Original Article

The effect of different inferior mesenteric artery ligation levels and different lymph node dissection areas on the short- and long-term outcomes of rectal cancer

Shidong Hu[1,2#], Songyan Li[2#], Xiaohui Huang[2#], Yang Yan[2], Da Teng[1,2], Haiguan Lin[1,2], Changzheng He[1,2], Zihe Gao[1,2], Yufeng Wang[3], Xiaohui Du[1,2]

[1]Medical School of Chinese PLA, Beijing, China; [2]Department of General Surgery, The First Medical Centre, Chinese People's Liberation Army General Hospital, Beijing, China; [3]Department of Hospital Management, The First Medical Centre, Chinese People's Liberation Army General Hospital, Beijing, China

Contributions: (I) Conception and design: X Du, S Hu, S Li, X Huang; (II) Administrative support: X Du, Y Wang; (III) Provision of study materials or patients: S Hu, S Li, X Huang; (IV) Collection and assembly of data: S Hu, Y Yan, D Teng; (V) Data analysis and interpretation: S Hu, H Lin, C He, Z Gao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Professor Xiaohui Du. Department of General Surgery, The First Medical Center of Chinese People's Liberation Army General Hospital, 28 Fuxing Road, Beijing 100853, China. Email: duxiaohui301pw@163.com.

Background: Surgery is the most effective treatment for rectal cancer patients, but its key steps, including selection of the level of inferior mesenteric artery ligation and removal of 253 lymph nodes, are still inconclusive. This study aimed to analyze the effects of different surgical methods, including levels of ligation (low *vs.* high) and lymph node dissection areas (D2 *vs.* D3) on the short-term and long-term outcomes.

Methods: Between March 2014 and August 2018, 253 rectal cancer patients were retrospectively analyzed; 113 patients underwent low ligation D2 lymph node dissection (LLD2), 75 patients underwent low ligation D3 lymph node dissection (LLD3), and 65 patients underwent high ligation (HL). We compared the short-term and long-term outcomes among the different groups.

Results: There were no significant differences among the groups in terms of the intraoperative variables, including operative time, blood transfusion, and conversion from laparoscopic to open surgery. The median blood loss was significantly lower in LLD3 (50 mL) than in LLD2 (100 mL) and HL (100 mL), but it was not significantly different between LLD2 and HL. There were no significant differences among the LLD2, LLD3, and HL groups in the incidence of postoperative complications (9.7% *vs.* 12.0% *vs.* 10.8%, respectively) and hospital stay (14 *vs.* 15 *vs*. 14, respectively). The anastomotic leakage Clavien-Dindo grade was significantly lower with LLD2 and LLD3 than with HL, but it was the same between LLD2 and LLD3. The total number of lymph nodes harvested in the LLD3 group (n=14) was higher than that in the LLD2 group (n=12), but it was not significantly different than that in the HL group (n=13). There were no significant differences among the groups in terms of 3-year overall survival rate and disease-free survival rate.

Conclusions: Low ligation was similar to HL in terms of major intraoperative and postoperative parameters, but it can reduce the severity of anastomotic leakage to a certain extent. D3 lymph node dissection can increase the total number of lymph nodes harvested, but it did not improve long-term prognosis.

Keywords: High ligation; low ligation; lymph node dissection

Submitted Aug 12, 2020. Accepted for publication Nov 27, 2020.
doi: 10.21037/jgo-20-327
View this article at: http://dx.doi.org/10.21037/jgo-20-327

Introduction

According to the latest research data, colorectal cancer is the third most common malignant tumor in men worldwide, with 861,663 deaths per year, making it a serious threat to people's health. Surgery is the most important treatment for colorectal cancer and rectal cancer, which accounts for the highest proportion of colorectal cancer (1).

In the operation of rectal cancer, the level of ligation of the inferior mesenteric artery (IMA) has received extensive attention from surgeons. Mile believed that rectal lymphatic drainage is from the bottom to the IMA and was the one who first proposed IMA low ligation (LL), which entails complete ligation of the blood vessels below the branching of the left colic artery (LCA) (2,3). On the other hand, Moynihan proposed high ligation (HL) of the IMA, from the level of the abdominal aorta to the blood vessels at the root of the IMA, in order to clear the 253 lymph nodes (regional lymph nodes at the root of IMA) located in the area (2,3).

Some scholars support HL of the IMA because they believed that this method can significantly increase the extent and number of lymph nodes dissected. For this purpose, laparoscopic operation can easily separate the colon and the spleen in order to decrease the risk of hematogenous tumor spread and to quickly find the correct anatomical gap to complete a total mesorectal excision (TME) (4-7). Although IMA HL can extend the lymph node dissection to include all 253 lymph nodes, other scholars support IMA LL, because the presence of metastases to 253 lymph nodes decreases the possibility of radical resection and cannot improve the prognosis, and HL may lead to insufficient anastomotic blood supply and serious complications (8,9).

