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ORIGINAL ARTICLE

Surgical and survival outcomes of laparoscopic colectomy for transverse colon cancer in elderly patients

Meng Yue, Yue Wang, Zhen-Hua Kang, Xu Wang, Lei Wang

Department of Colorectal and Anal Surgery, the First Hospital of Jilin University, Changchun 130012, Jilin, People's Republic of China

Summary

Purpose: *This study was designed to compare the survival and surgical outcomes of laparoscopic colectomy (LC) in elderly and non-elderly patients with transverse colon cancer (TCC).*

Methods: *From January 2011 to January 2018, 44 elderly (aged ≥70 years) and 72 non-elderly (aged <70 years) patients with TCC underwent LC at our institution. The survival and surgical outcomes of the two groups were compared retrospectively.*

Results: *Preoperatively, the Charlson Comorbidity Index (CCI) and American Society of Anesthesiologists score were higher in the elderly group than in the non-elderly group. There were no significant differences between the groups in operating time, intraoperative blood loss, conversion rate, pathologic data, 30-day postoperative mortality rate, incidence of 30-day postoperative complications, incidence of major complications, or compliance with adjuvant chemotherapy. During the follow-up period, differences in recurrence rate, 5-year overall survival (OS) rate, and 5-year disease-free survival (DFS) rate between the groups were not significant.*

Conclusion: *Although elderly patients with TCC have higher surgical risk than non-elderly patients, performing LC in elderly patients is safe and effective. The survival and surgical outcomes in elderly patients were similar to those in non-elderly patients.*

Key words: *laparoscopy, minimally invasive surgical oncology, transverse colon cancer, prognosis*

Introduction

Surgery is the primary treatment option for patients with colon cancer [1]. Since the American surgeon Jacobs performed the first laparoscopic colectomy (LC) for colon cancer in 1991 [2], with accumulation of surgical experience, improvements in surgical instruments, and continuous establishment of training institutions, an increasing number of medical centers have utilized LC to treat patients with colon cancer. In the recent decade, large-scale, multicenter, randomized, controlled trials have shown that LC has similar survival outcomes (OS and DFS) as conventional open colectomy and is associated with smaller surgical wounds [3-8]. However, all of these trials excluded patients with transverse colon cancer (TCC) [3-8] because LC is more difficult than laparotomic colectomy for TCC and because TCC accounts for only 10% of colon cancer cases [9]. The average life expectancy in China has been gradually increasing and accordingly, the incidence of colon cancer in the elderly has also been on the rise. Studies have shown that LC can achieve similar outcomes in both elderly and non-elderly patients with colon cancer [10-16]. However, currently, there is no English-language study reporting the outcomes of LC in elderly patients with TCC. Therefore, this study aimed to compare the survival and surgical outcomes of LC in elderly and non-elderly patients with TCC.

Corresponding author: Lei Wang, MD. Department of Colorectal and Anal Surgery, the First Hospital of Jilin University, Changchun 130012, Jilin, People's Republic of China.
Tel and Fax: +86 431-88782222, Email: leiwangusa@vip.163.com
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Methods

Patients

This study complied with the Declaration of Helsinki principles and was approved by the Ethics Committee of our hospital. 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.

From January 2011 to January 2018, a total of 137 patients with TCC underwent LC at our hospital. After screening according to the following inclusion and exclusion criteria, 116 patients were included in this study. Inclusion criteria were as follows: (1) pathologic diagnosis of colonic adenocarcinoma; (2) clinical stage T1-3, N0-2, M0; (3) receiving surgical treatment for the first time; (4) no other organs removed during surgery; and (5) complete clinical and follow-up data. Exclusion criteria were as follows: (1) emergency surgery for colonic perforation or intestinal obstruction; (2) synchronous or metachronous colorectal cancer and tumors in other organs; (3) other organs removed during surgery; and (3) recurrent tumor. Based on the age at which the patient underwent LC, patients were divided into the elderly group (aged ≥70 years; n=44) and non-elderly group (aged <70 years; n=72). This study retrospectively compared preoperative baseline data, surgical outcomes, and survival outcomes between the two groups. TCC was defined as cancer located between the hepatic and splenic flexures, while TNM stage was based on the seventh edition of TNM classification of colorectal cancer.

