Long-term oncologic outcomes of laparoscopic low anterior resection of rectal cancer with preservation of the left colic artery

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Abstract

Aim

To analyze the effect of preserving the left colic artery (LCA) on long-term oncologic outcomes during laparoscopic low anterior resection of rectal cancer.

Methods

Clinicopathological and follow-up patients undergoing laparoscopic low anterior resection of rectal cancer in general surgery department of Guangdong Provincial People's Hospital from January 2014 to December 2015 were retrospectively collected. According to the difference surgical methods of inferior mesenteric artery (IMA), 159 cases were divided into the LCA preservation group and 225 cases in the LCA non-preservation group. The 5-year rates of overall survival (OS) and disease-free survival (DFS) were compared between two group.

Results

384 patients were included in nal analysis. Anastomotic leakage occurred in 7 patients (4.4%) in the LCA preservation group and in 16 patients (7.1%) in the LCA non-preservation group. The follow-up rate was 91.2% (145/159) during 5–60 months in LCA preservation group, and 89.8% (202/225) during 5–60 months in the LCA non-preservation group. The number of patients who developed death, local recurrence and metastasis were 59 (37.1%), 13 (8.2%) and 60 (37.7%) in the LCA preservation group, and 86 (38.2%), 20 (8.9%) and 92 (40.9%) in the LCA non-preservation group, without signicant differences (all \( P \geq 0.05 \)). The 5-year OS and DFS rates were 69.0% and 59.3% in the LCA preservation group, and 68.8% and 55.9% in the LCA non-preservation group, without significant differences (all \( P \geq 0.05 \)). After stratification by TNM Stage, the difference on 5-year OS rates and DFS rates of I stage, II stage and III stage in two groups were no signicant as well (all \( P \geq 0.05 \)).

Conclusions

The long-term oncologic outcomes of laparoscopic low anterior resection of rectal cancer with preservation of the LCA are comparable with ligation at origin of IMA.

Introduction

Colorectal cancer is the third most commonly diagnosed cancer in men and the second in women [1]. In recent years, rectal cancer has developed into a comprehensive treatment mode mainly based on surgery, supplemented by radiotherapy and chemotherapy [2, 3]. Laparoscopic rectal cancer surgery has been proven to have the same clinical results as traditional open surgery in terms of safety and efficacy [4, 5]. During the laparoscopic low anterior resection of rectal cancer, the inferior mesenteric artery (IMA) can be treated in two ways: one is to identify and preserve the left colic artery (LCA) while ligating the IMA after the bifurcation of the left colic artery, the other is to ligate directly the root of the IMA without preserving the LCA [6].

Retrospective studies suggested that preserving the left colic artery may reduce the incidence of anastomose-related complications but had no effect on the long-term oncologic outcomes [7–9]. Nevertheless, preserving the LCA or not during laparoscopic low anterior resection of rectal cancer, is still debated. A randomized multicenter controlled trial showed that low ligation of the IMA in laparoscopic rectal cancer surgery resulted in better genitourinary function preservation without affecting initial oncological outcomes, while high ligation of the IMA did not increase the anastomotic fistula rate [10]. However, the effect of high or low ligation of IMA on long-term oncologic outcomes was not reported in this study.
Thus, the aim of our study is to analyze the clinicopathological data of patients who underwent laparoscopic low anterior resection of rectal cancer in the general surgery department of Guangdong Provincial People's Hospital to evaluate the long-term oncologic outcomes of intraoperative preservation of LCA.

Methods

Patients

This study was approved by the Ethics Committee of Guangdong Provincial People's Hospital [No. GDREC2019296H(R1)] and was carried out in adherence with the Declaration of Helsinki.

