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Open Complete Mesocolic Excision with Central Vascular Ligation Versus Laparoscopic Approach in Right Colon Cancer Patients

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ABSTRACT

Background: Complete mesocolic excision (CME) as a standard surgery for right sided colon cancer is proven however there is a great debate and deal of discussion if the extra effort needed for it in right sided colon cancer worth the gain that is achieved. We aimed in our study to assess the outcome of CME with central vascular ligation for treatment of right sided colon cancer performed either laparoscopic (lap.) assisted or by open technique.

Methods: Twenty-two patients with right colonic cancer were assigned to receive complete mesocolic excision with central vascular ligation in (Zagazig university hospitals) in the period from February, 2018 till February, 2020. Eleven cases for open approach and 11 cases for laparoscopic approach and their data were prospectively collected.

Results:the operative time in our study ranged from 120-210 minutes in open cases and 180-240 minutes in laparoscopic cases. The mean blood loss was 350±54.7 ml in open cases and 195.5±41.6 ml in laparoscopic cases and no intraoperative complications like ureteric or bowel injuries were recorded.The hospital stay ranged from 6 to 13 days in open cases and 4 to 6 days in laparoscopic cases and oral feeding was allowed in the second or third postoperative day in most of the patients.Clear advantages have been demonstrated for the laparoscopic approach in term of decreased intra-operative blood loss, faster post-operative recovery & return of bowel function, decreased pain, decreased hospital stay and improved quality of life.As regard post-operative complications, all patients were managed conservatively. Chest physician consultation for cases of chest infection and they improved with antibiotic treatment after, wound infection was noted in 6 patients of open group and it was superficial infection that had been treated easily. One patient developed UTI and was successfully treated and one case of abdominal collection for which US guided aspiration was done.

Conclusion: Short-term oncologic results of laparoscopic CME seem to be acceptable and outcome seems to be better than those obtained in other studies with conventional resection as laparoscopic procedure maintains intact embryological envelope of the mesocolon and allows high tight ligation

Key words: Right colon cancer, Complete mesocolic excision (CME), Laparoscopic CME with CVL.

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Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the fourth leading cause of cancer death worldwide. Globally, over 1.3 million new cases (9.7 % of all cancer diagnosis excluding non-melanoma skin cancer) were diagnosed and approximately 690,000 deaths (8.5 % of all cancer deaths excluding non-melanoma skin cancer) were attributed to this malignancy in 2012. Before the 1900s, CRC was relatively uncommon, but incidence rates have risen dramatically in parallel with economic development and adoption of the sedentary lifestyle and western diet**(1).**

Globally, the age standardized incidence rate is about 1.4 times higher in men (20.6/100,000 person-years) than in women (14.3/100,000 person-years). Yet, women on average live longer than men, with the median age at diagnosis higher (73 years) than that in men (69 years). There are only slightly more CRC deaths in men (373.631/year) than in women (320.250/year)**(2)**.

Hohenberger et al.(3) translated the concept of total mesorectal excision (TME) to colonic cancer, noting that traditionally more favorable oncologic results of colon neoplasia was eventually overtaken by rectal cancer and a more radical surgical approach performed along embryonic planes of development with higher quality specimens, produce better oncologic outcome; thus, complete mesocolic excision (CME) with central vascular ligation (CVL) was theorized, standardized and eventually validated by several studies **(4).**

The concept of complete excision of the involved organ along withits primitive mesentery,associated to central ligation of the supplyingblood vessels, isprogressively gaining acceptance as the next step towards a modern surgical oncology; surgicalresection of the primitive embryological mesenterium is in fact pivotal for optimal local clearance.The primitive mesenterium is the embryological envelope where the neurolymphovascular structures develop within a double-layered mesenchymal fibrofatty tissue and the initial pathway for cancerous diffusion: Its intact, complete excision is thus essential to clear residual disease in the surgical field, with consequent impact on local control. Furthermore, CVL allows for an extensive lymph node dissection along the feeding vessels, with significant effect on regionalrecurrence and systemic dissemination, as shown by improved survival in stageI-III colonic cancers treated with enhanced lymph node Harvesting**(5)**.

