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ORIGINAL ARTICLE

Outcomes of laparoscopic surgery for rectal cancer in elderly patients

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Summary

Purpose: *Elderly patients with rectal cancer are regarded as being at increased risk during radical resection because of lack of functional reserve and increased number of comorbidities. The aim of this study was to compare the short- and long-term outcomes of laparoscopic surgery with radical intent between elderly and young rectal cancer patients.*

Methods: *Three-hundred ten patients who underwent laparoscopic surgery with radical intent for rectal cancer at our institution between January 2008 and December 2014 were included in this retrospective study. Patients were divided into two age groups (younger than 70 years and older than 70 years) and were evaluated with respect to short- and long-term outcomes.*

Results: *Postoperative morbidity was similar in elderly and young groups (p=0.718). Overall survival and disease-free survival were not significantly different between the two groups. Advanced age was not independent predictor of overall survival and disease-free survival by univariate and multivariate analysis.*

Conclusion: *Our data indicate that laparoscopic surgery with radical intent can be performed as safely in elderly patients as in young patients, with comparable postoperative results and long-term outcomes.*

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

Introduction

Rectal cancer ranks fourth in terms of cancer-related deaths in China [1]. As life expectancy rises, the population is rapidly aging and the number of elderly patients with both neoplasm and comorbidities has significantly increased [2-5]. The proportion of elderly patients with rectal cancer is expected to increase gradually over the next few decades. Age exceeding 70 years is an independent predictor of increased morbidity, 30-day mortality, and a longer hospital stay because aging is associated with a gradual loss of reserve capacity, even in individuals without obvious underlying comorbidities [6-9]. Additionally, elderly patients usually have more comorbidities, and this may lead to more morbidity and a higher mortality rate than in younger patients undergoing surgical resection. Morbidity and mortality rates in particular are higher after laparotomy than after non-abdominal operations in the elderly [6-10].

During the past few decades, the treatment strategy for rectal cancer has shifted to minimally invasive approaches due to early detection of rectal cancer and improvements in minimally invasive surgery. Of these approaches, laparoscopic resection is an alternative surgical treatment because it can facilitate the removal of metastasized

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lymph nodes [11-16]. Some reports about positive short-term surgical outcomes of laparoscopic surgery compared with open surgery for elderly patients have been published [11-18]. However, there are few reports investigating long-term outcome after laparoscopic surgery in elderly patients with rectal cancer. This study investigated the impact of older age on surgical and long-term surgical outcomes of laparoscopic surgery for rectal cancer.

Methods

The therapeutic protocol was conducted in accordance with the Declaration of Helsinki. This research was approved by our local ethics committee. The need for informed consent from patients was waived because of the retrospective nature of the study.

We retrospectively reviewed the prospectively collected data of 319 patients who underwent laparoscopic surgery for rectal cancer with radical intent between January 2008 and December 2014 at our institution. Patients who underwent resection without radical intent were excluded. Patients whose procedures were converted to open resection were also excluded. The indication of laparoscopic surgery for rectal cancer was the patient with clinical stage T1-3N0-2M0.

Patients were categorized into young and elderly groups. Elderly patients were defined as 70 years or older, because previous reports demonstrated that age greater than 70 years was an independent predictor of increased morbidity, in-hospital mortality, and longer hospital stay [12,13]. Young patients were defined as younger than 70 years at surgical resection.

Preoperative clinical staging was defined by electronic colonoscopy, lower gastrointestinal endoscopic ultrasonography, magnetic resonance imaging (MRI) of the pelvis, and computed tomographic scans of the brain, chest, pelvis and abdomen. Positron emission tomography-computerized tomography (PET-CT) and bone scanning were performed when necessary. The TNM stage of rectal cancer was based on the 7th edition of the TNM classification of colorectal cancer which was proposed by Union Internationale Contre le Cancer (UICC) and American Joint Committee on Cancer (AJCC). For patients operated before 2010, their staging was recalculated to match the latest TNM classification by UICC and AJCC [19]. After thorough explanations of the operative and oncologic risks, patients provided informed consent. All procedures were based strictly on patients' individual decisions.

