ORIGINAL ARTICLE

Short- and long-term outcomes of laparoscopic complete mesocolic excision in elderly patients with right colon cancer

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Summary

Purpose: This study was designed to compare the shortand long-term outcomes between elderly and middle-aged patients who underwent laparoscopic complete mesocolic excision for right colon cancer.

Methods: A retrospective analysis was performed on the clinical and follow-up data of 108 patients undergoing laparoscopic complete mesocolic excision at our institution between January 2012 and January 2018. Patients were grouped according to their age at the time of operation into the elderly group (\geq 70 years old, 46 cases) and the middle-aged group (55 years old \leq age \leq 69 years old, 62 cases). Comparisons of short- and long-term outcomes were done between these two groups.

Results: When comparing baseline data, the Charlson comorbidity index and American Society of Anesthesiologists (ASA) scores were higher among elderly patients. Comparisons of other baseline data showed no statistically significant differences. With the exception of a higher intraoperative blood loss recorded among elderly patients, comparisons of other short-term outcomes such as operation duration, blood transfusion rate, conversion to open surgery, incidence and severity of complications 30 days after surgery, pathological results, and compliance with chemotherapy showed no statistically significant differences. Long-term follow-up results indicated that recurrences were somewhat similar between these two groups of patients. Multivariate analysis revealed that age was not an independent predictor of overall survival (OS) or disease-free survival (DFS).

Conclusion: Similar short- and long-term outcomes can be achieved among elderly and middle-aged patients with right colon cancer who underwent laparoscopic complete mesocolic excision. Age is not a limiting factor in the application of laparoscopic complete mesocolic excision.

Key words: complete mesocolic excision, laparoscopic surgery, minimally invasive surgical oncology, prognosis, right colon cancer

Introduction

Colon cancer is one of the most common malignancies [1-3]. As the average life expectancy rises, the number of old people with colon cancer shows an upward trend [4-6]. The main treatment for colon cancer patients is surgical removal of the tumor [7-9]. Currently, total mesorectal excision (TME) has become a standard technique for the surgical treatment of middle and lower rectal

cancer as it can reduce the incidence of local recurrence, making the long-term results of rectal cancer similar to those of colon cancer [10]. In 2009, Hohenberger et al. first mentioned complete mesocolic excision (CME), a procedure similar to TME [11]. Research had shown that CME could reduce the incidence of local recurrence and increase the survival rate of colon cancer patients [12-15]. Ever

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since US surgeon Jacobs first reported on using laparoscopic colectomy to treat colon cancer [16], laparoscopic colectomy became increasingly used as one of the treatments for colon cancer [17-22]. Studies have shown that when using laparoscopic CME as a treatment for colon cancer, this was associated with less blood loss, shorter hospitalization time, faster recovery time after surgery, similar or less complications, and long-term outcomes similar to those of an open CME [23-29]. However, these studies did not include older colon cancer patients. It is noted that there are no English-written papers about laparoscopic CME treatment for older colon cancer patients. This study aimed to compare the short- and long-term outcomes of laparoscopic CME treatment between elderly and middle-aged right colon cancer patients.

Methods

Patients

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 108 cases of primary right colon cancer patients who met the inclusion and exclusion criteria underwent laparoscopic CME at our Institute from January 2012 to January 2018. Inclusion criteria were as

follows: (1) pathologically confirmed adenocarcinoma of the colon; (2) cancer at clinical stage T1-3N0-2M0; (3) patients subjected to surgical treatment for the first time without any prior neoadjuvant therapy; (4) no removal of other internal organs; and (5) availability of complete clinical and follow-up information. Exclusion criteria were as follows: (1) emergency surgery had to be performed due to perforation of the colon or intestinal obstruction; (2) combined simultaneous or metachronous colorectal cancer and tumors in other organs; (3) removal of other internal organs during surgery; and (4) recurrent tumors.

Patients were grouped according to their age at the time of operation into the elderly group (\geq 70 years old, 46 cases) and the middle-aged group (55 years \leq age \leq 69 years, 62 cases). This study retrospectively compared the baseline information, as well as the short- and long-term outcomes between these two groups of patients. Pre-treatment examinations such as colonoscopy, computed tomography (CT) scans on the brain, chest and abdomen, tumor markers, lung function, electrocardiography (ECG), and ultrasonic cardiogram were conducted on all patients to determine their clinical stage, to exclude distant metastasis, and to determine whether patients could tolerate surgery. Examinations such as positron emission tomography–computed tomography (PET-CT) and bone scan were also conducted when necessary.

