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Laparoscopic versus open complete mesocolic excision for right cancer colon

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ABSTRACT

Introduction. This study aims to assess and compare the pathological, oncological and perioperative surgical outcomes of CME for right colon cancer by open and laparoscopic approaches.

Material and methods. This is a prospective randomized study that included all patients that underwent radical right hemicolectomy with CME for right colon cancer at the Department of General Surgery, Assiut University between January 2017 and December 2018. Follow up of the patients continued till January 2020.

Patients were randomized into two groups: the first group for open CME and the second group for laparoscopic CME. Demographic, operative, pathologic and oncological parameters were analysed.

Results. This study enrolled 35 patients with colon cancer that were randomly sub-grouped into the open CME group (n = 18) and laparoscopic CME group (n = 17) according to the surgical approach. Both groups had insignificant differences as regard mesocolon grading, vascular tie, circumferential safety margin, total lymph nodes and positive lymph nodes. Patients who underwent open CME had significantly shorter operative time [168.83 ± 23.50 *vs*. 205.17 ± 35.70 (minutes); $p < 0.001$] and significantly higher blood loss in comparison to those underwent laparoscopic CME [353.89 ± 85.70 *vs*. 224.11 ± 96.51 (cc); $p < 0.001$].

Patients underwent laparoscopic CME had significantly shorter time of passage of flatus [1.45 ± 0.23 *vs*. 2.34 ± 0.79 (days); $p < 0.001$] and first bowel motion [1.92 ± 0.38 *vs*. 2.79 ± 0.95 (days); $p = 0.01$], and less postoperative pain score and shorter hospital stay in comparison to those underwent open CME. There was no significant difference between the open group and the laparoscopic group as regard mean overall survival duration [23.44 *vs*. 23.29 (month); $p = 0.36$]

Conclusions. Our study supports the use of laparoscopic CME for right colonic cancer if good surgical expertise is present. It is a feasible and safe procedure with better postoperative short and long-term surgical outcomes and similar pathological and oncological outcomes if compared to the open approach.

Key words: cancer colon, complete mesocolic excision, right hemicolectomy

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Introduction

Colon cancer (CC) is the third most common cancer in both men and women in the world [1]. Surgery is still the cornerstone in the therapy of non-metastatic disease. The surgical principles and techniques regarding colonic resection for cancer colon had never been changed greatly in the last century. In 2009, a new concept of colonic resection referred as complete mesocolic excision (CME) was introduced by Hohenberger [2]. The concept of CME is similar to the total mesorectal excision (TME) proposed by Heald [3]. The wide application of TME led to a major improvement in the survival and local recurrence rates of rectal cancer. The rationale of CME is to resect a sufficient length of the affected colon with its mesocolon in an intact envelope of visceral peritoneum. This aims to minimize the risk of spillage of cancer cells into the peritoneal cavity and maximize the removal of potentially involved lymph nodes in a longitudinal direction. In addition, central

vascular ligation (CVL) of the relevant blood supply is performed as an integral part of CME to improve lymph node harvesting [4, 5].

Performing CME for left-sided resections is truly not much different compared to conventional resections performed by most expert colorectal surgeons. TME/CME principles are applied due to the feasibility of central vascular ligation of the inferior mesenteric vessels [6]. However, for right-sided resections, mobilization of the mesocolon needs to be more radical than a conventional resection, fully exposing the head of the pancreas and the anterior surface of the superior mesenteric artery and vein. This allows accurate identification of the origins of the ileocolic and middle colic vessels.

The concept CME with central vascular ligation (CVL) and D3 lymphadenectomy technique — which has a concept close to CME — has been adopted by many European and Asian colorectal centres. The results reported by these centres showed that CME and D3 lymphadenectomy are associated with higher reported survival rates than conventional colon resection surgery, especially for clinical stage II and III colon cancer [4, 5, 7, 8].

Since its introduction in 1991, the use of laparoscopy for colorectal surgery has shown to be associated with faster recovery and less morbidity as compared to the standard open approach without affecting oncologic outcomes. Hence it is hypothesized that CME using the laparoscopic approach will offer the best curative surgery for colon cancer patients [9–13].