Inclusion criteria: (1) Age 18-70 years; (2) Underwent laparoscopic low anterior resection for rectal cancer; (3) Postoperative pathology diagnosis of rectal adenocarcinoma. (4) Informed consent was signed prior to surgery in all cases. Exclusion criteria: (1) Preoperative neoadjuvant radiotherapy and chemotherapy; (2) Emergency surgery; (3) Preoperative and intraoperative detection of distant organ metastases or extensive implantation metastases in the abdominal cavity; (4) Intraoperative laparoscopic inability to complete the operation and intermediate open abdominal; (5) Postoperative pathology those who showed residual cancer cells at the proximal, distal, and circumferential incision margins; (6) Those who did not receive standard chemotherapy after TNM staging of stages II or III after surgery; (7) Patients with concomitant or atopic colorectal cancer and other organ tumors; (8) Patients with incomplete case data.

Based on the above criteria, we retrospectively collected data from the patients who undergone laparoscopic low anterior resection of rectal cancer at Guangdong Provincial People's Hospital from January 2014 to December 2015. A total of 384 cases were included in this study. Among them, 159 cases of LCA were preserved intraoperatively; while 225 cases of LCA were not preserved.

Surgical procedure

The patient was truncated under general anesthesia, pneumoperitoneum was established (pressure of 15 mmHg) and the abdominal cavity was explored. All patients underwent total mesenteric resection and D3 lymph node dissection with sphincter preservation [11]. For the LCA non-preservation group, the opening of the peritoneum proceeded cephalad, towards the duodenojejunal angle of Treitz, and the mesenteric root was incised 1 cm below the inferior margin of the pancreas. The aortomesenteric window was opened wide and the inferior mesenteric vessels were exposed. The inferior mesenteric artery was ligated and divided at 2 cm from its origin. The inferior mesenteric vein was ligated and divided below the pancreatic margin.

For the LCA preservation group, the opening of the peritoneum proceeded upward and then laterally towards the sigmoid colon. The left colic artery was identified and preserved while low ligation of the inferior mesenteric artery (the superior hemorrhoidal artery) was performed. Lymphadenectomy was performed medially along the inferior mesenteric artery as far as 2 cm from the aorta. For both groups, dissection was then continued windowing Toldt's and Gerota's fascias up to the parietocolic gutter. Intra-pelvic dissection was carried out through standardized planes. Dissection of the rectum starts by incision of the peritoneal fold in the pelvis. Mesorectal excision started posteriorly by dissection through Heald's "holy plane" [12], it carried on towards the lateral region of the rectum, sparing the lateral part of the lateral rectal ligaments, and extended on the anterior side in front of Denovvilliers’ fascia [13].

After resection of the tumor, with the proximal bowel to the pubic symphysis assured to be free of tension, if not, then freed the colonic splenic flexure. Reconstruct the gastrointestinal tract with a tubular anastomosis performed end-to-end. A diverting ileostomy was performed based on the surgeon's technical evaluation of the quality of the anastomosis.

Postoperative adjuvant chemotherapy
Patients with pathological stages II or III were treated with XELOX regimen (oxaliplatin, capecitabine) chemotherapy for 6-8 courses after surgery.

**Parameters and postoperative follow-up**

Parameters: operation time, intraoperative bleeding and intraoperative adverse events (e.g., presence of anastomotic tension, additional free colonic splenic flexure, etc.); postoperative anastomosis-related complications (anastomotic leakage, anastomotic bleeding and anastomotic stenosis, etc.); postoperative distance of the pathological tumor from the superior and inferior incision margins, total number of dissected lymph nodes and the number of positive lymph nodes.

Periodic patient follow-up with office visits for 5 years: every 3-6 months for 2 years after surgery; every 6-12 months for 3-5 years after surgery; once a year for 5 years after surgery. The follow-up included physical examination, CEA measurement, CT scan and colonoscopy. Confirmation of recurrence required imaging or pathological evaluation.

**Statistical analyses**

Statistical analyses were performed using SPSS (Statistical Product and Service Solutions 22.0 for Windows, SPSS Inc., Chicago, IL). Quantitative data are described as the mean ± standard deviation, and t-tests or rank sum tests were used to test the hypothesis. Qualitative data are described by the number of cases and percentages, and χ² or Fisher's tests were used to test the hypothesis. The Kaplan-Meier method was used to estimate survival, and the log-rank test was used to test differences between the survival curves. Statistical significance was considered to exist when \( P < 0.05 \).

