Apical lymph node dissection and low ligation of inferior mesenteric artery in the management of distal colorectal cancer

Ahmed F. Elkased, Ahmed S. Elgammal, Mohammed S. Ammar, Tamer Fakhry

Department of General Surgery, Faculty of Medicine, Menoufia University, Menoufia, Egypt

Correspondence to Ahmed S. Elgammal, MD, Department of General Surgery, Menoufia University, Menoufia, Egypt, Tel: +20 010 07789255; fax 0482304703; e-mail: ahmedegyptsabry@yahoo.com

Received 8 May 2016
Accepted 19 May 2016

The Egyptian Journal of Surgery
2016, 35:298–304

Aim
Curative resection of sigmoid and rectal cancer includes high ligation of the inferior mesenteric artery (IMA). However, IMA ligation compromises blood flow to the anastomosis, which may increase the leakage rate, and carries the possibility of injury of autonomic nerve plexus. Accordingly, in this study we employ a technique of lymph node (LN) dissection around the IMA, preserving the IMA and left colic artery (LCA) and compare it with high and low ligation

Background
Nowadays surgery for colorectal cancer has been standardized both ways in open and laparoscopic approaches. But there are still debates regarding the level of ligation of the IMA: at its origin from aorta (high ligation) or below the origin of left colic artery (low ligation). The technique of apical lymph node dissection with preservation of LCA has the advantage of both, better lymph node harvest and lower postoperative complications

Materials and methods
This is a prospective study which included 81 patients with operable distal colorectal cancer admitted to general surgery department in Menoufia University Hospitals from May 2012 to October 2015. Cases were divided by random serial number method into three groups: group (A) 27 cases for high ligation, group (B) 27 cases for low ligation and group(C) 27 cases for low ligation and apical lymph node dissection.

Results
There was high significant difference between the studied groups regarding to the number of harvested lymph nodes with Mean ± SD 18.3 ± 4.05 for high ligation versus 11.3+3.2 for low ligationand17.7+3.81 for apical dissection. also there was significant difference between studied groups as regarding the postoperativegenito-urinary complications.

Conclusions
Lymph node dissection around the IMA preserving the root of the IMA and LCA was feasible by our method, without compromising operation time, blood loss or the number of harvested lymph nodes with accepted rate of postoperative complications.

Keywords:
apical lymph node, inferior mesenteric artery, left colic artery

Egyptian J Surgery 35:298–304

1110-1121

Introduction

Incidence of colorectal cancer and mortality rates vary around the world. Globally, colorectal cancer is the third most commonly diagnosed cancer in men and the second in women [1].

Surgical treatment of colorectal cancer has changed radically in recent years. The introduction of total mesocolic excision, neoadjuvant therapy protocols, and the laparoscopic approach has made colorectal cancer treatment a multidisciplinary management [2].

Lymph node dissection carries prognostic and therapeutic implications. Lymphadenectomy for colorectal adenocarcinomas should extend to the level of the origin of the primary nurturing vessel. There is no consensus as to which is the best level of arterial ligation in the surgical treatment of distal colorectal cancer [3].

Previous guidelines did not advocate routine ligation of the inferior mesenteric artery (IMA) beyond left colic artery (LCA) takeoff unless there was evidence of tumor metastasis in this region. However, a retrospective analysis of more than 2400 patients,

comparing the outcomes of high and low ligation on survival, showed that high ligation reduced distant metastasis and local recurrence, and improved survival in certain stages of colorectal cancer [4].

The level of arterial ligation can affect genitourinary function (injury to the superior hypogastric plexus), the extent (and yield) of lymphadenectomy, and distal colonic arterial perfusion (especially in older people, in whom distal colonic arterial perfusion could be deficient due to arterial degenerative disease) [5].

The technique we adopted in this study carries the advantage of low ligation of the IMA, in securing good perfusion of the proximal colonic stump and avoidance of injury of parasympathetic plexus, and the oncological advantage of apical lymph node dissection.

