JBUON 2019; 24(2): 464-469
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

# Comparison of perioperative clinicopathologic outcome and postoperative survival of laparoscopic and open sphincter-sparing surgery in patients with rectal cancer: a retrospective study

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## Summary

***Purpose:*** *To investigate the perioperative clinicopathologic outcome and postoperative survival of sphincter-sparing surgery by laparoscopic and open approach for patients with rectal cancer.*

***Methods:*** *From January 1, 2008 to December 31, 2011, laparoscopic sphincter-sparing surgery and open sphincter-sparing surgery was performed in 228 patients with rectal cancer who were included in this study as open group (N=112) and laparoscopic group (N=116), respectively. The average follow-up time was approximately 5 years.*

***Results:*** *Spearman's test showed that there was a slight negative correlation in overall survival and American Society of Anesthesiologists (ASA) grade (Spearman's r=-0.146, p=0.028), History of abdominal surgery (Spearman's r=-0.134, p=0.044) of all patients was statistically significant. There was no significant difference in survival between laparoscopic and open group (p=0.988). Kaplan-Meier curves showed that the total overall survival rates after laparoscopic and open sphincter-sparing surgery were similar in both groups. Log rank test showed that there were significant differences in overall survival among different ypTNM stages (pathological TNM after neoadjuvant chemotherapy) (p=0.002) and Charlson comorbidity index (p=0.03).*

***Conclusions:*** *Compared with open approach, laparoscopic sphincter-sparing surgery of rectal cancer had less intraoperative bleeding, less postoperative complications and faster recovery of intestinal function after operation. Survival of open surgery and laparoscopic rectal sphincter preservation surgery was similar in both groups. ypTNM stage and Charlson comorbidity index are the risk factors affecting the survival of patients with rectal cancer.*

***Key words:*** *laparoscopic, open, rectal, sphincter-sparing, survival*

## Introduction

Rectal cancer is one of the most common malignant tumors in the clinic. Its incidence is relatively insidious [1] and the cause of the disease is not clear at present, while heredity and personal habits together may contribute to its genesis [2]. The main clinical symptoms are abdominal pain, digestive tract dominant or occult bleeding, abdominal distension, constipation, etc. In addition, anal digital examination with blood is the most important positive finding in the first diagnosis of rectal cancer [3]. In some patients, abdominal mass can be palpated during abdominal examination. The diagnosis of rectal cancer is based on clinical symptoms, gastrointestinal endoscopy, auxiliary examinations and biopsy [4].

The treatment of rectal cancer is now relatively mature, and some patients can survive long after tumor surgical removal, but tumor recurrence and

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Received: 13/07/2018; Accepted: 30/08/2018

metastasis are still the main hazard factors for the long-term survival of patients with rectal cancer. After laparoscopic surgery, patients with rectal cancer recover rapidly and have less postoperative complications, therefore, laparoscopic surgery can achieve good long-term oncological outcome in patients with rectal cancer [5]. Sphincter-sparing surgery (SSS) can improve the quality of life in patients with rectal cancer, and its application is gradually more frequently performed [6].

In this study, perioperative clinicopathologic outcome and postoperative survival of laparoscopic surgery and open SSS in patients with rectal cancer were compared and analyzed.

## Methods

*General information*

This study was approved by the ethics committee of Beijing Shijitan Hospital, Capital Medical University, and all patients gave written informed consent. From January 1, 2008 to December 31, 2011, laparoscopic sphincter-sparing surgery and open sphincter-sparing surgery was performed in 228 patients with rectal cancer in the General Surgery Department of Beijing Shijitan Hospital, Capital Medical University. In the process of entering the group, we fully respected the individual patient choice. After the full account of the advantages and disadvantages of the two kinds of operations, some patients considered that open approach is dominant in radical resection, and they chose SSS by open approach. Some patients considered that laparoscopic micro incision has the advantages of nice appearance, small trauma and quick recovery, and they chose SSS by laparoscopic approach. SSS by laparoscopic approach was performed in 112 patients with rectal cancer and SSS by open approach was performed in the other 116 patients. (Table 1).

