

Apical lymph nodes at the root of the inferior mesenteric artery in distal colorectal cancer: an analysis of the risk of tumor involvement and the impact of high ligation on anastomotic integrity

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Abstract

Background What level of arterial ligation is best in left-sided colon cancer and rectal cancer remains controversial. This study aims to assess the necessity and risk of high ligation from an oncological and technical perspective.

Methods The lymph nodes at the origin of the inferior mesenteric artery (IMA) were separated as apical nodes in all patients operated for distal colorectal cancer in our department. The number and status of the nodes were prospectively assessed, and demographic and tumor-related variables were evaluated as risk factors for apical tumor invasion. Anastomotic leaks were also evaluated.

Results A hundred and three patients (52 [50.5%] males, 60.3 ± 12.9 years old) were included. The number of non-apical lymph nodes harvested was 14.5 ± 7.1 with an additional 4.4 ± 3.2 apical nodes at the high ligation site. Tumor invasion of apical nodes was observed in 6 (5.8%) patients. Two of these (1.9%) had no other positive nodes (skip metastases). Although none of the variables evaluated was found significant for predicting apical node positivity, tumor invasion was detected in 8.5 and 22.2% of patients with pT3 and pN2 cancers, respectively. Among patients, who had an anastomosis ($n = 84$, 81.6%), anastomotic

leak was observed in 7(8.3%) and 1 (1.2%) of these patients required emergency relaparotomy. There was no mortality related to high ligation.

Conclusions High ligation of IMA may be routinely performed in patients with distal colorectal cancer, since tumor invasion of apical lymph nodes is neither rare (>5%) nor predictable, and skip metastases may also occur. This is especially true in case of an advanced disease for which apical node positivity peaks. The anastomotic leak rate is less than 10%, and mortality is low after high ligation of IMA.

Keywords Apical lymph nodes · Colorectal cancer · Inferior mesenteric artery · Anastomotic leak

Introduction

There is no consensus on what level of arterial ligation is best in the surgical treatment of distal colorectal cancer [1–5]. Previous guidelines did not advocate routine ligation of the inferior mesenteric artery (IMA) beyond the division of left colic artery unless there was evidence of tumor invasion in this region [1]. However, a retrospective analysis of more than 2,400 patients, comparing the outcomes of high and intermediate ligation on survival, showed that high ligation reduced distant metastasis and local recurrence, and improved survival, in certain stages of colorectal cancer [6]. In addition, as our understanding of regional lymphatic drainage in colorectal cancer evolved, most colorectal surgeons began to perform high ligation of IMA in order to achieve a more extensive mesenteric excision by reaching the origin of primary feeding arteries and to ensure an adequate oncological resection by increasing the number of lymph nodes harvested. This hypothesis has been confirmed by studies showing up to 8.6% of tumor

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involvement at high ligation sites [7, 8]. Moreover, understanding the factors that may affect the risk of tumor invasion at the root of IMA may be important and lead the surgeon to perform or omit high ligation in the presence or absence of these factors. However, little is known about the variables that may affect the positivity at apical nodes.

Another controversial aspect of high ligation of IMA is its effect on anastomotic integrity. Some authors believe that high ligation of IMA may be essential in order to ensure a tension-free anastomosis by maintaining a complete mobilization of the proximal limb [9, 10]. This hypothesis has been criticized by others who maintain that high ligation may decrease blood flow to the anastomosis [4]. Thus, the effect of high ligation on anastomotic complications deserves closer attention and may potentially be an important factor in the surgeon's decision to make a high- or low-intermediate tie.

The current study aims to reveal the incidence of positive lymph nodes located at the root of IMA in cases of distal colorectal cancer and analyze the potential risk factors increasing the rate of tumor invasion at apical nodes. The perioperative data and outcome in patients with an anastomotic leak were also evaluated.

Materials and methods

All patients selected for our prospective study had undergone surgery for distal colorectal cancer in our department between January 2005 and August 2007. The exclusion criteria were the following: synchronous, metastatic or recurrent disease, benign lesions or cancers except adenocarcinomas, macroscopic residual tumor, palliative resections and emergent surgery.