Patients and methods

This study included 81 patients diagnosed as having adenocarcinoma of the rectum or the sigmoid colon between May 2012 and October 2015 at the Surgical Department, Menoufia University Hospitals. The study was reviewed and approved by the ethics committee of Menoufia university hospital. Informed written consent was obtained from individual Patients.

Inclusion criteria

Only operable cases of sigmoid or rectal cancer fulfilling MRI or computed tomographic (CT) scan criteria, which include no permeation of surrounding fat planes, no encasement of major vascular structures, no extensive local spread, and no distant metastases or peritoneal infiltration, were included in this study.

Exclusion criteria

All cases with perforation or obstruction, metastatic cases, patients with low rectal tumors that necessitate abdominoperineal resection, and patients with synchronous lesions in a part of the colon other than the left colon or rectum were excluded from the study.

Preoperative work

All patients were subjected to the following.

(1) Colonoscopic biopsy of the tumor.
(2) Thorough clinical examination.
(3) Imaging studies: MRI or CT of the abdomen and pelvis and metastatic workup (ultrasound of the abdomen and chest radiography).

A total of 35 of our patients underwent neoadjuvant therapy.

All patients were eligible for general anesthesia (American Society of Anesthesiologists 1–4).

Preoperative assessment of genitourinary functions was carried out for all patients as follows.

(1) Uroflowmetric study and ultrasound measurement of postvoid bladder volume.
(2) Questionnaires for the International Index of Erectile Function [6].
(3) International Consultation on Incontinence Questionnaire [7].
(4) The Female Sexual Function Index [8] to assess the genitourinary functions both preoperatively and postoperatively.

The patients were randomly divided into three equal groups.

Group A included patients who underwent high ligation of the IMA.

Group B included patients who underwent low ligation of the IMA.

Group C included patients who underwent low ligation of the IMA with apical lymph node dissection.

Surgical technique

Standard (open or laparoscopic) resection of the sigmoid or the rectum was performed for all patients.

In group A, the IMA was flush ligated (1–1.5 cm) below its origin from the aorta.

In group B, the IMA was ligated below the takeoff of the LCA above the level of sacral promontory.

In group C, the IMA was low-ligated as in group B, whereas the lymph node around the origin of the artery was dissected by peeling the areolar and lymphatic tissue off the vascular sheath of the artery at its origin. The dissection was continued in caudal direction until the LCA was encountered and preserved.

Postoperative evaluation

In the immediate postoperative period, the patients were monitored closely for manifestations of fecal fistula.

In doubtful cases, CT of the abdomen and pelvis was performed to detect minor leakage (pericolic abscess or collection).

Histopathology of retrieved lymph nodes

Lymph nodes were collected for histopathological examination. The number of retrieved and positive lymph nodes on the root of the IMA, the total number of lymph nodes on the specimen, and the number of positive lymph nodes on the specimen were recorded.

Questionnaires for the International Index of Erectile Function, International Consultation on Incontinence Questionnaire, and the Female Sexual Function Index were administrated to every patient at 3 and 6 months postoperatively.

Uroflowmetry and ultrasound measurement of postvoid bladder volume was performed 3 and 6 months postoperatively.

Results

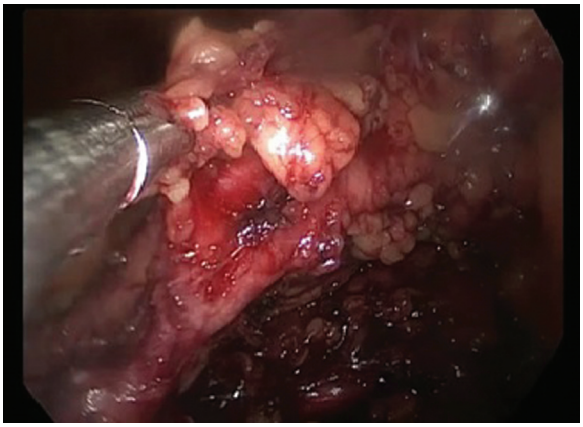
A total of 81 patients [50 (61.7%) male; mean age 55.3 ±12.9 years] were selected for this prospective study from all patients operated for distal colorectal cancer in our department. Tumors were located in the sigmoid (*n*=27; 33.3%), rectosigmoid and upper rectum (*n*=35; 43.2%), and midrectum (*n*=19; 23.4%) (Figs 1–6).