Blending Complete Mesocolic Excision with CVL is thus the logical step in gaining the highest locoregional control, removing both the intact mesocolon and the apical nodes, with relevant impact on long term outcome. To take advantage of minimally invasive techniques, laparoscopic approach to CME with CVL seems the natural consequence in the evolution of this procedure **(6).**

In our study we aimed in our study to assess the outcome of CME with central vascular ligation for treatment of right sided colon cancer performed either laparoscopic (lap.) assisted or by open technique.

Patients and Method

This study was a comparativestudy which included twenty-two patients with right colonic cancer who were assigned to receive complete mesocolic excision with central vascular ligation in Zagazig University Hospitals in the period from February, 2018 till February, 2020. Eleven cases were scheduled for open approach and 11 cases for laparoscopic approach (random selection was done) and their data were prospectively collected.

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Patients included in the study proved to have rt colon carcinoma, aged between 15 -75 years, and fit for laparoscopic approach.
Patients who were excluded included: Patientswho havetumors distal to the rt. colon, Patients with locally advanced tumors, Patientswith significant cardiovascular comorbidities, emergency cases admitted to emergency unit i.e., obstructed or perforated tumors, and contraindications for laparoscopic surgery.
All patients hadpreoperativeexaminations including complete blood count (CBC), kidney and liver functions, random blood glucose (RBS), prothrombin time (PT) and concentration (PC).Radiologicalinvestigations: Multidetector computed tomography (MD-CT) chest, abdomen and pelvis triphasic CT, Carcinoembryonic antigen and colonoscopy examinations and biopsies were done.

Surgical Technique:
a) Laparoscopic technique

Surgical approach was conducted under general anesthesia. The patient was placed in supine position and straps were used to secure the patient during steep changes of table position, the patient's left arm was tucked along his or her side and the right arm extended on an arm abroad. The surgical site shaved, prepared and an area from below the xiphoid to above pubis was exposed to allow conversion to open technique if necessary.Creation of pneumoperitoneum using veress needle which is inserted in the umbilicus and insufflation of CO2 is done until intrabdominal pressurereaches between 12-14 mmHg.

We used a diamond shaped configuration of ports. The first port is inserted inside the abdomen (10 mm umbilical port for the telescope) and then 3 other ports were inserted under direct vision (one 10 mm and two 5 mm) in the left upper abdomen, left lower, and right lower abdomen respectively. In cases of extracorporeal anastomosis only 3 ports were applied (no right lower abdominal port). In cases of intracorporeal anastomosis, one of 10mm sized ports is replaced by 12 mm in size.The operator stood on the left side of the patient, the camera man on the same side of the surgeon while the assistant on the opposite side.

Patientswereplacedinsteep Trendelenburgwiththe rightsideelevated. Once the workingspaceiscreated(byplacing thegreateromentumandtransversecolonover thetheliver),amedialtolateralapproachwas usedinallcases. Thefirststepisalwaysa thoroughexplorationoftheabdominalcavity. The right colon was pulled upwards and toward the right lower quadrant, stretching and exposingtheileo-colicpedicle. Mesenteric lymphadenectomy was conducted from the origin of ileo-colic vessels in a caudal direction along the SMV to the origin of the Henle's gastro-colic trunk, and then toward the terminal ileum (D3 lymph node dissection).
Completion of devascularization, the right colic vessels wereisolatedandsectionedifpresent. Thenpullingup thetransversecolon,its mesentery wasdissectedfromtherootandtherightbranchesofthemiddlecolicvesselswereidentifiedanddissectedb yEndoclips. Therightcolonwas thenreflectedmedially fromthehepaticflexuredownward, dividing

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theperitoneal reflection in the right gutter. The specimenswereexteriorizedthroughasmall incisionafterwoundretraction using Alexisport.Byusingharmonicdevice enterotomiesweredoneinboththesmall intestineandthecolon. Intracorporealsideto side ileo-transverse anastomosis was done using EndoGIAstaplerandclosureof enterotomy using 3/0 PDS sutures.