Table 1. Baseline characteristics of the two groups

Characteristics	*Elderly group (n=44)*	*Non-elderly group (n =72)*	*p value*
Age, years, median (range)	73 (70-77)	59 (50-69)	0.000
Gender (Male:Female)	25:19	46:26	0.448
ASA score, patients (n)			0.001
I	26	62	
II	14	9	
III	4	1	
CCI (n)			0.013
< 4	31	64	
≥ 4	13	8	
BMI (kg/m^2), median (range)	22 (19-26)	23 (18-28)	0.148
Clinical stage (7th AJCC- UICC), patients (n)			0.627
I	11	19	
II	14	26	
III	19	27	

Table 2. Operative and postoperative outcomes of the two groups

Outcomes	*Elderly group (n=44)*	*Non-elderly group (n=72)*	*p value*
Type of resection			0.876
Right hemicolectomy	21	31	
Left hemicolectomy	13	24	
Transverse colectomy	10	17	
Conversion to open surgery	3	5	1.000
Abdominal adhesions	1	2	
Hemorrhage	2	1	
Bulky tumor	0	2	
Operative time, min, median (range)	180 (190-240)	170 (180-250)	0.217
Blood loss (ml), median (range)	130 (80-300)	120 (90-300)	0.301
Time to pass first flatus (day)	3 (1-6)	2 (1-5)	0.457
Time to resume liquid diet (days), median (range)	4 (2-7)	3 (2-6)	0.289
Hospitalization (days), median (range)	11 (9-21)	10 (7-18)	0.181
Patients with postoperative complications (n)	7	11	0.927
Patients with major complications (n)	1	1	1.000
Intraoperative mortality (n)	0	0	-
Postoperative 30-day mortality (n)	0	0	-

Before treatment, patients underwent colonoscopy, pelvic magnetic resonance imaging, chest and abdominal computed tomography, detection of tumor markers, lung function tests, electrocardiography, and echocardiography to determine their clinical stage and whether they could tolerate LC. When necessary, positron emission tomography–computed tomography, bone scans, and other tests were performed to rule out tumor metastasis. LC was performed according to the principle of complete mesocolic excision (CME) [17,18]. Conversion was defined as an unplanned abdominal incision larger than what would have been necessary for specimen retrieval in the laparoscopic procedure.

Morbidity and mortality

Morbidity, defined as postoperative complications occurring within the postoperative 30 days, was classified using Clavien–Dindo classification [19-26]. Minor complications were classified as 1 and 2. Mortality was defined as death from any cause occurring within the postoperative 30 days.

Follow-up

Follow-ups were performed for all patients every 3 months in the first year after surgery, every 6 months in the second year after surgery, and every 12 months

Table 3. Pathological outcomes of the two groups

Outcomes	*Elderly group (n=44)* *n*	*Non-elderly group (n =72)* *n*	*p value*
Pathological TNM stage			0.556
I	5	10	
II	19	33	
III	20	29	
Tumor differentiation			0.469
Well	14	19	
Moderate	18	30	
Poor	12	23	
Harvested lymph nodes, median (range)	21 (15-30)	23 (18-32)	0.249
Lymphovascular invasion			0.711
Yes	15	27	
No	29	45	
Residual tumor (R0/R1/R2)	44/0/0	72/0/0	1.000

Table 4. Comparison of adjuvant chemotherapy compliance of the two groups

Outcomes	*Elderly group (n=44)*	*Non-elderly group (n=72)*	*p value*
Patients with at least one chemotherapy cycle (n)	24	47	0.250
Time to first chemotherapy (months), median (range)	6 (4-9)	5 (4-8)	0.204
Received full dose on schedule (n)	19	41	0.150
Cycles completed, median (range)	9 (3-12)	11 (5-12)	0.2774

Table 5. Tumor recurrence data of the two groups

Recurrences	*Elderly group (n=44)*	*Non-elderly group (n=72)*	*p value*
Tumor recurrence (n)	8	11	0.682
Recurrence site (n)			
Locoregional	1	2	
Distant	6	7	
Mixed	1	2	
Time to first recurrence (months), median (range)	21 (11-44)	17 (10-50)	0.079
Mortality (n)	9	10	0.357
Cancer-cause	7	8	
Non-cancer-cause	2	2	

thereafter. Follow-ups included routine physical examination, tumor marker detection, and chest and abdominal imaging. Electronic colonoscopy was performed annually [27-32]. When a suspected tumor recurrence was discovered, the patient was promptly referred to the hospital. OS was calculated from the date of radical resection to the last follow-up visit or death from any cause. DFS was calculated from the date of radical resection to the date of cancer recurrence or death from any cause. The last follow-up date was in May 2018.

