

High versus low ligation of inferior mesenteric artery during laparoscopic radical resection of rectal cancer

A retrospective cohort study

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Abstract

Laparoscopic radical resection is standard treatment for resectable rectal cancer. However, whether high or low inferior mesenteric artery (IMA) ligation should be performed remains controversial. This retrospective cohort study compared the advantages and disadvantages of low vs high IMA ligation in patients undergoing laparoscopic total mesorectal excision for rectal cancer.

Rectal cancer patients (n=322) undergoing total mesorectal excision at our institution in 2010 to 2017 were enrolled; 174 underwent high IMA ligation group and 148 low IMA ligation (LIMAL group). Baseline data on patients, operative indices, economic indices, pathology findings, perioperative complications, and survival in the 2 groups were analyzed retrospectively.

The low IMA ligation group had significantly higher anus retention ratio ($P=.022$), shorter hospital stay ($P=.025$), lower medical expenses ($P=.032$), fewer cases of anastomotic leakage ($P=.023$) and anastomotic stricture ($P<.001$), and lower incidence of postoperative genitourinary dysfunction ($P=.003$). Cox regression analysis indicated that local recurrence, distant metastasis, tumor differentiation, and tumor-node-metastasis stage were independently associated with survival.

Low ligation of the IMA during laparoscopic radical resection of rectal cancer appears to be associated with a lower risks for anastomotic leakage, anastomotic stricture, and genitourinary dysfunction, a shorter hospital stay, and lower costs. In contrast, the rate of lymph node harvest, tumor recurrence rate, metastasis, or mortality was not found to be related with the level of IMA ligation.

Abbreviations: ASA = American society of anesthesiologists, HIMAL = high inferior mesenteric artery ligation, IMA = inferior mesenteric artery, LIMAL = low inferior mesenteric artery ligation, TME = total mesorectal excision, TNM = tumor-node-metastasis.

Keywords: anastomotic leakage, anastomotic stricture, genitourinary function, inferior mesenteric artery, laparoscopic radical resection, left colonic artery, rectal cancer, total mesorectal excision

1. Introduction

Colorectal cancer is the third most commonly diagnosed cancer in both sexes worldwide, and the third and fourth leading cause

of cancer-related mortality in women and men, respectively.^[1] About 1.4 million new cases of colorectal cancer are diagnosed annually, and about 0.7 million die of colorectal cancer-related causes every year.^[1] Approximately 30% of colorectal cancers are rectal cancers, which are associated with worse clinical outcomes.^[2,3] Although neoadjuvant chemoradiation has a role in advanced rectal cancer, total mesorectal excision (TME)—first described by Heald et al^[4] in 1982—remains the gold standard treatment for rectal cancer.

Laparoscopic intra-abdominal surgery was introduced more than 3 decades ago, and laparoscopic colectomy has been performed since the early 1990s.^[5,6] Compared to open colectomy, laparoscopic colectomy has many advantages.^[7] In addition, patients undergoing laparoscopic colectomy have earlier return of bowel function, with the duration of ileus being about 24 hours less than that in patients undergoing open surgery.^[8,9] Because of these advantages laparoscopic TME has become standard therapy for rectal cancer worldwide. However, some controversies persist about whether the inferior mesenteric artery (IMA) should be ligated at its origin or not.^[10,11] Although high IMA ligation can simplify the operation and increase the extent and yield of lymphadenectomy, it is associated with risk of injury to the superior hypogastric plexus and sympathetic nerves, which may adversely impact distal rectal arterial perfusion and also cause genitourinary dysfunction.^[12,13] Inadequate rectal stump arterial perfusion and increased anastomosis tension may