b) Open technique:

The patient is placed in supine position. Arms are abducted and secured on padded arm boards. Straps are used to secure the patient during change of the table position when needed.
The surgical site shaved, prepared and an area from below the xiphoid to above pubis was exposed. The surgeon is positioned to the patient's right; the assistant is to the patient's left; the second assistant can stand either to the left of the first assistant or to the surgeon. The scrub nurse is to the right of the surgeon. Also, urinary catheter is inserted.Midline skin incision above and below the umbilicus, using 22-blade scalpel, extending cranially or caudally if needed.
Mobilization of the cecum and the ascending colon along the white line of Toldt, moving proximally toward the hepatic flexure, along the right paracolic gutter with identification of the right gonadal vessels and the right ureter within the retroperitoneum. Identification of the duodenum (dissection proceeds anterior to the duodenum). Dissection of the mesentery off the Gerota'sfascia.The patient is placed in the reverse Trendelenburg position then mobilization of the hepatic flexure (with care not to injure the second portion of the duodenum) is done. Dissection is complete when the second portion of the duodenum is exposed and the middle colic artery is identified.
Identification and ligation the ileocolic vessels at their origin then division of the mesentery, including the right colic and right branch of the middle colic artery, preserving the middle colic artery.
Transection of the terminal ileum (10 cm proximal to the ileocecal valve) and the proximal transverse colon (proximal and distal margin) between non-crushing intestinal clamps and specimen is removed. Anastomosis is done in isoperistaltic fashion (side to side) using 2/0 polyglactin sutures.

Data collection:
Patient data included gender, age, and tumor site and pathological type. Other data collected included operative time, intra-operative blood loss, conversion tolaparotomy, length of postoperative hospital stay, andintraoperative and postoperative complications.Quality of surgical specimens.

Statistical Analysis:
Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis.

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Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD(Standard deviation) for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively.
A P-value of < 0.05 was considered statistically significant &<0.001 for high significant result for two tailed tests.

Fig. (1): Identification of superior mesenteric vessels and ileocolic pedicle

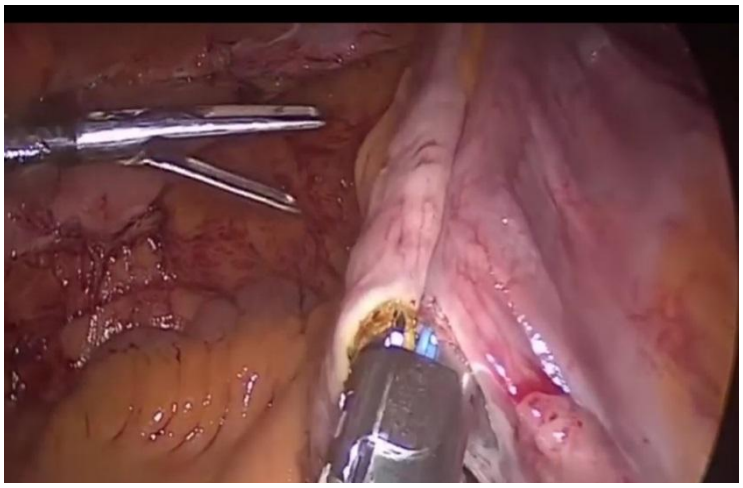

Fig. (2): Ileotransverse anastomosis was done using EndoGIA stapler.