*Inclusion criteria:* All patients with rectal cancer were clinically diagnosed as cT1-3N0-2 lesions after pelvic enhanced CT, pelvic enhanced MRI, transanal ultrasonography and positive biopsy of rectal carcinoma.

*Exclusion criteria:* Patients with synchronous distant metastasis; patients with invasion of adjacent tissues and organs; patients with tumors penetrating the serosa; patients with another malignancy; patients with severe cardiac or pulmonary disease; patients with intestinal obstruction and pregnant patients.

*Operation procedures*

Surgery was performed by surgeons having 5 years and above experience with laparoscopic colorectal resection. Total mesorectal excision (TME) and SSS were performed in all 228 patients, and the resection range of open and laparoscopic methods were the same. Clips were used to ligate the inferior mesenteric artery to its origin. After the patient's rectum was fully mobilized and sufficient distal resection margin passed through, we then introduced the endoscopic linear stapling devices and transected the rectum. The surgical specimens were removed through a short incision in the lower left quadrant under the wound. Bowel anastomoses were performed with a double staple or transanal suture.

*Follow up*

During 2 years after surgery, patients were followed up every 3 months, and during the next 3 years patients were followed up every 6 months. For the postoperative follow-up, CEA serum levels and chest radiography were performed every 3 months and abdominal and pelvic CT were performed every 6 months. Colonoscopic examinations were performed every year. The average follow-up time was approximately 5 years.

*Statistics*

SPSS 17.0 (Chicago, IL, USA) statistical software was used for statistical analyses. The clinicopathologic data of open group and laparoscopic group were compared with $x^2$ test and the survival outcomes were analyzed by Kaplan-Meier method and log rank test. Correlation was analyzed by Spearman test or Pearson test. $P<0.05$ was considered to be statistically significant.

**Table 1.** The baseline characteristics of Laparoscopic group and Open group

| *Characteristics* | *Laparoscopic group (n =112) n (%)* | *Open group (n=116) n (%)* | *p value* |
|---|---|---|---|
| Age, years (mean±SD) | 58.05±12.22 | 60.55±12.51 | 0.129 |
| Gender (male (%)) | 62 (55.4) | 61 (52.6) | 0.692 |
| Tumor distance from AV (cm) (mean±SD) | 5.92±3.84 | 6.20±3.85 | 0.585 |
| Preoperative CEA (ng/mL) (mean±SD) | 17.24±24.11 | 23.66±40.15 | 0.147 |
| ASA grade (N(Grade 1)/N(Grade 2)/N(Grade 3)) | 13/87/12 | 24/82/10 | 0.090 |
| Neoadjuvant chemoradiotherapy | 35 (31.2) | 38 (32.8) | 0.887 |
| Charlson comorbidity index | 1 (1,2) | 2 (1,2) | 0.097 |
| Past history of abdominal surgery | 13 (11.6) | 15 (12.9) | 0.761 |
| BMI (mean±SD) | 21.64±5.97 | 23.25±4.47 | 0.022 |
| Survival time (mean±SD) | 67.93±21.89 | 67.97±22.19 | 0.988 |

CEA: carcinoembryonic antigen, AV: anal verge, BMI: Body mass index

## Results

*Comparison of operation factors in the 2 groups*

The difference of operation time between laparoscopic group and open group was not statistically significant (p=0.291). The estimated blood loss volume in the open group was higher compared with the laparoscopic group (p=0.032), shunt ileostomy (p=0.037) and coloanal anastomosis (CAA), double stapling technique (DS) (p=0.0172). Time to pass the first flatus after laparoscopic surgery was shorter compared to the open surgery (p=0.024).

*Postoperative complications between laparoscopic and open group*

The incidence of postoperative ileus (p=0.033) and incisional infection (p=0.020) in the open group was higher than that in the laparoscopic group, but no significant difference in the incidence of postoperative anastomotic fistula was noted (p=0.419). The incidence of postoperative bleeding between the two groups was not statistically significant (p=0.517; Table 2).

