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Comparison between High and Low Binding of the Inferior Mesenteric Artery in Mesorectal Excision of Rectal Tumor

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ABSTRACT

Background: Colorectal tumor is one of the most common tumors in both men and women worldwide. However, whether high or low inferior mesenteric artery (IMA) ligation should be performed in the laparoscopic resection of resectable rectal tumor remains controversial.

Objectives: The aim of the work was to compare low vs high IMA binding in patients undergoing laparoscopic mesorectal excision for rectal tumor.

Patients and methods: This retrospective archived-based data study included a total of 161 patients with rectal tumor who were eligible for total mesorectal excision, attending at Al-Azhar University Hospitals. This study was conducted between 2010, and 2017. The high IMA binding (HIMAB) was conducted for 87 patients and low IMA binding (LIMAB) was conducted for 74 patients. Baseline data were retrospectively analyzed for patients in both groups.

Results: The LIMAB group showed more high anus retention ratio (P = 0.022), more brief hospital stay (P = 0.025), less medical costs (P = 0.032), lower anastomotic leakage (P = 0.023), and lower frequency of postoperative genitourinary dysfunction (P = 0.003) when compared with HIMAB group. Analysis of the Cox regression showed local recurrence, distant metastases, tumor differentials.

Conclusion: It could be concluded that laparoscopic radical rectal cancer resection with low IMA binding tends to be correlated with reduced anastomotic leakage risk, anastomotic stringency risk, the risk of instability of the genitourinary system, less time of hospitalization, and decreased costs. By comparison, it was found that the rate of excised lymph node, tumor recurrence, metastasis, or mortality was not associated with the level of IMA binding.

Keyword: Binding of inferior mesenteric artery; Rectal tumor; Mesorectal excision.

INTRODUCTION

Colorectal tumor is one of the most common tumors in both men and women worldwide and the third to fourth cause that lead to tumor-associated mortality[1]. 1.4 million cases were reported annually with high mortality up to 0.7 million per year [1]. Moreover, around 30 % of patients with colorectal tumor develop complications[2,3]. Despite the positive results of neoadjuvant chemoradiotherapy, total mesorectal excision (TME), is considered the best choice for management of rectal tumor[4].

In comparison with open colectomy, laparoscopic colectomy, that was implemented since the early 1990s, showed many advantages[5-7]. Moreover, the bowel function of patients, for them laparoscopic colectomy was conducted, was returned early, with the time of ileus return 24 hours prior patients underwent open surgery[8,9]. Therefore, the laparoscopic TME was considered the best choice for treatment of rectal tumor. However, there are debates regarding the site of inferior mesenteric artery (IMA) binding (whether on the origin or not) [10,11]. Despite high IMA binding is simpler and could increase the extent of lymphadenectomy, the risk of injury of the superior hypogastric plexus in addition to the sympathetic nerves is increased. This may cause genitourinary dysfunction and adversely affect distal rectal arterial perfusion[12,13]. Furthermore, inappropriate stump of the rectal arterial perfusion and the anastomotic tension could lead to the development of anastomotic leakage or anastomotic stricture[14–16].

However, few studies have discussed the association between the IMA binding level and the anastomotic leakage, lymph node affection, or 5-year survival.

The aim of the current work was to compare low vs high IMA binding in patients undergoing laparoscopic mesorectal excision for rectal tumor.

PATIENTS AND METHODS

This retrospective archived-based data study included a total of 161 patients with rectal tumor who were eligible for total mesorectal excision, attending at Al-Azhar University Hospitals. This study was conducted between 2010, and 2017.

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Ethical approval

This study was conducted in accordance with the declaration of Helsinki **and approval was obtained from the Clinical Research Ethics Committee of Faculty of Medicine, Al-Azhar University.** The informed consent wan not applicable as the study is retrospective archived-based data.

Inclusion criteria:

Patients with adenocarcinoma that was pathologically confirmed through preoperative biopsy, patients with tumor less than 10 cm above the anal verge, patients with laparoscopic TME as the operation of choice, patients without distant metastases prior the surgery, and patients with available follow-up data.

Exclusion criteria:

Patients with other malignancies or serious diseases, patients with local invasion that not eligible for radical resection, patients with bleeding at their tumor, patients with perforation or obstruction and the operation was conducted emergently.