In the textbook of *Colon and Rectal Surgery*, the American Society of Colon and Rectal Surgeons recommended LL, because HL can decrease the blood supply to the sigmoid colon; however, HL was recommended for patients who require additional vascular mobilization for the proximal colon, in order to avoid excessive tension on an anastomosis, with a consideration of the presence of metastatic nodes around the IMA (10). Japanese scholars believe that the lymph nodes around the IMA should be routinely cleaned. In fact, in Japan, D3 lymph node dissection for rectal cancer has become the standard procedure and D2 lymph node dissection is only used for tumors confined to the muscular layer and those that do not have lymph node metastasis found before surgery (11). Huang *et al.* showed HL and D3 lymph node dissection can be safely performed using the da Vinci robotic surgical system (12). Moreover, some surgeons routinely perform LL and D2 lymph node dissection which was proven an oncologically acceptable treatment strategy by Maeda *et al.* (13).

Selection of the level of IMA ligation and removal of the 253 lymph nodes are the key steps in the radical resection of rectal cancer. The most appropriate treatment remains inconclusive. This study retrospectively analyzed the effects of different surgical methods, including different levels of ligation and different lymph node dissection areas, on the short- and long-term outcomes of rectal cancer patients, in order to provide reference for the choice of rectal cancer surgical approach.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jgo-20-327).

Methods

This study retrospectively analyzed 253 patients who underwent anterior resection for rectal cancer at our hospital from March 2014 to August 2018 (*Figure 1*). The inclusion criteria were age >18 years, enteroscopy biopsy-confirmed malignancy, absence of distant metastasis on preoperative imaging assessment, American Society of Anesthesiologists (ASA) score I–III, body mass index (BMI) <30 kg/m^2, and complete medical records. The exclusion criteria were IMA root lymphadenopathy on the preoperative images; previous history of malignant tumors, abdominal aortic surgery, or arteriosclerosis of the IMA and its branch; and emergency surgery for intestinal obstruction, perforation, bleeding, etc. The primary and metastatic lesions were treated simultaneously in stage IV patients (surgical resection or radiofrequency ablation). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The TNM staging was in accordance with the American Joint Committee on Cancer colorectal cancer TNM staging system (eighth edition, 2017). The study was approved by the Ethics Committee of Chinese People's Liberation Army General Hospital (No. S2020-467-01). Because of the retrospective nature of the research, the requirement for informed consent was waived.

The surgeons were the deputy chief physicians of our hospital. In the LLD2 group, the abdominal cavity was routinely explored for the presence of distant metastasis and to identify tumor location and serosal penetration; the LCA was separated and retained, the IMA under the LCA was

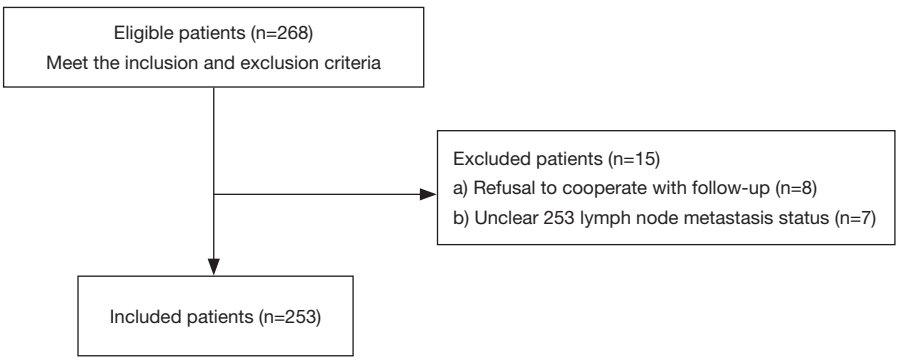

Figure 1 The flowchart of patient selection.

ligated and cut off [IMA changing to superior rectal artery (SRA) after LCA]. We identified the root of IMA for the confirmation of lymph node status through preoperative imaging and intraoperative exploration in LLD2 group. Complete anterior resection of the rectal cancer was performed according to the TME principle. In the LLD3 group, dissection of the 253 lymph nodes distributed along the IMA, from the its beginning to the beginning of the LCA, was performed; the other steps were the same as those for LLD2. In the HL group, the anterior space of the Toldt's fascia to the root of the IMA was freed, the blood vessels in the IMA were exposed, and the IMA was ligated at about 1 cm from the abdominal aorta; to complete the dissection of the 253 lymph nodes, the mesentery around the inferior mesenteric vein was freed and cut; the other steps were the same as those for LLD2.

The patients were followed-up through a series of phone calls until April 12, 2019. Overall survival (OS) was defined as the time from the completion of surgery to the death of the patient or the follow-up date. Disease-free survival (DFS) was defined as the time from the completion of surgery to recurrence or the follow-up date.

The baseline data collected from the three groups included age, gender, and BMI; distance (cm) of the tumor from the anal verge; preoperative chemoradiotherapy (CRT); ASA score; and tumor maximum diameter, differentiation, histopathologic type, and pathologic TNM stage. The intraoperative and postoperative parameters were operative time, blood transfusion, conversion from laparoscopic to open surgery, complications, anastomotic leakage grade, and hospital stay. The parameters for the oncological quality of surgery included the total number of harvested lymph nodes, metastatic lymph nodes, number of lymph nodes, number of metastatic 253 lymph nodes, and R0 resection. Clinical pathological information was obtained through the electronic medical record system. The long-term outcomes included OS and DFS. The first recurrence mode and cause of death were compared among the groups.