Patients with rectal cancer received neoadjuvant radiation therapy unless the tumor was intraperitoneal or early stage (T1-2 and N0). This therapy included 45–50 Gy of radiation therapy in 5 weeks, to the L5-S1 region and excluding the aorta, with the combination of 5-fluorouracil (320 mg/m²) during the first and last weeks, as determined by the radiation oncologist, generally based on the patient's general condition and the side effects of treatment.

All procedures were performed or supervised by a single surgeon (MO) in order to standardize the procedure. During the first 2 years of the study period, the operations were performed by laparotomy; however, since 2006, laparoscopy has gradually become the preferred approach. During the procedure, the fatty tissue at the root of IMA was swept to the specimen with meticulous blunt dissection in order to maximize the number of resected lymph nodes, and IMA was carefully tied, clipped or sealed 1–1.5 cm from the aorta in order to protect the nerves. The tissue between the origin of IMA and the points where superior rectal and left

colic arteries branch was marked with silk ties by the surgeon himself in the operating room, and the lymph nodes harvested from this area were defined as 'apical nodes' (Fig. 1). The pathological examination was done in a routine manner and reported as was suggested in the guidelines of the College of American Pathologists [11]. Specimens were fixated with formalin, and fatty tissues were examined both visually and by palpation and macroscopically searched for nodular elements, which were picked up as possible lymph nodes for further evaluations. These pieces were sampled and embedded in paraffin. The lymph nodes were stained with hematoxylin and eosin for histological analysis. Although some advanced pathological techniques including xylene clearance or immunohistochemistry have been shown to increase the number of harvested lymph nodes and to permit more accurate staging, none of those techniques, only standard protocols, was used in the current study [12]. The numbers of harvested and tumor-involved lymph nodes were reported separately. If tumor involvement was observed in a lymph node, it was defined as a positive node. In addition, besides demographic data, the following tumor characteristics were analyzed as possible risk factors for tumor involvement at apical lymph nodes: pT and pN stages, localization (distal colon or rectum), differentiation (well, moderate, poorly or undetermined), and neoadjuvant radiation therapy.

The postoperative data were retrospectively obtained from a chart review analysis. Anastomotic leak was diagnosed or confirmed with clinical or radiological findings such as nature of the drainage, abdominal signs, contrast computerized tomography, or X-rays. Perioperative data and related mortality were also reported. The following characteristics were analyzed as possible risk factors for an anastomotic leak: demographics, location of the tumor, pT and pN stages, location of the anastomosis, operative technique (laparoscopic, converted or open), and neoadjuvant radiation therapy. Location of the anastomosis was classified as intraperitoneal after left colonic and sigmoidal and anterior resections or intrapelvic after low anterior resections.

Distal cancer included adenocarcinoma in the distal (distal descending, sigmoid, rectosigmoid) colon and rectum for which high ligation of IMA was required, since IMA is the primary feeding artery. The location of the tumor was reported according to the surgeon's observations. The peritoneal attachments between the beginning of sigmoid colon and left inferior side of the abdominal cavity were accepted as the border between ascending and sigmoid colon. Similarly, the transition between the sigmoid colon and upper rectum was defined as the point where the tenia coli of sigmoid form the circumferential longitudinal muscle of the rectal wall, or clinically, where the distal large intestine commences opposite the sacral promontory [11]. If the tumor was just on the border, or had extensions

