

ORIGINAL ARTICLE

Short- and long-term outcomes of laparoscopic complete mesocolic excision for transverse colon cancer

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Summary

Purpose: To compare the short- and long-term outcomes of open and laparoscopic complete mesocolic excision (CME) for transverse colon cancer (TCC) using propensity score matching (PSM).

Methods: The clinical and follow-up data of 97 TCC patients who were subjected to CME in our institution from January 2012 to October 2017 were retrospectively analyzed. The patients were divided into the laparoscopic and open group according to the surgical approaches. The patients were 1:1 matched using the PSM method. The matching variables included age, sex, body mass index (BMI), clinical stage, and American Society of Anesthesiologists (ASA) score. Forty-three patients were included in each study group. Short- and long-term outcomes were compared between the two groups.

Results: Compared with the open group, the laparoscopic

group showed benefits including less intraoperative blood loss, faster postoperative recovery, and shorter hospital stay. There was no significant difference in the incidence of 30-day postoperative complications, the incidence of major complications, and the pathological results between the two groups. The intraoperative and postoperative 30-day mortality rates in both groups were 0%. There was no significant difference in the tumor recurrence rate, 5-year overall survival (OS), and 5-year disease-free survival (DFS) between the two groups.

Conclusion: Short-term outcomes were better with laparoscopic CME than with open surgery although the long-term outcomes were similar in both groups.

Key words: complete mesocolic excision, laparoscopy, minimally invasive surgical oncology, prognosis, transverse colon cancer

Introduction

Minimally invasive surgery is becoming one of the acceptable treatment options for patients in the field of surgical oncology [1]. Since the first reported case of laparoscopic colectomy for a colon tumor that was conducted by Jacobs et al. in 1941 [2], several multicenter, large-sample, randomized controlled trials (RCT) have indicated that laparoscopic surgery for colon cancer can be very beneficial for patients [3-8]. Minimally invasive surgery has advantageous surgical features including less blood loss, shorter hospital stays, faster postopera-

tive recoveries, comparable or fewer complications, and comparable oncological outcomes (tumor recurrence rate, OS rate, and DFS rate) to traditional laparotomy [3-8]. However, all of the above studies excluded TCC due to the difficulty experienced with laparoscopic surgery for this condition [3-8]. The concept of CME was first proposed by Hohenberger et al. in 2009 [9]. Studies have shown that using CME can improve the 5-year OS rate by 15% in patients with colon cancer [9]. Currently, only a few studies have examined laparoscopic CME

for the treatment of TCC, and these studies have drawbacks such as small sample sizes and no long-term follow-up results [10-12]. This study aimed to compare the short-term and long-term outcomes between laparoscopic and open CME for the treatment of TCC using PSM.

Methods

Patients

This retrospective study complied with the Declaration of Helsinki and was approved by the ethics review board of our Institute. The need for informed consent from all patients was waived because of its retrospective design.

From January 2012 to October 2017, a total of 97 patients with primary TCC were subjected to radical surgery in our hospital based on specified inclusion and exclusion criteria. TCC was defined as cancer located between the hepatic and splenic flexures. Inclusion criteria were: (1) the pathological type was colon adenocarcinoma; (2) clinical stage was T1-3N0-2M0; (3) patients were subjected to surgery only, no neoadjuvant therapy was prescribed; (4) no other organs were resected; and (5) clinical and follow-up data were available and complete. Exclusion criteria: (1) patients received emergency surgery due to colon perforation or intestinal obstruction; (2) patients had combined synchronous or metachronous colorectal cancer or other organ tumors; (3) other organs were resected during surgery; (4) recurrent tumors.

Patients were divided into laparoscopic and open groups according to the surgical approach. R software was used for PSM, and patients in the laparoscopic CME and open CME groups were 1:1 matched based on age, sex, BMI, clinical stage and ASA score. Ultimately, 43 patients in each group were included in the study. This study retrospectively compared the preoperative baseline data and the short- and long-term outcomes between the two groups. Patients were examined routinely including electronic colonoscopy, pelvic magnetic resonance imaging (MRI), chest and abdominal computed tomography (CT), tumor marker testing, pulmonary function testing, electrocardiography and echocardiography, and any other tests deemed necessary to determine the clinical stage and patient tolerance to surgery [13-19]. If needed, examinations including positron emission tomography-computed tomography (PET-CT) and bone scans were used to exclude tumor metastasis. The tumor TNM stage was based on the 7th edition of the TNM classification of colorectal cancer.