This study aimed to assess and compare the pathological, oncological and perioperative surgical outcomes of CME for right colon cancer by open and laparoscopic approaches.

Material and methods

This is a prospective study that included all patients that underwent radical right hemicolectomy with CME for right colon cancer at the Department of General Surgery, Assiut University between January 2017 and December 2018. Follow up of the patients continued till January 2020.

Exclusion criteria include stage IV disease, extracolonic infiltration (T4b), emergency conditions caused by cancer (bleeding, perforation and obstruction), recurrent cases and previous significant abdominal surgery (except appendectomy or cholecystectomy). Also, patients with deranged cardiopulmonary and hepatorenal functions not suitable for the laparoscopic surgery group are excluded from the study.

All eligible patients during the period of the study were included (total coverage) as the authors are not a specialized colorectal centre. Thirty-five patients with colon cancer were assigned to receive either open or laparoscopic complete mesocolon resection. The cases will be randomized simply into two groups: the first group for open CME and the second group for laparoscopic CME. Random assignment of intervention will be done after subjects have been assessed for eligibility and recruited. The first case will be assigned for its group by tossing a coin, the second case will be assigned for the other group and third case for the first group and so on.

History and clinical examination, basic laboratory investigations and carcinoembryonic antigen (CEA) were routinely done for all patients. All patients had computed tomography (CT) of the abdomen and pelvis, colonoscopy and punch biopsy. Routine plain chest radiograph was done as a metastatic workup and MSCT-chest was performed in some cases when indicated.

Written informed consents were taken from all patients. All patients scheduled for resection underwent bowel preparation for three days before surgery in the form of a low fibre diet, clear fluid intake and multiple enemas the day before surgery. Elastic compression stockings worn by patients and low molecular weight heparin (LMWH) given 12 hours before surgery are measures used for prophylaxis against deep venous thrombosis (DVT). The protocol of an enhanced recovery program (fast track surgery) was not followed in this study.

Surgical technique

Open approach

For open surgery, a lateral-to-medial approach is used, starting with an incision of the lateral peritoneal fold. The visceral and parietal fasciae are separated by sharp dissection to ensure an intact mesocolon. The dissection continues medially in the mesofascial interface. The mesenteric root up to the origin of the superior mesenteric pedicle is mobilized, and the dissection continues over the duodenum and pancreatic uncinate process to allow complete access to the superior mesenteric vein and artery. After the complete colonic mobilization, the supplying vessels transected close to their origin from the superior mesenteric vessels (CVL) (Fig. 1A).

For cecal and ascending colon tumours, the ileocolic, right colic (if present), and right branch of middle colic vessels are divided with a division of the mid-transverse colon. For tumours at and distal to hepatic flexure tumour, extended right hemicolectomy is performed with resection of proximal 2/3 of the transverse colon and division of middle colic vessels at their origin. In addition, a part of the greater omentum is removed en bloc with the specimen. An end-to-end or end-to-side ileocolic anastomosis is performed using a hand-sewn technique with 3–0 Vicryl suture.

