JBUON 2021; 26(6): 2425-2432
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

ORIGINAL ARTICLE

Outcomes of laparoscopic complete mesocolic excision for transverse colon cancer in elderly patients

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Summary

Purpose: *To investigate the short- and long-term outcomes of laparoscopic complete mesocolic excision (LCME) for the treatment of transverse colon cancer (TCC) in elderly patients.*

Methods: *Data from 147 TCC patients who underwent LCME at our hospital between January 2014 and January 2019 were retrospectively analyzed. The patients were stratified into two groups for the analysis of the clinical effectiveness of LCME: elderly group (54 patients) and non-elderly group (93 patients).*

Results: *The Charlson comorbidity index score of the elderly group was higher than that of the non-elderly group. The difference in the overall complications between the elderly and non-elderly groups was not statistically significant, while the incidence of pulmonary infection was higher in the elderly group than in the non-elderly group. No statistical differences were seen in the 5-year disease-free survival (DFS) and overall survival (OS) rates between the elderly and non-elderly groups. Poor tumor differentiation, T3-4 and N2 stage were independent risk factors for TCC recurrence and survival among patients.*

Conclusions: *LCME is a safe and effective method for the treatment of TCC in elderly patients, with comparable clinical effectiveness between the elderly and non-elderly patients.*

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

Introduction

Presently, colorectal cancer (CRC) has the third highest incidence rate and fourth highest mortality rate among all malignancies in the world [1]. It is the third most common cancer among men and the second most common cancer among women [1]. The occurrence of malignant neoplasms in the transverse colon is known as transverse colon cancer (TCC), and it accounts for approximately 10% of all CRC cases [2]. Comprehensive treatment for TCC includes surgery as the primary modality [2]. Laparoscopic colectomy (LC), first described by Jacobs in 1991 [3], has evolved rapidly with the development of laparoscopic equipment and accumulation of operator experience and is now widely applied in the treatment of CRC [4-7]. As the treatment of TCC by LC involves complex maneuvers, cases of TCC have not been included in randomized controlled trials (RCTs) [8-13]. However, with the emergence of the complete mesocolic excision (CME) technique [14], the prognosis of TCC patients may be improved [14]. In the recent years, the number of elderly patients with CRC has followed an upward trend, and changes in physiological function in such patients have led to decreased surgical tolerance and increased rates of postoperative complications and mortality. This

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Received: 03/02/2021; Accepted: 11/04/2021

has created doubts in clinical practice regarding the feasibility of laparoscopic treatment among elderly patients. Therefore, the present study aimed to investigate the short-term and long-term outcomes of laparoscopic CME (LCME) in the treatment of TCC among elderly patients.

Methods

Patients

This study complied with the Declaration of Helsinki principles. This retrospective research was approved by the Ethics Committee of our hospital (Decision approval number 1680). The need for informed consent from all patients was waived because this was a retrospective study. All data had no personal identifiers and were kept confidential.

The data of patients diagnosed with TCC who underwent LCME between January 2014 and January 2019 at our hospital were retrospectively analyzed, and the subjects were selected based on the following inclusion and exclusion criteria: (1) Inclusion criteria: 1. TCC, clinical stage T1-3N0-2M0; 2. Patients with no distant metastases and those eligible for surgery as confirmed by preoperative examinations; 3. Patients who had undergone CME; 4. Patients whose data were complete (2). Exclusion criteria: 1. Patients with other malignant tumors detected through postoperative examinations or a history of other malignancies; 2. Patients with a history of abdominal surgery, extensive adhesion in the abdominal cavity, poorly controlled severe underlying diseases, or patients who had undergone preoperative radiochemotherapy; 3. Patients who had undergone palliative resection or combined surgery on organs of the abdominal cavity; 4. Patients who had undergone emergency surgery caused by hemorrhage, bowel obstruction, or perforation.