Patients with pathological stage III were given capecitabine + oxaliplatin (XELOX) or oxaliplatin + calcium folinate/fluorouracil (mFOLFOX6) as chemotherapy. Patients with pathological high-risk stage II were given single-agent capecitabine as chemotherapy [30-32].

Table 1. Baseline characteristics of the two groups

Characteristics	Middle-aged group (n=62) n	Elderly group (n=46) n	p value
Age (median vears: range)	63 (55-69)	74 (70-77)	0.000
Sex (Male: Female)	38.24	27.10	0.785
	50.24	27.17	0.785
ASA SCOLE			0.047
Ι	47	27	
II	12	13	
III	3	6	
Charlson comorbidity index			0.014
≥ 3	8	15	
< 3	54	31	
BMI (median, kg/m²; range)	21 (18-28)	22 (19-27)	0.548
Clinical stage			0.886
Ι	9	7	
II	24	29	
III	10	9	
Tumor site			0.943
Cecum	6	5	
Ascending colon	45	32	
Transverse colon	11	9	

Postoperative 30-day complications were graded according to the Clavien-Dindo classification system. Major complications were defined those of grades 3, 4, and 5, while minor complications were defined those of grades 1 and 2 [33-36]. Operative death was defined as mortality occurring intraoperatively or within 30 post-operative days.

Follow-up

Patients were followed-up after being discharged. Follow-up was performed in the form of outpatient visits, house visits, or communications through letters, among other approaches. Following discharge from the hospital, follow-up was once every 3 months in the first year, once every 6 months in the second year, and once every year thereafter. During follow-up, standard examinations such as physical examinations, tumor marker estimations, and chest and abdomen imaging examinations were carried out. Colonoscopy was conducted once a year [37-41]. The last follow-up took place in February 2018.

Statistics

All calculations were performed using IBM SPSS 13.0 software. For variables with normal distribution, data were 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. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). The Cox proportional hazard model was used to identify significant predictive factors for patient survival outcomes. All analyses were performed using SPSS version 13 for Microsoft Windows version. p<0.05 indicated statistical significance.

Results

Short-term outcomes

The Charlson comorbidity index and ASA score were higher among elderly patients when comparing the baseline data of these two groups of patients. Comparisons of the remaining baseline data, such as sex, body mass index (BMI), clinical stage, and tumor site, showed no statistically significant differences (Table 1).

Table 2 shows the short-term outcomes of these two groups, which indicate that blood loss during surgery was higher in the elderly group.

Table 2. Short-term outcomes of the two groups

Outcomes	Middle-aged group (n=62)	Elderly group (n=46)	p value
	п	п	
Conversion to open surgery			1.000
Tumor reasons	4	3	
Technical reasons	1	1	
Operative time (median, min; range)	140 (110-200)	130 (100-210)	0.247
Blood loss (median, ml; range)	80 (50-300)	120 (100-280)	0.040
Blood transfusion	1	1	1.000
Time to pass first flatus (median, d; range)	3 (1-5)	3 (2-6)	0.254
Time to resume liquid diet (median, d; range)	4 (2-6)	4 (3-5)	0.587
Hospitalization (median, d; range)	11 (8-19)	12 (8-29)	0.158
Patients with postoperative complications	9	7	0.919
Anastomotic leakage	2	1	
Ileus	1	0	
Wound infection	1	2	
Chylous leakage	2	2	
Gastroplegia	1	1	
Intra-abdominal sepsis	2	1	
Patients with major complications	1	2	0.792
Intraoperative mortality	0	0	-
Postoperative 30-day mortality	0	0	-
First chemotherapy after surgery (median, weeks; range)	7 (6-9)	8 (7-10)	0.208

There were no statistically significant differences when comparing the operation duration, blood transfusion rate during and after surgery, number of days in hospital, and incidence and severity of complications 30 days after surgery between these two groups. The rate of conversion to open surgery was similar between the two groups of patients, and the cause of conversion to open surgery among these two groups was mainly due to the disease itself. None of the patients died at the operating table. A comparison of the pathological results between the two groups showed no statistically significant differences (Table 3).

Long-term outcomes

The median follow-up period of the elderly and middle-aged groups were 41 and 45 months

respectively, without statistical significance. During follow-up, 9 patients from the elderly group passed away, of which 7 cases were due to recurrence of cancer while the other 2 deaths were not caused by cancer (one was due to ischemic stroke while the other was due to a hemorrhagic stroke). Nine patients from the middle-aged group passed away, of which 8 cases were due to recurrence of cancer while the other death was not related to cancer (sudden cardiac death) (Table 4). Comparisons of the sites of recurrent disease, treatment of recurrence, etc. between the two groups of patients showed no statistically significant differences (Table 4).