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. Only variables associated with survival with p values ≤ 0.100 in the univariate analysis were used for multivariate analysis using a stepwise Cox proportional hazards regression model. The results are reported as hazard (HR) with 95% confidence intervals (95% CI). All analyses were performed using the SPSS version 13.0 for Microsoft® Windows® version (SPSS Inc., Chicago, IL, USA). P<0.05 was considered to be significant.

Results

Surgical outcomes

Comparing the preoperative baseline data between groups, the Charlson Comorbidity Index and American Society of Anesthesiologists score were higher in the elderly group than in the non-elderly group (Table 1). Differences in other characteristics, such as sex, body mass index, and clinical stage, between groups were not significant.

Three patients in the elderly group and 5 in the non-elderly group were converted to laparotomy (Table 2). There were no significant differences between groups in operating time, intraoperative blood loss, incidence of 30-day postoperative complications, incidence of severe complications, or pathologic diagnosis (Table 3). There was no intraoperative or 30-day postoperative mortality in either group. Adjuvant chemotherapy was performed in 24 and 47 patients in the elderly and non-elderly groups, respectively. There were no significant differences in initiation time of or compliance with adjuvant chemotherapy between groups (Table 4).

Follow-up and survival

The median follow-up in the elderly and non-elderly groups was 38 and 43 months, respectively. During the follow-up period 9 and 10 patients died in the elderly and non-elderly groups, respectively. Of the 9 deaths in the elderly group, 7 were due to tumor recurrence and 2 to stroke; of the 10 deaths in the non-elderly group, 8 were due to tumor recurrence and 2 to non-cancer-cause (Table 5). The 5-year OS rates in the elderly and non-elderly groups were 71% and 76%, respectively, which were not significantly different (Figure 1, p=0.223). Multivariate analysis showed that T stage, N stage, and tumor differentiation status were independent predictors of OS (Tables 6 and 7).

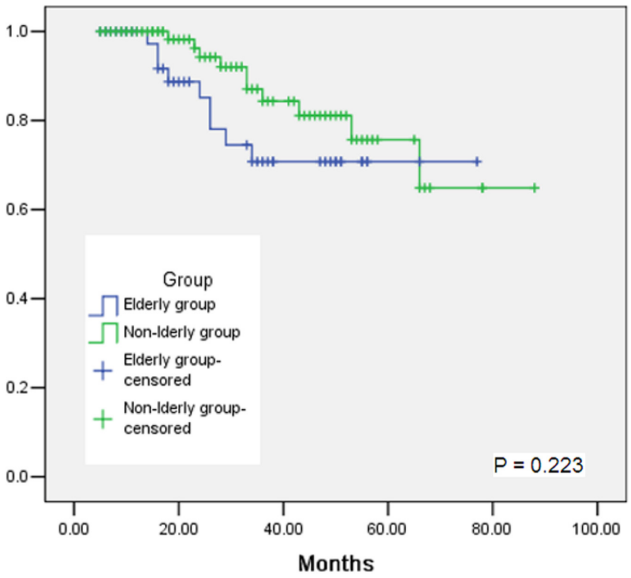

Figure 1. Comparison of overall survival rate between elderly (aged ≥70 years) and non-elderly (aged <70 years) group. There was no significant difference between the two groups (p=0.223).

