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Original Article

Comparison of outcomes after open total and laparoscopy-assisted radical resection for early rectal cancer

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Abstract: Background: The study was aimed to compare the outcomes of open total and laparoscopy-assisted radical resection for early rectal cancer. Methods: Patients with rectal cancer who underwent total radical resection in Xinan hospitals between August 2007 and November 2014 were analyzed in this retrospective and propensity score-matched cohort study. The association between methods of operation and survival was evaluated by cox proportional hazards regression models. Results: Only 783 patients were included finally in this cohort study. There was no significant difference found between the group of open total and laparoscopy-assisted radical resection. The comparative items include overall survival (open total versus laparoscopy-assisted radical resection: hazard ratio (HR) for 0.97, 95% c.i. 0.67 to 1.75), recurrence-free survival (HR 3.20, 0.41 to 8.52), postoperative death (2.6%/1.3%; P=0.045) and the severity of complications (following the Clavien-Dindo classification). However, we found the pattern of complication was different between two groups. Anastomosis-related complication is more common in laparoscopy-assisted group (8.0%/4.2%; P=0.015) and wound-related complication is more common in the group of open total radical resection (1.6%/5.6%; P=0.003). Conclusion: In terms of the long term outcomes (survival and recurrence), laparoscopy-assisted total radical resection for early rectal cancer is more feasible than open total radical resection. However, an increased risk of anastomotic leakage and a higher postoperative mortality rate is found significantly after laparoscopic-assisted total radical resection, which suggests an urgent need of anastomotic innovation for the total laparoscopy-assisted radical resection of rectal cancer in the future.

Keywords: Early rectal cancer, open total radical resection, laparoscopy-assisted radical resection, outcome

Introduction

Laparoscopy-assisted radical resection of rectal cancer is considered to be safer and patient's quality of life is superior when compared with the total open radical resection [1, 2]. With the improvement of laparoscopicinstruments and accumulated experience of laparoscopic-surgery, laparoscopy-assisted radical resection of rectal cancer has been used worldwide [3]. However, some researches have shown that total open radical resection of rectal cancer ismore feasible in terms of the superior survival and less recurrence [4-6]. But, on the one hand, the results in these studies were not conclusive for the smaller sample size; on the other hand, the controlled clinical trials were not qualified, and the potential bias and heterogeneity were considered to be the major limitations of this study. Additionally, because the complexity of laparoscopy-assisted radical resection of rectal cancer could lead to a high possibility of selection bias. Hence, the propensity score matching method [7] is used alternatively to obtain the well-matched results. So, our study focus on comparing the outcomes after open total and laparoscopy-assisted radical resection for early rectal cancer via the propensityscore matching method.

Methods

Our databases of rectal cancer were carried out in a prospectively retrospective review. The individuals in this cohort study were those who have received the total radical resection

Table 1. Baseline characteristics of propensity score-matchedpatients who underwent open or laparoscopy-assisted totalradical resection of rectal cancer

	Open group (n=512)	Laparoscopy group (n=271)	P*
Demographic characteristics			
Age (years)			
Mean (s.d.)	47.6 (12.6)	48.4 (13.7)	
Median (range)	47 (33-84)	48 (33-84)	0.492†
Sex ratio (M:F)	319:183	160:91	0.967
Body mass index (kg/m^2)			
Mean (s.d.)	23.1 (11.6)	23.1 (3.0)	
Median (range)	23.6 (15-37)	23.6 (15-37)	0.768†
ASA fitness grade			0.480
I	216 (41.0)	82 (36.7)	
II	238 (55.4)	168 (59.0)	
III	58 (3.6)	21 (4.4)	
Tumour characteristics			
Location			
Upper third	371 (73.9)	200 (79.7)	
Middle third	131 (26.1)	51 (20.3)	
Size (cm)			
Mean (s.d.)	3.8 (2.6)	3.2 (2.5)	
Median (range)	2.4 (0.1-9.0)	2.4 (0.1-16)	0.004†
Histology			0.796
Differentiated	229 (45.6)	112 (44.6)	
Undifferentiated	273 (44.4)	139 (45.4)	
Morphology			
Ulcer	304 (60.6)	163 (64.9)	
No ulcer	198 (39.4)	85 (35.1)	
No lymphovascular invasion	429 (85.5)	210 (87.3)	0.679
Depth of tumour invasion			0.834
Mucosa	218 (41.4)	106 (42.2)	
Submucosa	284 (58.6)	143 (57.8)	
Lymph node metastasis	43 (8.4)	26 (8.0)	0.751

Values in parentheses are percentages unless indicated otherwise. ASA, American Society of Anesthesiologists. *χ^2 test, except †Mann-WhitneyU test.

in Xinan hospitals between August 2007 and November 2014. The pathological types of rectal cancer were confirmed histologically. All the data were obtained with appropriate institutional review board waivers and without revealing any information personally.