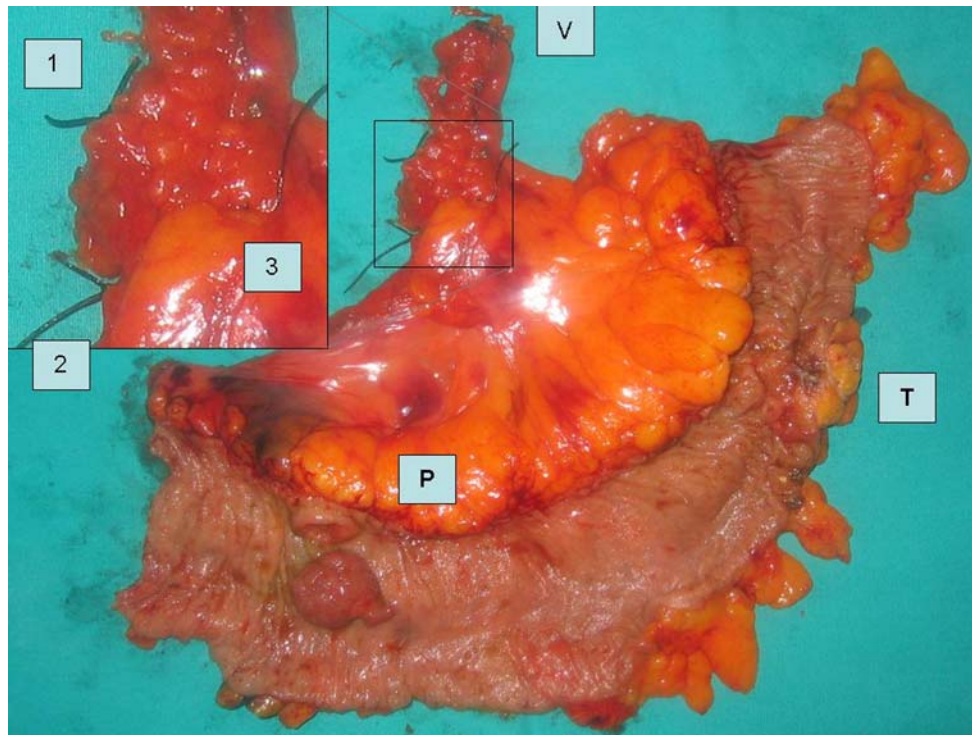


Fig. 1 A 65-year-old male patient underwent laparoscopic anterior resection for sigmoid cancer (C) and a rectosigmoid polyp (P). Apical lymph nodes included those harvested from the area between the

origin of inferior mesenteric artery (1), superior rectal artery (2), and left colic artery (3). High ligation of the inferior mesenteric vein (V) was performed in order to secure a tension-free anastomosis

to the both sites, it was quite difficult to establish whether it belonged to the distal sigmoid or proximal rectum. These tumors were classified as rectosigmoid cancer.

All statistical analysis was done using SPSS for Windows 15.0. The results were presented as percentages, means, and standard deviations. Student's *t*-test, Mann–Whitney U test, and Pearson's Chi-square test were used for evaluation of numeric and continuing values. A *P* value less than 0.05 was considered significant.

Results

A total of 103 patients (52 [50.5%] males, 60.3 ± 12.9 years old) were selected for this prospective study from all patients operated for distal colorectal cancer in our department. Tumors were located in the distal colon ($n = 58$, 56.3%) (distal descending [$n = 17$; 16.5%], sigmoid [$n = 27$; 26.2%], and rectosigmoid [$n = 14$; 13.6%]) or rectum ($n = 45$; 43.7%). Out of 45 patients with rectal tumors, all except 14 (31.1%), who had either intraperitoneal ($n = 10$; 71.4%) or early-stage (T1-2 and N0) ($n = 4$; 28.6%) disease, received neoadjuvant radiation therapy. Patients underwent left colonic and sigmoidal ($n = 17$; 16.5%), anterior ($n = 27$; 26.2%), low anterior ($n = 40$; 38.2%) or abdominoperineal ($n = 19$; 18.4%) resection

either via laparotomy ($n = 60$; 58.3%) or laparoscopy ($n = 43$; 41.7%); There were 7 (16.3%) conversions to open surgery. The anastomoses were intraperitoneal ($n = 44$, 42.7%) or intrapelvic ($n = 40$, 38.8%) in the 84 patients who did not have an abdominoperineal resection. Thirty-five (41.7%) of these had a diverting stoma. All anastomoses in laparoscopic and open procedures were performed using a double stapler technique, except in 7 (8.3%) patients (4 in the laparoscopic and 3 in the open group), who underwent an intersphincteric anastomosis, done with manual suturing. The hospitalization period was 9.7 ± 6.9 days, and 30-day morbidity and mortality were observed in 23 (22.3%) and 9 (8.7%) patients, respectively. Among patients who had an anastomosis ($n = 84$), anastomotic leak was observed in 7 (8.3%). One patient required relaparotomy and had a Hartmann's procedure 3 days after the first operation. Although the hospitalization period was lengthened in patients who had an anastomotic leak, none of these patients died within 30 days postoperatively; but a stoma was not necessitated, or closure could be achieved in only 2 patients (Table 1).