Surgical method

The abdominal cavity was first explored to determine the presence or absence of ascites, adhesions, and distant metastases in the liver, stomach, greater omentum, and abdominal cavity. Subsequently, the transverse colon was examined to determine the tumor location and size and occurrence of serosal invasion. After complete examination, the greater omentum was reflected upward, and the small intestine was retracted to the left lower abdomen to expose the mesenteric root. Upon locating the projection of the superior mesenteric vein (SMV), the retroperitoneum was opened along the direction of the SMV for access to the right Toldt's space. Dissection was performed rightward to the front of the prerenal fascia, laterally toward the peritoneal reflection, and upward to the hepatocolic ligament. Sharp medial dissection was performed superiorly for access to the prepancreatic space and advanced rightward to the lateral margin of the descendant duodenum. The vascular sheath was opened along the SMV to the root, exposing the left and right branches of the middle colic vein; ligation and separation were then performed at the root. Subsequently, baring of the middle colic artery was performed at the inferior margin of the pancreas and mesenteric root of the transverse colon, followed by ligation and separation at the root. Lymph node dissection was then performed at the root of the superior mesenteric artery. The Toldt's space was extended leftwards to the pancreatic tail, and the mesentery of the transverse colon was dissected at the surface of the pancreas, with care taken to protect the splenic vessels. From the point of dissection, the gastrocolic ligament was separated from the outer side of the gastroepiploic arch along the greater curvature of the stomach, advancing rightward to the duodenal bulb and leftward to the splenic flexure. The mesentery of the transverse colon was dissected along the surface of the pancreas to connect with the separated prepancreatic space inferior to the mesentery and subsequently separated at the anterior margin of the pancreas. This was followed by adequate separation of the hepatic flexure, splenic flexure, and portions of the ascending and descending colon. After making a median incision on the upper abdomen, an incision protector was inserted, followed by *ex vivo* resection of the transverse colon tumors, mesentery of the transverse colon, and entire greater omentum. Finally, anastomosis, peritoneal lavage, drain placement, and abdominal closure were sequentially performed.

Statistics

Categorical variables were presented as frequencies and percentages, and continuous variables were presented as median values with range. Statistical analyses were performed with the x^2 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. Only variables associated with survival with p values ≤ 0.10 in the univariate analysis were used for multivariate analysis using a stepwise Cox proportional hazards regression model. The results were reported as hazard ratios with 95% confidence intervals. All analyses were performed using SPSS version 13.0 for Microsoft® Windows® version (SPSS Inc., Chicago, IL, USA). P<0.05 was considered to be significant.

Results

With the exception of the Charlson comorbidity index (CCI) scores, the differences in the preoperative data between the two groups of patients were statistically insignificant (Table 1).

The perioperative complications of the patients were graded according to the Clavien–Dindo classification system [15]. The postoperative complications among the subjects in the present study were grade I and II; none of the subjects developed complications that were grade III or above. Although postoperative complications occurred in 9 patients from the elderly group, none of the patients experienced two or more concomitant complications. The

difference in the overall complications between the elderly and non-elderly groups was not statistically significant (Table 2), while the incidence of pulmonary infection was higher in the elderly group than in the non-elderly group. Patients of both groups who presented with postoperative complications recovered after treatment and were discharged. There were no differences between groups in pathological data in terms of histologic differentiation, excised lymph nodes, surgical margins and pathologic TNM stage (7th AJCC-UICC) (Table 3).