*Pathologic characteristics of tumors*

No significant difference was noted in the tumor differentiation (p=0.575), ypTNM stage (p=0.535) and macroscopic quality of the TME specimen (p=0.526) between the open and laparoscopic group. However, the circumferential resection margin (CRM) positivity in open group was higher than that in laparoscopic group (p<0.001; Table 3).

*Postoperative survival between laparoscopic and open group*

Spearman's test showed a slight negative correlation in overall survival and ASA score (Spearman's r=-0.146, p=0.028); the higher the score, the shorter the survival time. Spearman's test also showed a slight negative correlation in overall survival and history of abdominal surgery (Spearman's r=-0.134, p=0.044). The survival time of patients with history of abdominal surgery was shorter than that of patients without abdominal surgery.

Kaplan-Meier curves showed no significant difference in overall survival between laparoscopic and open group after SSS (p=0.931; Figure 1). Five-year overall survival in stage I, stage II, stage III and in the total number between the two groups were 89.5 vs. 86.8%, 83.4 vs. 82.5%, 59.8 vs. 62.7% and 70.7 vs. 72.3%, respectively.

The log rank test results showed no significant difference in survival of all 228 patients with rectal cancer after SSS in relation to age (p=0.5), tumor distance from anal verge (AV) (p=0.151), preoperative CEA level (p=0.844), and tumor differentiation (p=0.191), but there was significant difference in pTNM stage (p=0.002) (Figure 2) and Charlson comorbidity index (p=0.03).

**Table 2.** Operation-related data

| *Variables* | *Laparoscopic group (n =112)* | *Open group (n=116)* | *p value* |
|---|---|---|---|
| Operation time (hrs, median (range)) | 3 (3.5) | 4 (3.5) | 0.291 |
| EBL (ml) (mean±SD) | 194.20±137.84 | 234.95±140.44 | 0.032 |
| Procedures SSS with CAA /DS | 11/101 | 19/97 | 0.172 |
| Diverting ileostomy (Y/N) | 15/97 | 21/95 | 0.367 |
| Time to pass first flatus (days, median) | 2 (1.6) | 4 (1.25) | 0.024 |
| Anastomotic leakage, n (%) | 6 (5.4) | 8 (6.9) | 0.419 |
| Postoperative bleeding, n (%) | 2 (1.8) | 3 (2.6) | 0.517 |
| Postoperative ileus, n (%) | 5 (4.5) | 15 (12.9) | 0.033 |
| Incisional infection, n (%) | 2 (1.8) | 10 (8.6) | 0.020 |

SSS: spincter-sparing surgery, Y/N: Yes/No, CAA: colo anal anastomosis, DS: double stapling technique

**Table 3.** Pathologic characteristics of tumors

| *Variables* | *Laparoscopic group (n =112)* | *Open group (n=116)* | *p value* |
|---|---|---|---|
| Tumor differentiation (W/P) | 73/39 | 80/36 | 0.575 |
| ypTNM (I/II/III) | 39/50/23 | 48/49/19 | 0.535 |
| CRM, mean±SD | 4.47±1.93 | 6.68±2.47 | <0.001 |
| Macroscopic quality of TME specimen (C/I) | 106/6 | 109/7 | 0.526 |

W: Well or moderately differentiated; P: Poorly differentiated or mucinous; CRM=circumferential resection margin; C: Complete or near complete; I: Incomplete