**Results**

**Patient clinical characteristics**

A total of 384 rectal cancer patients, including 257 males (66.9%) and 127 females (33.1%) were enrolled in this study. Based on grouping criteria, 159 cases were assigned to the LCA preservation group and 225 to the LCA non-preservation group. The clinicopathological characteristics of the two groups are provided in Table 1. There were no statistically significant differences between the two groups regarding sex, age, BMI (Body Mass Index, BMI) and tumor distance from anal margin distribution.

| Cases          | Gender | Age(year) | BMI (kg/m²) | Preoperative Hb (g/L) | Preoperative Alb (g/L) | Tumor distance from anal margin(cm) |
|----------------|--------|-----------|-------------|-----------------------|------------------------|------------------------------------|
|                | Male   | Female    | Male        | Female               | Male                   | Female               |                                    |
| LCA non-preservation | 225    | 72(32.0%) | 58.3 ± 10.0 | 22.5 ± 3.2           | 128.5 ± 12.2          | 34.2 ± 3.4          | 8.1 ± 2.1                           |
| LCA preservation  | 159    | 55(34.6%) | 60.7 ± 8.0  | 22.4 ± 3.3           | 130.4 ± 11.8          | 34.4 ± 3.7          | 7.8 ± 2.0                           |
| Statistical value | χ²=0.283 | t=1.485  | t=0.088     | t=-0.905             | t=-0.329              | t=0.797              |                                     |
| P value          | 0.595  | 0.140     | 0.930       | 0.367                | 0.743                 | 0.427                |                                     |

Abbreviations: BMI, body mass index; Hb, hemoglobin; Alb, albumin; LCA, left colic artery.

**Surgical Outcomes**
The surgical outcomes are presented in Table 2. The mean operating time of the LCA preservation group was 75 minutes longer than that of the LCA non-preservation group (288.3 v 213.3 minutes; \( P = 0.030 \)). Operative bleeding showed no significantly difference in the two groups (93.2 v 86.4 min; \( P = 0.284 \)). The rate to free colonic splenic flexure in the LCA preservation group was higher than that in the LCA non-preservation group (12.6% v 5.8%; \( P = 0.019 \)). Anastomotic bleeding occurred in 10 patients (6.3%) in the LCA preservation group and 13 patients (5.8%) in the LCA non-preservation group; anastomotic stenosis occurred in 4 patients (2.5%) in the LCA preservation group and 6 patients (2.7%) in the LCA non-preservation group; anastomotic fistula occurred in 7 patients (4.4%) in the LCA preservation group and 16 patients (7.1%) in the LCA non-preservation. These rates were not significantly different (All \( P > 0.05 \)).

| Cases                  | Operating time(min) | Operative bleeding(ml) | Free colonic splenic flexure(%) | Anastomotic bleeding(%) | Anastomotic stenosis(%) | Anastomotic leakage(%) |
|------------------------|---------------------|------------------------|---------------------------------|-------------------------|------------------------|------------------------|
| LCA non-preservation   | 225                 | 213.3 ± 46.1           | 86.4 ± 19.3                     | 13(5.8%)                | 6(2.7%)                | 16(7.1%)               |
| LCA preservation       | 159                 | 288.3 ± 30.9           | 93.2 ± 45.3                     | 20(12.6%)               | 10(6.3%)               | 4(2.5%)                |
| Statistical value      | t=-2.200            | t=-1.122               | \( \chi^2 = 5.485 \)            | \( \chi^2 = 0.043 \)    | \( \chi^2 = 0.517 \)  | \( \chi^2 = 1.214 \)  |
| \( P \) value          | 0.030               | 0.284                  | 0.019                           | 0.835                   | 0.472                  | 0.271                  |

Abbreviations: LCA, left colic artery.