A total of 14.5 ± 7.1 non-apical lymph nodes were harvested, with an additional 4.4 ± 3.2 apical nodes at the high ligation site. Pathology evaluation revealed the T and N status as pT1 ($n = 1$, 1.0%), pT2 ($n = 6$, 5.8%), pT3 ($n = 71$, 68.9%), and pT4 ($n = 25$, 24.3%), and pN0

Table 1 Demographic and disease-related data in patients with an anastomotic leak

Demographics	Localization/stage	Operation	Diagnosis of the leak	Treatment	Outcome
M, 51	Sigmoid/T3N0	Anterior resection (open)	Physical and laboratory findings secondary to intra-abdominal sepsis	Reoperation on day 3 (Hartmann's procedure). Discharged from the hospital on day 11	Deceased due to hepatic metastasis 21 months, postoperatively
M, 80	Rectosigmoid/T4N1	Low anterior resection (open) + diverting ileostomy + segmental bladder and ureteral resection with Boari flap	Nature of the drainage fluid (Uro-colo-cutaneous fistula)	Conservative. Multiple attempts with nephrostomy to heal urinary fistula. Discharged from the hospital on day 34	Hartmann's procedure for uro-colo-cutaneous fistula 6 months postoperatively. Deceased due to cardiac pathology while having no recurrent or metastatic disease 11 months postoperatively
M, 61	Rectosigmoid/T3N0	Low anterior resection (laparoscopic) + diverting ileostomy	Nature of the drainage fluid	Conservative. Discharged on day 25	Alive without recurrent or metastatic disease, but with an ileostomy 15 months postoperatively
F, 68	Rectum/T3N2	Low anterior resection (laparoscopic) + diverting ileostomy	Nature of the drainage fluid	Conservative. Discharged on day 14	Alive without recurrent or metastatic disease, but with an ileostomy 14 months postoperatively
M, 72	Sigmoid/T3N0	Anterior resection	Nature of the drainage fluid	Conservative. Discharged on day 7	Underwent low anterior resection with a diverting ileostomy 2 months postoperatively. Stoma closure 10 months after the 2nd operation. Alive without recurrent or metastatic disease 27 months postoperatively
F, 67	Rectosigmoid, T3N1	Anterior resection (open)	Nature of the drainage fluid	Conservative. Discharged on day 27	Deceased due to hepatic metastasis 51 months, postoperatively
M, 49	Rectum, T4N1	Low anterior resection + partial bladder resection + primary bladder repair + diverting ileostomy	Nature of the drainage fluid	Conservative. Discharged on day 19	Deceased due to hepatic metastasis 14 months, postoperatively

Table 2 Demographics and histological findings in patients ($n = 6$) with positive apical lymph nodes

Demographics	Localization	Differentiation	T–N stage	Total harvested nodes	Positive nodes (apical + non-apical)	Prognosis
m, 71	Rectosigmoid	Moderately	T3N2	8	1 + 4	Deceased during postoperative period secondary to a cerebrovascular event
m, 60	Rectum	Moderately	T3N2	15	4 + 0*	Deceased due to hepatic metastasis 15 months after the operation
m, 62	Rectosigmoid	Poorly	T3N2	10	9 + 0*	Deceased due to hepatic metastasis 8 months after the operation
f, 66	Rectum	Moderately	T3N2	11	3 + 4	Lost to the follow-up
m, 54	Distal descending	Moderately	T3N1	13	1 + 2	Deceased due to hepatic metastasis 25 months after the operation
f, 60	Sigmoid	Moderately	T3N1	10	1 + 1	Alive without recurrent or metastatic disease 23 months after the operation

* Skip metastases

($n = 62$, 60.2%), pN1 ($n = 23$, 22.3%), and pN2 ($n = 18$, 17.5%), respectively. Tumor invasion was observed at apical nodes in 6 (5.8%) patients, and 2 (1.9%) of these had no other positive nodes except in the high ligation area (skip metastases) (Table 2).