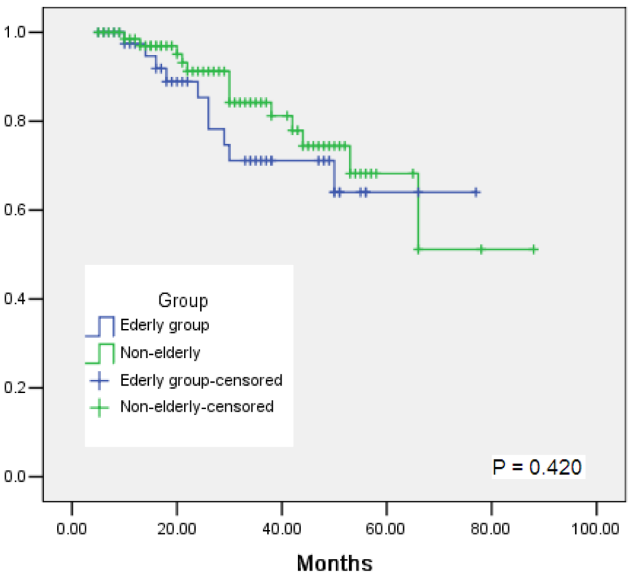

Figure 2. Comparison of disease-free survival rate between elderly (aged ≥70 years) and non-elderly (aged <70 years) group. No significant difference was observed (p=0.420).

During the follow-up period, the tumor recurred in 8 and 11 patients in the elderly and non-elderly groups, respectively. There were no significant differences between the groups in tumor recurrence rate or recurrence site (Table 5). The 5-year DFS rates in the elderly and non-elderly groups were 64% and 68%, respectively, which were not significantly different (Figure 2, p=0.420). Multivariate analysis showed that T stage and N stage were independent predictors of DFS (Tables 6 and 7).

Table 6. Univariate analysis of survival

Variables	*Five-year overall survival* *n*	*p value*	*Five-year disease-free survival* *n*	*p value*
Age, years		0.223		0.420
<70	76		68	
≥70	71		64	
Gender		0.451		0.284
Male	77		74	
Female	73		68	
Charlson comorbidity index		0.078		0.080
< 4	81		73	
≥ 4	68		62	
ASA score		0.069		0.057
I-II	78		71	
III	65		63	
T stage		0.029		0.017
T_1-T_2	87		74	
T_3-T_4	64		59	
N stage		0.011		0.023
N_0-N_1	89		71	
N_2	62		58	
Tumor differentiation		0.041		0.047
Well- Moderate	75		68	
Poor	66		57	

Table 7. Cox proportional hazards model for survival

Variables	*Hazard ratio (95% CI)*	*p value*
Overall survival		
Charlson comorbidity index ≤4 versus>4	1.218 (0.784-1.587)	0.154
ASA score I-II versus III	1.328 (0.689-1.889)	0.235
T stage T_1-T_2 versus T_3-T_4	2.088 (1.458-3.748)	0.016
N stage N_0-N_1 versus N_2	2.581 (1.587-3.698)	0.010
Tumor differentiation		
Well-moderate versus poor	1.978 (1.578-3.057)	0.032
Disease-free survival		
Charlson comorbidity index ≤4 versus>4	1.358 (0.670-1.684)	0.239
ASA score I-II versus III	1.189 (0.510-1.401)	0.130
T stage T_3-T_4 versus T_3-T_4	1.780 (1.350-2.741)	0.025
N stage N_0-N_1 versus N_2	1.980 (1.248-2.900)	0.011
Tumor differentiation		
Well-moderate versus poor	1.289 (0.789-1.905)	0.090

Discussion

Despite the lack of high-level, evidence-based, well-designed studies, retrospective reports have shown that LC can achieve better surgical outcomes and similar survival outcomes for elderly patients with colon cancer compared with laparotomic colectomy [10-16]. However, these studies excluded patients with TCC [10-16], primarily because LC is difficult to perform in patients with TCC for several reasons. First, the anatomical structure adjacent to the transverse colon is complicated, making dissection difficult. Second, lymphadenectomy involves the pancreas, stomach, spleen, kidney, and other important organs, such that even a slight mistake can easily lead to critical organ damage. Third, there are great vascular variations in the area of lymphadenectomy. The authors found no English-language study reporting the outcomes of LC in elderly patients with TCC after searching multiple databases, including PubMed, Embase, and Chemical Abstracts. Thus, this study demonstrated for the first time that elderly patients with TCC treated with LC can achieve survival and surgical outcomes similar to those in non-elderly patients.