### Pathology Outcomes

The pathology outcomes are presented in Table 3. As expected, the length of proximal margin was significantly longer in the LCA preservation group (\( P = 0.000 \)), whereas distal margin, number of collected lymph nodes, metastasized positive lymph nodes and tumor TNM staging were not significantly different in the two groups (All \( P > 0.05 \)).

| Cases                  | Proximal margin(cm) | Distal margin(cm) | Number of lymph nodes dissected | Number of stage III positive lymph nodes | Tumor TNM a staging |
|------------------------|---------------------|-------------------|---------------------------------|----------------------------------------|---------------------|
| LCA non-preservation   | 225                 | 6.1 ± 0.8         | 2.7 ± 0.8                       | 15.8 ± 7.7                             | 31(13.8%) 95(42.2%) 99(44.0%) |
| LCA preservation       | 159                 | 6.8 ± 0.9         | 2.6 ± 0.8                       | 17.1 ± 8.9                             | 19(11.9%) 65(40.9%) 75(47.2%) |
| Statistical value      | t=-3.724            | t=0.829           | t=-1.242                        | t=0.312                                | \( \chi^2 = 0.486 \) |
| \( P \) value          | 0.000               | 0.409             | 0.216                           | 0.756                                  | 0.782               |

\( a \) According to the Cancer Staging Manual, 7th edition.

Abbreviations: LCA, left colic artery.
Table 4
Postoperative Follow-up Outcomes for LCA preservation and LCA non-preservation Groups

|                      | loss of follow-up | Local recurrence | Tumor metastasis | Death    |
|----------------------|-------------------|------------------|------------------|----------|
| LCA non-preservation | 23(10.2%)         | 20(8.9%)         | 92(40.9%)        | 86(38.2%)|
| LCA preservation     | 14(8.8%)          | 13(8.2%)         | 60(37.7%)        | 59(37.1%)|
| $\chi^2$ value       | 0.215             | 0.060            | 0.387            | 0.049    |
| $P$ value            | 0.643             | 0.806            | 0.534            | 0.824    |

Abbreviations: LCA, left colic artery.

Follow-up Outcomes

The follow-up rate was 91.2% (145/159) during 5–60 months in the LCA preservation group, and 89.8% (202/225) during 5–60 months in the group non-preservation. The number of patients who developed death, local recurrence and metastasis were 59 (37.1%), 13 (8.2%) and 60 (37.7%) in the LCA preservation group, and 86 (38.2%), 20 (8.9%) and 92 (40.9%) in the LCA non-preservation group, without significant differences (all $P > 0.05$).

There was no significant difference in the OS rate and DFS rate between the LCA preservation group and LCA non-preservation group as analyzed by the Kaplan–Meier method (Fig. 1). We further performed analysis of stage-by-stage OS rates and DFS rates in stage I to stage III cases. There was no statistically significant difference in OS and DFS rates between the LCA preservation group and the LCA non-preservation group in all stage I to stage III (Fig. 2).

Discussion

Since Heald et al proposed total mesorectal excision (TME) in 1982, the clinical outcomes of middle and low rectal cancer have been significantly improved [14, 15], but anastomotic leakage is still an important factor affecting the short-term and long-term postoperative outcomes of rectal cancer, and greatly increases the total cost of treatment [16–18]. It has been reported that the incidence of anastomotic leakage after rectal cancer surgery is 5% ~ 26% [19, 20]. To date, no consensus has been reached on whether LCA preservation during rectal cancer surgery can reduce anastomose-related complications and improve long-term prognosis [9, 21].

Excessive anastomotic tension and poor blood supply are important factors for anastomotic leakage [22]. High ligation of IMA can loosen the mesentery and make the proximal colon more free and drooping, theoretically reducing the tension between the colon and the anastomotic site of the rectum or anal canal [23]. However, after the high ligation of IMA, the proximal colon could only supply blood from the middle colon artery from the superior mesenteric artery, the blood perfusion of the marginal arterial arch was reduced, and the blood supply of the terminal colon was deteriorated [24].