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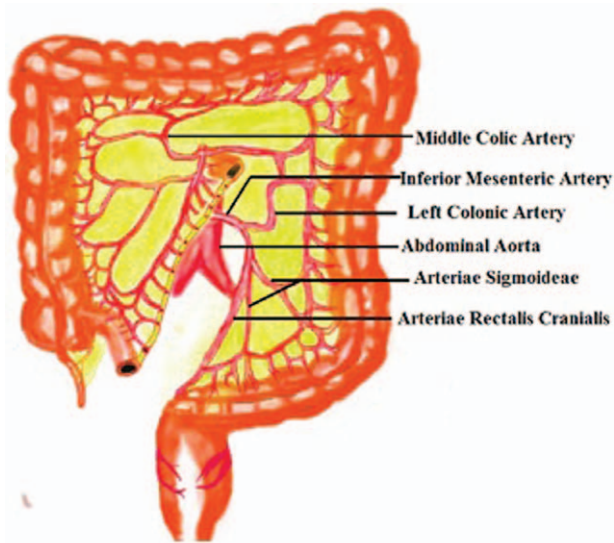


Figure 1. Illustration of mesenteric vessels.

lead to the development of anastomotic leaks and stricture following rectal surgery^[14–16] (illustration of mesenteric vessels is shown in Fig. 1). However, there are scant data in the literature on the association between the level of IMA ligation and the rate of anastomotic leakage, lymph node harvest, or 5-year survival. The aim of this retrospective cohort study was to determine whether low IMA ligation or high IMA ligation is more beneficial in laparoscopic TME for rectal cancer.

2. Methods

2.1. Power calculation and sample size

Before we initiate the full-scale study, we performed a pilot study of 40 patients, 20 in the high inferior mesenteric artery ligation (HIMAL) group and 20 in the low inferior mesenteric artery ligation (LIMAL) group. We found that the rate of anastomotic leak was 10% in the HIMAL group (2/20) and 5% in the LIMAL group (1/20). Based on the results, power and sample size.com/Calculators/ 1-Sample, 2 sided Equality was used to calculate the sample size. We set a cut-off level of significance at $\alpha=0.05$ and a power of $1-\beta=0.80$, and identify the sample size of 282 for this study, minimum sample size for each group was 141. We then included all consecutive eligible cases who underwent laparoscopic radical resection of rectal cancer for the past 8 years. We were able to analyze a total of 322 patients (174 patients in HIMAL group and 148 patients in LIMAL group), which provided a sample size adequate for meaningful statistical analysis.

2.2. Patients

A total of 322 patients undergoing laparoscopic TME between January 2010 and December 2017 at the TaiZhou People's Hospital Affiliated 5 to Nantong University were enrolled in this retrospective cohort study. Due to surgeon preference, 174 patients were selected for HIMAL before October 2013, and 148 patients were selected for LIMAL since October 2013.

Patients were eligible for inclusion if

- (1) pathologic diagnosis of adenocarcinoma had been confirmed with preoperative colonoscopy and biopsy;
- (2) the tumor was situated <10cm from the anal verge;
- (3) treatment was with laparoscopic TME;
- (4) no distant metastases were present prior to surgery; and
- (5) complete clinicopathological and follow-up data were available.

Patients were excluded from the study if

- (1) radical resection had not been performed because of local invasion;
- (2) other synchronous malignancy or serious disease was present; or
- (3) surgery had been performed as an emergency procedure because of tumor bleeding, perforation, or obstruction.

The study protocol was in accordance with the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of TaiZhou People's Hospital (TZRY-CR-18-0016). The need for obtaining informed consent was waived because of the retrospective nature of the study.

2.3. Preoperative preparation

Enhanced MRI or CT scan of the abdomen and pelvis was performed for preoperative staging and exclusion of distant metastasis. All patients underwent chest radiography, cardiac ultrasonography, lung function testing, electrocardiogram, and other examinations to exclude surgical contraindications. Preoperatively, patients received only fluids for 24 hours before surgery. Bowel preparation was with 2000 mL of 6.8% polyethylene glycol-electrolyte solution.