During the follow-up period, tumor recurrence occurred in 15 and 27 patients from the elderly and non-elderly groups, respectively (Table 4). No statistical differences were seen in the 5-year DFS and OS rates between the elderly and non-elderly groups (Figures 1 and 2). Univariate analysis was performed on the risk factors for tumor recurrence,

Table 1. Baseline characteristics of the two groups

	Elderly group (n=54)	*Non-elderly group (n =93)*	*p value*
Age (years)	74 (70-76)	61 (50-69)	0.000
Gender (Male: Female)	35: 19	62: 31	0.819
ASA score (n)			0.137
I	32	56	
II	17	28	
III	5	9	0.021
CCI (n)			
<3	42	85	
≥3	12	8	0.147
BMI (kg/m^2)	21 (17-26)	20 (18-25)	
Clinical stage (7th AJCC- UICC) (n)			0.320
I	19	22	
II	21	46	
III	14	25	

Table 2. Operative and postoperative outcomes of the two groups

	Elderly group (n=54)	*Non-elderly group (n=93)*	*p value*
Conversion to open surgery (n)	2	3	0.878
Abdominal adhesions	1	2	
Hemorrhage	2	1	
Bulky tumor	0	2	
Operative time (min)	190 (170 - 230)	180 (160 - 260)	0.247
Blood loss (ml)	140 (100 - 250)	130 (90 - 260)	0.170
Time to pass first flatus (d)	2 (1 - 3)	2 (1 - 4)	0.247
Time to resume liquid diet (d)	3 (2 - 5)	3 (2 - 6)	0.108
Hospitalization (d)	11 (8 - 24)	10 (8 - 20)	0.297
Patients with postoperative 30-day complications (n)	9	12	0.530
Pneumonia	5	1	0.047
Anastomotic leakage	2	4	
Atelectasis	1	3	
Chylous ascites	1	1	
Ileus	0	3	-
Patients with major complications (n)	0	-	-
Intraoperative mortality (n)	0	0	-
Postoperative 30-day mortality (n)	0	0	-

and the results indicated that ASA score III, poor tumor differentiation, T3-4 and N2 stage were correlated to tumor recurrence (Table 5). Results of multivariate analysis showed that poor tumor differentiation, T3-4 and N2 stage were independent risk factors for tumor recurrence (Table 6). Univariate analysis was performed on the risk factors for mortality, and the results indicated that Charlson comorbidity index > 3, ASA score III, poor tumor differentiation T3-4 and N2 stage were correlated to mortality (Table 5). Results of multivariate analysis showed that poor tumor differentiation, T3-4 and N2 stage were independent risk factors for mortality (Table 6).

Discussion

In this study, the CCI score was higher in the elderly group than in the non-elderly group. While the incidence of pulmonary infection was higher in the elderly group, the overall complications between the two groups were not statistically different. Furthermore, no statistical differences were seen in the 5-year DFS and OS rates between the elderly and non-elderly groups. Poor tumor differentiation, T3-4 and N2 stage were seen as independent risk factors for TCC recurrence and survival among patients.

Multiple RCTs have demonstrated superior short-term clinical effectiveness and long-term effectiveness with LC as that with open surgery during treatment of colon cancer [17-24]. Therefore, clinical practice guidelines recommend LC as a standard approach for the treatment of colon cancer [16]. However, given the proximity of the transverse colon to several key organs, such as the liver, pancreas, spleen, stomach, and duodenum, as well as the greater degree of mobility owing

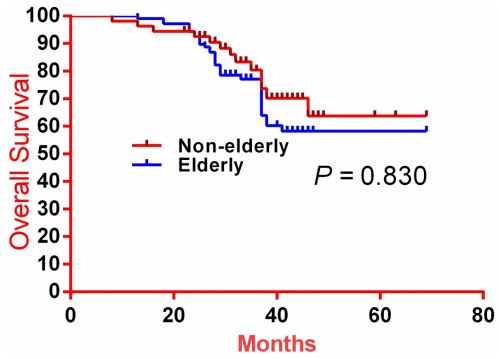

Figure 1. Comparison of overall survival rate between elderly (aged ≥70 years) and non-elderly (aged <70 years) group. There was no significant difference between the two groups (p=0.830).