Patient characteristics and clinical data

All the patients' characteristics were obtained from medical records. Patient Characteristics includes: age, gender, BMI, tumor stage, tumor location, tumor size, tumor differentiation, degrees of invasion and metastasis and the operative methods. The tumor stage was determined follow the guidance of National Comprehensive Cancer Network in 2015 [8, 9]. If the patients are found to have multiple synchronous rectal cancer, the rectal wall with the deepest infiltration was considered uppermost, and other characteristics were considered accessionaly. The main pathological characteristics were used in the following analysis.

Patients' follow-up

Patients were followed through the accepted clinical practice. Generally, the follow-up procedure includes: digital rectal examination every 6 months for 5 years after surgery, abdominopelvic CT annually for 5 years. The recurrence of rectal cancer was diagnosed if there was any positive evidence found. The endpoints of follow-up were death or the cut-off date of 30 November 2014. All recurrence of patients was documented pathologically or by radiological imaging. Complications of surgery were graded following the Clavien-Dindo classification [8, 10, 11]. The overall survival and recurrence-free survival (RFS) was calculated from the time of surgery to the endpoint of study. And those lost to follow-up and operative deaths were treated as censored.

Statistical analysis

T test was used to compare the continuous variables and χ^2 testused to compare the categorical variables. In order to perform in a randomized clinical trial setting as possible as we can, we employed the propensity score matching methods. And a multiple logistic regression model was used to generate the propensity

Table 2. Short-term surgical outcomes of propensity score-matched patients who underwent open or laparoscopy-assisted total radical resection of rectal cancer

	Open group (n=512)	Laparoscopy group (n=271)	P†
No.of dissected lymph nodes			
Mean (s.d.)	43.7 (17.0)	40.8 (16.8)	0.003‡
Median (range)	31 (4-103)	32 (3-100)	
Duration of operation (min)			
Mean (s.d.)	175.8 (63.0)	227.6 (81.4)	<0.001‡
Median (range)	174 (84-490)	215 (70-555)	
Complications			
Clavien-Dindo classification			
None	414 (82.5)	197 (78.5)	
I	15 (2.4)	22 (4.8)	
II	31 (5.8)	17 (6.0)	
IIIA	39 (7.4)	18 (6.0)	
IIIB	10 (1.6)	9 (2.8)	
IV	1 (0.2)	3 (0.4)	
V	1 (0.2)	6 (1.6)	
Site of complication			
None	414 (825)	201 (78.5)	
Anastomosis	24 (4.2)	39 (15)	
Wound	27 (5.1)	5 (1.6)	
Intra-abdominal	12 (2.2)	11 (3.6)	
Other	18 (3.6)	19 (6.0)	
Hospital stay (days)	9.4 (0.5)	11.2 (0.6)	0.001‡
No. receiving ICU care	39 (8.2)	12 (14.1)	0.054
Length of ICU stay (days)	0.3 (1.0)	0.8 (3.3)	0.083‡

Values in parentheses are percentages unless indicated otherwise; *values are mean (s.d.). ICU, intensive care unit. †χ^2 test, except ‡t test.

score. The received treatments of patients were considered as dependent variables, and variables involved in this multivariable model include: age, gender, BMI, tumor stage, tumor location, tumor size, tumor differentiation and degrees of invasion and metastasis. The propensity score-matched pairs were carried out without replacement (2:1 match for open: laparoscopic) via using the 5→1 digit match macro of SAS ®Greedy (SAS Institute, Cary, North Carolina, USA). Because of the mixed-effect model, the effect of matched pair was considered randomly. The statistical significance and the outcome of surgery were evaluated by appropriate statistical methods for matched data. In the propensity score-matched cohort, mixed linear model was used to compare the continuous variables and conditional logistic regression was used to compare the categorical variables. Cox proportional hazards regression model with robust standard errors was used to compare the risks of recurrence, death and metachronous rectal cancer. The log (survival curve) was used to exam the proportional hazards assumption, which was generated by the Kaplan-Meier method and analyzed by log rank test. Statistical significance was set at P<0.050.

Results

From August 2007 to November 2014, there are 921 patients with early rectal cancer underwent total radical resection in Xinan hospital. In this study, patients who need combined resection or have another cancer were excluded. There were 834 patients available finally and only 783 patients were included after propensity score matching. Patients' baseline characteristics are shown in **Table 1**. And there is no statistical significance based on baseline characteristics.