The 5-year OS rate of the elderly and middleaged groups was 71 and 75% respectively, without statistical significance (p=0.411, Figure 1). Multivariate analysis revealed that the T-stage and

Table 3. Pathological outcomes of the two groups

Outcomes	Middle-aged group (n=62)	Elderly group (n=46)	p value
	п	n	
Pathological TNM stage			0.415
Ι	5	4	
II	22	20	
III	35	22	
Tumor differentiation			0.711
Well differentiated	19	14	
Moderately differentiated	29	24	
Poorly differentiated	9	6	
Mucinous	5	2	
Harvested lymph nodes (median, range)	19 (13-42)	18 (12-29)	0.107
Lymphovascular invasion			0.681
Yes	45	35	
No	17	11	
Residual tumor (R0/R1/R2)	62/0/0	46/0/0	1.000

Table 4. Tumor recurrence data of the two grou

Recurrences	Middle-aged group (n=62)	Elderly group (n=46)	p value
	n	п	
Tumor recurrence	12	9	0.978
Recurrence site			
Locoregional	2	1	
Distant	9	7	
Mixed	1	1	0.300
Time to first recurrence (median, months, range)	19 (11-48)	17 (8-43)	0.486
Mortality	9	9	
Died of cancer recurrence	8	7	
Died of non-cancer-related causes	1	2	

Factors	Univariate Favorable vs unfavorable	p value	OR	Multivariate 95% CI	p value
Age	<70 vs ≥ 70 years	0.411	-	-	-
Sex	Male vs female	0.284	-	-	-
ASA score	I-II vs ≥ III	0.085	1.584	0.557 – 1.874	0.284
T stage	T1-T2 vs ≥T3-T4	0.021	2.254	1.680 - 3.014	0.001
N stage	N0-N1 vs \ge N2	0.033	2.584	1.541 - 2.987	0.018

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

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

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

Age <70 vs > 70 years 0.318	
nge (70 vo 2 / 0 years 0.510	-
Sex Male vs female 0.254	-
ASA score I-II vs ≥ III 0.047 1.214 0.487 - 1.547 0).128
T stage T1-T2 vs ≥T3-T4 0.025 2.238 1.541 - 3.258 0).021
N stage N0-N1 vs ≥ N2 0.021 2.008 1.321 - 2.357).028

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



1.0 0.8 **Proportion surviving** 0.6 Group 0.4 Elderly grou Middle-aged group Elderly group 0.2 censored Middle-aged group censored 0.0 0.00 10.00 20.00 30.00 40.00 50.00 70.00 60.00 Months

Figure 1. Comparison of overall survival rate between elderly group (\geq 70 years old, 46 cases) and the middle-aged group (55 years < age < 69 years, 62 cases). There was no significant difference between the two groups (p=0.411).

Figure 2. Comparison of disease-free survival rate between elderly group (\geq 70 years old, 46 cases) and the middle-aged group (55 years old \leq age \leq 69 years old, 62 cases). There was no significant difference between the two groups (p=0.318).

N-stage were identified as independent predictors for the patient OS (Table 5).

The 5-year DFS rate of the elderly and middleaged groups was 55 and 59% respectively, showing no statistically significant difference (p=0.318, Figure 2). Multivariate analysis revealed that the T-stage and N-stage of disease were identified as independent predictors for DFS (Table 6). Age was not an independent predictor for OS or DFS.

Discussion

Based on similar principles of embryo anatomy for TME procedures [10], Hohenberger et al. introduced the concept of CME in 2009 in which sharp dissection is carried out in the fascial gap between the colon and the wall of the colon [11], preserving the intactness of colon visceral fascia, clearing as much regional lymph nodes as possible through ligation of the corresponding blood vessels in the mesangial root [11], reducing the chances of abdominal tumor spreading, and thereby improving the prognosis of colon cancer patients [11]. Since 2011, the National Comprehensive Cancer Network (NCCN) began recommending CME as a standard procedure for locally advanced colon cancer [42]. However, doubts exist over the suitability of performing CME on elderly patients as the excision area is larger in CME than in non-CME, coupled with the physiological degeneration of this group of patients. Based on information retrieved from retrieval databases such as MEDLINE, Embase, Web of Science, Google Scholar and Chemical Abstracts, there are currently no studies written in English on the use of CME for treating elderly colon cancer patients. This study is the first paper to indicate that similar short- and long-term outcomes can be achieved among elderly and middle-aged right colon cancer patients who underwent laparoscopic CME treatment. Hence, laparoscopic CME can be used effectively and safely on elderly right colon cancer patients.