The included 161 patients with rectal tumor were divided into two groups;

Group 1 (HIMAB**)** consisted of 87 patients,

Group 2 (LIMAB**)** consisted of 74 patients.

Preoperative preparation

Enhanced abdomen and pelvis MRI and CT scan were conducted for preoperative staging and to rule out the presence of metastasis. Chest X-ray, cardiac ultrasonography, respiratory function tests, electrocardiogram, in addition to other investigations were conducted to exclude any surgical contraindication. Furthermore, patients drink only fluids for one day prior to the surgery. Powel preparation was performed through drinking 2000 mL of polyethylene glycol-electrolyte 6.8%.

Surgical procedure

The same surgical team executed both procedures. Following the general anesthesia, operable patient was in the lithotomy position. Pneumoperitoneum was continued at 11-15 mm Hg as a pressure. After the incision of sigmoid mesentery, the Toldt space was entered then a separate presacral space was created along the submesenteric plexus. At this point, the deep left pelvic nerves and vessels in addition to the lest ureter were clearly identified and preserved. Then, the incision in the peritoneum was conducted at the Treitz angle to let the inferior mesenteric vessels appear.

Having the HIMAB group, the binding and amputation of IMA was conducted one cm from its origin, while the binding and amputation of the inferior mesenteric vein was conducted below the pancreatic margin. Regarding the LIMAB group, the root of the IMA was appeared, and lymphadenectomy was conducted till the origin of IMA. Then, after the preservation of the left colic artery, the binding and amputation of the IMA was performed lowly.

After either up or down binding, the left part of transverse mesocolon was divided to open the gastrocolic ligament. Then, the left colonic angle was dissected up to the level of the levator ani muscle. Then, TME was conducted to remove the tumor completely at least two cm from it.

Adjunctive therapy and follow-up

Adjuvant chemotherapy of XELOX (capecitabine plus oxaliplatin) for six months was conducted postoperatively for the patients having stage II or more. In addition, radiotherapy was conducted for patients having T4b stage. The follow up was conducted regularly starting three months after the surgery for mean duration 39.4 ± 24.5 months.

Preoperative and postoperative data

After collection the demographic characteristic data, surgical indices like; surgery duration, excised lymph nodes, intraoperative blood loss, proximal margin, the recovery time of the powel function, distal margin, and anus retention ratio were gathered from the archived data. Moreover, the economic factors, duration of hospitalization and the hospital expenses, as well as the pathological findings, tumor size, histological stage, and tumor-node-metastasis (TNM) staging, were gathered. The perioperative complications, postoperative complications in addition to the survival were also assessed.

Statistical analysis

Data analysis was executed via SPSS software version 22. Continuous data was presented by means and standard deviation (SD), while categorical data was represented by percentages.

The comparison of continuous data was executed using student t test, while the categorical data was compared using chi-square test. The correlation analysis was conducted using Spearman correlation, while Kaplan-Meier curve was executed for the survival analysis. Furthermore, univariate analysis was executed with the level of significance was set when $P \leq 0.05$.

RESULTS

Included patients

Throughout the study period, we included 161 patients. Among them, 87 were in the HIMAB group and 74 were in the LIMAB group. The mean age of the patients in the HIMAB group was 57.20 ± 10.54 years, and 58 patients in this group were males. Furthermore, most patients had BMI 25 kg/m^2 or more, and the majority of patients reported ASA score between I and II. Among the HIMAB group, the tumor was distant from the anal verge by 5 cm or more in majority of the patients and only 26 patients reported their tumor less than 5 cm from the anal verge. Among the same group, neoadjuvant chemo- or radiotherapy was executed for 40 patients. On the other hand, the mean age of patients in the LIMAB group was 58.10 ± 10.78 years, and 49 of the patients in it were males. Similarly, the majority of patients had BMI 25 or more, and the majority of patients reported ASA score between I and II. Furthermore, the tumor was distant from the anal verge by 5 cm or more in majority of the patients and only 26 patients reported their tumor less than 5 cm from the anal verge. Among the same group, neoadjuvant chemo- or radiotherapy was executed for 36 patients. There was np difference between the two groups regarding the demographic characteristics (Table 1).