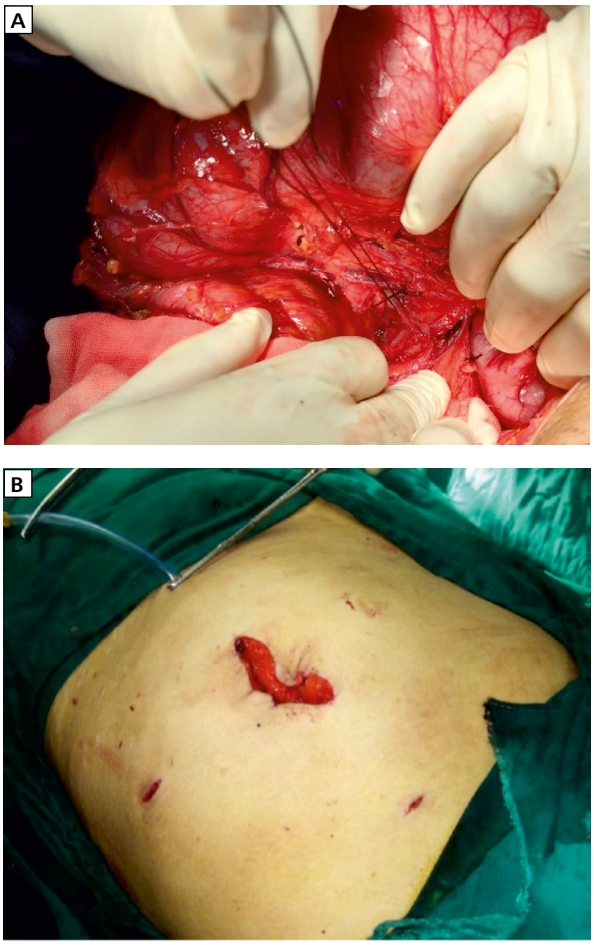

Figure 1. A. Central vascular ligation in right hemicolectomy: division of middle colic pedicle and hanging of ileocolic pedicle at their origin from superior mesenteric vessels; **B.** Periumbilical incision (5 cm) for specimen retrieval and creation of anastomosis

Laparoscopic approach

For laparoscopic cases, the medial-to-lateral approach is used. The mesentery at the junction of the terminal ileum and cecum is pulled to the right lower quadrant to identify the ileocolic pedicle. The peritoneum on the caudal aspect of the ileocolic vessels is incised to reach the retroperitoneal plane. Sharp dissection proceeds in caudal-cephalic direction and from the medial to lateral to separate the posterior layer of the mesocolon from the parietal fascia. After exposing the right gonadal vessels, ureter, duodenum, and head of the pancreas, the division of vessels proceeds in a fashion similar to that discussed in the open approach. Finally, the gastrocolic ligament and lateral peritoneum fold of the colon are divided.

The specimen was extracted from a small periumbilical midline incision (Fig. 1B). An extracorporeal end-to-end or end-to-side ileocolic anastomosis is performed using hand-sewn or stapling techniques.

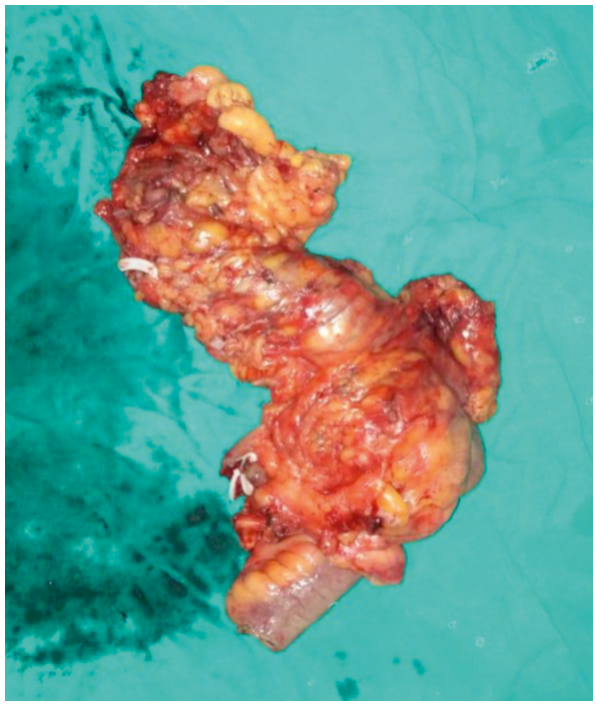

Figure 2. Resection specimen of right hemicolectomy: cancer cecum removed by laparoscopic CME show divided ileocolic and right colic pedicles marked by clips

Follow up

After completion of adjuvant therapy, all patients were subjected to follow up schedule. Patients were reviewed every 3 months in outpatient clinic visits for the 1st postoperative year, every 6 months in the 2nd year and then annually. During visits, history and clinical examination were taken and blood samples were obtained to check CEA. Computed tomography of the abdomen was done every six months and colonoscopy after one year.