Statistical analysis

Statistical analyses were performed using SPSS 22.0 (SPSS Institute, Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to evaluate normality of data and Levene's test was used to evaluate the homogeneity of variance. The continuous variables were expressed as median (min–max). For the measurement data that were consistent with the normality and homogeneity of variance, comparison of two groups was performed by the *t*-test, comparison of multiple groups was performed by one-way analysis of variance, and comparison between groups was performed using the Student-Newman-Keuls. For the measurement and grade data that did not meet the normality or homogeneity of variance, comparison of two groups was performed using the Mann-Whitney U-test and comparison of multiple groups was performed using the Kruskal-Wallis rank sum test. The count data were compared using the chi-square test. Multivariate analysis was performed using a logistic regression model. Survival analysis was performed using the Kaplan-Meier method; the difference was compared using the log-rank test, and the influencing factors were analyzed using the COX regression model. $P<0.05$ was considered to be statistically significant.

Results

Baseline cohort characteristics

Of the 253 rectal cancer patients included in this study, 113

underwent LLD2, 75 underwent LLD3, and 65 underwent HL. There were no significant differences in the basic clinic pathologic characteristics including age, gender, BMI, distance of tumour from anal verge, preoperative CRT, ASA score, and tumor maximum diameter, differentiation, histopathologic type, and pathologic TNM stage among the three groups (*Table 1*).

Short-term outcomes

There were no significant differences among the three groups in terms of the intraoperative variables, including operative time, blood transfusion, and conversion from laparoscopic to open surgery. The median blood loss of LLD3 was 50 mL, which was significantly lower than that of LLD2 (100 mL) and HL (100 mL). There was no significant difference in blood loss between LLD2 and HL.

There was no significant difference in the incidence of postoperative complications among the LLD2, LLD3, and HL groups (9.7% *vs.* 12.0% *vs.* 10.8%, respectively; P=0.885). The anastomotic leakage Clavien-Dindo (CD) grade was significantly lower (P<0.05) with LLD2 and LLD3 than with HL, but there was no significant difference between LLD2 and LLD3 (*Table 2*). There was no significant difference in the hospital stay among the three groups (14 *vs.* 15 *vs.* 14 days, respectively; P=0.809).

To analyze the risk factors for anastomotic leakage, a logistic regression model analysis with backward method was used and included age, gender, distance (cm) of the tumor from the anal verge, operative time, blood loss, blood transfusion, preoperative CRT, conversion from laparoscopic to open surgery, and pathologic TNM stage. Among these factors, blood transfusion was the independent risk factor for anastomotic leakage [odds ratio (OR): 1.001, 95% confidence interval (CI): 1.000–1.002, P=0.042] (*Table 3*).

The total number of lymph nodes harvested in the LLD3 group (n=14) was higher than that in the LLD2 group (n=12, P<0.05), but it was not significantly different from that in the HL group (n=13, P>0.05). The total number of lymph nodes harvested tended to be higher in the HL group than in the LLD2 group (P>0.05). There was no significant difference in the number of metastatic lymph nodes among the LLD2, LLD3, and HL groups (P=0.707). Of the 253 lymph nodes, the number of lymph nodes harvested in the LLD3 group was significantly higher than that in the HL group (1 *vs.* 0, P<0.05) and LLD2 group (P<0.05). There were no significant differences in number of positive 253 lymph nodes and R0 resection among the three groups (*Table 4*).

Long-term outcomes

The median follow-up period was 26 months. There was no significant difference in 3-year OS rates among the LLD2, LLD3, and HL groups (91.2% *vs.* 88.2% *vs.* 97%, respectively; P=0.379) (*Figure 2*). During the follow-up period, the primary tumor was the cause of death in four cases of LLD2, four cases of LLD3, and one case of HL, but there was no significant difference among the groups (*Figure 2*, *Table 5*).

The LLD2, LLD3, and HL groups had no significant differences in 3-year DFS rates (84.0% *vs.* 83.9% *vs.* 86.1%, respectively; P=0.517) and number of relapses during the follow-up period (13 *vs.* 11 *vs.* 9, respectively; P=0.800) (*Figure 3*). The sites of recurrence were the liver (n=4), lung (n=3), and other locations (n=6) in the LLD2 group; liver (n=3), lung (n=3), local (n=1), and other locations (n=4) in the LLD3 group; and liver (n=1), lung (n=4), local (n=2), and other locations (n=2) in the HL group (*Table 5*).

Discussion

In 1982, Professor Heald proposed the concept of TME, which surgeons widely accepted and applied to the clinic and significantly improved the local recurrence and long-term survival of patients with rectal cancer (14,15). In the academic world of laparoscopic TME surgery, there are two opposing views on the site of IMA ligation, in particular, LL and HL. With the development of technology, more emphasis had been placed on IMA root lymph node dissection. The best IMA ligation level and the decision to clean the 253 lymph nodes or not are not well-documented. This study compared the short- and long-term effects of three different surgical methods LLD2, LLD3, and HL, in order to explore the best surgical procedure for anterior resection of rectal cancer.

