187, Figure 1). Moreover, no significant differences were found when analyzing individual TNM stages (Table 4). Multivariate Cox regression analysis of OS in all

Table 1. Demographics and clinical data of the two groups

Data	*Laparoscopy group n=62 n (%)*	*Open group n=62 n (%)*	*p value*
Age, years, median, (range)	54 (41-70)	52 (43-72)	0.759
Gender (male: female)	42:20	38:24	0.453
BMI (kg/m²), median (range)	21 (19-26)	23 (19-27)	0.450
Clinical stage (cTNM)			0.992
I	21 (33.9)	19 (30.6)	
II	22 (15.5)	26 (41.9)	
III	19 (30.6)	17 (27.4)	
ASA score			0.559
I	42 (67.7)	45 (72.6)	
II	14 (22.6)	12 (19.4)	
III	6 (9.7)	5 (8.0)	

BMI: body mass index

Table 2. Surgical outcomes of the two groups

Outcomes	*Laparoscopy group (n=62)*	*Open group (n=62)*	*p value*
Operative time (min), median (range)	210 (190-300)	170 (140-240)	0.041
Blood loss (ml), median (range)	100 (70-150)	160 (100-240)	0.034
Conversion	8	-	-
Time to pass flatus (d), median (range)	3 (2-4)	4 (3-5)	0.040
Postoperative stay (d), median (range)	9 (7-21)	14 (8-31)	0.038
Patients with postoperative 30-day complications, n (%)	13 (21.0)	15(24.2)	0.668
Anastomotic leakage	4 (6.5)	6 (9.7)	
Anastomotic stenosis	3 (4.8)	3 (4.8)	
Intra-abdominal bleeding	1 (1.6)	2 (3.2)	
Abdominal abscess	1 (1.6)	1 (1.6)	
Ileus	2 (3.2)	1 (1.6)	
Pneumonia	1 (1.6)	1 (1.6)	
Wound infection	1 (1.6)	1 (1.6)	
Patients with major complications	1 (1.6)	2 (3.2)	1.000
Patients with minor complications	12 (19.4)	13 (21.0)	0.823

Table 3. Pathological data of the two groups

Pathological data	*Laparoscopy group n=62 n (%)*	*Open group n=62 n (%)*	*p value*
Histologic differentiation			0.597
Well	21 (33.9)	24 (38.7)	
Moderately	18 (29.0)	17 (27.4)	
Poorly	23 (37.1)	21 (33.9)	
Retrieved lymph nodes, median (range)	16 (12-24)	17 (14-28)	0.528
Pathological stage (pTNM)			0.540
I	14 (22.6)	18 (29.0)	
II	19 (30.6)	17 (27.4)	
III	29 (46.8)	27 (43.5)	
Residual tumor			1.000
R0	62 (100)	62 (100)	
R1	0 (0)	0 (0)	
R2	0 (0)	0 (0)	

patients revealed that tumor statuses of T3 or T4a, lymph node statuses of N2 or N3, and poor tumor differentiation were significant predictors of worse OS (Table 5). The type of surgical approach was not found to be a significant predictor of OS.

The 5-year DFS rate was 56.4% and 52.6% in the laparoscopy and open groups, respectively, with no statistically significant difference (p=0.184, Figure 2). Multivariate Cox regression analysis of DFS in all patients revealed that tumor statuses of T3 or T4a, and lymph node status of N2 were significant predictors of worse DFS (Table 6). The type of surgical approach was not found to be a significant predictor of DFS.

Table 4. Five-year survival following laparoscopy and open group with regard to pathological stage

Pathological stage	*Laparoscopy group (n=62)* %	*Open group (n=62)* %	*p value*
I	79	76	0.541
II	69	67	0.297
III	49	45	0.110

Table 5. Prognostic factors related to overall survival

Regression variables	*Adjusted hazard ratio*	*95%CI*	*p value*
Pathological T stage			
T_1-T_2	1.00		
T_3-T_{4a}	2.69	1.69-3.97	0.029
Pathological N stage			
N_0-N_1	1.00		
N_2	2.02	1.55-3.54	0.018
Differentiation grade			
Well-moderately	1.00		
Poor	3.15	2.32-3.99	0.015

Table 6. Prognostic factors related to disease-free survival

Regression variables	*Adjusted hazard ratio*	*95%CI*	*p value*
Pathological T stage			
T_1-T_2	1.00		
T_3-T_{4a}	1.87	1.59-4.36	0.024
Pathological N stage			
N_0-N_1	1.00		
N_2	2.30	1.45-3.02	0.010

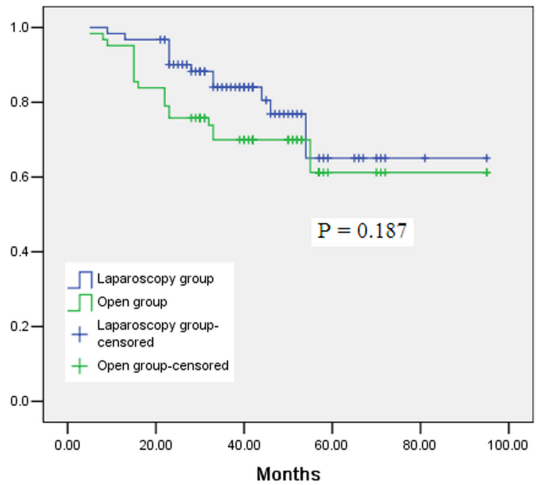

Figure 1. Comparison of overall survival rate between laparoscopy and the open group (p=0.187).