The risk factors for apical tumor invasion were also investigated in the current study. The evaluation of demographic data showed that age and gender (62.2 ± 5.9 vs. 60.4 ± 13.2 years ($P = 0.741$) and $n = 4$ (67%) vs. $n = 48$ (49.5%) males ($P = 0.414$) among apical node positive and negative cases, respectively) were not statistically significant. Further analysis also showed that none of the studied variables was a significant risk factor for tumor invasion of apical lymph nodes. We failed to find a parameter for determining apical lymph node positivity (Table 3). However, apical lymph node positivity occurred quite often in pT3 and pN2 tumors (8.5 and 22.2%, respectively). In contrast, none of the T1 or T2 tumors was associated with positive apical lymph nodes, although it must be kept in mind that there was a very small number of patients in these groups.

The details of the operative techniques (open and laparoscopic) were also compared to ensure homogeneity of the data. Gender (33 (55.0%) and 19 (44.2%) males, $P = 0.279$) and age (59.9 ± 12.7 and 60.9 ± 13.2 years, $P = 0.720$) were not statistically different in open and laparoscopic groups. The numbers of non-apical and apical lymph nodes harvested in the open (14.1 ± 7.0 and 4.8 ± 3.4) and laparoscopic (14.8 ± 7.2 and 3.8 ± 2.8) groups were similar as well ($P = 0.89$ and 0.44). Of the 6 patients with positive apical lymph nodes, 4 (6.7%) and 2 (4.7%) were underwent open and laparoscopic resections, respectively. The search for a risk factor that increased the rate of anastomotic leak failed in the current study (Table 4).

Table 3 Risk factors for tumor invasion of apical lymph nodes

	Status of apical lymph nodes		<i>P</i>
	Involved ($n = 6$) (%)	Not involved ($n = 97$) (%)	
T and N stages			
T1 ($n = 1$)	0	1 (100)	$P = 0.433$
T2 ($n = 6$)	0	6 (100)	
T3 ($n = 71$)	6 (8.5%)	65 (91.5%)	
T4 ($n = 25$)	0	25 (100)	
N1 ($n = 23$)	2 (8.7%)	21 (91.3%)	$P = 0.224$
N2 ($n = 18$)	4 (22.2%)	13 (77.8%)	
Localization			
Colon ($n = 58$)	4 (6.9%)	54 (93.1%)	$P = 0.598$
Rectum ($n = 45$)	2 (4.4%)	43 (95.6%)	
Neoadjuvant radiation therapy ($n = 45$)*			
Received ($n = 31$)	1 (3.2%)	30 (96.8%)	$P = 0.565$
Not received ($n = 14$)	1 (7.1%)	13 (92.9%)	
Differentiation			
Well ($n = 4$)	0	4 (100%)	$P = 0.676$
Moderately ($n = 74$)	5 (6.8%)	69 (93.2%)	
Poorly ($n = 11$)	1 (9.1%)	10 (90.9%)	
Undetermined [†] ($n = 14$)	0	14 (100%)	

* Calculated only for rectal cancer

[†] Including 2 patients with complete response after neoadjuvant radiation therapy

Discussion

The level of lymph node invasion and the number of nodes involved have been shown to be significant prognostic factors in patients with colorectal cancer. However, there is no consensus on the level of arterial ligation in distally