Anastomotic leakage is a serious complication after rectal cancer surgery and is an important index for evaluating the short-term curative effect of radical resection of rectal cancer. Anastomotic leakage was reported to have an incidence of about 5% to 15% after low anterior resection for rectal cancer and had been closely related to anastomotic blood supply and anastomotic tension (16-18). The effects of the different IMA ligation levels on the short-term efficacy of radical surgery for rectal cancer are controversial.

Table 1 Patient characteristics

Characteristics	LLD2 (n=113)	LLD3 (n=75)	HL (n=65)	P
Age (years) [P25–P75]	62 [52–67]	61 [53–66]	60 [53–68]	0.787
Gender				0.594
Male	77	46	44	
Female	36	29	21	
BMI (kg/m^2) (P25–P75)	24.3 (22.0–26.1)	24.1 (22.4–25.5)	23.7 (21.8–26.2)	0.924
Distance of tumour from anal verge (cm) [P25–P75]	8 [5–10]	7 [5–11]	8 [5–10]	0.996
Preoperative CRT				0.234
Yes	5	7	7	
No	108	68	58	
ASA				0.051
I	11	4	13	
II	86	64	47	
III	16	7	5	
Tumor max diameter (cm) (P25–P75)	3.5 (2.5–5.0)	3.0 (2.5–4.0)	4.0 (2.7–4.5)	0.184
Differentiation				0.320
Well	5	0	2	
Moderately	92	62	48	
Poorly	7	7	11	
Dysplasia	3	2	2	
Other	6	4	2	
Histopathological type				0.941
Adenocarcinoma	92	65	54	
Mucinous adenocarcinoma	6	3	4	
Signet-ring cell carcinoma	1	1	0	
Other	14	6	7	
Pathological TNM stage				0.784
Stage 0	5	1	2	
Stage 1	18	17	11	
Stage 2	45	32	23	
Stage 3	39	21	23	
Stage 4	6	4	6	

LLD2, low ligation D2 lymph node dissection; LLD3, low ligation D3 lymph node dissection; HL, high ligation; BMI, body mass index; CRT, chemoradiotherapy; ASA, American Society of Anesthesiologists.

Table 2 Intraoperative and postoperative parameters

Parameters	LLD2 (n=113)	LLD3 (n=75)	HL (n=65)	P
Operative time: minutes [min–max]	175 [142–234]	178 [140–212]	176 [136–218]	0.619
Blood loss (mL), median [min–max]	100 [50–200]	50 [50–100]*	100 [50–200]#	0.022
Blood transfusion				0.669
Yes	11	10	6	
No	102	65	59	
Conversion to open from laparoscopic surgery				0.256
Yes	3	0	0	
No	110	75	65	
Complication, n (%)	11 (9.7)	9 (12.0)	7 (10.8)	0.885
Anastomotic leakage	2	4	3	
Intra-abdominal infection	2	1	0	
Surgical site infection	1	1	1	
Pulmonary infection	1	1	0	
Bowel obstruction	2	0	0	
Urinary dysfunction	2	2	0	
Hemorrhage	1	0	2	
Vaginal pelvic fistula	0	0	1	
Anastomotic leakage grade				0.009
CD 2	2	4	0*#	
CD 3	0	0	3	
Hospital stay (days), median [min–max]	14 [7–101]	15 [5–43]	14 [8–36]	0.809

*, compared to LLD2 P<0.05; #, compared to LLD3 P<0.05. CD indicates Clavien-Dindo classification of postoperative complications. LLD3, low ligation D3 lymph node dissection; HL, high ligation.

The anatomical types of IMA and its branches include types I to IV. In type I, the LCA is the first to branch off, and the sigmoid artery (SA) and SRA coexist; in type II, the IMA first branches into the common trunk of the LCA and SA; in type III, the LCA, SA, and SRA are separated at the same point; in type IV, there is no LCA (19). The Riolan's arterial arch is an important collateral circulation of the IMA and superior mesenteric artery and was reported by Chinese scholars to be present in about 7.6% (20-22). Some studies have shown that LL has certain advantages on the short-term efficacy in some patients. One study that used laser Doppler flowmetry to confirm retention in the LCA and its ascending branch showed that increasing the perfusion of the anastomosis could theoretically reduce the incidence of anastomotic leakage (23). Other studies showed that IMA type III and absence of the Riolan's arterial arch were independent risk factors for anastomotic leakage (19,24). Retrospective studies recommended IMA LL for patients with IMA type III and absence of the Riolan's arterial arch, in order to reduce the incidence of postoperative anastomotic leakage (25). Trencheva *et al.* reported a prospective cohort study on 616 patients and showed that the incidence of anastomotic leakage increased with HL than with LL (P=0.0281) (26). Mari *et al.* conducted a multicenter randomized controlled trial (RCT) on 214 patients and reported better preservation of genitourinary functions (i.e., urinary symptoms, quality of life, sexual function) in the LL group (n=103) than in the HL group (n=111) at nine months postoperatively (P<0.05) (27).