Table 1: Baseline demographic characteristics of patients in the two groups

	HIMAB group (n= 87)	LIMAB group (n= 74)	*P*
Gender			0.85
Male, n (%)	59 (67.24)	49 (66.22)	
Female, n (%)	28 (32.76)	25 (33.78)	
Age, years	57.19 ± 10.54	58.10 ± 10.78	0.44
BMI (kg/m^2)			0.15
<25, n (%)	24 (27.01)	25 (34.46)	
≥25, n (%)	63 (72.99)	49 (65.54)	
ASA			0.70
I-II, n (%)	77 (88.51)	67 (89.87)	
III, n (%)	10 (11.49)	7 (10.13)	
Distance of cancer from anal verge			0.26
<5 cm	25 (29.31)	26 (35.13)	
≥5cm Preoperative neoadjuvant	62 (70.69)	48 (64.87)	
Abbreviation; ASA = American Society of Anesthesiologists, HIMAB = high inferior mesenteric artery binding, BMI = body mass index, LIMAB= low inferior mesenteric artery binding.			

Surgical and economic outcomes

The anus retention ratio was significantly higher in the LIMAB group (P = 0.022). Moreover, the duration of the hospital stay and the operation cost was significantly lower in the LIMAB group (P = 0.025 and P = 0.032, respectively). Otherwise, there was no difference between the two groups regarding other variables (Tables 2 and 3) .

Table 2: The surgical and economic outcomes.

	HIMAB group (n= 174)	LIMAB group (n= 148)	*P*
Surgery duration, min	167.53 ± 12.56	166.51 ± 11.48	0.45
Intraoperative blood loss, mL	31.82 ± 13.96	30.52 ± 6.54	0.30
Lymph nodes harvested, n	16.02 ± 2.12	15.63 ± 2.63	0.16
Proximal margin, cm	15.96 ± 2.36	16.33 ± 1.79	0.11
Distal margin, cm	3.85 ± 0.80	3.81 ± 0.67	0.69
Bowel function recovery time, h	35.95 ± 8.05	35.92 ± 4.33	0.97
Hospital stay, d	16.77 ± 11.95	14.32 ± 6.80	0.03
Medical costs, EP	42390 ± 23220	38140 ± 16620	0.03
Anus retention ratio	19.61%	40.39%	0.02
Abbreviations; HIMAB = high inferior mesenteric artery binding, LIMAB = low inferior mesenteric artery binding.			