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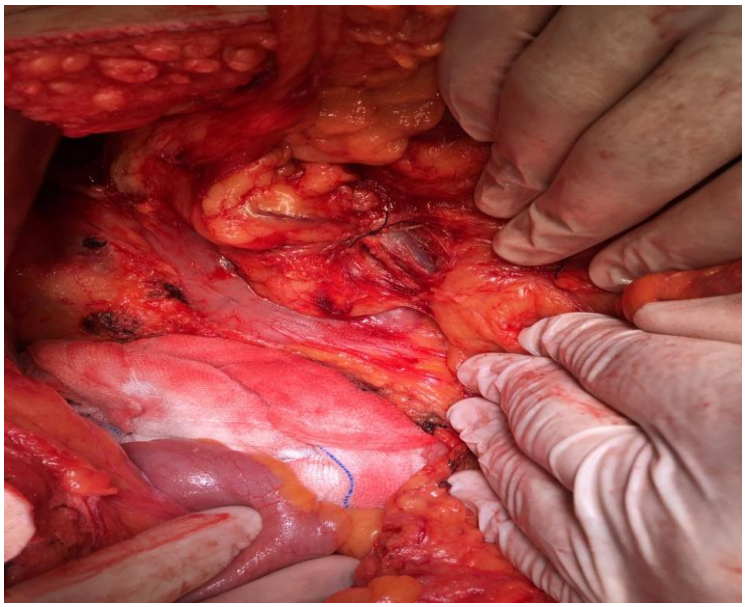

Fig. (3): Full exposure of the 2nd part of duodenum and CVL on flush with exposed SMV.

Results

There was no statistically significant difference between open and laparoscopic groups as regard the age, gender and co-morbidities. Many patients had combined co-morbidities in both groups**(Table1) (Fig. 4).**

There was statistically significant difference between open and laparoscopic groups as regard operative time, length of incision, hospital stay, blood loss and type of incision ($p<0.05$). There was no statistically significant difference between open and laparoscopic groups as regard time of first flatus and type of anastomosis in laparoscopic cases ($p>0.05$)**(Table 2)**.

There was statistically significant difference between open and laparoscopic groups as regard wound complications which was more in group I. The majority of group II cases had nocomplications. Many patients had combined complications in both groups. There was statistically significant difference as regard hospital stay in favour of group II**(Table 3)**.

There was no statistically significant difference between open and laparoscopic groups as regard follow-up and recurrence ($p>0.05$)**(Table 4)**.

There was no statistically significant difference between open and laparoscopic groups as regard positive and total number of LNs, pathology and grade ($p>0.05$)**(Table 5)**.

Table (1): Demographic data among the studied groups.

Item	**Group I (Open)** *(n=11)*		**Group (Laparoscopic)** *(n=11)*		**Test**	**P-value**
Age *(years)* Mean ± SD Range	53 ± 16.6 25-75		52.2 ± 12.3 36-73		T-Test	0.886
	N	**%**	**N**	**%**		
Gender Male Female	5 6	45.5% 54.5%	4 7	36.4% 63.6%	X^2	1.00

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Co-morbidities						
No	5	45.5%	5	45.5%		
DM	2	18.2%	1	9.1%		
Hypertension	4	36.4%	4	36.4%	X^2	0.515
Renal failure	0	0%	1	9.1%		
Hypothyroidism	1	9.1%	0	0%		
Smoking	2	18.2%	0	0%		

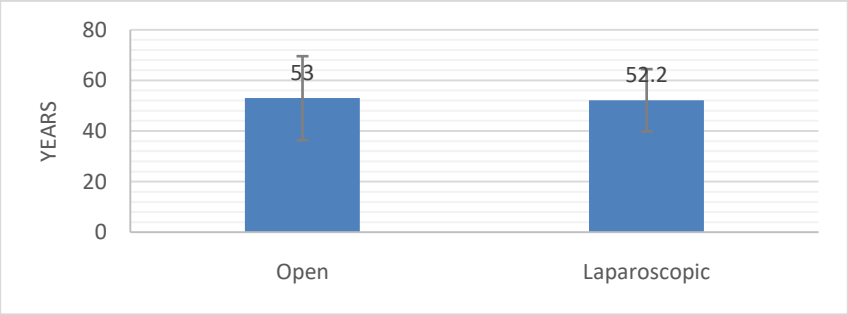

Fig. (4): Age among the studied groups.

Table (2): Operative data among the studied groups.