Other studies have found no significant differences

Table 3 Risk factors for anastomotic leakage

Risk factors	Univariate analysis		Multivariate analysis	
	P	Odds ratio (95% CI)	P	Odds ratio (95% CI)
Gender	0.996	0 (0–0)	0.997	0 (0–0)
Blood transfusion (mL)	0.035	1.002 (1.000–1.003)	0.042	1.001 (1.000–1.002)
Age	0.615	0.982 (0.916–1.053)	–	–
Distance of the tumor from the anal verge (cm)	0.463	0.925 (0.753–1.138)	–	–
Operative time	0.612	0.996 (0.981–1.011)	–	–
Blood loss	0.170	0.988 (0.971–1.005)	–	–
Preoperative CRT	0.740	1.461 (0.156–13.655)	–	–
Conversion from laparoscopic to open surgery	0.999	0.000 (0.000–0.000)	–	–
Pathologic TNM stage	0.526	0.787 (0.376–1.648)	–	–

Table 4 Oncological quality of surgery

Variables	LLD2 (n=113)	LLD3 (n=75)	HL (n=65]	P
Total harvested lymph nodes [min–max]	12 [4–18]	14 [4–31]*	13 [6–26]	0.003
Metastatic lymph nodes [min–max]	0 [0–13]	0 [0–20]	0 [0–12]	0.707
IMA root lymph nodes (n=253) [min–max]	–	1 [0–5]*	0 [0–3]*#	0.000
Number of metastatic lymph nodes (n=253) [min–max]	–	0 [0–3]	0 [0–1]	0.192
R0 resection				0.423
Yes	99	61	57	
No	14	14	8	

*, compared to LLD2 P<0.05; #, compared to LLD3 P<0.05. LLD3, low ligation D3 lymph node dissection; HL, high ligation; IMA, inferior mesenteric artery.

in the short-term efficacy among the different ligation methods. A prospective study that used laser Doppler flowmetry found no significant difference in colonic perfusion between HL and LL (1.19 *vs.* 1.71, respectively; P=0.28) and that the risk of postoperative anastomotic leakage did not increase (28). Yamamoto *et al.* showed no significant difference in the incidence of anastomotic leakage between HL and LL (29). Fujii *et al.* conducted a single-center RCT and showed no differences between HL and LL in the incidence of anastomotic leakage, operative time, blood loss, and postoperative hospital stay (3). Another RCT showed no significant difference between HL and LL in the incidence of anastomotic leakage; defecation function; and defecation, quality of life, and sexual life scores (30). Mari *et al.* found no differences in blood loss, surgical time, and postoperative complications between LL and HL (P>0.05) (27). A meta-analysis showed that HL did not increase the incidence of anastomotic leakage and genitourinary dysfunction (31). Another meta-analysis showed no significant difference in the incidence of anastomotic leakage between HL and LL (32).

Our study found no significant difference between LL (i.e., LLD2, LLD3) and HL in the incidence of anastomotic leakage, postoperative complication rates, and other major intraoperative and postoperative parameters, such as operative time, blood transfusion, conversion from laparoscopic to open surgery, and hospital stay. The median blood loss of LLD3 was significantly lower than that of LLD2 and HL, which might be related to the individual surgeons who performed LLD3 tending to pay more

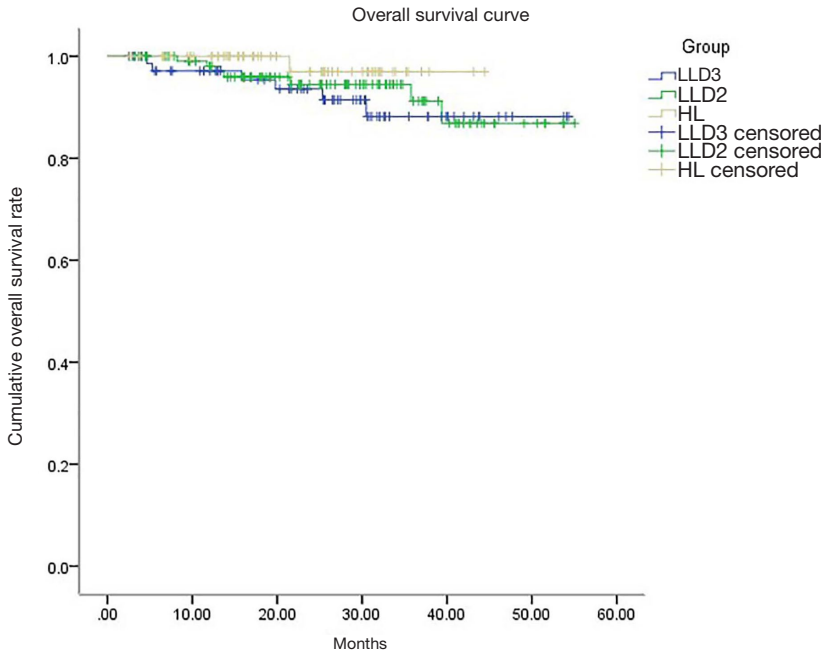

Figure 2 Overall survival curve of these groups.