Table 4 Risk factors for anastomotic leak

	Leak (<i>n</i> = 7)	No leak (<i>n</i> = 77)	<i>P</i>
Age (years) (Mean ± SD)	64 ± 11,2	59.2 ± 12.7	0.341
Gender (male/female) (%)	5/2	36/41	0.211
Location of the tumor	<i>n</i> = 7	<i>n</i> = 77	
Distal descending colon (<i>n</i> = 17) (%)	0	17 (100)	0.192
Sigmoid (<i>n</i> = 27) (%)	2 (7.4)	25 (92.6)	
Rectosigmoid (<i>n</i> = 14) (%)	3 (14.2)	11 (85.8)	
Rectum (<i>n</i> = 26) (%)	2 (3.8)	24 (96.2)	
Operative technique	<i>n</i> = 7	<i>n</i> = 77	
Open (<i>n</i> = 48)	5 (10,4)	43 (89,6)	0.694
Laparoscopic (<i>n</i> = 36)	2 (5,6)	34 (94,4)	
Converted (<i>n</i> = 4)	0 (0)	4 (100)	
Location of the anastomosis	<i>n</i> = 7	<i>n</i> = 77	
Intraperitoneal (<i>n</i> = 44)	3 (6,8%)	42 (93,2%)	0.598
Intrapelvic (<i>n</i> = 40)	4 (10%)	37 (90%)	
Radiation			
Among low anterior resections (<i>n</i> = 40)			
Received (<i>n</i> = 12)/omitted (<i>n</i> = 28)	2 (16,7%)/2 (7,1%)	10 (83,3%)/26 (92,9%)	0.358
Among rectal cancers with a low anastomosis (<i>n</i> = 26)			
Received (<i>n</i> = 12)/omitted (<i>n</i> = 14)	2 (16,7%)/0 (0%)	11 (83,3%)/14 (100%)	0.112
T and N stages			
T1 (<i>n</i> = 1)	0 (0%)	1	0.822
T2 (<i>n</i> = 5)	0 (0%)	5	
T3 (<i>n</i> = 61)	5 (8,2%)	56 (91,5%)	
T4 (<i>n</i> = 17)	2 (11,8%)	15 (88,2%)	
N0 (<i>n</i> = 51)	3 (5,9%)	48 (94,1)	0.399
N1 (<i>n</i> = 19)	3 (15,8%)	16 (84,2%)	
N2 (<i>n</i> = 14)	1 (7,1%)	13 (92,9%)	

* Nineteen (18.4%) patients underwent an abdominoperineal resection. The other 84 (81.6%) patients had an anastomosis. (SD standard deviation)

located disease [4]. Studies evaluating survival rates between high (at the origin of IMA) and low-intermediate (after the branching of left colic artery) ligation have generally shown no significant difference between the two techniques [3, 13–17]. In contrast, a retrospective analysis, evaluating more than 2,400 patients who underwent high ligations of IMA versus ligation of the superior rectal artery, showed reduced distant metastasis and local recurrence rates as well as improved survival in the IMA group in certain stages of colorectal cancer [6]. It has been asserted that this study was flawed, since the authors ignored the stage migration phenomenon, which might arise as a result of more accurate staging in patients who underwent extensive lymphadenectomy [4]. Other retrospective studies assessing the outcomes of high and low tie techniques might also be biased due to their study design, since high ligation was generally performed selectively, mostly according to what the surgeon decided based on preoperative and intraoperative findings [13–17]. Thus, patients with more advanced tumors probably underwent more aggressive resection including high ligation of IMA, limiting the equivalency of the groups. Due to these

restrictions in interpreting the survival results, we believe that tumor invasion rates at apical lymph nodes may be more informative, while analyzing whether or not high ligation of IMA is routinely required to achieve an oncologically adequate surgery in patients with distal colorectal cancer. Data in the literature have revealed that the apical lymph node positivity rate might reach 8.6%, and the pathology evaluation in our study showed that the tumor invasion rate at apical nodes is 5.8% [4, 7]. In our opinion, this is an important finding which may lead surgeons to perform high ligation of IMA for all patients with distal colorectal cancer, because otherwise, more than 5% patients would actually have a R2 instead of the desired R0 resection. It is important to note that in our study, the pathologists were not blinded to the ongoing collection of prospective data during the study period, which might have encouraged them to perform more detailed examinations on the specimens. It may be hypothesized that patients with positive apical lymph nodes may have a higher risk of diminutive, undetectable distant metastases at the time of resection. This may be true, since 3 out of 4 patients who had an appropriate follow-up in our series died a short time

(8, 15, and 25 months) after surgery due to hepatic metastases (Table 2). However, we believe that this hypothesis should be tested in larger series of patients.

It should also be taken into consideration that the number of lymph nodes and the rate of positivity might be increased with advanced pathology examinations such as xylene clearance [12]. We preferred not to include any advanced examinations or evaluations except standard pathological procedures in our study design in order to reveal the importance of high ligation using regular examinations which reflected routine daily practice. An advantage of the current study was its prospective design, which may guarantee the accurate evaluation of the lymph nodes, since the high ligation area was marked in the operating room (Fig. 1). Moreover, we believe that our results may confirm the necessity of high ligation of IMA in two additional perspectives. First, our data suggest that skip metastases are not rare ($n = 2$, 1.9%) and may sometimes occur in patients with distally located colorectal cancer as previously mentioned in another study [18]. However, we are not sure whether these were really skip metastases, or whether there were non-identified metastases in the proximal lymph nodes; since there was a possibility of micrometastasis in non-apical nodes, which could not be identified with hematoxylin and eosin staining, the technique used in the study [19, 20]. Our study also evaluated the variables predicting the status of apical lymph nodes, but failed to find any significant parameters, probably due to the limited number of patients with positive apical lymph nodes.