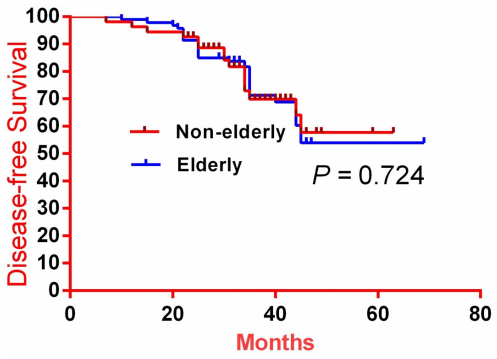

Figure 2. Comparison of disease-free survival rate between elderly (aged ≥70 years) and non-elderly (aged <70 years) group. No significant difference was observed (p=0.724).

Table 3. Pathologic outcomes of the two groups

	Elderly group (n=54)	*Non-elderly group (n =93)*	*p value*
Pathologic TNM stage (n)			0.498
I	12	15	
II	20	37	
III	22	41	
Tumor differentiation (n)			0.576
Well	7	17	
Moderate	28	45	
Poor	19	31	
Harvested lymph nodes	21 (15- 30)	23 (18 - 32)	0.249
Lymphovascular invasion (n)			0.494
Yes	18	26	
No	36	67	
Residual tumor (R0/R1/R2) (n)	54/0/0	93/0/0	1.000

Table 4. Tumor recurrence data of the two groups

	Elderly group (n=54)	*Non-elderly group (n=93)*	*p value*
Tumor recurrence (n)	15	27	0.995
Recurrence site (n)			
Locoregional	4	7	
Distant	10	18	
Mixed	1	2	
Time to first recurrence (months)	20 (7- 46)	23 (10- 45)	0.291
Mortality (n)	13	21	0.836
Cancer-cause	11	18	
Non-cancer-cause	2	3	

Table 5. Univariate analysis of survival

Variable	*Five-year overall survival*	*p value*	*Five-year disease-free survival*	*p value*
Age, years (n)		0.830		0.724
<70	69		62	
≥70	64		58	
Gender (n)		0.747		0.425
Male	67		64	
Female	64		58	
Charlson comorbidity index (n)		0.087		0.148
<3	71		64	
≥3	62		57	
ASA score (n)		0.074		0.087
I-II	70		64	
III	61		56	
T stage (n)		0.024		0.017
T_1-T_2	84		71	
T_3-T_4	54		51	
N stage (n)		0.013		0.001
N_0-N_1	79		73	
N_2	50		49	
Tumor differentiation (n)		0.010		0.000
Well-moderate	74		69	
Poor	49		44	

Table 6. Cox proportional hazards model for survival

Variables	*Hazard ratio (95% CI)*	*p value*
Overall survival		
Charlson comorbidity index ≤3 versus >3	1.247 (0.780-1.994)	0.244
ASA score I-II versus III	1.201 (0.659-2.189)	0.201
T stage T_1-T_2 versus T_3-T_4	2.247 (1.501-3.363)	0.025
N stage N_0-N_1 versus N_2	2.014 (1.470-2.570)	0.011
Tumor differentiation Well-moderate versus Poor	1.980 (1.301-3.013)	0.020
Disease-free survival		
ASA score I-II versus III	1.157 (0.591-2.265)	0.147
T stage T_1-T_2 versus T_3-T_4	1.870 (1.402-2.494)	0.020
N stage N_0-N_1 versus N_2	2.180 (1.507-3.154)	0.009
Tumor differentiation Well-moderate versus Poor	1.980 (1.418-2.765)	0.012

to non-fixation of the transverse colon to the retroperitoneum, LC and lymph node dissection in the transverse colon are challenging [17-24]. In addition, the incidence of TCC is lower than that with other types of CRC [17-24]. These reasons have resulted in the exclusion of TCC cases in RCTs [8-13].