Table 5 Long-term outcomes

Outcomes	LLD2 (n=113)	LLD3 (n=75)	HL (n=65)	P
Three-year overall survival rate	91.2%	88.2%	97.0%	0.379
Death reason				1.000
All reasons	6	6	1	
Rectal cancer	4	4	1	
Other disease except malignancy	2	2	0	
Three-year disease-free survival rate	84.0%	83.9%	86.1%	0.517
Recurrence				0.800
All sites	13	11	9	
Liver	4	3	1	
Pulmonary	3	3	4	
Local recurrence	0	1	2	
Other	6	4	2	

attention to the details of the operation. Theoretically, HL could free the sigmoid colon. Autopsy studies have shown that HL could result in a colonic intestine that was about 10 cm longer than that with LL (33). Buunen *et al.* found that a tension-free anastomosis was possible in 80% of patients who underwent LL (34). Another main factor for anastomotic leakage is anastomotic blood supply. In patients with Riolan's arterial arch, the IMA and Riolan's arterial arch can both supply blood to the intestine. A small or absent Riolan's arterial arch can decrease colonic blood supply, which is an important cause of ischemic damage in the left colon. In HL, the LCA is not retained and the

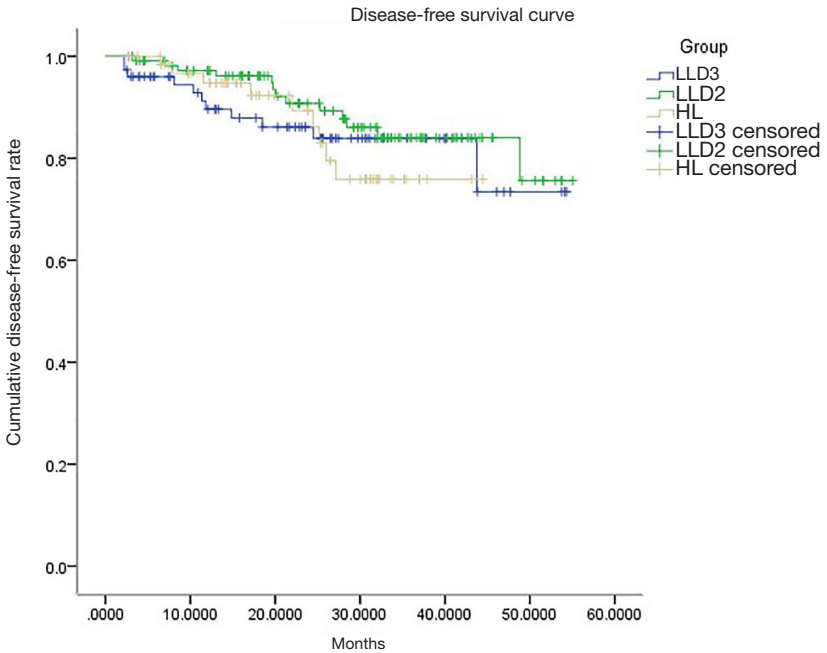

Figure 3 Disease-free survival curve of these groups.

blood supply from the middle colic artery could only reach the splenic flexure of the colon; this leads to insufficient blood supply to the peripheral arteries of the colon distal to the splenic flexure and of the anastomotic region, thereby, leading to intestinal ischemia, which can cause anastomotic leakage and more severe complications, such as intestinal necrosis (35). In patients without a Riolan's arterial arch, HL might reduce the blood supply to the distal colon, causing severe anastomotic leakage; our findings of significantly lower CD grade of anastomotic leakage after LL than after HL, but a similar grade between LLD2 and LLD3, might support this principle. However, multivariate logistic regression analysis revealed that ligation level was not an independent risk factor for anastomotic leakage.

Our study found that the total number of lymph nodes harvested with LLD3 was higher than that with LLD2, but it was not significantly different from that with HL. The total number of lymph nodes harvested tended to be higher with HL than with LLD2. D3 lymph node dissection improved the total number of lymph nodes harvested, and LLD3 achieved lymph node dissection that was similar to that with HL. These results were similar to the results of previous Italian and Japanese RCTs (3,27). Moreover, in this study, the number of 253 lymph nodes detected was higher in the LLD3 group than in the HL group, but the median number of both groups was low. Due to the fact that LLD3 surgery is yet to be popularized, surgeons should pay more attention to the 253 lymph nodes areas during LLD3 surgery, in order to increase the number of 253 lymph nodes detected. Japanese scholars routinely performed LLD3, and the number of 253 lymph nodes cleaned was not significantly different between LL and HL (3); the median number of positive 253 lymph nodes in both groups was 0 and the 253 lymph nodes were in the third station of rectal cancer lymphatic drainage. The median number of total lymph nodes harvested was few, which was related to the skewed distribution of the data and the presence of some patients with therapy. The quality of pathological detection may also affect the total harvested lymph nodes. Similar to our study, one study found that the rates of metastasis to the 253 lymph nodes were 1% for pT1, 1% for pT2, 2.7% for pT3, and 10% for pT4 rectal cancer patients (11). This study showed no significant differences in the R0 resection, 3-year OS, and 3-year DFS rates; cause of death; and location of recurrence among the three groups. Although 253 lymph node dissection improved the total number of lymph nodes harvested, it did not improve the long-term outcomes. Matsuda *et al.* showed no significant differences between HL and LL in the 5-year OS, 5-year DFS, and site of first recurrence; moreover, in group of