Of the 54 patients with rectal tumors, 35 underwent neoadjuvant chemoradiation (*n*=35; 64.8%).

Patients underwent sigmoidal resection (*n*=27; 33.3%), anterior resection (*n*=35; 43.2%), or low anterior resection (*n*=19; 23.4%) either by means of laparotomy (*n*=68; 83.9%) or laparoscopy (*n*=13; 16.1%).

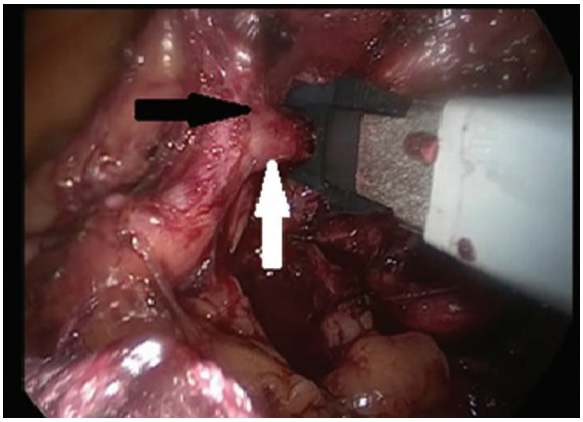
No patient in this study needed covering ileostomy.

Figure 1



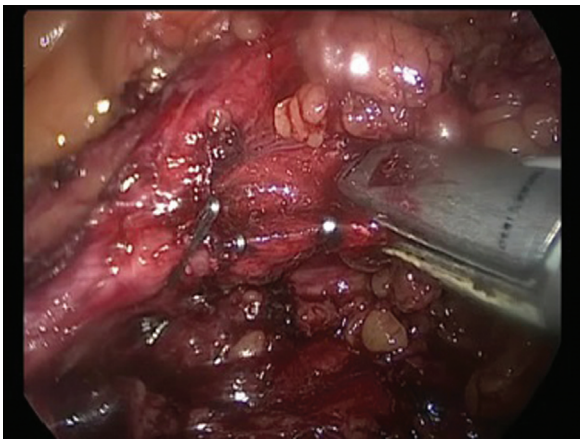
Apical lymph node dissection.

Figure 2



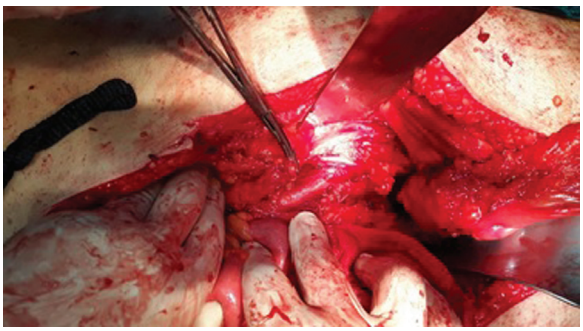
Clipping of the superior rectal artery (black arrow=left colic artery; white arrow=inferior mesenteric artery).

Figure 3



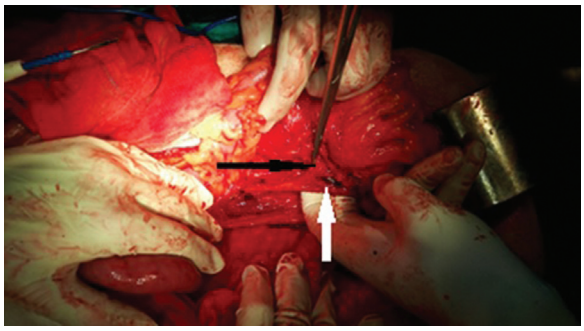
Clipping.