The concept of CME, which is similar to the total mesorectal excision (TME) approach [25], was first proposed by Hohenberger, based on the anatomic and histologic similarities between colic and rectal mesentery and because the entire colic mesentery is enclosed by the visceral fascia [14]. Laparoscopic CME (LCME) refers to the procedure in which the visceral and parietal fascia are subjected to sharp dissection under direct vision to achieve complete excision of the colic mesentery, ligation of the main blood vessels at the root, and lymph node dissection to the greatest extent. Compared with traditional surgery, CME significantly improves prognosis in patients with colon cancer [25]. With the development of minimally invasive surgical techniques, LCME has also been applied in the treatment of TCC [17]. In a study that compared the effectiveness of LCME and open CME in TCC treatment, it was found that the LCME group achieved better short-term effectiveness, including lesser intraoperative blood loss, faster postoperative recovery, and comparable perioperative complication rates as compared with open surgery [17]. The advantages of LCME in the treatment of TCC have also gained gradual recognition by surgeons in clinical practice [17-19].

As the population structure of China faces gradual aging in the 21st century [1], the proportion of elderly TCC patients has also increased progressively [1]. The incidence of TCC is higher among elderly men than that among elderly women, which may be related to factors such as poor lifestyle habits and a longer duration of exposure to carcinogenic factors in men. This is also reflected by the proportions of male and female subjects in this study.

TCC in the elderly patients is characterized by increased preoperative complications; in the present study, the elderly group had significantly more preoperative complications than the non-elderly group. At present, the common methods used for the clinical assessment of preoperative complications are the CCI [26] and simplified comorbidity score (SCS) scoring systems [27]. The SCS system is mainly used for lung cancer patients [27]. In a study by Huang et al the CCI score correlated with the 30-day postoperative complication rate and long-term survival rate in patients with colon cancer [28]. In the present study, the incidence of infectious pulmonary complications was higher in the elderly group than in the non-elderly group. This may be related to the degenerative changes in vital organ functions among the elderly patients, which leads to a higher number of preoperative complications, higher tendency of reduced compensative ability in the organs, greater stress and traumatic responses, and weaker postoperative immunologic function, ultimately resulting in higher proneness to infectious pulmonary complications. Furthermore, as the LCME procedure involves the establishment of a pneumoperitoneum, the resulting increase in intra-abdominal pressure leads to elevation of the diaphragm, which affects ventilation and gas exchange functions of the lungs and venous return. The combination of these effects with reduced pulmonary functional reserve and poorer compliance in elderly patients results in an increased incidence of pulmonary infection. However, the overall postoperative complication rate in the elderly patients was not increased, and all patients successfully recovered after active treatment. To prevent pulmonary complications in elderly patients, in consideration of the weaker cough strength and pulmonary function among elderly patients, an emphasis should be placed on strengthening of the perioperative pulmonary function and training for active and passive sputum expectoration during the early postoperative period [25]. Treatment methods, such as back-patting, repositioning of the patient and aerosol inhalation at periodic intervals may be adopted.

LCME is a feasible approach in both minimally invasive and radical surgery. The feasibility of LCME in minimally invasive surgery has been reported in previous studies [17-19], and long-term follow-up has been established as the optimum method for assessment of the radicality of LCME [17-19]. In the present study, we analyzed the risk factors related to postoperative recurrence and survival in the elderly and non-elderly patient groups and found that poor tumor differentiation, T3-4 and N2 stage were independent risk factors for tumor recurrence and survival, while age was not an independent prognosis-determining factor. This provides evidence to support the use of the LCME approach in elderly TCC patients.

The results presented in this article are based on a single-center retrospective study with a small sample size and lack evidence-based validation. Therefore, multi-center prospective RCTs with a large sample size are required to further validate the influence of age on the surgical and oncologic effects of LCME in the treatment of TCC.

Conclusion

LCME is a safe and effective method for the treatment of TCC in elderly patients, with comparable clinical effectiveness between the elderly and non-elderly patients.

Funding

This study was supported by grants from the Research Project of Medical and Sanitary Institution of Yunnan Province (2017NS194).

Acknowledgements

We sincerely thank our hospital colleagues who participated in this research.

Conflict of interests

The authors declare no conflict of interests.

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