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ORIGINAL ARTICLE

Short- and long-term outcomes of laparoscopic surgery in elderly patients with rectal cancer

Guangyuan Sun, Jun Xue, Yue Zhang, Xiaobin Gao, Fei Guo

Department of Surgery, the First Affiliated Hospital of Hebei North University, Hebei Province, People's Republic of China

Summary

Purpose: *This study aimed to use propensity score matching (PSM) to compare the short- and long-term outcomes of laparoscopic surgery for the treatment of rectal cancer in elderly and middle-aged patients.*

Methods: *Data were retrospectively obtained from 588 patients aged ≥60 years when they underwent laparoscopic surgery for rectal cancer in our hospital between January 2009 and December 2016. The patients were divided into an elderly group (≥70 years) or a middle-aged group (60–69 years), and were subsequently matched 1:1 using PSM for sex, body mass index, Charlson comorbidity index (CCI), tumor location, clinical stage, and American Society of Anesthesiologists (ASA) score. A total of 115 patients from each group were matched and included in the study, and their short-term and long-term outcomes were compared.*

Results: *The elderly group had greater intraoperative blood loss and a higher surgical conversion rate, although the other outcomes were similar between the two groups (surgical time, pathology results, 30-day incidence of complications, and incidence of major complications). No patients died intraoperatively or within 30 days after surgery. There were no significant differences in the two groups' rates of tumor recurrence, 5-year overall survival, and 5-year disease-free survival.*

Conclusion: *Although elderly patients had greater intraoperative blood loss and a higher surgical conversion rate, laparoscopic surgery for rectal cancer provided similar short-term and long-term outcomes among middle-aged and elderly patients.*

Key words: *elderly, laparoscopy, minimally invasive surgery, prognosis, rectal cancer*

Introduction

Recent improvements in life expectancy, health awareness, and screening technology have resulted in increasing numbers of elderly patients presenting with rectal cancer [1-3]. Radical surgical resection is the primary treatment for rectal cancer, and studies have confirmed that surgical treatment is feasible and effective for elderly patients with rectal cancer [4-6]. However, elderly patients have relatively high rates of impaired organ function and medical comorbidities, which makes some elderly patients unable to tolerate traditional open surgery [1-6]. The first case of laparoscopic surgery for rectal cancer was reported in the 1990s [6], and laparoscopic surgery had become widely used because it causes minimal trauma. High-quality randomized controlled trials have confirmed that, compared to open surgery, laparoscopic rectal surgery is associated with less blood loss, shorter hospital stay, similar or fewer complications, and similar oncological outcomes (e.g., pathology results, tumor recurrence, overall survival, and disease-free survival) [7-12]. However, laparoscopic surgery is only gradually being applied for treating rectal cancer. This study aimed to use PSM to compare the short- and long-term outcomes of laparoscopic surgery for rectal cancer among elderly and middle-aged patients.

Correspondence to: Jun Xue, MD. Department of Surgery, First Affiliated Hospital of Hebei North University, Zhangjiakou 075000, Hebei Province, People's Republic of China.
Tel/Fax: +86 313 8046973, E-mail: junxuecn@163.com
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Methods

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 the retrospective nature of the study.

Between January 2009 and December 2016, 588 patients aged ≥60 years underwent laparoscopic surgery for rectal cancer. The inclusion criteria were: (1) the pathological type was rectal adenocarcinoma, (2) the clinical stage was T1–3N0–2M0 before treatment, and (3) the patient did not undergo resection of any other organs. The exclusion criteria were: (1) the patient underwent emergency surgery or (2) underwent only exploratory laparoscopy. Based on their age at the time of surgery, the patients were divided into an elderly group (≥70 years) or a middle-age group (60–69 years). R software was subsequently used for the PSM, which was based on sex, body mass index, CCI, tumor location, clinical stage, and ASA score. Based on the matching results, a total of 115 patients in each group were matched 1:1, and their short-term and long-term outcomes were compared.

All patients had undergone pelvic magnetic resonance imaging, thoracic and abdominal computed tomography, and other examinations to confirm their clinical stage before treatment. Positron-emission tomography-computed tomography or bone scans were performed as needed [13]. The patients' ability to tolerate laparoscopic surgery was confirmed based on the results of laboratory tests, lung function tests, electrocardiography, echocardiography, and other examinations [13]. Patients with a clinical stage T3N+ underwent long-course neoadjuvant radiochemotherapy, and their laparoscopic surgery was performed 6–8 weeks after the radiochemotherapy was completed [14,15]. The specific surgical procedures have been previously reported [12].