Anastomotic leakage is one of the common serious complications after laparoscopic rectal cancer surgery. There are many factors affecting anastomotic leakage, including the patient's age, BMI, distance between tumor and anal border, etc., among which anastomotic blood supply and anastomotic tension are closely related [25]. The results of our study showed that anastomotic leakage occurred in 7 patients (4.4%) in the LCA preservation group and in 16 patients (7.1%) in the LCA non-preservation group. The incidence of anastomotic leakage in the LCA preservation group was lower than that in the LCA non-preservation group, but the difference was not statistically significant. At the same time, there were no statistically significant differences in anastomotic bleeding and anastomotic stenosis between the two groups. For the anastomotic tension, there was no statistically significant difference in the length of the proximal resection margin in postoperative pathological specimens.
The intraoperative parameters and postoperative complication rates were important indexes for demonstrating the efficacy of quality control in a surgical procedure. A previous RCT study showed that the LCA preservation or not does not increase the duration of laparoscopic low anterior resection of rectal cancer [10]. Our study revealed the mean operating time of the LCA preservation group was 75 minutes significantly longer than that of the LCA non-preservation group. It was considered that this may be the result of a higher rate of freeing splenic flexure colon in the LCA preservation group, thus resulting in prolonged operative time for the whole group (12.6% vs 5.8%, \( P = 0.019 \)). Despite the prolonged operative time in the LCA preservation group, there was no significant difference in operative bleeding between the two groups. Despite the prolonged operative time in the LCA preservation group, there was no significant difference in operative bleeding between the two groups. When passing the laparoscopic learning curve, intraoperative bleeding does not increase significantly as the surgical area expands [26].

IMA root lymph nodes are the third station of lymphatic drainage in rectal cancer and the most important route of metastasis in progressive rectal cancer [27]. Studies have shown that IMA root lymph node metastasis has an impact on patients’ 5-year survival and tumor recurrence rates [28]. Our results suggest that the surgical approach of preserving LCA and IMA low level ligation does not reduce the detection and positivity rate of lymph nodes. The difference between the total number of lymph nodes obtained and the number of positive lymph nodes was not statistically significant between the two groups.

Our long-term follow-up of patients, survival analysis showed that preserving LCA or not during laparoscopic low anterior resection of rectal cancer, there was no statistically significant difference on five years of OS and DFS. When further analysis of stage-by-stage OS rates and DFS rates in stage I to stage III cases, there was still no statistically significant difference in OS and DFS rates between the LCA preservation group and the LCA non-preservation group in all stage I to stage III. Several previous studies have also shown that, whether preserving LCA or not, there were no significant differences with respect to the 5-year mortality in patients underwent laparoscopic rectal cancer, and it seemed to achieve comparable success with acceptable safety outcomes [7–9], but data from JCOG0404 showed that preserving LCA, five-year relapse-free survival and OS tended to be better in the LCA preservation group than the LCA non-preservation group (RFS: 83.7% and 80.5%, HR 0.80 [95% CI 0.51–1.26], OS: 96.3% and 91.1%, HR 0.41 [95% CI 0.19–0.89]) [29].

In conclusion, our data suggest that the long-term oncologic outcomes of preservation of the LCA in laparoscopic low anterior resection of rectal cancer are comparable with ligation at origin of IMA, but more multicenter randomized controlled trials are required.

Declarations

**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study was approved by the Ethics Committee of Guangdong Provincial People's Hospital and was carried out in adherence with the Declaration of Helsinki [No. GDREC2019296H(R1)]. The need for informed consent from all patients was waived due to the study's retrospective nature.

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**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form (available at [http://dx.doi.org/10.21037/atm-20-2556](http://dx.doi.org/10.21037/atm-20-2556)). The authors have no conflicts of interest to declare.
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Figures

Figure 1

Kaplan–Meier estimates of overall survival and disease-free survival for all anterior resection cases (a and b, respectively). The red line and the green line indicate, respectively, survival curves of the LCA preservation group and the LCA non-preservation group. Abbreviations: LCA, left colic artery.
Figure 2

Kaplan–Meier estimates of overall survival and disease-free survival for all anterior resection cases in stage I (a and b, respectively), stage II (c and d, respectively), and stage III (e and f, respectively). The red line and the green line indicate, respectively, survival curves of the LCA preservation group and the LCA non-preservation group. Abbreviations: LCA, left colic artery.