2.4. Surgical procedure

All patients were operated on by the same team of experienced surgeons. After general anesthesia and tracheal intubation, the patient was placed in the bladder lithotomy position, with the head end lowered by 20° to 30° and the body inclined 15° to 20° to the right. The 5-trocar technique was adopted for laparoscopy. The umbilical foramen was used as the observation port. The lower right 10-mm hole was used as the main operating hole, and the right upper 5-mm hole and the 2 left 5-mm holes were used as assistant working ports. Pneumoperitoneum was established and maintained at a pressure of 11 to 15 mm Hg. Through the middle approach, the sigmoid mesentery was incised using an ultrasound knife, and the Toldt space was entered. The left retroperitoneal space was expanded and a separate presacral space was created along the surface of the submesenteric plexus; the hypogastric nerves, the genitofemoral nerve, the left ureter, the common iliac veins, and the gonadal vessels were identified and preserved. The peritoneum was incised toward the duodenojejunal angle (Treitz) until the root of the mesentery which was located 1 cm below the lower edge of the pancreas. The inferior mesenteric vessels were then exposed easily. In the HIMAL group, the IMA was ligated and amputated 1 cm from its origin, and the inferior mesenteric vein was ligated and amputated below the pancreatic margin (Fig. 2). In the LIMAL group, incision of the peritoneum was extended upward to expose the root of the IMA. Lymphadenectomy was performed as far as the origin of IMA. The left colic artery was identified and preserved. Then the IMA was ligated and amputated lowly (Fig. 3). In both groups, the left part of transverse mesocolon was divided and the left part of the

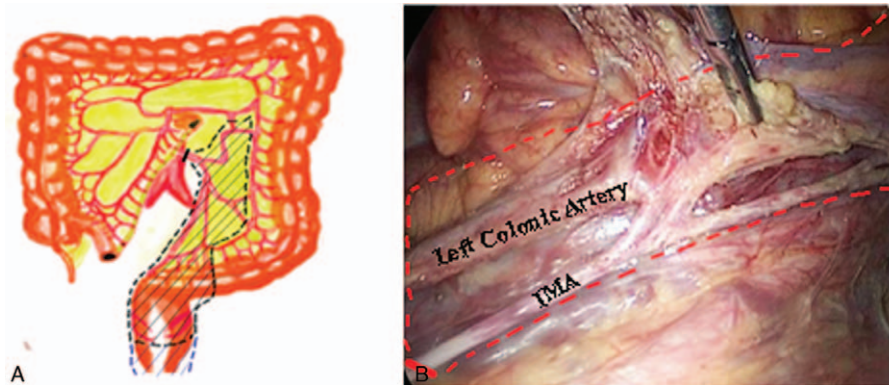


Figure 2. High ligation, the IMA was ligated 1 cm from its origin and dissection the inferior mesenteric lymph nodes as D3. A. Illustration of surgical resection range. B. Laparoscopy displays the amputation of vessels and area of mesenteric. IMA = inferior mesenteric artery.

gastrocolic ligament was opened, thus dissecting free the left colonic angle completely. Dissection was then continued up to the level of the levator ani muscle.

In both groups, the TME technique was the same, with care being taken to achieve complete removal of the tumor. The common principle was to achieve sharp separation in the membrane space and minimal or no blood loss. The rectal proper fascia of the excised specimen was <5 cm, and resection of intestinal tube was at least 2 cm from the distal end of the tumor. The aim was to have a smooth pelvic wall wound and excision of the rectal proper fascia without creation of a coloboma.

2.5. Adjunctive therapy and follow-up

All patients with pathological stage II and above received 6 months of XELOX (capecitabine plus oxaliplatin) postoperatively. Those with T4b stage received, in addition, pelvic radiotherapy. First follow-up was at 3 months after surgery via telephone interview or clinic visit. All patients were followed up regularly up to February 28th 2018. The mean follow-up duration was 39.4 ± 24.5 months (range: 2.066–94.433 months).

2.6. Preoperative and postoperative data

Data were collected on baseline characteristics (age, gender, body mass index [BMI], American Society of Anesthesiologists (ASA)

score, distance from anal verge); surgical indices (surgery duration, intraoperative blood loss, number of lymph nodes harvested, proximal margin, distal margin, bowel function recovery time, anus retention ratio); economic factors (hospitalization days, medical expenses); pathology findings (mean size of tumor, tumor-node-metastasis (TNM) stage, histology stage); perioperative complications (anastomotic leakage, anastomotic stricture, genitourinary dysfunction, local recurrence, metastasis); and postoperative survival (overall survival and survival of patients with different stages). Univariate and multivariate analysis were used to identify the factors associated with survival.