Table 3: The pathology findings

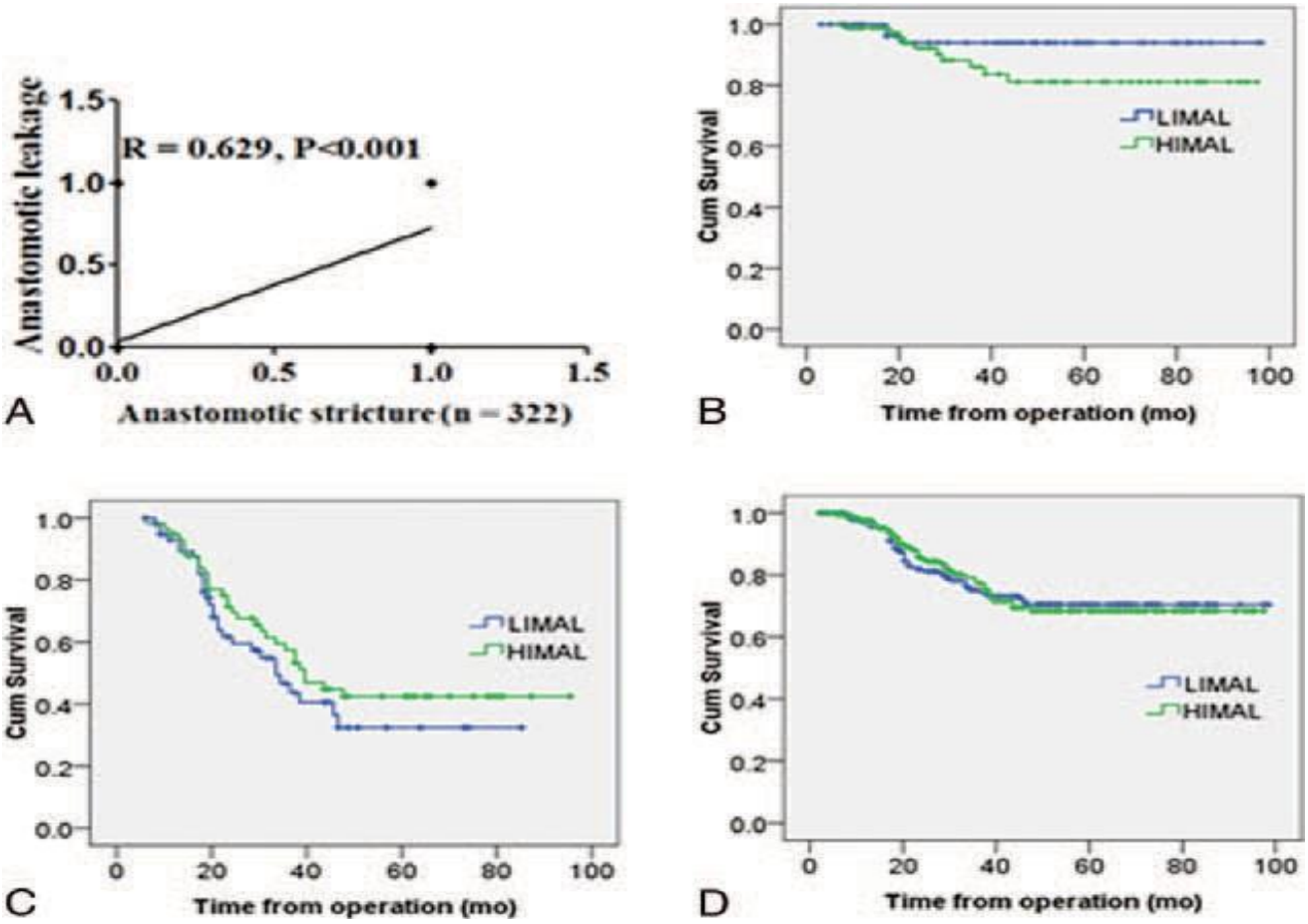
	HIMAB group (n= 87)	LIMAB group (n= 74)	*P*
Tumor diameter, cm	2.85 ± 0.84	2.78 ± 1.08	0.48
Differentiation			0.13
Well-to-moderately differentiated, n (%)	61 (70.11)	52 (69.59)	
Poorly differentiated, n (%)	21 (24.14)	14 (18.92)	
Mucinous cancer, n (%)	5 (5.75)	8 (11.49)	
TNM stage			0.54
0, n (%)	1 (0.58)	1 (1.35)	
I, n (%)	19 (21.84)	28 (18.92)	
II, n (%)	38 (44.25)	59 (39.87)	
III, n (%)	29 (33.33)	59 (39.86)	
Abbreviations; HIMAB = high inferior mesenteric artery binding, LIMAB = low inferior mesenteric artery binding, TNM = tumor-node-metastasis.			

Postoperative complications and survival

By comparison between the two groups, anastomotic leakage and the anastomotic stricture were higher in HIMAB group (P = 0.023 and P < 0.001, respectively). Among the patients in the HIMAB group with anastomotic stricture, four patients underwent fan-shaped incision. Therefore, anastomotic leakage was highly associated with anastomotic stricture (R = 0.629; P < 0.001, Figure 1A). Furthermore, postoperative genitourinary dysfunction was more common in patients with HIMAB (P =.003).

The follow-up duration for all patients was 39.4 ± 24.5 months. In the HIMAB group, five patients developed local recurrence, 21 reported distant metastases, and 20 died due to cancer-associated conditions. Having the LIMAB group, four patients developed local recurrence, 18 reported distant metastases, and 17 died due to cancer-associated conditions. The rates of recurrence and metastasis were not different among the two groups (P = 0.899 and P = 0.969, respectively). Similarly, the survival was not different between the two groups (Table 4 and Figure 1).

Figure 1:
A: The correlation between anastomotic stricture and anastomotic leakage.
B-D: The survival in patients with different TNM stages.
B: Stage II; C: Stage III; **D:** Overall survival. inferior mesenteric artery binding.