Thus, since the positivity of apical lymph nodes is unpredictable, we believe that high ligation should be performed in all patients with distally located colorectal cancer, until risk factors for apical node positivity are determined. Besides, current data reveal that tumor involvement at apical lymph nodes is relatively high reaching 8.5 and 22.2%, respectively, in particular groups of patients with pT3 and pN2 tumors, and this suggests that high ligation is especially necessary during surgery for advanced tumors [1, 5]. High ligation of IMA has been recommended in recent guidelines, when a macroscopically involved lymph node is observed in this location at the time of surgery [1, 5]. Although the rates of apical node positivity were 0% in T1 or T2 tumors in the current study, we do not know whether or not high ligation of IMA may be omitted in early-stage cancers, due to the limited number of patients. Thus, we believe that prospective studies on larger patient populations are necessary to find definitive parameters for using or omitting high ligation of IMA in specific cases.

Anastomotic leak is a major and challenging complication of colorectal procedures. From the technical point of view, the effect of high ligation on anastomotic integrity is

controversial. After high ligation of IMA, the vascularization of the proximal limb completely depends on the middle colic and marginal arteries. Some authors therefore believe that high ligation significantly reduces the blood flow and consequently may jeopardize the safety of the anastomosis [21]. Others, however, maintain that high ligation is often essential in order to secure a tension-free anastomosis [9, 10].

The only study evaluating patients who underwent high versus low tie techniques showed no significant difference in anastomotic leak rates [13–15]. On the other hand, we can accept that the incidence of an anastomotic leak after a major colorectal operation should be less than 10%. In a recent study by Kanemitsu et al., a leak was detected in 3.3% of 1,188 patients who underwent a high ligation of IMA with curative intent [18, 22]. In our series, among 84 patients who had a colonic anastomosis, the risk of anastomotic leak was 8.3% ($n = 7$), which is, in our opinion, reasonable and comparable with the previously presented data. The operative technique namely performing the operation with a laparoscopic or open approach was not significantly associated with the leak rates (5.0 and 10.4%, respectively, NS). In contrast to data reported in the literature, we did not find any significant factor that increases the risk of anastomotic leak in the current study (Table 4), probably because of the limited number of patients suffering from anastomotic dehiscence [23]. It is interesting that the leak rate was higher than expected in patients with intraperitoneal anastomoses, where theoretically there was a better blood supply, but we believe that this was an incidental finding, since no statistical difference was observed.

The first patients in the study were operated with an open technique, but then laparoscopy gradually became the preferred method. Our data may arouse criticism, since different methods may affect the number of lymph nodes harvested, especially because of the steep learning curve in laparoscopic colorectal procedures. However, our study revealed that the numbers of lymph nodes harvested, both non-apical (14.1 ± 7.0 vs. 14.8 ± 7.2) and apical (4.8 ± 3.4 vs. 3.8 ± 2.8), were similar in patients who underwent laparoscopic surgery and those who underwent open surgery.

We believe that laparoscopic operations did not adversely affect our results, because in our experience, it is much easier to identify the region at the root of the inferior mesenteric artery and to guarantee appropriate high ligation of IMA at its origin during a laparoscopic operation due to the advantages of the direct vision provided by this technique.

In conclusion, our study shows that high ligation of IMA is necessary, since apical lymph node positivity is more than 5% in patients with distal colorectal cancer. Skip

metastases are not rare. The positivity in high ligation lymph nodes is unpredictable, but may rise in advanced disease, thus, high ligation of IMA is especially important for these cases. In our series, none of the patients with T1 or T2 tumors had positive apical lymph nodes; however, this may be due to the limited number of patients in the study. The risk of anastomotic leak after high ligation of IMA is less than 10% and comparable to the data in the literature. Further well-designed large volume studies are needed to confirm the above findings.

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