Item	**Group I (Open)** *(n=11)*	**Group II (Lap.)** *(n=11)*	**Test**	**P-value**
Operation type Rt. Hemicolectomy Extended Rt. Hemicolectomy	6 (54.5%) 5 (45.5%)	8 (72.7%) 3 (27.3%)	X^2	0.659
Operative time *(min)* Mean ± SD Range	147.3±36.6 (120-210)	198.2±22.7 (180-240)	T-test	**0.001* (HS)**
Type of incision Midline incision Pfannenstiel incision Rt. subcostal incision	11 (100%) 0 (0%) 0 (0%)	0 (%) 3 (27.3%) 8 (72.7%)	X^2	**<0.001* (HS)**
Length of incision *(cm)* Mean ± SD Range	21.4±3.2 (15-25)	6.5±0.93 (5-7)	T-test	**<0.001* (HS)**
Blood loss *(cc)* Mean ± SD Range	350±54.7 (300-500)	195.5±41.6 (150-250)	T-test	**<0.001* (HS)**
Type of anastomosis in laparoscopic cases Intracorporeal Extracorporeal	0 0	0 0	3 8	27.3% 72.7%	—	—

Table (3): Post-operative course and complications among the studied groups.

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Item	**Group I (Open)** *(n=11)*		**Group II (Laparoscopic)** *(n=11)*		**Test**	**P-value**
	N	**%**	**N**	**%**		
Time of first flatus *(hours)* Mean±SD Range	38.2±9 (24-48)		33.8±10.5 (24-48)		T-test	0.308
Complications						
No Complications	5	45.5%	9	81.8%		0.08
Wound complication	6	54.5%	0	0%		**<0.001***
Leakage	0	0%	0	0%	X^2	NA
Chest infections	5	45.5%	1	9.1%		0.06
UTI	1	9.1%	0	0%		0.31
Abdominal Collection	0	0%	1	9.1%		0.31
DVT	0	0%	1	9.1%		0.31
Hospital stay*(days)* Mean±SD Range	8.5±2.2 (6-13)		5±0.89 (4-6)		T-test	**<0.001* (HS)**

Table (4): Follow-up among the studied groups.

Item	**Group I (Open)** *(n=11)*	**Group II (Laparoscopic)** *(n=11)*	**Test**	**P-value**
Follow-up *(months)* Mean ± SD Range	17.9 ± 6.6 6-24	16.7 ± 5.96 7-24	T-test	0.665
Recurrence within 6 months Number	0\11 (0%)	0\11 (0%)	X^2	—

Table (5): LNs, pathology and grade among the studied groups.

Item	**Group I (Open)** *(n=11)*		**Group II (Laparoscopic)** *(n=11)*		**Test**	**P-value**
Positive LNs Mean ± SD Median Range	2.7 ± 2.9 2 0-9		2 ± 2.6 0 0-7		MW	0.543
Total LNs Mean ± SD Median Range	22 ± 8.8 19 12-41		22 ± 12.1 17 13-46		MW	0.858
Pathology	**N**	**%**	**N**	**%**	X^2	0.368

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Adenocarcinoma Neuroendocrine tumor Squamous cell carcinoma	10 0 1	90.9% 0% 9.1%	10 1 0	90.9% 9.1% 0%		
Grade I II III	 0 7 4	 0% 63.6% 36.4%	 1 8 2	 9.1% 72.7% 18.2%	X^2	0.420

Discussion

In the early 1990s, laparoscopic colectomy was an evolving technique. Shortly then after, its short-term benefits have been proved including decreased blood loss, decreased postoperative pain, early regain of bowel function and shorter hospital stay. Therefore, laparoscopic colectomy has been well accepted in the management of benign colorectal diseases including rectal prolapse, inflammatory bowel diseases, diverticular disease and endometriosis. But concerns about its oncological safety held most surgeons from performing it in colorectal malignancies. There were concerns about port site metastasis, resection margins, number of harvested lymph nodes, long term overall survival and recurrence free survival**(7).**