2.7. Statistical analysis

SPSS 16.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. Categorical variables were summarized as percentages and compared using the chi-square test. Continuous variables were summarized as means (\pm standard error) and compared between groups using Student *t* test. Correlations were assessed by the nonparametric Spearman rank correlation method. Survival analysis was performed using the Kaplan-Meier method, and the log-rank test was applied to analyze the differences between groups. Univariate analysis was performed to identify the variables associated with prognosis. Cox regression analysis was used to identify the independent predictors of prognosis in

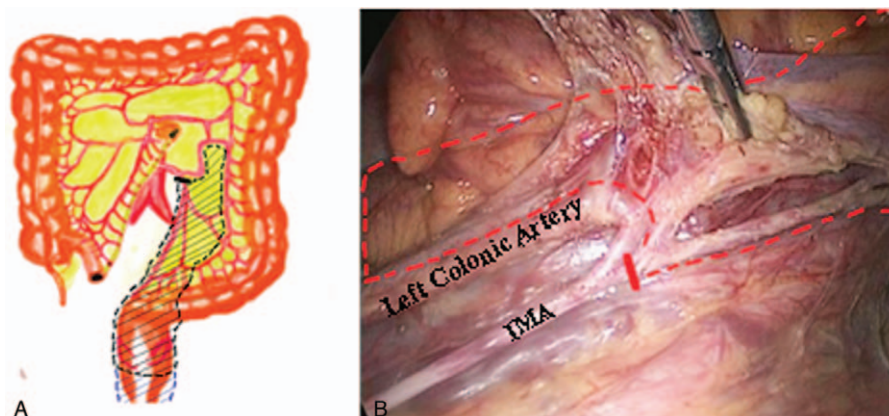


Figure 3. Low ligation, the IMA was ligated identified and preserved the left colic artery, and dissection the inferior mesenteric lymph nodes as D3. A. Illustration of surgical resection range. B. Laparoscopy displays the amputation of vessels and area of mesenteric. IMA = inferior mesenteric artery.

rectal cancer patients. $P \leq .05$ was considered statistically significant.

3. Results

3.1. Patients

A total of 322 patients were enrolled in the study: 174 in the HIMAL group and 148 in the LIMAL group. Of the 174 patients in the HIMAL group 117 were males and 57 females. Mean age was 57.20 ± 10.54 years. BMI was ≥ 25 in 127 patients and < 25 in 47 patients. ASA score was I-II in 154 patients and III in 20 patients. Distance of the cancer from the anal verge was ≥ 5 cm in 123 patients and < 5 cm in 51 patients. 80 patients had preoperative neoadjuvant chemotherapy or radiotherapy. Of the 148 patients in the LIMAL group 98 were males and 50 females. Mean age was 58.10 ± 10.78 years. BMI was ≥ 25 in 97 patients and < 25 in 51 patients. ASA score was I-II in 133 patients and III in 15 patients. Distance of the cancer from the anal verge was ≥ 5 cm in 96 patients and < 5 cm in 52 patients. Seventy-one patients had preoperative neoadjuvant chemotherapy or radiotherapy. Gender composition, age, BMI, ASA score, distance from anal verge, and preoperative neoadjuvant chemotherapy or radiotherapy were all comparable between the 2 groups (all $P > .05$; Table 1).

3.2. Comparison of surgical and economic indices between HIMAL and LIMAL

Operation time, intraoperative blood loss, mean number of lymph nodes harvested, Sample length of proximal and distal margins, and bowel function recovery time were not significantly different between the groups. However, hospital stay (14.32 ± 6.80 days vs 16.77 ± 11.95 days; $P = .025$) and medical costs (38140 ± 16620 vs 42390 ± 23220 RMB; $P = .032$) were significantly lower in LIMAL than in HIMAL. The anus retention ratio in those with lower rectal cancer was significantly higher in the LIMAL group than in the HIMAL group (40.385% [21/52] vs 19.608% [10/51]; $P = .022$). The details are presented in Table 2.

Table 1
Baseline characteristics of patients in the 2 groups.