Figure 4



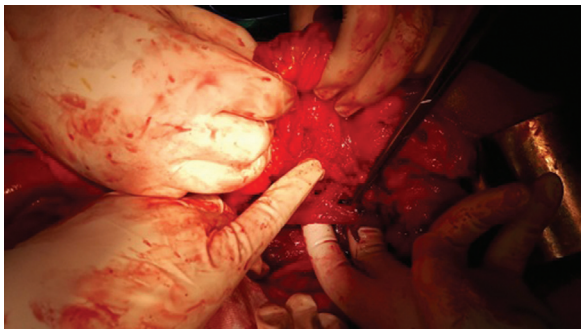
Apical lymph node dissection.

Figure 5



Preservation of the left colic artery (black arrow=left colic artery; white arrow=inferior mesenteric artery).

Figure 6



Ligation of the superior rectal artery.

Table 1 The number of harvested LNs and the positive LNs in the studied groups

	Group A	Group B	Group C	Test	*P*-value
Number of harvested LNs					
Mean±SD	18.3±4.05	11.33±0.2	17.73±0.81	ANOVA: 29.68	0.001
Range	16.00–24.00	9.00–15.00	14.00–21.0		
Positive LNs				χ^2: 7.43	0.24
Number of cases (%)	18 (66.7)	8 (29.63)	13 (48.15)		

ANOVA, analysis of variance; LN, lymph node.

Table 2 The number of cases with detected apical LNs and the percentage of its positivity

	Studied surgical techniques for ligation of IMA [*n* (%)]			
Apical lymph nodes	Group A (*n*=27)	Group C (*n*=27)	Test	*P*-value
Cases with apical nodes	24 (88.9)	26 (96.2)	Fisher's exact: 0.52	0.30
Cases with positive apical nodes	3 (11.1)	4 (14.8)	χ^2: 0.50	0.68

IMA, inferior mesenteric artery; LN, lymph node.

The hospitalization period was 10.6 4±0.7 days.

The mean number of harvested lymph nodes was 18.3, 11.3, and 17.7 for groups A, B, and C, respectively. Lymph node metastasis was detected in 16, 13, and 15 cases in the groups A, B, and C respectively. There was a high significant difference between each of groups A and C and group B as regards the number of retrieved nodes, whereas there was no significant difference between the studied groups as regards the number of positive nodes (Table 1).

The apical nodes were detected in about 89 and 96% of cases in groups A and C, respectively. There was no significant difference between the two groups as regards the number of retrieved and positive apical nodes (Table 2).

The overall positivity of apical nodes was 12.9%.

Skip metastasis was found only in one specimen in both groups A and C (1.8%).

Genitourinary dysfunction occurred in 8, 1, and three patients in groups A, B, and C, respectively. There was a significant difference between the studied groups as regards the postoperative genitourinary dysfunction, the incidence being higher in group A in comparison with groups B and C, with an overall incidence of 14.8% (Table 3).

Table 3 The incidence of postoperative complications

Postoperative complications	Group A [*n* (%)]	Group B [*n* (%)]	Group C [*n* (%)]	χ^2	*P*-value
Genitourinary dysfunction	8 (29.6)	1 (3.7)	3 (11.1)	7.62	0.022
Anastomotic leak	3 (11.1)	1 (3.7)	2 (7.4)	7.07	0.29

Postoperative anastomotic leakage occurred in 7.4% of all patients, with no significant difference between the studied groups as regards this entity (Table 3).

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 located disease [9].

Studies evaluating survival rates, conducted by Lange and colleagues, between high (at the origin of IMA) and low–intermediate (after the branching of the LCA) ligation have generally shown no significant difference between the two techniques [10].

In contrast, Pezim and Nichols, in a retrospective analysis evaluating more than 2400 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 [11].