Patients were considered for neoadjuvant chemoradiotherapy in case of clinical T3 or N+ disease. Radiotherapy was delivered to the whole pelvis at a dose of 45Gy in 25 fractions, followed by a boost to the primary tumor of 5.4Gy in 3 fractions during 5.5 weeks. Chemotherapy was 5-fluorouracil or Xeloda-based. Laparoscopic surgery was performed 6-8 weeks after neoadjuvant therapy. Laparoscopic surgery was performed with 5 trocars. The rectum was mobilized and dissected between the visceral and parietal pelvic fascia without injuring the hypogastric nerves. A detailed procedure of laparoscopic surgery has been described in previous reports [13,14,20].

Operative mortality was defined as death within 30 days after radical laparoscopic surgery, and morbidities were defined as complications occurring up to postoperative day 30. The severity of postoperative 30-day complications was graded according to the Clavien-Dindo classification [21,22]. Major complications were defined as grades 3b, 4a, 4b and 5. Minor complications were defined as 1, 2 and 3a.

After surgery, patients underwent blood and serum examinations every 3-4 months, computed tomographic scans of the chest, pelvis and abdomen every 6 months, and an annual endoscopy. If gastrointestinal symptoms were reported, an additional electronic colonoscopy was carried out when indicated. Disease recurrence was defined as locoregional or distant metastasis proven radiologically or pathologically, when available [23]. The last follow up was April 2015. Overall survival was assessed from the date of surgery until the last follow up or death of any cause. Disease-free survival was calculated from the date of surgery until the date of cancer recurrence or death of any cause.

Statistics

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Variables were presented as mean and standard deviations for variables following normal distribution and were analyzed by t test. For variables following non-normal distribution, data were expressed as median and range and were compared by Wilcoxon test. Differences of semiquantitative results were analyzed by Mann–Whitney *U*-test. Differences of qualitative results were analyzed by chi-square test or Fisher exact test. Survival rates were analyzed using the Kaplan-Meier method and differences between two groups were analyzed 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 less than 0.10 were selected for inclusion in the multivariate Cox proportional hazard regression model. Adjusted hazard ratios (HR) along with the corresponding 95% confidence intervals (CI) were calculated. All statistical tests were two-sided, with the threshold of significance set at $p<0.05$ level.

Results

Of 319 identified patients, 9 were excluded because they were converted to open surgery. Of 310 eligible patients, 226 (72.9%) were in the young group and 84 (27.1%) in the elderly group.

Table 1. Preoperative data

	Elderly (N=84)	*Young (N=226)*	*p value*
Age (years)	76.5 ± 3.9	57.0 ± 6.8	0.010
Gender (male: female)	57:27	154:72	0.962
BMI (kg/m^2)	23 (17-27)	24 (21-26)	0.568
ASA score			
I	38	128	0.105
II	42	86	
III	4	12	
Clinical stage (cTNM)			
I	21	59	0.911
II	47	119	
III	16	48	
Number of comorbidities			
0	38	159	0.010
1	32	54	
2	12	9	
>2	2	4	
Tumor location (distance from anal verge,cm)			
Lower rectum (<5)	32	89	0.457
Middle rectum (5 - 10)	25	80	
Upper rectum (10 - 15)	27	57	

BMI: body mass index

Table 2. Operative results

	Elderly (N=84)	*Young (N=226)*	*p value*
Operative time (min, range)	160 (140-240)	180 (150-260)	0.325
Blood loss (ml, range)	210 (160-360)	240 (180-320)	0.240
Postoperative stay (days, range)	9 (7-16)	8 (6-18)	0.569
Type of resection			
Low anterior	63	173	0.776
Abdominoperineal	21	53	

Table 1 presents the preoperative data for all patients who underwent laparoscopic resection for rectal cancer. The frequency of preoperative comorbidities was significantly higher in the elderly group. In both groups, cardiovascular disease was the most frequent comorbidity, followed by type 2 diabetes mellitus, and pulmonary disease. There were no significant differences in gender ratio, body mass index (BMI), American Society of Anesthetists (ASA) score, clinical stage, and tumor location (Table 1).

Table 2 shows the operative data between elderly and young patients. No significant between-group differences were observed in blood loss, operation time, hospital stay and type of resection.

There were no differences between groups in pathological data in terms of histologic differentiation, circumferential resection margin, excised lymph nodes, surgical margins and pathological TNM stage (7th AJCC-UICC) (Table 3).

There was no significant difference in the postoperative 30-day complication rate between the two groups (Table 4). Major complications occurred in 2 elderly and 4 young patients. No significant difference was noted between groups in the severity of postoperative 30-day complications. No 30-day death occurred in this study.