Complete excision of the primitive dorsal mesentery along the anatomo-embryological and surgical planes by means of CME is the standard of care for colonic cancers. Technical strategies for CME include two aspects: sharp separation of visceral and parietal fascia, and ligation at the root of central supply vessels and more radical lymph node dissection for improving oncological outcomes**(8).**However, the right hemicolectomy is performed routinely worldwide, the feasibility and safety of complete mesocolic excision has been showed in open and laparoscopic surgeries**(9).**

In our study, the mean age of patients (5 (45.5%) males and 6 (54.5%) females) was 53±16.6 years in group 1 (open) and (4 (36.4%) males and 7 (63.6%) females) was 52.2±12.3 in group 2 (laparoscopic). According to a study done by **Siani and Pulica(5)**, the mean age of patients (75 males and 40 females with a male to female ratio of 1.8) was 65±1.3 years. while in a study done by **El-Fol et al. (10)**, the mean age of patients (14 males (46.7%) and 16 (53.3%) females) was 58.33±5.88 years. **Shin et al. (11)**in their study reported that the mean age of patients (445 (44.1%) males and 565 (55.9%) females) was 60±11years. The patient demographics and baseline clinical data were similar between the treatment groups; the L-CME group exhibited a mean age of 69.91 years, and the O-CME group exhibited a mean age of 65.41 years. Women comprised 46.20% and 41.23% of the L-CME and O-CME patients, respectively. None of the studies were blinded, and all of the studies were powered to demonstrate the non-inferiority of the laparoscopic approach **(12).**

In our study the majority of operations were rt. hemicoectomy although we didn't exclude hepatic flexure or proximal transvers colon lesions as in majority of cases the lesion was in the rt. colon (caecum and ascending colon). There was no statistically significant difference between open and laparoscopic groups as regard operative type ($p>0.05$). **Storli et al. (13)** performed 9 (7.3%) transverse colectomies in the open approach but none in the laparoscopic group. In a second paper, **Storli et al. (13)**published their experience regarding CME only in transverse colon cancer. **Gouvas et al. (14)** managed all of the transverse colon cancers using an extended right

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hemicolectomy. **Munkedal et al. (5)** excluded all cancers in the transverse colon or flexures from their analysis. But, **Bae et al. (16)** and **Zhao et al. (17)** managed all cases by a right or extended right hemicolectomy. All studies exhibited remarkable similar exclusion criteria: Stage IV disease and emergency surgery.

In our study, there was statistically significant difference between open and laparoscopic groups as regard operative time (120-210min. vs 180-240 min.) (p =0.001). This is similar to data reported by **Hewett et al. (18)**asthe mean duration of surgery was 95-135 compared to 145-180 min. Also, it's similar to data reported by **Shin et al. (11)** as the total operation time was significantly longer in the laparoscopic group than the open group (165 vs. 139 min, p < 0.001). Also,**Mori et al. (19)** reported that the mean operative time after laparoscopic CME ranges from 136 min to 269 min. In contrast, the study conducted by **Kim et al. (9)**reported that the mean operative time was similar between the open and laparoscopic CME groups (175 min vs. 178 min).

One of advantages of laparoscopic surgery over open surgery is less blood loss and less need for blood transfusion **(20)**. In our study there was statistically significant difference between open and laparoscopic groups as regard blood loss and length of incision (P<0.05); blood loss is more in O-CME. This is similar to data reported in the majority of studies published previously as that reported *by* **Adamina et al. (21)**and**Negoi et al. (12)**where the laparoscopic approach was associated with statistically significant lower intraoperative bleeding, with a mean difference of 52.11ml (P<0.001).

Less blood loss in laparoscopic surgery may be caused by usual using of modern energy devices during laparoscopic surgery like Harmonic® scalpel or Ligasure ™ V as minor oozing compromise the laparoscopic view therefore, dissection must be performed with this tools that optimize precise tissue cutting and coagulation **(22)**.
As regard to the length of incision, our results correlate with data reported by **Bae et al. (16)**where Patients from the laparoscopic group had a shorter incision, with a mean difference of 14.01 cm (P<0.001). It was also reported that incision length was approximately three times shorter in L-CME than O-CME by **Sheng et al. (23).** Reduced incision length, significantly decreases abdominal wall complications and postoperative pain, hospital stay and could affect patient recovery **(24).**