Outcome measures

Surgical outcome parameters included operative time, blood loss, conversion rate, gastrointestinal recovery (time of 1st bowel motion and time of 1st passing flatus), postoperative pain score, duration of hospital stay, and postoperative morbidity and mortality within 30 days after surgery.

Pathological outcome parameters include circumferential resection safety margin (CRM), proximal and distal resection margins, number of harvested lymph nodes, number of positive lymph nodes, mesocolon grade and distance between the tumour and the central arterial high tie (Fig. 2).

Oncological outcomes include pattern and rate of recurrence and 2-years survival rate.

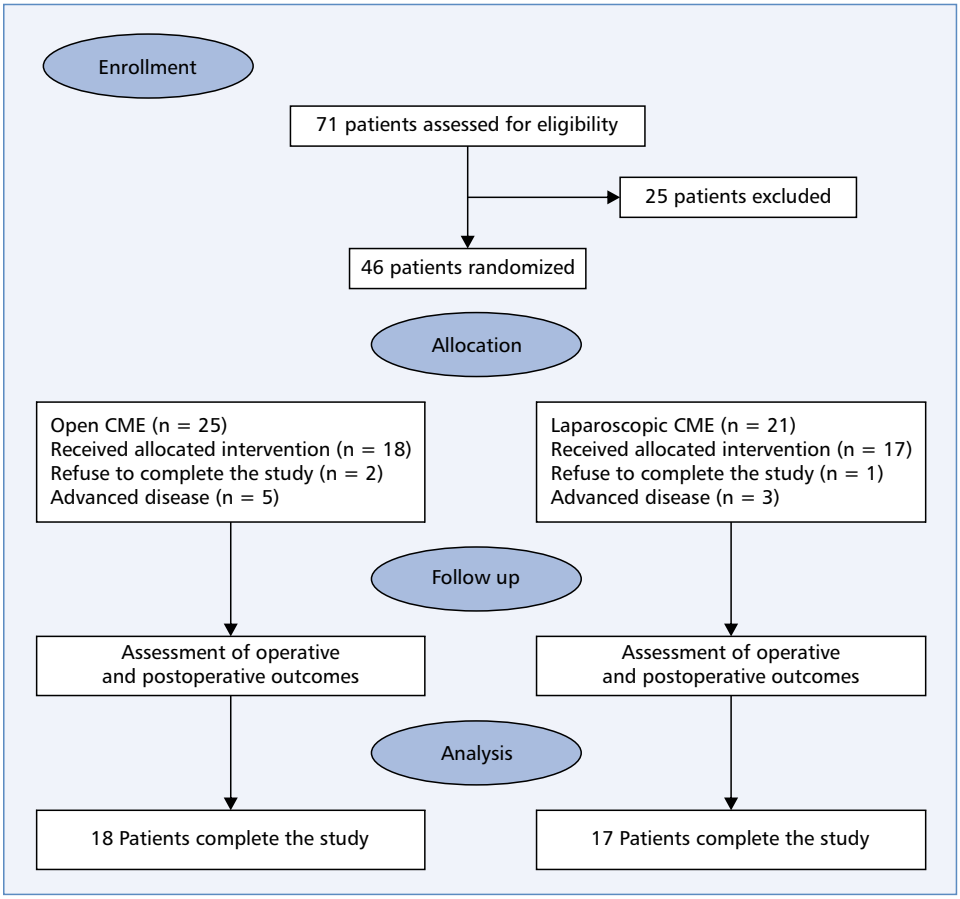

Figure 3. The enrollment process (CONSORT flow diagram); CME — complete mesocolic excision

Statistical analysis

Data analysis was performed using SPSS v20.0 (Statistical Product and Service Solutions Inc., Chicago, IL, USA). Quantitative data were expressed as medians, means, minimum and maximum and were compared by Mann-Whitney U test. Qualitative data were expressed as numbers and percentages and were compared by the Chi-square test or Fischer's exact test when appropriate. A log-rank test was used to compare the time to recurrence between the two groups. A significance level of p-value less than 0.05 was used in all statistical tests.