The severity of complications during the first 30 days after surgery was evaluated using the Clavien-Dindo classification (Grade 1–2: mild complications, Grade 3–5: severe complications) [16-23]. All-cause mortality was also tracked during the first 30 days after surgery. Patients with pathological stage III or high-risk pathological stage II (T4, positive margins, <12 lymph nodes, or a high-grade tumor) received adjuvant chemotherapy unless contraindicated [13].

Follow-up visits were performed at surgery clinics, the patient's home, or through physician correspondence with the patients. Follow-up was performed every 3 months during the first postoperative year, every 6 months during the second postoperative year, and annually thereafter [24-29], with the final follow-up being completed in July 2017.

Statistics

Data were calculated as means and standard deviations for variables following normal distribution and were analyzed using *t*-test. For data not normally distributed, results were expressed as medians and ranges and compared by using nonparametric tests. Differences in semiquantitative results were analyzed using the Mann-Whitney *U* test. Differences in qualitative results were analyzed using the chi-square test or Fisher's exact test, as appropriate. Survival rates were analyzed using the Kaplan-Meier method and differences between the 2 groups were assessed with the log-rank test. Univariate analyses were performed to identify prognostic variables related to overall survival and disease-free survival. Univariate variables with probability values <0.10 were selected for inclusion in the multivariate Cox proportional hazard regression model. Adjusted hazard ratios (HR) along with the corresponding 95% confidence interval (CI) were calculated. P< 0.05 was considered to indicate statistical significance. The Statistical Package for the Social Sciences (SPSS) 13.0 (SPSS Inc., Chicago, IL, USA) was applied.

Results

The patient general characteristics are shown in Table 1. No significant differences were observed between the two groups in terms of sex, body mass index, CCI, tumor location, clinical stage and ASA score.

The short-term outcomes are shown in Table 2. Compared to the middle-aged group, the elderly group had greater intraoperative blood loss and a higher surgical conversion rate. No significant differences were observed in the two groups' surgical times, intraoperative or postoperative blood transfusion rates, postoperative recovery, or length of hospitalization. No patient died within 30 days after surgery, and there were no significant differences in the two groups' 30-day incidence of all complications or major complications. Furthermore, no significant differences were observed in the two groups' pathology results (TNM stage, tumor differentiation, and resection margin status) (Table 3).

Adjuvant chemotherapy was administered to 36 patients in the elderly group and 40 patients in the middle-aged group. No significant differences were observed in the two groups' start times and compliance rates (Table 2).

The overall median follow-up was 42 months, with 38 months for the elderly group and 45 months for the middle-aged group; this difference was not statistically significant (p=0.450). At the last follow-up, 32 patients in the elderly group and 26 patients in the middle-aged group had died. In the elderly group, the deaths were related to tumor recurrence (22 patients) and non-oncological causes in 4 cases (2 cases of acute myocardial infarction, 1 case of ischemic stroke, and 1 case of hemorrhagic stroke). In the middle-aged group, the causes of death were tumor recurrence (30 patients) and non-oncological causes in 2 cases (1 case of acute myocardial infarction and 1 case of sudden

cardiac death). The differences between the two groups were not statistically significant (Table 4).

The 5-year overall survival rates were 60.5% for the elderly group and 65.4% for the middle-aged group; this difference was not statistically significant (p=0.239; Figure 1). Multivariate analysis revealed that T stage and N stage were independent predictors of overall survival. The 5-year disease-free survival rates were 52.1% for the elderly group and 55.4% for the middle-aged group; this difference was not statistically significant (p=0.105; Figure 2). Multivariate analysis revealed that N stage and tumor differentiation status were independent predictors of disease-free survival.

Table 1. Baseline characteristics of the elderly and middle-aged group

Characteristics	*Elderly (n=115)*	*Middle-aged (n=115)*	*p value*
Age (years)	73 (70-77)	66 (60-69)	0.000
Gender			0.677
Male	77	74	
Female	38	41	
BMI (kg/m²; range)	22 (18-28)	23 (19-28)	0.548
ASA score			0.488
I	68	73	
II	34	31	
III	13	11	
Clinical stage (cTNM)			0.817
I	54	49	
II	38	47	
III	23	19	
Charlson comorbidity index			0.544
< 3	84	88	
≥ 3	31	27	
Tumor location (distance from anal verge), cm			0.621
Upper rectum (10-15)	39	42	
Middle rectum (5-10)	44	37	
Lower rectum (<5)	32	36	