After a median follow-up period of 34 months (range 3-86), 82 (26.5%) of the 310 patients died during the follow-up period: 23 (7.4%) in the elderly group (2 from cardiac episodes and the others from rectal cancer recurrence) and 59 (19.0%) in the young group (3 from acute coronary syndrome, one from stroke and the others from rectal cancer recurrence).The 5-year overall survival rate in the elderly group was 66%, compared to 75% in the young group (p=0.313; Figure 1). As shown in Figure 2, the disease-free survival rate was 56% in the elderly group and 62% in the young group,

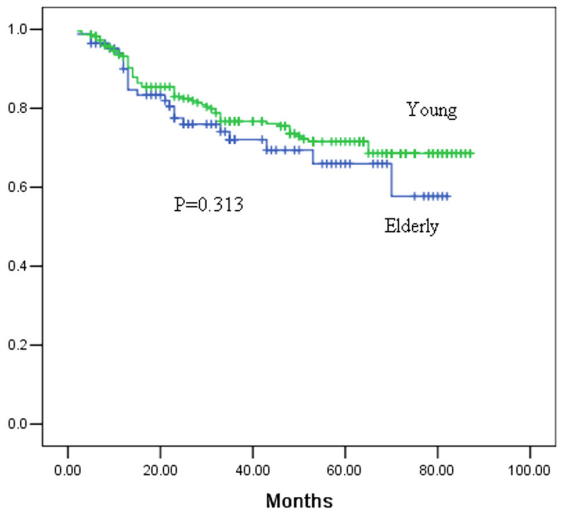

Figure 1. Overall survival of elderly and young patients.

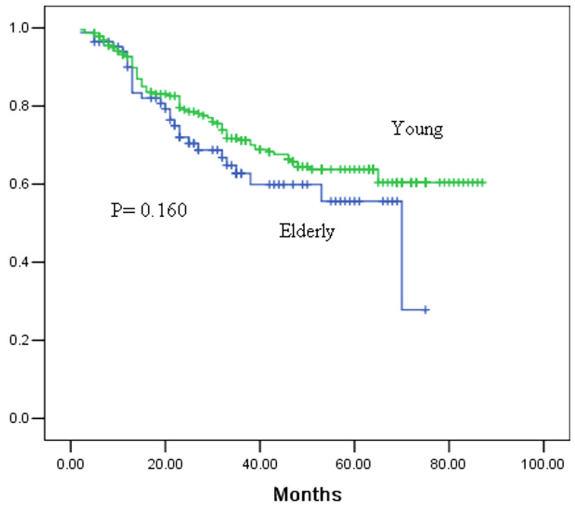

Figure 2. Disease-free survival of elderly and young patients.

Table 3. Pathological results

	Elderly (N=84)	*Young (N=226)*	*p value*
Pathological stage (pTNM)			
pCR	6	18	
I	26	62	0.831
II	40	115	
III	12	31	
Grade of differentiation			
Good	43	105	0.681
Moderate	18	62	
Poor	23	59	
Circumferential resection margin (mm)			
Positive (≤1)	5	19	0.472
Negative (>1)	79	207	
Retrieved lymph nodes (N, range)	11 (5-19)	13 (7-22)	0.102
Residual tumor (R0/R1/R2)	80/2/0	221/5/0	0.906

pCR: pathological complete response after neoadjuvant therapy

Table 4. Postoperative complications

Complications	*Elderly (N=84)*	*Young (N=226)*	*p value*
Post-operative complications	15	23	0.067
Pneumonia	2	3	
Ileus	2	3	
Anastomotic leakage	6	10	
Heart failure	1	3	
Intra-abdominal bleeding	2	1	
Intra-abdominal abscess	2	3	
Severity of complications			0.836
Major (3b, 4a, 4b and 5)	2	4	
Minor (1, 2 and 3a)	13	19	

respectively (p=0.160). No significant differences with respect to type of recurrence was noticed (Table 5).

Advanced age was not independent predictor of overall survival and disease-free survival by univariate and multivariate analysis.