Results

All patients diagnosed with right colonic cancer and matching eligibility criteria were recruited to the study in the period between January 2017 and December 2018. Twenty-six patients were excluded before randomization because they are not meeting inclusion criteria. Two patients refused participation, 7 required urgent surgery, 8 were inoperable, 5 patients with T4 disease, 2 patients were had previous explorations with dense adhesions and 2 patients had cardiac problems. After allocation, 3 patients refused to complete the study while 8 patients were found to have advanced disease. This study enrolled a total number of 35 patients with colon cancer who were randomly sub-grouped into the open CME group (n = 18) and laparoscopic CME group (n = 17) according to the surgical approach. Figure 3 shows the enrollment process (CONSORT flow diagram).

Patients' demographic data

The mean age of the open group was 50.61 ± 13.69 years and the majority (61.1%) of them were males while the mean age of the laparoscopic group was 49 ± 13.55 years and, the majority (52.9%) of them were males (Tab. 1). Both groups had no significant differences as regard age (p = 0.72) and sex (p = 0.31).

Pathological outcomes

It was noticed that the common tumour location in both groups was the cecum (n = 14). The majority of

Table 1. Patients' demographic data

	Open CME (n = 18)	Laparoscopic CME (n = 17)	p-value
Age [years]	50.61 ± 13.69	49 ± 13.55	0.72
Age group			0.44
< 40 years	5 (27.8%)	4 (23.5%)	
40–60 years	7 (38.9%)	10 (58.8%)	
> 60 years	6 (33.3%)	3 (17.6%)	
Sex			0.31
Male	11 (61.1%)	9 (52.9%)	
Female	7 (38.9%)	8 (47.1%)	
Body mass index (kg/m^2)	26.53 ± 3.10	26.40 ± 3.48	0.90

CME — complete mesocolic excision

both groups had tumour stage III (n = 15). Stage T3 and stage N2 were frequently found in both groups. The majority of patients had moderately differentiated carcinoma. Regarding tumour location, TNM stage, and tumour differentiation, there are no significant differences between the studied groups (Tab. 2). Both groups had insignificant differences as regard mesocolon grading, vascular tie, circumferential safety margin, total lymph nodes and positive lymph nodes. All patients had negative proximal, distal and circumferential resection margins.

Perioperative data among the study population

Patients who underwent open CME had significantly shorter operative time [168.83 ± 23.50 *vs.* 205.17 ± 35.70 (minutes); $p < 0.001$] and significantly higher blood loss in comparison to those underwent laparoscopic CME [353.89 ± 85.70 *vs.* 224.11 ± 96.51 (cc); $p < 0.001$].

Only one patient in case of open CME had a minor injury to a superior mesenteric vein (SMV) which was easily repaired without significant morbidity.

Conversion to open approach was required in 2 patients in the laparoscopic group due to extensive adhesions. Difficult adhesiolysis by laparoscopic approach with prolonged operative time lead to conversion. Yet, these patients are reported in the laparoscopic group. A smooth postoperative course ensues with no specific morbidities observed in these 2 patients.

It was noticed that patients who underwent laparoscopic CME had a significantly shorter time of passage of flatus [1.45 ± 0.23 *vs.* 2.34 ± 0.79 (days); $p < 0.001$] and first bowel motion [1.92 ± 0.38 *vs.* 2.79 ± 0.95 (days); $p = 0.01$], and less postoperative pain score and shorter hospital stay in comparison to those underwent open CME.

Ileus, leakage, pneumonia, and wound infection occurred more in patients of the open group than laparoscopic group, despite not reaching statistical significance (Tab. 3). Fourteen (77.8%) and 16 (94.1%) patients of the open and laparoscopic group respectively received postoperative chemotherapy. No reported cases of 30-day mortality.

Long-term oncological and surgical outcomes

One patient in each group developed lung metastasis during long-term follow up. Also, two patients of the open group and three patients of the laparoscopic group developed liver metastasis. Local recurrence was reported in only one case with laparoscopic CME.

Adhesive intestinal obstruction occurred in only one patient with open CME while incisional hernia occurred in three patients with open CME and one patient with laparoscopic CME (Tab. 4).