BMI: body mass index, ASA: American Society of Anesthesiologists

Table 2. Short-term outcomes of the elderly and middle-aged group

Outcomes	*Elderly (n=115)*	*Middle-aged (n=115)*	*p value*
Type of resection			0.634
Low anterior	91	88	
Abdominoperineal	24	27	
Operative time (min; range)	210 (150-250)	190 (160-270)	0.210
Blood loss (ml; range)	190 (150-340)	150 (130-300)	0.038
Conversion to open surgery	10	3	0.046
Blood transfusion	11	8	0.472
Time to pass first flatus (d; range)	4 (3-7)	4 (3-6)	0.528
Time to resume liquid diet (d; range)	5 (4-10)	5 (3-8)	0.258
Hospitalization (d; range)	12 (8-24)	10 (7-21)	0.108
Patients with postoperative complications	19	15	0.457
Patients with major complications	6	4	0.518
Postoperative 30-day deaths	0	0	-
Patients with at least one cycle adjuvant chemotherapy	36	40	0.575
Time interval to initiate chemotherapy (d; range)	40 (30- 84)	37 (26- 68)	0.105
More than 75% of total planned regimen without delay or dose reduction	31	35	0.560

Table 3. Pathological outcomes of the elderly and middle-aged group

Outcomes	*Elderly (n=115)*	*Middle-aged (n=115)*	*p value*
Pathological stage (pTNM)			0.777
pCR	16	19	
I	38	34	
II	32	36	
III	29	26	
Histological differentiation			0.404
Good	37	43	
Moderate	43	41	
Poor	35	31	
Circumferental resection margin			0.424
Positive (≤1mm)	6	9	
Negative (>1mm)	109	106	
Residual tumor (R0/R1/R2)	115/0/0	115/0/0	1.000

pCR: pathological complete response after neoadjuvant therapy

Table 4. Follow-up data of the elderly and middle-aged group

Data	*Elderly (n=115)*	*Middle-aged (n=115)*	*p value*
Tumor recurrence, n	38	33	0.475
Locoregional	21	19	0.728
Distant	9	8	1.000
Mixed	8	6	0.581
Time to first recurrence (median, months, range)	21(5-74)	24(5-45)	0.215
Last follow up			
Died of cancer recurrence	22	30	0.207
Died of non-oncological causes	4	2	0.679

Table 5. Multivariate analysis of overall survival

Regression variables	*Adjusted hazard ratio*	*95% CI*	*p value*
Pathological T stage		1.87–4.52	0.008
T_0-T_2	1.00		
T_3-T_4	3.54		
Pathological N stage		1.45–3.89	0.018
N_0-N_1	1.00		
N_2	2.45		

Table 6. Multivariate analysis of disease-free survival

Regression variables	*Adjusted hazard ratio*	*95% CI*	*p value*
Pathological N stage		1.25–3.08	0.024
N_0-N_1	1.00		
N_2	1.89		
Differentiation grade		1.55–2.57	0.015
Good-moderate	1.00		
Poor	2.05		

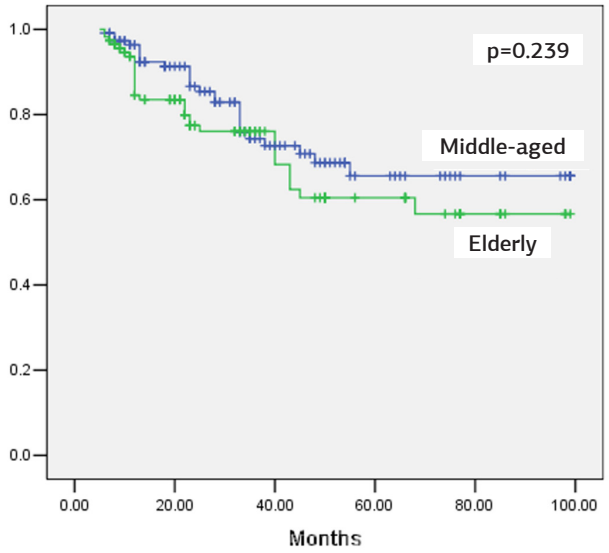

Figure 1. Kaplan-Meier overall survival between elderly and middle-aged group. There was no significant difference between the 2 groups (p=0.239).

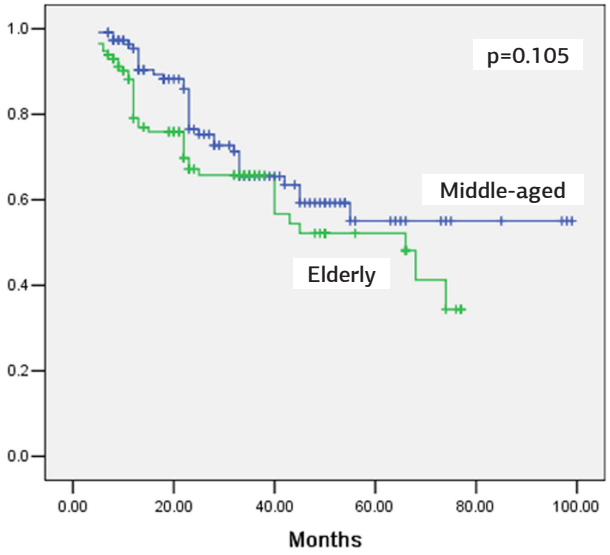

Figure 2. Kaplan-Meier disease-free survival of the elderly and middle-aged group. No significant difference was observed (p=0.105).