	HIMAL group (n=174)	LIMAL group (n=148)	P
Gender			.85
Male, n (%)	117 (67.24)	98 (66.22)	
Female, n (%)	57 (32.76)	50 (33.78)	
Age, yr	57.19 ± 10.54	58.10 ± 10.78	.44
BMI			.15
< 25 , n (%)	47 (27.01)	51 (34.46)	
≥ 25 , n (%)	127 (72.99)	97 (65.54)	
ASA			.70
I-II, n (%)	154 (88.51)	133 (89.87)	
III, n (%)	20 (11.49)	15 (10.13)	
Distance of cancer from anal verge			.26
< 5 cm	51 (29.31)	52 (35.13)	
≥ 5 cm	123 (70.69)	96 (64.87)	
Preoperative neoadjuvant chemotherapy or radiotherapy			.72
Yes	80 (45.98)	71 (47.97)	
No	94 (54.02)	77 (52.38)	

ASA=American Society of Anesthesiologists, BMI=body mass index, HIMAL=high inferior mesenteric artery ligation, LIMAL=low inferior mesenteric artery ligation.

Table 2
Surgical and economic indices in the 2 groups.

	HIMAL group (n=174)	LIMAL group (n=148)	P
Surgery duration, min	167.53 ± 12.56	166.51 ± 11.48	.45
Intraoperative blood loss, mL	31.82 ± 13.96	30.52 ± 6.54	.30
Lymph nodes harvested, n	16.02 ± 2.12	15.63 ± 2.63	.16
Proximal margin, cm	15.96 ± 2.36	16.33 ± 1.79	.11
Distal margin, cm	3.85 ± 0.80	3.81 ± 0.67	.69
Bowel function recovery time, h	35.95 ± 8.05	35.92 ± 4.33	.97
Hospital stay, d	16.77 ± 11.95	14.32 ± 6.80	.03
Medical costs, RMB	42390 ± 23220	38140 ± 16620	.03
Anus retention ratio	19.61% (10/51)	40.39% (21/52)	.02

HIMAL=high inferior mesenteric artery ligation, LIMAL=low inferior mesenteric artery ligation.

3.3. Pathology findings

Tumor diameter, tumor differentiation, and tumor TNM stages were not significantly different between the groups (Table 3).

3.4. Perioperative complications and postoperative survival

There were no perioperative deaths. Anastomotic leakage was significantly more common in HIMAL than in LIMAL (17 vs 5; $P = .023$). At colonoscopy, performed 6 months after surgery, anastomotic stricture was significantly more common in HIMAL than in LIMAL (24 patients vs 4 patients; $P < .001$). In the HIMAL group, closure of prophylactic enterostomy could not be performed in 3 patients because of serious stricture of the anastomosis. Another 9 patients required fan-shaped incision of the anastomotic stricture by the insulation-tipped diathermic knife. In the LIMAL group none of the cases of stricture were serious. Spearman correlation analysis showed significant positive correlation between anastomotic leakage and anastomotic stricture ($R = 0.629$; $P < .001$, Fig. 4A). Postoperative genitourinary dysfunction—assessed 3 months after surgery using the International Index of Erectile Function -5 questionnaire^[17]—was significantly more common in HIMAL than in the LIMAL patients (29 vs 9; $P = .003$).

Mean follow-up was for 39.4 ± 24.5 months. In the HIMAL group, 10 patients had local recurrence, 42 patients developed distant metastasis, and 40 patients died of cancer-related causes.

Table 3
Pathology findings.

	HIMAL group (n=174)	LIMAL group (n=148)	P
Tumor diameter, cm	2.85 ± 0.84	2.78 ± 1.08	.48
Differentiation			.13
Well-to-moderately differentiated, n (%)	122 (70.11)	103 (69.59)	
Poorly differentiated, n (%)	42 (24.14)	28 (18.92)	
Mucinous cancer, n (%)	10 (5.75)	17 (11.49)	
TNM stage			.54
0, n (%)	1 (0.58)	2 (1.35)	
I, n (%)	38 (21.84)	28 (18.92)	
II, n (%)	77 (44.25)	59 (39.87)	
III, n (%)	58 (33.33)	59 (39.86)	

HIMAL=high inferior mesenteric artery ligation, LIMAL=low inferior mesenteric artery ligation, TNM=tumor-node-metastasis.