In our study there was no statistically significant difference between open and laparoscopic groups as regard time of first flatus (p>0.05); what was expected is that L-CME group would have recovery of gastrointestinal function earlier than O-CME group, but both groups were comparable.
In contrast to a study by **Huang et al. (25)** which reported thatthe laparoscopic approach was associated with a shorter time interval to first flatus and the time to liquid diet was shorter for the L-CME patients with a mean difference of 0.90 d (P= 0.002). Explanation for this may be related to long operation time in L-CME group and small sample size in our study.
In our study there was no statistically significant difference between open and laparoscopic groups as regard complications (p>0.05) except in wound complication (p<0.05). But, in general postoperative complications were lower in L-CME groups. This is similar to the data in a study by

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Shin et al. (11)which reported that differences in overall postoperative morbidity rates between the groups did not reach significance; however, the rate of surgical site infection was significantly lower in the laparoscopic group.

In our study we reported 6 cases of wound infection in O-CME group. Postoperative wound infections contribute predominantly to the morbidity and mortality related to colorectal surgery. Surgical site infections (SSI) associated with colorectal surgery are 4 times more than any other abdominal surgery. Factors leading to a higher incidence of infections include; advanced age, type of surgical wound (clean, clean-contaminated, contaminated or dirty) and surgeries for neoplasm. Other factors such as diabetes mellitus, chemotherapy and steroid use can also increase the risk of SSI **(26).**

In our study none of both groups had recurrence within 6-24 months and the majority of them had no complications. This is in contrast to data reported in a study by **Chaouch et al. (27)**which reported recurrence in six patients out of 175 patients in the O-CME group and 6 patients out of 171 patients in the L-CME group with no statistically significant differences between these two groups.

In our study there was no statistically significant difference between open and laparoscopic groups as regard positive and total LNs. This is compatible the previous studies which documented that with respect to pathologic outcomes, the total number of retrieved lymph nodes was significantly greater in the open group (28.6 vs. 25.7, $p = 0.005$). However, no significant differences were noted between the two groups in terms of the number of positive lymph nodes and number of patients with more than 12 lymph nodes harvested**(11).**

However, in contrast to **Kim et al. (9)** where the median number of lymph nodes retrieved in our study was 26 and 29 inthe laparoscopic and open groups respectively, the median number of lymph nodes retrieved in our study was 17 and 19 inthe laparoscopic and open groups respectively but this difference may be related smaller size of our sample.

Number of harvested lymph nodes in our study is more in O-CME than in L-CME and this is correlates with a study by **Shin et al. (28)***as*there were several possible explanations for this difference: in some cases of open surgery, more meticulouslymph node dissection could be performed and a more aggressive dissection of the lymph nodes over the head of the pancreas or along the gastroepiploic arcade. However, the difference in the number of harvested lymph nodes between the two groups might be related to the total length of the specimen.

Other important point in our study is that we have no case with retrieved number of lymph nodes less than 12. According to a study by **Provenzale et al. (29)** it was reported that; Although O-CME allows removal of more lymph nodes than L-CME, both the open and laparoscopic approaches satisfy the current recommendation of a minimum of 12 lymph nodes.

Also, we think that smaller number of retrieved lymph nodes in L-CME may be due to lack of our experienceas reported by**Negoi et al. (12)**thatthere was a high heterogeneity between the studies. Meta-regression of retrieved lymph nodes according to the number of patients revealed that the equivalence between laparoscopic and open approach is stronger with the increased experience in laparoscopic approach.

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Conclusion

Laparoscopic CME in rt. colon cancer can be performed with good technical efficiency, quick functional recovery, mild disability and less operative blood loss and operative trauma. The short-term oncologic results of laparoscopic CME seem to be acceptable and outcome seems to be better than those obtained in other studies with conventional resection as laparoscopic procedure maintains intact embryological envelope of the mesocolon and allows high tight ligation.

Conflict of Interest: No conflict of interest.

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