Discussion

The present study revealed that, although the elderly group had greater intraoperative blood loss and a higher surgical conversion rate, laparoscopic surgery for rectal cancer provided similar short- and long-term outcomes among the elderly and middle-aged groups. Furthermore, our searches of Medline, Embase, Google Scholar, and major academic publishers (e.g., Elsevier, Nature and Springer) did not identify any studies that have used PSM to compare the short- and long-term outcomes of laparoscopic surgery for rectal cancer among elderly and middle-aged patients. In the present study, approximately 25% of the elderly group of patients had a CCI of >3, which reflects a high-risk of complications and/or mortality after open surgery. Thus, these concerns may motivated surgeons to not recommend surgical treatment for elderly patients, and may cause the patients to refuse surgical treatment in favor of non-surgical treatment. However, the 5-year overall survival rate after non-surgical treatment of rectal cancer is significantly lower, compared to surgical treatment [30-32]. Therefore, the advantages of laparoscopic surgery for elderly patients with rectal cancer are that it causes minimal trauma, is safe, and is effective for high-risk patients.

In the present study, the elderly group had greater intraoperative blood loss, which is likely related to relatively poor coagulation and vascular elasticity in that group [33] compared to middle-aged patients. However, the intraoperative and postoperative blood transfusion rates were similar between the two groups, and the median blood loss in the elderly group was only 40 ml more than that in the middle-aged group. Moreover, the increased intraoperative blood loss in the elderly group had no significant effect on their postoperative complications or long-term prognosis. Although we did not detect any obvious abnormalities in the four conventional coagulation test results for the elderly group [33], coagulation is a complicated process that is imperfectly characterized by these four tests. The higher surgical conversion rate in the elderly group was likely related to poor coagulation and difficulty achieving intraoperative hemostasis [33], which led to conversion to open surgery in order to maintain a clear surgical field and ensure patient safety.

Adjuvant chemotherapy helps improve the prognosis of patients with rectal cancer, and better compliance with the chemotherapy protocol is associated with improved prognosis [34-37]. To the best of our knowledge, no studies have evaluated the role of adjuvant chemotherapy among elderly patients who underwent laparoscopic treatment of rectal cancer, and our study is the first to confirm that elderly patients had similar start times and compliance rates for adjuvant chemotherapy compared to middle-aged patients.

There is no clear definition of "elderly" in the field of clinical oncology, although our literature search indicated that researchers in developed countries have generally defined elderly patients with rectal cancer as being ≥75 years old. However, researchers in developing countries have generally defined these patients as being ≥65-70 years old [38-40]. Thus, we defined "elderly patients" those aged ≥70 years, as China is a devel-

oping country with a lower life expectancy (vs. developed countries) and other Chinese researchers have generally defined elderly patients with rectal cancer as being ≥70 years old.

Most deaths in the present study were related to tumor recurrence, and both groups had similar long-term prognoses. Previous English-language reports regarding laparoscopic treatment of elderly patients with rectal cancer have described 5-year overall survival rates of 51-69%, and large randomized controlled trials have revealed 5-year overall survival rates of 52-74% [8,12]. In the present study, the 5-year overall survival rate was 62% among elderly patients who underwent laparoscopic surgery for rectal cancer, which agrees with the previous findings [8,12]. However, the previous studies have indicated that elderly patients experienced inferior overall survival compared to non-elderly patients [41,42]. This discrepancy is likely related to the elderly patients having more comorbidities compared to their non-elderly counterparts. Moreover, patients with comorbidities are less likely to receive adjuvant therapy, and it is difficult to target and prevent tumor recurrence among these patients.

The limitations of the present study are the retrospective single-center design and the relatively small sample size. However, to the best of our knowledge, this is the first study to use PSM to compare laparoscopic treatment of rectal cancer among elderly and middle-aged patients, and our results provide a foundation for implementing larger multicenter studies.

Conclusion

In conclusion, the elderly group had greater intraoperative blood loss and a higher surgical conversion rate, although laparoscopic surgery for rectal cancer provided similar short-term and long-term outcomes among the elderly and middle-aged patients.

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Conflict of interests

The authors declare no conflict of interests.

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