patients in clinical stage III, there were no differences in the DFS and OS between HL and LL (36). Mari *et al.* showed no significant difference in the 1-year local recurrence and distant metastasis rates between HL and LL. Yasuda *et al.* found no significant differences in the OS and relapse-free survival between HL and LLD3 (37). Several meta-analyses showed no significant difference in the 5-year OS between HL and LL, but further subgroup analysis of 253 lymph node-positive patients showed superior 5-year survival rate after HL than after LL [hazard ratio (HR): 0.77, 95% CI: 0.66–0.89] (31,32,38). The low rates of detection and metastasis to the 253 lymph nodes may be the reason for the failure to reflect the effect of D3 lymph node dissection in improving the long-term prognosis. If the root lymph nodes are found to be enlarged through preoperative imaging or intraoperative exploration, our team will clean the root lymph nodes.

Our study analyzed the short- and long-term effects of LLD2, LLD3, and HL. Urinary function and quality of life need to be further compared. This study was a single-center study with risk of bias; a multicenter research should to be carried out. Future studies need to explore the benefits of LCA retention in preventing anastomotic leakage in high-risk populations and D3 lymph node dissection for high-risk populations with 253 lymph node metastases.

In conclusion, in postoperative rectal cancer patients, LL was similar to HL in the incidence of anastomotic leakage, other complications, and major intraoperative and postoperative parameters, but it can reduce the severity of anastomotic leakage to a certain extent. D3 lymph node dissection can increase the total number of lymph nodes harvested, but it did not improve long-term prognosis.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/jgo-20-327

Data Sharing Statement: Available at http://dx.doi.org/10.21037/jgo-20-327

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jgo-20-327). The authors have no conflicts of interest to declare.

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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The TNM staging was in accordance with the American Joint Committee on Cancer colorectal cancer TNM staging system (eighth edition, 2017). The study was approved by the Ethics Committee of Chinese People's Liberation Army General Hospital (No. S2020-467-01). Because of the retrospective nature of the research, the requirement for informed consent was waived.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Miles WE. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon (1908). CA Cancer J Clin 1971;21:361-4.
3. Fujii S, Ishibe A, Ota M, et al. Short-term and long-term results of a randomized study comparing high tie and low tie inferior mesenteric artery ligation in laparoscopic rectal anterior resection: subanalysis of the HTLT (High tie vs. low tie) study. Surg Endosc 2019;33:1100-10.
4. Hartley JE, Mehigan BJ, Qureshi AE, et al. Total mesorectal excision: assessment of the laparoscopic approach. Dis Colon Rectum 2001;44:315-21.
5. Morino M, Parini U, Giraudo G, et al. Laparoscopic total mesorectal excision: a consecutive series of 100 patients. Ann Surg 2003;237:335-42.
6. Pikarsky AJ, Rosenthal R, Weiss EG, et al. Laparoscopic