HIMAB = high inferior mesenteric artery binding, LIMAB = low

Table 4: Operative and postoperative complications

	HIMAB group (n= 87)	LIMAB group (n= 74)	*P*
Anastomotic leakage, n (%)	9 (9.77)	3 (3.38)	0.02
Anastomotic stricture, n (%)	12 (13.79)	2 (2.70)	0<.01
Genitourinary dysfunction, n (%)	15 (16.67)	5 (6.08)	0.003
Local recurrence, n (%)	5 (5.75)	5 (6.08)	0.90
Metastasis, n (%)	21 (24.14)	18 (24.32)	0.97
Overall survival, n (%)	67 (70.01)	57 (77.02)	0.98
Stage I survival, n (%)	19 (100)	14 (96.43)	0.24
Stage II survival, n (%)	33 (87.01)	28 (94.92)	0.12
Stage III survival, n (%)	14 (48.28)	15 (49.15)	0.92
Abbreviations; HIMAB = high inferior mesenteric artery binding, LIMAB = low inferior mesenteric artery binding, TNM = tumor-node-metastasis.			

Factors associated with thee survival

The univariate analysis revealed that the site of the tumor from the anal verge, the size of the mass, the recurrence rate, metastasis rate, the distal margin length, the differentiation degree, and the TNM staging were significantly correlated with the survival rate (Table 5). Furthermore, local recurrence, degree of differentiation, distant metastasis, and TNM were independent factor for survival (Table 6).

Table 5: Univariate regression of the variable correlated with the survival

	Died (n= 37)	Survived (n= 124)	P
Gender			0.66
Male, n (%)	25 (68.92)	82 (66.13)	
Female, n (%)	12 (31.08)	42 (33.87)	
Age, years	57.19 ± 11.38	57.73 ± 10.44	0.70
BMI (kg/m^2)			0.67
<25, n (%)	12 (32.43)	37 (29.84)	
≥25, n (%)	25 (67.57)	87 (70.16)	
ASA			0.68
I-II, n (%)	33 (87.84)	111 (89.52)	
III, n (%)	4 (12.16)	13 (10.48)	
Distance from anal verge			0.04
<5 cm, n (%)	16 (41.89)	72 (29.03)	
≥5 cm, n (%)	21 (58.11)	88 (70.97)	
Surgery duration, min	166.59 ± 12.33	167.21 ± 12.01	0.70
Intraoperative blood loss, mL	30.39 ± 6.22	31.47 ± 12.28	0.47
Lymph nodes harvested, n	15.81 ± 2.54	16.15 ± 2.07	0.77
Proximal margin,cm	16.07 ± 2.29	16.33 ± 1.79	0.11
Distal margin,cm	3.62 ± 0.80	3.90 ± 0.73	0.01
Bowel function recovery time, h	36.55 ± 7.45	35.75 ± 6.33	0.36
Mean hospitalization d	17.43 ± 12.08	15.076 ± 9.22	0.08
Mean medical costs,RMB	44950 ± 24900	39470 ± 18950	0.08
Tumor diameter, cm	3.60 ± 0.84	2.59 ± 0.87	<0.01
Differentiation			<0.01
Well-to-moderately	15 (40.54)	195 (78.63)	
differentiated, n (%)			
Poorly differentiated, n (%)	12 (32.43)	46 (18.55)	
Mucinous cancer, n (%)	10 (27.03)	7 (2.82)	
TNM stage			<0.01
0, n (%)	0	3 (1.21)	
I, n (%)	1 (1.35)	65 (26.21)	
II, n (%)	63 (17.57)	123 (49.60)	
III, n (%)	30 (81.08)	57 (22.98)	
Local recurrence, n (%)	8 (21.66)	3 (1.21)	<0.01
Metastasis, n (%)	37 (100.00)	4 (1.61)	<0.01
HIMAB vs LIMAB			0.997
HIMAB, n (%)	20 (54.05)	67 (54.03)	
LIMAB, n (%)	17 (45.95)	57 (45.97)	
Abbreviations; HIMAB = high inferior mesenteric artery Binding, LIMAB = low inferior mesenteric artery binding, TNM = tumor-node-metastasis.			

Table 6: The regression analysis showing variables associated with the survival

	B	SE	Wald	sig	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.							