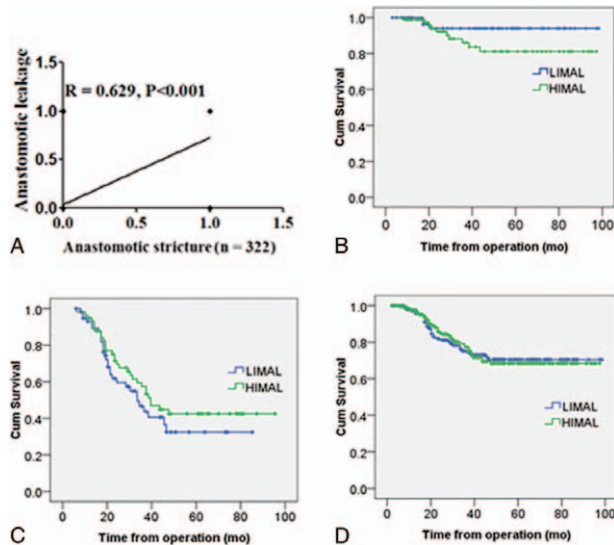


Figure 4. A: Positive correlation of anastomotic stricture with anastomotic leakage. B-D: Postoperative survival in different TNM stage subgroups in HIMAL and LIMAL. B: Stage II; C: Stage III; D: Overall survival for both groups. LIMAL=low inferior mesenteric artery ligation, HIMAL=high inferior mesenteric artery ligation, TNM=tumor-node-metastasis.

In the LIMAL group, 9 patients had local recurrence, 36 patients developed distant metastasis, and 34 patients died of cancer-related causes. The differences in recurrence rate and metastasis rate were not significantly different ($P=.899$ and $P=.969$, respectively).

Overall survival and survival in patients with different TNM stages were comparable in the two groups. Table 4 and Figure 4 B-C show the details.

3.5. Factors associated with survival of patients with rectal cancer

On univariate analysis, distance of the cancer from the anal verge, the sample length of distal margin, tumor size, local recurrence, distant metastasis, degree of differentiation, and TNM stage were significantly associated with survival (Table 5). On Cox regression analysis, local recurrence, distant metastasis, degree of differentiation, and TNM stage were independently associated with survival of patients with rectal cancer (Table 6).

Table 4
Perioperative complications and postoperative survival.

	HIMAL group, n (%)	LIMAL group, n (%)	P
Anastomotic leakage, n (%)	17/174 (9.77)	5/148 (3.38)	.02
Anastomotic stricture, n (%)	24/174 (13.79)	4/148 (2.70)	<.01
Genitourinary dysfunction, n (%)	29/174 (16.67)	9/148 (6.08)	.003
Local recurrence, n (%)	10/174 (5.75)	9/148 (6.08)	.90
Metastasis, n (%)	42/174 (24.14)	36/148 (24.32)	.97
Overall survival, n (%)	7134/174 (7.01)	114/148 (77.02)	.98
Stage I survival, n (%)	38/38 (100)	27/28 (96.43)	.24
Stage II survival, n (%)	67/77 (87.01)	56/59 (94.92)	.12
Stage III survival, n (%)	28/58 (48.28)	29/59 (49.15)	.92

HIMAL=high inferior mesenteric artery ligation, LIMAL=low inferior mesenteric artery ligation, TNM=tumor-node-metastasis.

Table 5
Univariate analysis showing variables associated with survival of rectal cancer patients.