Right hemicolectomy was performed for cancers located at the hepatic flexure, and left hemicolectomy was performed for cancers located at the splenic flexure. Transverse colectomy was performed for cancers located between the hepatic and splenic flexures. Surgical details had been previously reported [10]. Conversion was defined as an unplanned abdominal incision larger than what would have been necessary for specimen retrieval in the laparoscopic group.

Morbidity and mortality

Morbidity, defined as postoperative complications occurring within 30 postoperative days, was classified using the Clavien–Dindo classification [20-26]. Minor complications were classified as 1 and 2. Mortality was defined as death from any cause occurring within the 30 postoperative days.

Follow-up

All patients were followed-up after hospital discharge. Patients were followed-up once every 3 months in the first year, once every 6 months in the second year, and then once every year afterward. The follow-up examination included a routine physical examination, tumor marker testing, and chest and abdominal imaging. An annual electronic colonoscopy was performed [27-30]. When tumor recurrence was suspected, patients were subjected to timely diagnosis in the hospital. OS was calculated from the date of radical resection to the last follow-up visit or death from any cause. DFS was assessed from the date of radical resection until the date of cancer recurrence or death from any cause. The follow-up was closed in November 2017.

Statistics

Categorical variables are presented as frequencies and percentages, and continuous variables are presented as median values with range. Statistical analyses were performed with the Chi-square test, Fisher's exact test, and Mann–Whitney *U* test for categorical and continuous variables, respectively. OS and DFS rates were estimated by the Kaplan–Meier method, with differences in survival between groups compared by the log-rank test. The Cox proportional hazard model was used to identify significant predictive factors for patient survival outcomes. Results are expressed as odds ratios (OR) with 95% confidence intervals (CI). All analyses were performed using the Statistical Package for Social Sciences (SPSS) 13.0 for Microsoft Windows version. $P < 0.05$ was considered to be statistically significant.

Results

Short-term outcomes

The baseline data including age, sex, BMI, clinical stage, and ASA score showed no significant difference among all patients (Table 1).

In the laparoscopic group, 5 patients were converted to open surgery due to abdominal adhesions (2 cases) and hemorrhage (3 cases). The laparoscopic CME had benefits that included less intraoperative blood loss, faster postoperative recovery, and a shorter hospital stay (Table 2). However, the duration of the surgical procedure in the laparoscopic group was longer than in the open surgery group (Table 2). There was no significant difference in the incidence of postoperative complications and the incidence of major complications

Table 1. Baseline characteristics of the two groups

Characteristics	Laparoscopic group (n=43)	Open group (n=43)	p value
Age (median, years; range)	64 (55-72)	65 (51-70)	0.587
Sex (male: female)	25:18	22 :21	0.516
ASA score	29		
I	32	0.420	
II	11	10	
III	3	1	
BMI (median, kg/m ² ; range)	22 (18-27)	21 (19-28)	0.200
Clinical stage			0.886
I	9	7	
II	24	29	
III	10	9	

Table 2. Short-term outcomes of the two groups

Outcomes	Laparoscopic group (n=43)	Open group (n=43)	p value
Type of resection			0.628
Right hemicolectomy	21	17	
Left hemicolectomy	14	15	
Transverse colectomy	8	11	
Conversion to open surgery			-
Abdominal adhesions	2	-	
Hemorrhage	3	-	
Operative time (median, min; range)	160 (120-220)	140 (110-200)	0.030
Blood loss (median, ml; range)	130 (80-240)	150 (100-310)	0.038
Time to pass first flatus (median, d; range)	3 (1-5)	4 (2-5)	0.040
Time to resume liquid diet (median, d; range)	4 (2-7)	5 (3-7)	0.032
Hospitalization (median, d; range)	10 (7-19)	12 (8-22)	0.034
Patients with postoperative complications	7	9	0.579
Patients with major complications	1	1	1.000
Intraoperative mortality	0	0	-
Postoperative 30-day mortality	0	0	-