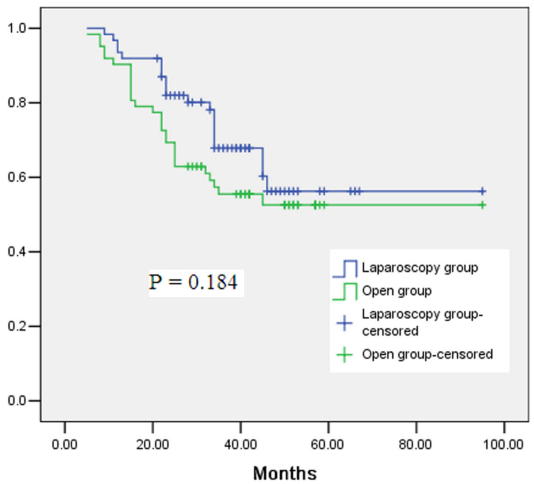

Figure 2. Comparison of disease-free survival rate between laparoscopy and the open group (p=0.184).

Discussion

SFC is rarely seen in clinical practice [15-17] and is difficult to treat with laparoscopic-assisted colectomy. Therefore, previous large-scale RCTs have tended to exclude SFC to ensure that the studies be conducted smoothly [9-14]. A literature review performed by us retrieved only 7 reports on laparoscopic-assisted colectomy for SFC [18-24], and 5 of these only reported short-term outcomes without comparing them with those of open abdominal surgery [19-23]. Only one report compared laparoscopic colectomy versus open abdominal colectomy for treating SFC [24]. One report from Japan by Nakashima et al. [24] included 55 SFC patients (33 undergoing laparoscopic-assisted colectomy and 22 undergoing open abdominal surgery) and showed that, in contrast to open abdominal surgery, laparoscopic-assisted colectomy for SFC was associated with less intraoperative blood loss, fewer postoperative complications, and faster postoperative recovery. However, the report did not compare the long-term outcomes [24]. Another study by Kim et al. from South Korea [18] indicated that laparoscopic-assisted colectomy for SFC could have similar long-term outcomes to open abdominal surgery. However, their study analyzed a small sample size (only 33 patients in the laparoscopy group and 18 in the open group) [18]. Our review of the PubMed, Google Scholar, and EMBASE databases indicates that our study was the English report with the largest sample size among studies comparing the long-term outcomes of laparoscopic-assisted and open abdominal surgery for SFC.

In previous studies, the mean volume of intraoperative bleeding in laparoscopic-assisted colectomy for SFC was 15-120 ml [18-24]. In this study, the median volume was 100 ml, a value similar to that reported in past studies [18-24]. The mean duration of operation in the laparoscopy group was longer than that in the open group, a phenomenon similar to the observations in past studies [18-24], which may be due to the technical complexity of laparoscopic-assisted colectomy for SFC [18-24]. We believe that with continual improvement in surgical instruments and physicians' laparoscopic surgical experience, operative times will decrease [18-24].

The incidence of complications after laparoscopic colectomy for SFC in previous studies was 6-37.5% [18-24], with the most common complications including anastomotic leak and intestinal obstruction [18-24]. One study showed that the incidence of postoperative complications after laparoscopic-assisted colectomy for SFC was lower than that of open abdominal surgery [24], but another study reported comparable rates [18]. In this study, it was found that the incidence of minor and major complications on day 30 after surgery was comparable between the two surgical methods. These discrepancies were likely due to differences between studies in the definition of complications [18-24].

Despite a number of studies comparing the long-term outcomes between laparoscopic-assisted colectomy and open abdominal surgery for CRC having been conducted [9-14], they have all excluded patients with SFC [9-14]. To date, only one study has compared the long-term outcomes of different surgical approaches for SFC, which showed that the 5-year OS and tumor-free survival rates were similar [18]. In this study, it was found that the 5-year OS and DFS rates were also similar. This was in accordance with previous large studies of laparoscopic-assisted colectomy for CRC [9-14,38-43], indicating that laparoscopic-assisted colectomy for SFC may achieve a similar long-term outcome to open abdominal surgery.

To date, there is no high-quality evidence summarizing the relative advantages and disadvantages of laparoscopic-assisted and open abdominal surgery for SFC. Although prospective RCTs are the gold standard for evaluating the clinical efficacy of a treatment, its practical use is usually confronted with great difficulty due to issues with patient recruitment, time, funding, and ethics. In contrast, PSM can achieve results similar to prospective RCTs by effectively utilizing observational data from clinical practice while limiting confounding and selection bias. This approach has been widely accepted to be a statistical method of great practicality, novelty, and authority. In recent years, a growing number of authors have applied PSM to the study of lung and gastric cancers, but its application to SFC research is still lacking. The use of PSM in this study maximally decreased the bias inherent to retrospective studies and further verified the oncological safety of laparoscopic-assisted colectomy for SFC patients.

The present study has some limitations. This was a retrospective study from a single institution. The findings of this study may be limited by the retrospective nature of the analysis. Therefore, we cannot rule out the possibility of selection bias. The surgeons may have tended to select laparoscopic colectomy only in relatively simple and straightforward cases. In addition, the total number of patients was relatively small in both groups. Nevertheless, we believe that the present study could be useful as a stepping stone to future RCTs on laparoscopic colectomy for SFC. We expect to conduct further large, robust observational

studies or RCTs as we accumulate experience with laparoscopic colectomy for SFC.

In summary, laparoscopic colectomy for SFC had acceptable morbidity and mortality rates and had no effect on patient survival and recurrence rates. Based on the present results, we consider laparoscopic colectomy to be a safe and feasible procedure for patients with SFC.

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Conflict of interests

The authors declare no conflict of interests.

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