DISCUSSION

There is a controversy regarding the optimum level of IMA binding during the laparoscopic TME; however, there is a consensus regarding being the best managing procedure for the resection of rectal tumor[11]. Some literature was in the favor of low binding revealing that it is more feasible and associated with less complications; however, the data was not satisfactory and did not cover all the aspects[17]. (Reference number 17 should be number 12, correct and rearrange the subsequent references) Therefore, we conducted this study to compare between HIMAB and LIMAB in laparoscopic TME for rectal tumor as regard the operative and postoperative outcomes. In comparison with HIMAB, LIMAB needs more technical expertise as it preserves the left colon artery after dissection, while the HIMAB is easier. However, the risk of injury of hypogastric plexus or sympathetic fibers is increased in HIMAB, which in turn would be reflected on the genitourinary function and the arterial perfusion[12]. (Reference number 12 should be number 13, correct and rearrange the subsequent references)There is no doubt that inappropriate blood supply to the stump is a risk factor for anastomotic leakage[14]. The literature showed that LIMAB may increase the blood supply to the site of the anastomosis[18]. (Reference number 18 should be number 15, correct and rearrange the subsequent references) Previous studies revealed that the incidence of leakage from the site of the anastomosis as a consequence of TME is ranging between 3.2% and 11.6%[19,20]. However, LIMAB was reported to be correlated with reduced rate of anastomotic leakage[21,22]. Similarly, postoperative anastomotic leakage in our study occurred in 6.83% of the patients. A previous clinical study revealed that the level of IMA binding during either open or laparoscopic surgery did not affect the rate of leakage at the anastomosis site[23]. However, our results showed that anastomotic leakage is directly correlated with HIMAB. In some cases, the marginal artery supplying the anastomosis site may be absent, which in turn will cause insufficient supply of blood to the site of the anastomotic, and in turn would cause leakage at that site. Therefore, it is recommended to extend the resection in such cases for only that reason even if it is not needed from the oncosurgical view, but this may in turn increase the tension in the anastomosis site which may also cause leakage.

The stricture at the anastomosis site is another metric that denote the god speed of any surgery in the gastrointestinal tube. The stricture at the anastomosis site is diagnosed by the aid of endoscopy when the stoma diameter is less than 12 mm[24]. Hereby, we reported that the stricture at the anastomosis site as higher in HIMAB group when compared with the LIMAB group. I addition, there was positive relationship between it and leakage at the anastomosis site. This may donate that the leakage at the anastomosis site may be a risk factor for the stricture at the same site.

In addition to the cells that form the gastrointestinal tube, it contains a great amount of microbial flora[25]. Therefore, the stricture at the site of the leakage may be a result of interaction between host and microbial cells[26]. A previous study revealed that lack of blood supply, the tension at the anastomosis site, and the use of narrow-diameter staplers were correlated with stricture at the anastomosis site. This can explain the increased incidence of stricture at the site of the anastomosis in the HIMAB group in our data as the hematogenous supply to the anastomosis site was relatively lower and the tension at that site was relatively higher at that group.

The dysfunction in the genitourinary systems can be a result of hypogastric nerve plexus injuery[12]. Therefore, sparing this plexus during the operation make the genitourinary dysfunction less likely[27]. This support the LIMAB as in it the binding is far from the sympathetic nerves and the hypogastric plexus. This support the decreased incidence of genitourinary dysfunction in our data in the LIMAB group.

Having the TNM staging, the accurate staging is an important as it can assess the outcomes of colorectal tumor[28-31]. Furthermore, the number of dissected lymph nodes can be used for the assessment of the success of the

surgery. A previous study revealed that HIMAB did not increase the number or the extension of the existed lymph nodes[32]. Hereby, we revealed no difference between the two groups regarding the number of excised lymph nodes. However, we could get the information regarding the involvement of the apical lymph node in the LIMAB.

Another point that favor the LIMAB is that it provides more length of the colon. Sparing the left colonic artery can increase the hematogenous supply to the proximal colon allowing it to be preserved, which in turn would decrease the tension at the anastomosis site. The more preservation of colonic length, the more success of anastomosis during the anterior resection of the rectum.

Unlike other previously reported data that revealed that high binding achieves advantages regarding the survival, our study did not agree with that[23,32-34]. Our results regarding the lack of correlation between the site of IMA binding and the survival were consistent a previously-published study discussing a surgery rather than TME[35]. The increased hospitalization time in HIMAB group can be owed to that the anastomotic leakage is the cause of increase the duration of hospitalization and also the costs.

CONCLUSION

In conclusion, during radical resection for rectal tumor by laparoscopy, LIMAB was associated with decreased risks of leakage and stricture at the anastomosis site in addition to decrease the risk of dysfunction in the genitourinary systems.

The duration of the stay at the hospital and the subsequent costs were lower in LIMAB group. However, the number or the extension of excised lymph nodes, the rate of recurrence, rate of metastasis, and rate of mortality were not correlated with the IMA binding level.

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