Table 3. Pathological outcomes of the two groups

Outcomes	Laparoscopic group (n=43)	Open group (n=43)	p value
Pathological TNM stage			0.810
I	5	4	
II	21	24	
III	17	15	
Tumor differentiation			0.489
Well	13	15	
Moderate	14	18	
Mucinous	8	7	
Poor	8	6	
Harvested lymph nodes (median, range)	19 (14-24)	18 (15-28)	0.587
Lymphovascular invasion			0.479
Yes	14	11	
No	29	32	
Residual tumor (R0/R1/R2)	43/0/0	43/0/0	1.000

between the two groups within 30 days after surgery (Table 2). The intraoperative mortality and mortality within 30 days after surgery were 0% in both groups (Table 2). The pathological results (TNM stage, tumor differentiation, margin condition, and lymph node dissection results) in the two groups were not significantly different (Table 3).

Follow-up and survival

The median follow-up time for the laparoscopic group and the open group was 44 and 42 months, respectively, with no significant difference between groups. During the follow-up, 6 pa-

tients died in the laparoscopic group, and 8 in the open group. The cause of death in all cases was tumor recurrence. No significant differences were found with respect to the tumor recurrence site, the median time to recurrence, and the treatments for recurrence between the two groups (Table 4). The 5-year OS rates of patients in the laparoscopic CME and open surgery group were 71 and 68%, respectively, the difference being not significant (Figure 1, $p=0.671$). Multivariate Cox regression analysis of OS in all patients revealed that T3 or T4, N2 or N3, and poor tumor differentiation were significant predictors of a worse OS (Table 5). The

Table 4. Tumor recurrence data of the two groups

Recurrence	Laparoscopic group (n=43)	Open group (n=43)	p value
Tumor recurrence	6	8	0.559
Recurrence site			0.825
Locoregional	2	3	
Distant	3	4	
Mixed	1	1	
Time to first recurrence (median, months, range)	19 (13-40)	17 (11-50)	0.200
Treatment for recurrence			1.000
Chemotherapy	3	4	
Surgery	1	1	
Radiotherapy	1	2	
Supportive care only	1	1	

Table 5. Univariate and multivariate analysis for predictive factors of overall survival

Factors	Univariate Favorable vs unfavorable	p value	OR	Multivariate 95% CI	p value
Age	<65 vs \geq 65 years	0.071	1.158	0.504-1.600	0.125
Sex	Male vs female	0.402	-	-	-
ASA score	I-II vs \geq III	0.085	1.258	0.687-1.504	0.189
T stage	T1-T2 vs \geq T3-T4	0.033	2.001	1.587-3.890	0.021
N stage	N0-N1 vs \geq N2	0.038	2.187	1.280-2.897	0.040

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

Table 6. Univariate and multivariate analysis for predictive factors of disease-free survival

Factors	Univariate Favorable vs unfavorable	p value	OR	Multivariate 95% CI	p value
Age	<65 vs \geq 65 years	0.201	-	-	-
Sex	Male vs female	0.154	-	-	-
ASA score	I-II vs \geq III	0.069	1.158	0.887-1.258	0.320
T stage	T1-T2 vs \geq T3-T4	0.021	2.540	1.687-3.027	0.018
N stage	N0-N1 vs \geq N2	0.028	2.014	1.450-2.580	0.011