In 1982, the British surgeons Heald, Husband and Ryall proposed the concept of total mesorectal excision (TME) [33], which aimed to standardize the quality control of radical surgery for rectal cancer [34]. TME can significantly reduce the local recurrence rate of rectal cancer and improve the 5-year survival rate [35]. However, there had always been a lack of surgical quality standards for colon cancer. In 2009, the German surgeon Hohenberger first used the concept of CME to regulate the surgical treatment of colon cancer [17]. Studies have shown that CME can reduce the 5-year local recurrence rate from 6.5% to 3.6% and increase the 5-year survival rate by 5% compared with conventional radical surgery for colon cancer [17]. The scope of surgical resection in CME is larger than that in conventional radical surgery for colon cancer [36-38]. It is well known that the surgical risk of elderly patients is higher compared with non-elderly patients. However, in this study, the overall incidence of complications and severe complications were similar between elderly and non-elderly patients. In addition, none of the patients died during the operation or within 30 days after surgery. These results confirm that LC is safe in elderly patients with TCC.

All guidelines for diagnosis and treatment of colorectal cancer recommend postoperative adjuvant chemotherapy for patients with stage II colon cancer with high-risk factors and those with stage III colon cancer, starting 4 weeks after surgery, to reduce the tumor recurrence rate and improve survival [29]. Studies have shown that, compared with laparotomic colectomy, LC can advance the initiation of adjuvant chemotherapy and improve patient compliance [39-42]. In this study, the initiation time of and compliance with adjuvant chemotherapy were similar between elderly and non-elderly patients; the tumor recurrence rate, OS and DFS rate were also similar, which may be due to better compliance with chemotherapy in elderly patients.

Under the premise of accomplishing the therapeutic goal, the development direction of modern surgery is to pursue minimum invasion in order to facilitate more rapid recovery [43-45]. As a minimally invasive surgical technique, single-incision laparoscopic surgery has gradually been applied to various benign diseases, such as cholecystectomy and appendectomy. Since a team of American surgeons first reported in 2008 that single-incision LC could be used to treat colon cancer [46], the procedure has been gradually applied. In 2017, Japanese surgeons were the first to use single-incision LC to treat TCC [47]. They demonstrated that, compared with multiple-incision LC, single-incision LC has the advantages of shorter hospital stay and better cosmetic results [47]. Our hospital has introduced single-incision laparoscopic surgical instruments in recent years; lately, single-incision LC has been used to treat several cases of TCC, with a plan to summarize our experiences in a relevant article when the sample size is large enough.

Conversion to laparotomy is often inevitable when LC is performed. The reported conversion rate in the literature is 0% to 18% when LC is used to treat TCC [18,48-54], with variations based on different cases and surgical experience [18,48-54]. In this study, the conversion rates in the elderly and non-elderly groups were 6.8% and 6.9%, respectively, which are similar to previous studies. Currently, there is no English-language study reporting the conversion rate of LC in elderly patients with TCC. This study showed for the first time that such a conversion rate was similar between elderly and non-elderly patients.

In this study, survival outcomes, including tumor recurrence, OS, and DFS, were similar between elderly and non-elderly patients. The previously reported 5-year OS rate in patients with TCC undergoing LC was 70% to 90%, while the 5-year DFS rate was 60% to 80%, which are similar to those in the present study [18,48-54]. There is currently no study reporting the 5-year OS

rate or 5-year DFS rate in elderly patients with TCC treated with LC. Thus, this study demonstrated for the first time that elderly patients can achieve similar long-term outcomes as non-elderly patients.

The present study has two important limitations. First, the retrospective design is associated with known risks of bias, and a prospective, randomized, controlled trial is needed to confirm that LC is safe and effective in elderly patients with TCC. Second, we only examined data from a single center with a small sample size, and it is possible that our findings may not be generalized to other centers and/or patient groups. The fact that the study failed to find a significant difference between groups in survival may be due to the small sample size.

Conclusion

The results of this study suggest that LC in elderly patients with TCC does not increase the incidence of postoperative complications and can achieve similar survival outcomes as those in non-elderly patients. Thus, in elderly patients with TCC, age is not a contraindication for LC.

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Conflict of interests

The authors declare no conflict of interests.

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