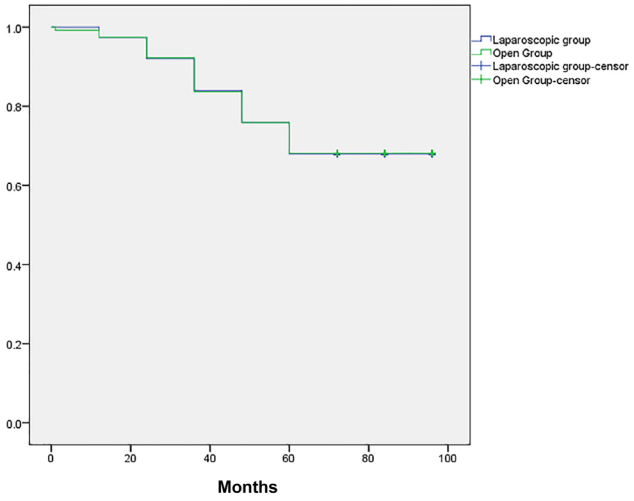


**Figure 1.** Kaplan-Meier curves showing overall survival of all patients.

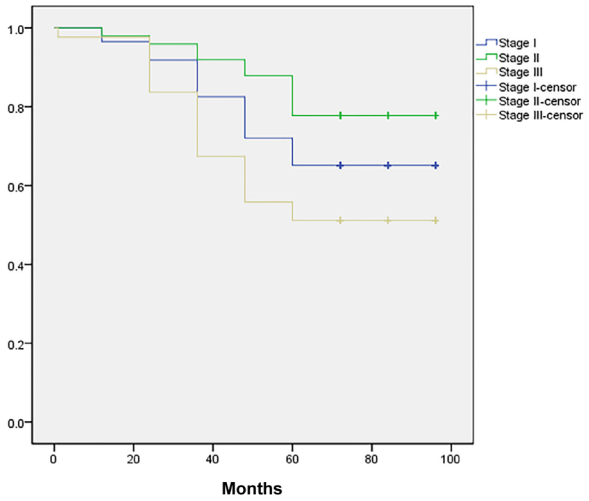


**Figure 2.** Kaplan-Meier curves showing overall survival of different ypTNM stages of all patients (p=0.002).

## Discussion

According to statistics from the World Health Organization published in 2012, colorectal cancer (CRC) was the third most common form of cancer in males (10.0% of all patients with cancer) and the second in females (9.2% of all patients with cancer) worldwide [7]. With the improvement of living conditions and changes in eating habits, the incidence of CRC in China has been increasing in recent years. With the increasing popularity of CRC screening, the detection and diagnosis rates of rectal cancer are higher than before, and the treatment effectiveness continues to improve. Therefore, improving the therapeutic effectiveness and prolonging survival are the main significant targets in the treatment of rectal cancer. Young patients with CRC may face greater threats, but whether age is an independent factor affecting the long-term survival of patients with rectal cancer is still controversial [8]. In this study, there was no significant difference in survival of rectal cancer patients with age (p=0.5).

Young people are easily misdiagnosed, leading to late staging of tumors at the time of detection, which may affect overall survival [9]. However, in this study, there was no significant difference in survival time between different age groups (p=0.500). Previous evidence [10] indicates that the 5-year survival of patients with rectal cancer is more significantly improved than in patients with colon cancer, due to increased use of local and comprehensive treatment, such as perioperative chemoradiotherapy and TME in patients with rectal cancer [11]. in our study, ypTNM stage (p=0.002) was an independent prognostic factor in patients with CRC and this conclusion was consistent with a previous relevant report [12].

The 5-year overall survival of stage I is much higher than that of stage IV, indicating that early diagnosis plays an important role in improving of the survival of CRC patients. There were some studies [13,14] reporting that the application of comprehensive treatment, such as chemotherapy and radiotherapy which reduce the recurrence and metastasis of CRC, has contributed to the gradual improvement of overall survival in the last 30 years. With the widely use of new investigating technologies, more CRC metastases are found in early stage, and this will be helpful to improve the survival rate of this disease [15]. Local tumor invasion and lymph node metastasis are common in malignant tumors [16]. Due to lack of complete visible mesentery anatomy in low perirectal and serosal invasion of tumor into the surrounding tissue, the position of cancer mass is one of the factors closely related to the prognosis of CRC, which leaves local residual tumor and causes early postoperative recurrence.