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

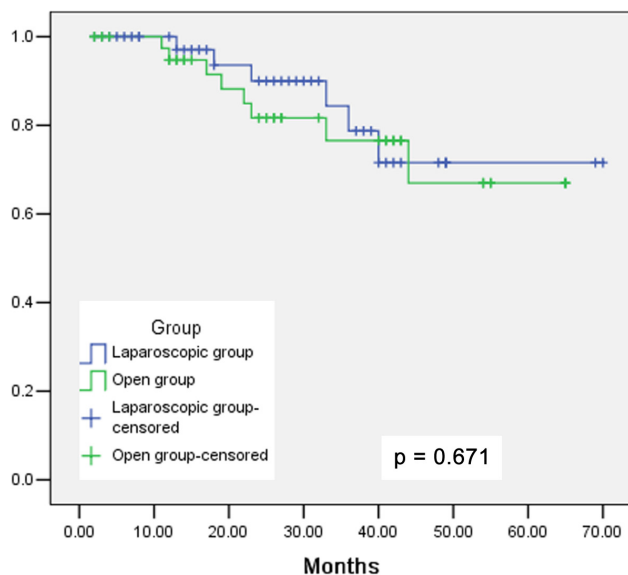


Figure 1. Comparison of overall survival rate between laparoscopic and open group. There was no significant difference between the 2 groups ($p=0.671$).

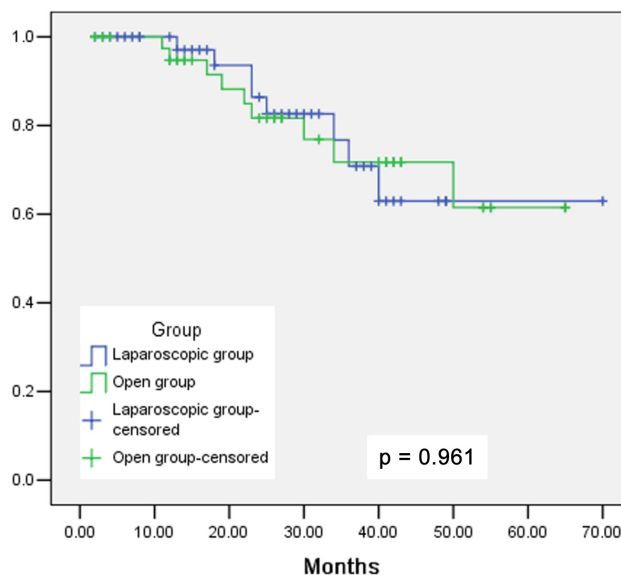


Figure 2. Comparison of disease-free survival rate between laparoscopic and open group. No significant difference was observed ($p=0.961$).

type of surgical approach was not found to be a significant predictor of OS.

The 5-year DFS rates in patients in the laparoscopic and the open groups were 63 and 61%, respectively, without significant difference (Figure 2, $p=0.961$). Multivariate Cox regression analysis of DFS in all patients revealed that T3 or T4, and N2 were significant predictors of worse DFS (Table 6). The type of surgical approach was not found to be a significant predictor of DFS.

Discussion

In the past 30 years, the survival of patients with rectal cancer has been significantly improved compared with that of patients with colon cancer, mainly due to the technique of TME [31]. In 1982, the concept of TME proposed by Heald et al., became the globally accepted gold standard for rectal cancer surgery [31]. This procedure can significantly reduce the local recurrence rate of rectal cancer and significantly improve the 5-year OS rate of these patients [32-35]. However, there has been no consensus on the choice of surgical methods for colon cancer in the past 10 years, leaving the quality of surgery uncontrolled. Based on similar anatomic principles as TME surgery, Hohenberger et al. proposed the concept of CME in 2009 [9]. The technique of CME proceeds as follows: the space between the visceral and parietal fascia of the colon is separated using sharp dissection, the visceral fascia is maintained intact, and the blood vessels are ligated at the mesenteric root, so that regional lymph nodes can be maximally dissected

[9]. The goal of this surgical technique is to reduce the dissemination of the tumor in the abdominal cavity, reduce the tumor recurrence rate, and improve the patient OS rates [9]. Currently, the concept of CME has been accepted by the global surgical oncology community [9]. Previously reported local recurrence rates after CME for the treatment of colon cancer ranged from 2 to 10% [36-38]. The local recurrence rate in this study was 8.1%, similar to the previously reported rates.