total mesorectal excision. Surg Endosc 2002;16:558-62.
7. Zhou ZG, Hu M, Li Y, et al. Laparoscopic versus open total mesorectal excision with anal sphincter preservation for low rectal cancer. Surg Endosc 2004;18:1211-5.
8. Kim JC, Lee KH, Yu CS, et al. The clinicopathological significance of inferior mesenteric lymph node metastasis in colorectal cancer. Eur J Surg Oncol 2004;30:271-9.
9. Cirocchi R, Trastulli S, Farinella E, et al. High tie versus low tie of the inferior mesenteric artery in colorectal cancer: a RCT is needed. Surg Oncol 2012;21:e111-23.
10. Bleday R, Garcia Aguilar J. Surgical treatment of rectal cancer. In: Wolff BG, Fleshman JW, Beck DE, et al. editors. The ASCRS textbook of colon and rectal surgery. New York: Springer, 2007.
11. Watanabe T, Itabashi M, Shimada Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. Int J Clin Oncol 2015;20:207-39.
12. Huang CW, Yeh YS, Su WC, et al. Robotic surgery with high dissection and low ligation technique for consecutive patients with rectal cancer following preoperative concurrent chemoradiotherapy. Int J Colorectal Dis 2016;31:1169-77.
13. Maeda Y, Shinohara T, Futakawa N, et al. The Oncologic Outcomes of Inferior Mesenteric Artery-Preserving Laparoscopic Lymph Node Dissection for Upper-Rectal or Sigmoid Colon Cancer. J Laparoendosc Adv Surg Tech A 2018;28:1352-8.
14. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? Br J Surg 1982;69:613-6.
15. Martling AL, Holm T, Rutqvist LE, et al. Effect of a surgical training programme on outcome of rectal cancer in the County of Stockholm. Stockholm Colorectal Cancer Study Group, Basingstoke Bowel Cancer Research Project. Lancet 2000;356:93-6.
16. Tanaka J, Nishikawa T, Tanaka T, et al. Analysis of anastomotic leakage after rectal surgery: A case-control study. Ann Med Surg (Lond) 2015;4:183-6.
17. Read TE, Mutch MG, Chang BW, et al. Locoregional recurrence and survival after curative resection of adenocarcinoma of the colon. J Am Coll Surg 2002;195:33-40.
18. Taflampas P, Christodoulakis M, Tsiftsis DD. Anastomotic leakage after low anterior resection for rectal cancer: facts, obscurity, and fiction. Surg Today 2009;39:183-8.
19. Murono K, Kawai K, Kazama S, et al. Anatomy of the inferior mesenteric artery evaluated using 3-dimensional CT angiography. Dis Colon Rectum 2015;58:214-9.
20. van Gulik TM, Schoots I. Anastomosis of Riolan revisited: the meandering mesenteric artery. Arch Surg 2005;140:1225-9.
21. Gourley EJ, Gering SA. The meandering mesenteric artery: a historic review and surgical implications. Dis Colon Rectum 2005;48:996-1000.
22. Cheng BC, Chang S, Huang J, et al. Surgical anatomy of the colic vessels in Chinese and its influence on the operation of esophageal replacement with colon. Zhonghua Yi Xue Za Zhi 2006;86:1453-6.
23. Komen N, Slieker J, de Kort P, et al. High tie versus low tie in rectal surgery: comparison of anastomotic perfusion. Int J Colorectal Dis 2011;26:1075-8. Erratum in: Int J Colorectal Dis. 2011 Jun;26(6):821. Gosselink, Martijn [corrected to Gosselink, Martijn P].
24. Huang J, Zhou J, Wan Y, et al. Influences of inferior mesenteric artery types and Riolan artery arcade absence on the incidence of anastomotic leakage after laparoscopic resection of rectal cancer. Zhonghua Wei Chang Wai Ke Za Zhi 2016;19:1113-8.
25. Shi W, Yu DG. Relationship between the absence of Riolan arterial arch and anastomotic leakage after radical resection of rectal cancer. Journal of Colorectal & Anal Surgery 2017;23:591-4.
26. Trencheva K, Morrissey KP, Wells M, et al. Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. Ann Surg 2013;257:108-13.
27. Mari GM, Crippa J, Cocozza E, et al. Low Ligation of Inferior Mesenteric Artery in Laparoscopic Anterior Resection for Rectal Cancer Reduces Genitourinary Dysfunction: Results From a Randomized Controlled Trial (HIGHLOW Trial). Ann Surg 2019;269:1018-24.
28. Rutegård M, Hassmen N, Hemmingsson O, et al. Anterior Resection for Rectal Cancer and Visceral Blood Flow: An Explorative Study. Scand J Surg 2016;105:78-83.
29. Yamamoto M, Okuda J, Tanaka K, et al. Oncological impact of laparoscopic lymphadenectomy with preservation of the left colic artery for advanced sigmoid and rectosigmoid colon cancer. Dig Surg 2014;31:452-8.
30. Matsuda K, Hotta T, Takifuji K, et al. Randomized clinical trial of defaecatory function after anterior resection for rectal cancer with high versus low ligation of the inferior mesenteric artery. Br J Surg 2015;102:501-8.
31. Guraya SY. Optimum level of inferior mesenteric artery ligation for the left-sided colorectal cancer. Systematic review for high and low ligation continuum. Saudi Med J

2016;37:731-6.
32. Yang Y, Wang G, He J, et al. High tie versus low tie of the inferior mesenteric artery in colorectal cancer: A meta-analysis. Int J Surg 2018;52:20-4.
33. Bonnet S, Berger A, Hentati N, et al. High tie versus low tie vascular ligation of the inferior mesenteric artery in colorectal cancer surgery: impact on the gain in colon length and implications on the feasibility of anastomoses. Dis Colon Rectum 2012;55:515-21.
34. Buunen M, Lange MM, Ditzel M, et al. Level of arterial ligation in total mesorectal excision (TME): an anatomical study. Int J Colorectal Dis 2009;24:1317-20.
35. Lange JF, Komen N, Akkerman G, et al. Riolan's arch: confusing, misnomer, and obsolete. A literature survey of the connection(s) between the superior and inferior mesenteric arteries. Am J Surg 2007;193:742-8.
36. Matsuda K, Yokoyama S, Hotta T, et al. Oncological Outcomes following Rectal Cancer Surgery with High or Low Ligation of the Inferior Mesenteric Artery. Gastrointest Tumors 2017;4:45-52.
37. Yasuda K, Kawai K, Ishihara S, et al. Level of arterial ligation in sigmoid colon and rectal cancer surgery. World J Surg Oncol 2016;14:99.
38. Singh D, Luo J, Liu XT, et al. The long-term survival benefits of high and low ligation of inferior mesenteric artery in colorectal cancer surgery: A review and meta-analysis. Medicine (Baltimore) 2017;96:e8520.

Cite this article as: Hu S, Li S, Huang X, Yan Y, Teng D, Lin H, He C, Gao Z, Wang Y, Du X. The effect of different inferior mesenteric artery ligation levels and different lymph node dissection areas on the short- and long-term outcomes of rectal cancer. J Gastrointest Oncol 2021;12(2):580-591. doi: 10.21037/jgo-20-327