	Died (n=74)	Survived (n=248)	P
Gender			.66
Male, n (%)	51 (68.92)	164 (66.13)	
Female, n (%)	23 (31.08)	84 (33.87)	
Age, yr	57.19±11.38	57.73±10.44	.70
BMI			.67
<25, n (%)	24 (32.43)	74 (29.84)	
≥25, n (%)	50 (67.57)	174 (70.16)	
ASA			.68
I-II, n (%)	65 (87.84)	222 (89.52)	
III, n (%)	9 (12.16)	26 (10.48)	
Distance from anal verge			.04
<5cm, n (%)	31 (41.89)	72 (29.03)	
≥5cm, n (%)	43 (58.11)	176 (70.97)	
Surgery duration, min	166.59±12.33	167.21±12.01	.70
Intraoperative blood loss, mL	30.39±6.22	31.47±12.28	.47
Lymph nodes harvested, n	15.81±2.54	16.15±2.07	.77
Proximal margin,cm	16.07±2.29	16.33±1.79	.11
Distal margin,cm	3.62±0.80	3.90±0.73	.01
Bowel function recovery time, h	36.55±7.45	35.75±6.33	.36
Mean hospitalization d	17.43±12.08	15.076±9.22	.08
Mean medical costs,RMB	44950±24900	39470±18950	.08
Tumor diameter, cm	3.60±0.84	2.59±0.87	<.01
Differentiation			<.01
Well-to-moderately differentiated, n (%)	30 (40.54)	195 (78.63)	
Poorly differentiated, n (%)	24 (32.43)	46 (18.55)	
Mucinous cancer, n (%)	20 (27.03)	7 (2.82)	
TNM stage			<.01
0, n (%)	0	3 (1.21)	
I, n (%)	1 (1.35)	65 (26.21)	
II, n (%)	13 (17.57)	123 (49.60)	
III, n (%)	60 (81.08)	57 (22.98)	
Local recurrence, n (%)	16 (21.66)	3 (1.21)	<.01
Metastasis, n (%)	74 (100.00)	4 (1.61)	<.01
HIMAL vs LIMAL			.997
HIMAL, n (%)	40 (54.05)	134 (54.03)	
LIMAL, n (%)	34 (45.95)	114 (45.97)	

HIMAL=high inferior mesenteric artery Ligation, LIMAL=low inferior mesenteric artery ligation, TNM=tumor-node-metastasis.

4. Discussion

Although laparoscopically assisted TME is widely applied for radical resection of rectal cancer, the ideal level for IMA ligation is still controversial.^[11] Previous studies have reported that the low ligation of the IMA appears to be safe and feasible during traditional TME.^[18] This study, we compared advantages and disadvantages of the low and high IMA ligations during laparoscopic TME for patients with rectal cancer. Compared with HIMAL, LIMAL makes dissection and preservation of the left colon artery, which requires greater technical expertise of the surgeons. While HIMAL makes resection and lymphadenectomy easier, the approach increases the risk of injury to the superior hypogastric plexus and sympathetic nerves, which may adversely affect distal colonic arterial perfusion and genitourinary function.^[12] Insufficient blood supply to the colonic stump is a major factor associated with anastomotic leaks after rectal surgery.^[14] Low ligation of the IMA may ensure better blood supply to the anastomosis.^[19]

Table 6
Cox regression analysis showing variables independently associated with survival of rectal cancer patients.

	B	SE	Wald	sig	Exp (B)	95.0% CI for Exp (B)	
						Lower	Upper
TNM stage	1.303	0.309	17.796	0.00	3.681	2.009	6.745
Recurrence	1.606	0.407	15.555	0.00	4.980	2.243	11.061
Metastasis	1.906	0.332	32.973	0.00	6.726	3.509	12.892
Differentiation	0.717	0.174	17.027	0.00	2.048	1.457	2.879

TNM = tumor-node-metastasis.

Anastomotic leakage is an important index of the success of gastrointestinal surgery. According to previous reports, the incidence of anastomotic leakage after rectal cancer surgery is in the range of 3.2% to 11.6%.^[20,21] However, low ligation of the IMA has been shown to significantly reduce incidence of anastomotic leakage.^[22,23] In our sample postoperative anastomotic leakage of varying degrees occurred in 22/322 (6.83%) patients, which is similar to the previous reports. A Randomized clinical trial shown that the level of ligation of the IMA during anterior resection for rectal cancer with open or laparoscopic surgical approach did not influence the rate of anastomotic leakage.^[24] However, our study found anastomotic leakage to be significantly more common in HIMAL patients than in LIMAL patients ($P = .023$). When the IMA was ligated at the root, the left colonic artery is also cut off. The blood supply to the proximal part of the anastomosis is from the marginal artery of the middle colic artery (Fig. 1). However, this supply is not always adequate, especially in patients with degenerative disease of microvascular. In some patients, the marginal artery between the middle colic artery and the left colon artery may even be absent. Insufficient blood supply to the anastomotic stoma affects its healing and is a key cause of anastomotic leakage. Hence, when this blood supply is inadequate, a more extended intestinal resection should be performed, even it is oncologically unnecessary. However, extensive intestinal resection is bound to increase the tension of the anastomosis, which may itself increase the risk of anastomotic leakage.