Multivariate Cox regression analysis of overall survival showed that significant predictors

Table 5. Tumor recurrence data

Recurrence data	*Elderly (N=84)*	*Young (N=226)*	*p value*
Tumor recurrence, N (%)	27 (32.1)	71 (31.4)	0.903
Recurrence site			
Brain	1	3	
Lung	1	4	
Liver	6	15	0.656
Locoregional	3	12	
Distant lymph nodes	3	9	
Peritoneal seeding	13	28	
Time to recurrence (median, months)	15	29	0.279

Table 6. Multivariate analysis of overall survival

Regression variables	*Adjusted hazard ratio*	*95%CI*	*p value*
Pathological T stage			
T_{is}-T_2	1.00		
T_3-T_4	3.45	1.58-5.98	0.002
Pathological nodal invasion			
No	1.00		
Yes	2.55	1.88-3.66	0.023
Differentiation grade			
Good-Moderate	1.00		
Poor	1.58	1.48-2.05	0.036

Table 7. Multivariate analysis of disease-free survival

Regression variables	*Adjusted hazard ratio*	*95%CI*	*p value*
Pathological N stage			
N_0-N_1	1.00		
N_2	2.78	1.24-3.25	0.012
Differentiation grade			
Good-Moderate	1.00		
Poor	2.12	1.25-3.13	0.008

of worse overall survival were pathologic T3/T4 disease, lymph node metastasis and tumors with poor differentiation (Table 6). Significant predictors of worse disease-free survival were pathologic N2 disease, and tumors with poor differentiation (Table 7).

Discussion

Elderly cancer patients have increased number of comorbidities and decreased functional reserve. In particular, elderly patients with comorbid conditions often have difficulty with anesthesia and postoperative recovery. For the above-mentioned reasons, some patients and their physicians are often reluctant to treat operable rectal cancer surgically and tend to choose conservative or palliative management [12]. However, several studies have shown that the elderly patient can safely undergo a major abdominal surgery and advanced age should not be a determining factor in the decision to perform radical resection [11-18].

Previous studies have reported that morbidity and mortality rates after laparoscopic surgery for rectal cancer are not higher than those following open resection, with the benefits of more rapid recovery and less blood loss [11-18]. In elderly patients, laparoscopic resection is associated with less morbidity and shorter hospital stay than open surgery for selected cases. Previous studies have shown that the overall complication rates of laparoscopic surgery for rectal cancer were similar between elderly and young patients [24-26]. In our series, the overall and severity of complication rates after laparoscopic surgery did not differ between the two groups, results that were similar to those in previous reports.

It is also important to consider the potential

disadvantages of laparoscopic surgery for elderly patients. Pneumoperitoneum may cause an increase in intra-abdominal pressure and absorption of carbon dioxide, particularly from the peritoneum. The effects of pneumoperitoneum on cardiopulmonary physiology have not been clearly elucidated during laparoscopy, especially for elderly patients. In our series, we did not encounter any elderly patients who suffered from the disadvantages of pneumoperitoneum. Previous reports have suggested that low pneumoperitoneum pressure or a gasless laparoscopic technique might be preferable for elderly patients with cardiopulmonary comorbidity [26,27]. To the best of our knowledge, no study has investigated this problem with respect to laparoscopic surgery for rectal cancer. A well-designed study (low-pressure vs normal-pressure pneumoperitoneum) is needed to clarify such effects in the elderly in the future.

Although laparoscopic surgery for rectal cancer is classified as a clinical research category, it is not yet a standard treatment under the current guidelines, despite its equal or superior performance compared with open resection. Most previous studies have investigated the short-term outcomes of laparoscopic surgery, although multicenter studies also discussed its long-term oncological outcomes [28-31]. Oncological outcomes of laparoscopic surgery for rectal cancer have been shown to be as good as those of open surgery. However, most previous studies of laparoscopic surgery in the elderly have investigated only short-term outcomes [11-18]. It remains unclear whether laparoscopic surgery is suitable for elderly patients with rectal cancer from the standpoint of oncological outcome. In the current study, the overall and disease-free survival of elderly patients did not differ from that of the nonelderly. Most patients in the elderly group died of rectal cancer recurrence.

This study has several limitations. Firstly, it is based on a single-center experience and also based on retrospective non-randomized analysis, not prospective randomized analysis. Secondly, the size of sample is small and the follow up period was not very long, which should be taken into account when interpreting the results.

In the present study, laparoscopic surgery for rectal cancer was a safe and effective treatment for elderly patients with comparable postoperative results and long-term outcomes,, although elderly patients had greater comorbidity than younger patients.

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