It has been found in our study that the amount of blood loss during surgery is higher among elderly patients than the middle-aged group. The cause of this is the physiological degeneration of elderly patients, which results in the corresponding degeneration of the coagulative function [1-5]. In addition, vascular elasticity is weaker in elderly patients [1-4]. As such, their blood loss during surgery is comparatively higher. Even though their platelet count and coagulation tests prior to surgery showed no obvious abnormalities, coagulation is, however, a very complicated process. At present, the platelet count and coagulation tests, which are routinely used in the clinic, can only give a rough indication of the body's coagulation state. Notwithstanding, the blood transfusion ratio of these two groups was similar, and when compared with previous reports on laparoscopic colectomy, the blood transfusion ratio was also similar [23-29]. This showed that even though elderly right colon cancer patients have higher blood loss when subjected to laparoscopic CME, as long as the perioperative period is properly managed, the blood transfusion ratio will be similar to that of middle-aged patients.

Conversion to open surgery during laparoscopic CME for colon cancer is unavoidable in some cases, as it is in other laparoscopic procedures (such as laparoscopic gastrectomy and laparoscopic liver resection). Previous studies showed that the conversion rate during laparoscopic CME is 2-14% [23-29] and the reasons for the conversion can be classified into cancer-related reasons (such as bulky tumors and T4 stage cancers) and technical-related reasons (such as hemorrhage and adhesions) [23-29]. Our research showed that the difference in conversion rate of both elderly and middle-aged groups, at 9 and 8% respectively, was not significantly different between these two groups of patients and these rates were also similar to conversion rates in past reports. Most of the conversion cases in these two groups were mainly due to tumor reasons.

Relevant guidelines for treating colorectal cancer recommend the commencement of adjuvant chemotherapy 4-8 weeks after surgery for high-risk stage II and stage III cancer patients [30-32]. This showed that similar chemotherapy compliance can be achieved for elderly right colon cancer patients who underwent laparoscopic CME. Our study showed that the OS and DFS rates were similar between the two groups, which is related to their similarity in chemotherapy compliance.

There is currently no consensus on the definition of elderly colon cancer patients. Different studies set different standards with defined age groups ranging from those above 65 years old to those above 80 years old [43-49]. However, most of the clinical studies, both locally and overseas, defined this age group to be between 65 and 75 years old. Our study has defined this age group as those who are 70 years old and above.

It was noted that presently there are no studies written in English on the long-term outcomes of elderly colon cancer patients who underwent CME. Our study is the first to report on the long-term outcomes of elderly colon cancer patients who underwent laparoscopic CME. Based on previous studies, the 5-year OS and 5-year DFS rates of right colon cancer patients who underwent laparoscopic CME is 70-90% and 51-59%, respectively. The 5-year OS and 5-year DFS rates of right colon cancer patients in our study were similar to past papers and between the two groups. In our study, the cause of death among elderly patients was mainly due to the recurrence of cancer while a handful of them passed away due to non-cancer-related causes. This showed that as long as an elderly right colon cancer patient is deemed suitable for laparoscopic CME, such treatment ought to be given to the elderly patient so as to achieve a similar long-term survival rate to that of middle-aged patients. For colon cancer treatments, non-surgical treatments have limited effects and their 5-year OS is 0%. Currently in China, the expected life expectancy among the older population shows a rising trend. Therefore, old age is not a limiting factor in the application of laparoscopic CME.

However, we acknowledge that this study has several limitations. First, it was a retrospective study based on a single center and not a prospective randomized analysis. Second, the sample size was small and the follow-up period was not very long. These limitations should be considered when interpreting our study results. In the future, a multicenter prospective randomized controlled study with longer follow-up period is necessary to validate the safety of laparoscopic CME for elderly patients with right colon cancer.

Conclusion

In conclusion, our study shows that the application of laparoscopic CME in elderly right colon cancer patients did not increase the incidence

of complications and death, and it is possible to achieve similar long-term outcomes comparable to that of middle-aged patients. Old age is not a limiting factor for elderly right colon cancer patients to undergo laparoscopic CME.

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Conflict of interests

The authors declare no conflict of interests.

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