The incidence of anastomotic stricture is another index for evaluating the success of gastrointestinal surgery. Under endoscopy, anastomotic stricture is diagnosed when the diameter of anastomotic stoma is <12 mm.^[25] In the present study 27 patients had anastomosis stricture at review 6 months after operation, with significantly more cases occurring in the HIMAL group. Anastomotic stricture was also positively correlated with anastomotic leakage ($R=0.629$; $P < .001$), which may indicate that anastomotic leakage is an important cause of anastomotic stricture.

The intestinal tract is made up of stromal cells, epithelial cells, and immune cells, and contains massive amounts of microbial organisms.^[26] Complex host-microbial cells interactions underlie the development of stricture after anastomotic leakage.^[27] Guyton KL et al^[27] also reported that ischemia, an increased anastomotic tension, and the use of circular or narrow-diameter staplers were causes of anastomotic strictures. In our study, the anastomotic stricture rate was significantly higher in HIMAL patients than in LIMAL patients ($P < .001$), which supports the theory that ligation of the IMA at its origin decreases blood supply and increases tension at the rectal anastomosis and thus increases the risk of anastomotic stricture.

Postoperative genitourinary dysfunction may occur when there is injury to the superior hypogastric nerve plexus.^[12] The

introduction of TME and autonomic nerve-sparing techniques has decreased the incidence of genitourinary dysfunction after rectal surgery.^[28] In our study postoperative genitourinary dysfunction was significantly lower in the LIMAL group ($P = .003$), which suggests that ligation of the IMA far from the hypogastric plexus helps preserve pelvic autonomic functions and thereby contributes to better postoperative quality of life.

TNM stage is the gold standard for assessing prognosis in colorectal cancer,^[29–32] and therefore thorough lymph node dissection is essential for accurate staging. The thoroughness of lymph node dissection is also an index of the success of radical surgery. Mohammed A et al^[33] compared high and low IMA ligation in a large number of patients with rectal cancer and found that high IMA ligation did not seem to increase the number of total harvested lymph nodes. Our study also found that there was no significant difference between HIMAL and LIMAL patients in the mean number of harvested lymph nodes. Extending lymphadenectomy to the origin of the IMA in LIMAL will provide information on apical node involvement.

In a cadaveric study Bonnet et al^[34] found that low ligation of the IMA can provide additional colonic length. In practice, we have found that preservation of the left colonic artery and cutting the left colonic mesentery along the marginal vessels can extend the length of mesentery from 10 cm to nearly 40 cm. The blood supply to the proximal colon is more abundant when the left colonic artery is preserved, and allows more of the proximal colon to be retained; this helps make the anastomosis tension free. The availability of sufficient length of colon increases the success rate of anastomosis during ultra-low anterior rectal resection. In the present study, among those with lower rectal cancer, the anus retention ratio was higher in patients undergoing LIMAL.

While some authors have reported that high ligation provides a survival benefit in selected subgroups of rectal cancer patients,^[35] this has not been consistently demonstrated.^[24,33] In our study also there were no differences between the HIMAL and LIMAL patients in recurrence and metastasis rates or in mortality (either overall mortality or mortality in different TNM stage subgroups). Both univariate and Cox regression analyses did not show the association between the level of IMA ligation the survival of patients with rectal cancer. The findings of our current study are consistent with previous results obtained by other type of surgery.^[36] However, mean duration of hospitalization and the medical expenses were significantly lower in LIMAL than in HIMAL (all $P < .05$). Detailed analysis showed that anastomotic leakage was primarily responsible for extended hospitalization and increased costs in HIMAL patients.

5. Conclusions

Low ligation of IMA during laparoscopic radical resection for rectal cancer appears to be associated with lower risks of

anastomotic leakage, anastomotic stricture, and genitourinary dysfunction. Duration of hospital stay and medical costs were significantly lower in patients undergoing low IMA ligation. Meanwhile, lymph nodes harvest, recurrence rate, metastasis rate, and mortality were not associated with the level of IMA ligation.

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