According to our search, currently there are only 3 articles in English that have reported on the treatment of TCC using laparoscopic CME [10-12]. Of them, only one reported on the short-term outcomes after laparoscopic colectomy for TCC [12], but did not compare it with those of open laparotomy. Two research papers have reported on a comparison between laparoscopic CME and open CME for TCC [10,11]. One of these was presented by Wang et al. [10], in which 78 patients with TCC were included, 39 of them underwent laparoscopic surgery and 39 underwent laparotomy. The report indicated that laparoscopic colon resection for splenic flexure carcinoma had better short-term outcomes than open surgery; however, the long-term outcomes were not compared [10]. Another article by Storli et al. showed that laparoscopic CME for the treatment of TCC had long-term outcomes similar to that of open surgery [11]; however, the sample size was small (only 33 patients in the laparoscopic surgery group and 23 patients in the open surgery group) [11]. To the best of our knowledge, our study has currently the largest sample size among English language

reports comparing short- and long-term outcomes between laparoscopic and open CME for TCC. This study indicates that compared to open surgery, laparoscopic CME can achieve better short-term outcomes and similar long-term outcomes.

Compared with open surgery, the advantages of laparoscopic CME that we observed included less intraoperative blood losses, faster postoperative recoveries, and shorter hospital stays, similar to the results of previous RCT studies [3-8]. In this study, the incidence of postoperative complications and the incidence of major complications within 30 postoperative days in the laparoscopic CME group were similar to those in the open surgery group. In some studies, the incidence of complications in the laparoscopic CME group is lower than that in the open surgery group [3-5], while in others they are similar between the two groups [6-8]. This is probably due to the different definition of complications in each study.

Lymphadenectomy is crucial in CME [9]. An insufficient number of excised lymph nodes during dissection may result in inaccurate pathological staging and the assignment of an artificially low tumor stage, which influences the determination of prognosis [9]. Colorectal cancer treatment guidelines recommended the excision of at least 12 lymph nodes. In this study, the number of positive lymph nodes in the two groups were similar, and the number of lymph nodes dissected in each patient was all greater than 12. Similar to previous reports, this indicated that laparoscopic CME achieves similar lymphadenectomy results as open CME [10-12].

Currently in big-sample studies of open CME for treating colon cancer, the 5-year OS rate ranges from 74 to 90% [3-8]. At present, only one study compared long-term outcomes between laparoscopic CME and open CME in the treatment of TCC [11]. No statistically significant difference was found in the 5-year OS rates [11]. In our study, the 5-year OS rates and the 5-year DFS rates after laparoscopic and open CME for TCC were similar. Our results are similar to those of previous large-sample studies that showed that long-term outcomes after treatment of colon cancer with laparoscopic CME for TCC were similar to those after open surgery [39-44].

Although RCTs would be the gold standard for evaluating laparoscopic surgery for CME in patients with TCC, this type of study would be logistically difficult to perform due to constraints

including research objectives, time, funds, and ethics. It is well-known that the incidence of TCC is relatively low, approximately 10% of all colon cancers, and laparoscopic CME for TCC surgery is more difficult. Thus, initiating an RCT for laparoscopic CME would be very difficult. PSM effectively utilizes the observational data in clinical practice and reduces hybrid bias and selectivity bias in observational studies. This can achieve an RCT-like effect and is generally considered to be a very practical, novel and reliable statistical method. In recent years, more and more researchers have utilized PSM for investigations on rectal cancer, ascending colon cancer, descending colon cancer, and sigmoid colon cancer. However, studies on TCC are less frequent than those for the other forms of colon cancer. In this study, PSM was used to minimize the bias inherent in retrospective studies, further confirming that the use of laparoscopic CME for TCC can achieve oncologic outcomes similar to that of open surgery.

The present study had several limitations. First, this study was performed retrospectively, which may introduce selection bias despite propensity matching. Second, although the number of laparoscopic CME for TCC in our study was greater than that in previous studies, the low incidence of TCC limits the opportunity for prospective randomized clinical trials, which are needed to establish definitive conclusions. Despite these limitations, we believe that our results provide valuable support for laparoscopic CME for TCC. A larger scaled, prospective, randomized controlled study is needed to confirm the safety and efficacy of laparoscopic CME for TCC.

Conclusion

In conclusion, the use of laparoscopic CME in the treatment of TCC leads to better short-term outcomes than laparotomy, but comparable long-term outcomes.

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Conflict of interests

The authors declare no conflict of interests.

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