Kanemitsu *et al.* [4] and chin *et al.* [12] indicated that the high tiecontributed to survival prolongation. They reported that the 5-year survival rate of patients who had lymph node metastasis around the IMA but underwent lymph node dissection up to the root of the IMA was as good as 40%.

In our study, lymph nodes could be visualized in all patients (100%). For group A, the mean number of harvested lymph nodes was 18.3±4.05 (range 6–24), For group B, the mean number was 11.3±3.2 (range 9–15), whereas in group C the mean was 17.7±3.8 (range 14–21).

The number of harvested lymph nodes was significantly higher in both groups A and C than in group B, whereas there was no significance difference between groups A and C as regards this number.

Data collected by West *et al.* [13] were very similar to our study, and their meta-analysis reported a greater lymph node yield (median, 30 vs. 18; $P<0.0001$) in high versus low ligation, which was highly significant.

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 was 12.9% [14,15].

This is an important finding, which may lead us to perform apical lymph node dissection for all patients with distal colorectal cancer, because, otherwise, more than 10% patients would actually have metastasis at this site.

The second reason that may lead us to perform such dissection is skip phenomena. Skip metastasis occurred in apical nodes in 1.8% of our patients. This coincides with the findings of Palma *et al.* [16], who found it in 1.9% of his patients.

However, the investigators are not sure whether these were really skip metastases or whether there were nonidentified metastases in the proximal lymph nodes, as there was a possibility of micrometastasis in nonapical nodes, which could not be identified with hematoxylin and eosin staining [4].

Despite the oncological advantage of high ligation, it has many drawbacks such as reduced blood flow to the descending colonic limb and the possible injury of the superior hypogastric autonomic plexus and nerves.

Anastomotic leak, in the form of fecal fistula or pericolic abscess, is a major and devastating 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 [17].

Dworkin and Allen-Mersh [18] assessed the influence of clamping of the IMA using Doppler flowmetry. They showed that the blood flow to the sigmoid colon

fell by 50% within 5 days postoperatively. Others, however, maintain that high ligation is often essential to secure a tension-free anastomosis [19].

In our study, among 81 patients who underwent colorectal anastomosis, the incidence of risk for anastomotic leak was 7.4% (n=6), which is reasonable and comparable to other studies in the literature, such as that by Hida *et al.* [14], who found 6.3% leakage rate among their patients (seven of 112).

Two of these patients required re-exploration and Hartman procedure was performed, whereas the other four patients were managed conservatively.

In our study, there was no significant difference between the studied groups as regards the leakage rate (P=0.29). This is in disagreement to the results obtained by Buunen *et al.* [20], who showed an anastomotic leak rate of 20% in high ligation versus a 0% leak rate in low ligation.

For many years, severe urogenital dysfunction has been accepted as normal following colorectal cancer surgery. Reasons for the high rates of denervated bladder and impotence were the anatomy and pathophysiology of autonomic pelvic nerves that were only poorly understood by surgeons, and the commonly used blunt dissection technique [21].

Genitourinary dysfunction occurred in 14.8% of our patients; this is similar to data collected by Havenga *et al.* [22], who reported that the total mesorectal excision and high ligation of the IMA is compatible with autonomic nerve preservation and reported preservation of sexual function in 85% of cases with no observed loss in urinary function. In our study, genitourinary complications were significantly higher in group A than in both groups B and C.

This is explained by resection of the superior hypogastric plexus and/or resection of the hypogastric nerve on both sides of aorta, with high ligation of the IMA, and this will cause serious urogenital complications as retrograde ejaculation and impotence in men, diminished or loss of orgasm in women, and urinary incontinence in both sexes.

Conclusion

Lymph node dissection around the IMA preserving the root of the IMA and LCA was feasible with our method, without compromising operation time, blood loss, or the number of harvested lymph nodes. It has the advantage of both preservation of blood flow, which could contribute to improvement of the leakage rate, and avoidance of inadvertent injury of autonomic nerve plexus around the origin of the IMA.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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