Tumor differentiation is one of the most important factors for the biological behavior of malignant tumors. Low differentiated tumors are more prone to rapid progression and metastasis, and may cause distant micrometastases, which lead to postoperative tumor recurrence. Preoperative serum levels of CEA are of prognostic significance. CEA levels ≥5ng/mL have an adverse impact on survival, which is independent of tumor stage [17,18]. An elevated preoperative CEA level was associated with a significantly increased risk of overall mortality [19]. Elevated CEA was an independent prognostic factor in all stages, and within each stage grouping, and the prognosis of the subset of patients with elevated CEA was similar to or worse

than a subset of patients who were identified with a normal preoperative CEA level [20]. A study at the ASCO 2006 meeting concluded that the data at that time were insufficient to support the use of CEA for risk stratification individually in patients with using of adjuvant therapy [21]. Duffy et al. [22] reported that CEA was not sufficiently sensitive or specific to be used for screening or as a diagnostic test for CRC. However, CEA levels do have value in the pretreatment staging and follow-up of patients with diagnosed CRC. Because of the abundant blood supply and sufficient lymph nodes in the peritoneal reflection site, rectal cancer is more likely to transfer to this area in the early stage [23].

Laparoscopic rectal cancer surgery has less blood transfusion, less intestinal obstruction and less pain. [24,25]. Several other studies reported that short-term quality of life was improved in patients who underwent laparoscopic versus and those who underwent open TME [26]. Three years after, the disease-free survival was similar in the open and laparoscopic surgery groups (72.5 vs. 79.2%) [27]. Laparoscopic radical resection of rectal cancer, especially the laparoscopic SSS, has become the main surgical treatment of rectal cancer at present. Anastomotic leakage is a common complication of patients with rectal cancer with tumor margin and anus distance been the important factors in the occurrence of anastomotic leakage. The risk of anastomotic leakage increases when the distance between the lower edge of the tumor and the anal verge is less than 7 cm [28]. The distance between the lower edge of the tumor and the anal verge is one of the key factors that determine the kind of operation for patients with rectal cancer [29].

Clinical and pathological data of all the 228 patients with rectal cancer who underwent laparoscopic and open SSS in our hospital showed significant difference in the estimated blood loss between the laparoscopic and open group (p=0.032). Time to pass the first flatus after laparoscopic surgery was significantly shorter compared to open surgery (p=0.024). Postoperative ileus (p=0.033) and incisional infection (p=0.020) were statistically different between the open and the laparoscopic group. The postoperative complication rates of anastomotic leakage and postoperative bleeding were similar in both groups. ypTNM stage (p=0.002) was risk factor affecting the survival in this study. The postoperative survival time of patients who were in late tumor stages and without postoperative or preoperative chemoradiotherapy was significantly shortened. Radiotherapy and chemotherapy are important parts of the comprehensive treatment of rectal cancer. Local residual tumor and micrometastases could be diminished or eliminated, the incidence of postoperative tumor recurrence could be reduced, and the treatment effect could be improved to a great extent. Preoperative chemoradiotherapy combined with surgery has become a standard treatment for patients with locally advanced rectal cancer, which improved local recurrence control and disease free survival [30]. In the Sauer et al. study [31], 823 patients clinically staged as T3/4 or lymph node-positive rectal cancer were administered the same chemoradiotherapy regimen either preoperatively or postoperatively and the 5-year overall survival rates (76 vs. 74%) were similar.

The greatest limitation of our study is its retrospective nature, and as such, a selection bias is a possibility. The insufficient sample size is also a limitation of this article.

## Conclusions

Compared with open approach, laparoscopic sphincter-sparing surgery of rectal cancer has less intraoperative bleeding, less postoperative complications and faster recovery of intestinal function after operation. Survival of open surgery and laparoscopic rectal-sphincter preservation surgery was similar. ypTNM stage and Charlson comorbidity index are the risk factors affecting the survival of patients with rectal cancer.

## Author contribution

Conception and design; Administrative support; Provision of study materials or patients: Zhanzhi Zhang; Collection and assembly of data: Zhipeng Sun; Data analysis and interpretation: Nengwei Zhang; Manuscript writing; Final approval of manuscript: Zhanzhi Zhang; Zhipeng Sun; Nengwei Zhang

## Acknowledgement

This work was supported by Key Medical Specialties of Beijing Municipal administration of hospitals (Sail plan, ZYLX201512).

## Disclosure

The authors declare no conflicts of interest in this work. This study was reviewed and approved by the ethics committee of Beijing Shijitan Hospital, Capital Medical University, and all patients gave written informed consent.

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