Effect of operation method on short-term outcomes

In the group of laparoscopy-assisted total radical resection, the average of duration of operation was longer and dissected lymph nodes were lower when compared with the open total radical resection group. Although there is no apparent significance between the severity of complication between two groups, which are followed the Clavien-Dindo classification. The patterns of complications are different. Wound-related complications are commonly found in open radical resection group, including hernia (3 patients, 0.5%), infection (20 patients, 3.9%) and dehiscence (4 patients, 0.7%). Whereas, the most common complication is anastomosis-related one in laparoscopy-assisted radical resection group, including stricture (22 patients, 8.1%), leakage (11 patients, 4.05%) and bleeding (8 patients, 2.9%), especially the stricture of rectum. In addition, except for the patterns of complications, the overall operation-related

Table 3. Long-term surgical outcomes of propensity score-matched patients who underwent open or laparoscopy-assisted total radical resection of rectal cancer

	Open group (n=512)	Laparoscopy group (n=271)	P*
Recurrence	19 (3.8)	14 (5.6)	0.681
Site of recurrence			0.669
Peritoneum	2 (0.4)	1 (0.4)	
Liver	7 (1.4)	5 (2.0)	
Distant lymph node	4 (0.8)	0 (0)	
Lung	1 (0.2)	2 (0.8)	
Bone	1 (0.2)	1 (0.4)	
Operation bed	1 (0.2)	1 (0.4)	
Spleen	1 (0.2)	1 (0.4)	
Others	2 (0.4)	3 (1.2)	
5-years OS rate	100%	99%	0.894
5-years RFS rate	97%	93%	0.291

Values in parentheses are percentages, *χ^2 test are Recurrence and Site of recurrence. log rank test are 5-years OS/RFS rate.

deaths were also significant between two groups (1 in the open group, 4 in the laparoscopy group) (**Table 2**).

Effect of operation method on long-term outcomes

During the follow-up, there were 87 patients (9.4%) lost finally. The average follow-up duration was 55 (37-69) and 58 (44-67) months for laparoscopy-assisted and open groups respectively. There are 33 patients that recurred during the follow-up. There were no significant differences found between the group of open total and laparoscopy-assisted radical resection. The comparative items include overall survival (open total versus laparoscopy-assisted radical resection: hazard ratio (HR) for 0.97, 95% c.i. 0.67 to 1.75), recurrence-free survival (HR 3.20, 0.41 to 8.52), postoperative death (2.6%/1.3%; P=0.045), risk of death (HR 0.96, 0.57 to 1.65) and the risk of recurrence (HR 2.20, 0.51 to 9.52) (**Table 3**).

Discussion

Our study compare the outcomes between open total and laparoscopy-assisted radical resection for early rectal cancer both in short and long term. Although some researches have shown that total open radical resection of rectal cancer is more feasible in terms of the superior survival and less recurrence [12]. But, on the one hand, the results in these studies were not conclusive for the smaller sample size; on the other hand, the controlled clinical trials were not qualified, and the potential bias and heterogeneity are considered to be the major limitations of this study. Additionally, because the complexity of laparoscopy-assisted radical resection of rectal cancer could lead to a high possibility of selection bias. Hence, in our study, we used the propensity score matching method [7] alternatively to obtain the well-matched results.

In this study, although the overall survival in laparoscopy-assisted group was comparable to that in open total group, and the average of dissected lymphnodes was similar, the operating time of laparoscopy-assisted total radical resection was longer. This might attribute to a more difficult rectal reconstruction. In addition, results showed that the severity of postoperative complications was of little significant difference between two groups when followed the Clavien-Dindo classification. However, the pattern of complications was different. The most common complication is anastomosis-related one in laparoscopy-assisted radical resection group, including stricture, leakage and bleeding. These complications require longer hospital days which just explain why the hospital day in laparoscopy-assisted groupis longer in our study.

Another item that is more common in laparoscopy-assisted group is the postoperative death. In our research, 4 operation-associated deaths in laparoscopy-assisted group proved to have anastomosis-related complications. So, an effective methodis needed to restore the continuity of rectum which could significantly decrease the rate of postoperative mortality. Although some methods for reconstruction have been reported recently, and could help in reducing the rate of anastomosis-related complications [13-16]. There is still no standard method for this kind of restoration. Therefore, it is evident that the operation-associated death is more common after undergoing the laparoscopy-assisted total radical resection.

In a word, our data suggest that the laparoscopy-assisted total radical resection is not inferior

to open total radical resection in terms of the outcomes in long-terms. However, an increased risk of anastomotic leakage and a higher postoperative mortality rate is found significantly after laparoscopic-assisted total radical resection, further technological innovations and development of anastomotic reconstruction methods for laparoscopy-assisted total radical resection are of great need.

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Disclosure of conflict of interest

None.

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