Survival analysis among the study population

Two patients (11.7%) of laparoscopic CME and two patients (11.1%) of open CME were deteriorated and died during long-term follow-up. There was no significant difference between the open group and the laparoscopic group as regards the mean overall survival duration [23.44 *vs.* 23.29 (months); $p = 0.36$] (Fig. 4, Tab. 5).

Discussion

CME is considered by colorectal surgeons as a more radical operation rather than the conventional one. There is still a significant debate regarding the safety of CME right hemicolectomy, especially if performed via a laparoscopic approach. Here, the authors report a series of 35 patients who underwent CME right hemicolectomy and were randomly assigned to receive either open or laparoscopic CME.

It is noted that most of the patients (66.7% of open group and 76.5% of laparoscopic group) had tumour stage III. This may be attributed to the patient's education in seeking medical advice late so the tumour stage was advanced.

Table 2. Pathological outcomes

	Open CME (n = 18)	Laparoscopic CME (n = 17)	p-value
Anatomical site			0.80
Cecum	7(38.9%)	7 (41.2%)	
Ascending colon	5(27.8%)	4 (23.5%)	
Hepatic flexure	2 (11.1%)	1 (5.9%)	
Proximal transverse colon	4 (22.2%)	5 (29.4%)	
Tumour stage			0.78
Stage I	2 (11.1%)	1 (5.9%)	
Stage II	4 (22.2%)	3 (17.6%)	
Stage III	12 (66.7%)	13 (76.5%)	
T stage			
T2	2 (11.1%)	2 (11.8%)	0.99
T3	14 (77.8%)	13 (76.5%)	
T4	2 (11.1%)	2 (11.8%)	
N stage			0.75
N0	6 (33.3%)	5 (29.4%)	
N1	3 (16.6%)	5 (29.4%)	
N2	9 (50%)	7 (41.2%)	
Grade of adenocarcinoma			0.03
Well-differentiated	4 (22.2%)	3 (17.6%)	
Moderately differentiated	9 (50%)	8 (47.1%)	
Poorly differentiated	3 (16.7%)	1 (5.9%)	
Mucinous	2 (11.1%)	5 (29.4%)	
Mesocolon grading			0.44
Mesocolic plane	11 (61.1%)	9 (52.9%)	
Intramesocolic plane	7 (38.9%)	8 (47.1%)	
Vascular tie [cm]	10.97 ± 0.51 (95% CI 10.3 to 11.7)	10.91 ± 0.58 (95% CI 10.6 to 11.2)	0.63
Total lymph nodes	29 ± 5.07 (95% CI 28.8 to 29.2)	27.05 ± 5.52 (95% CI 24.4 to 29.7)	0.62
Positive lymph nodes	3.67 ± 2.34 (95% CI 2.59 to 4.75)	3.29 ± 2.91 (95% CI 1.91 to 4.67)	0.29

CME — complete mesocolic excision; CI — confidence interval

Central vascular ligation (CVL) can be assessed by the distance of the tumour to the high arterial tie (vascular tie). The mean vascular tie for the open group was 10.97 ± 0.51 and for the laparoscopic group was 10.91 ± 0.58. There were no significant differences between both groups as regard to vascular tie and these results agree with a systematic review and meta-analysis reported by Negoi et al. [14]. On other hand, Munkedal et al. [15] reported significantly high vascular tie after laparoscopic CME in comparison to the open CME.

The integrity of mesocolon was commonly assessed by the method described by Hohenberger et al. and classified as a mesocolic plane, intramesocolic plane or muscularis propria plane. It was noticed that mesocolon plane and intramesocolic plane were present in 11 (61.1%), and 7 (38.9%) patients of the open group and present in 9 (52.9%), and 8 (47.1%) patients of the laparoscopic group, respectively. Both groups had no significant differences as regard mesocolon grading and these results agree with the results reported by Gouvas et al. [16] and systematic review and meta-analysis by Negoi et al. [14].

The number of lymph nodes retrieved reflects the extent of regional lymphadenectomy. It is a key indicator of the quality of CME and is associated with recurrence rate and survival rate postoperatively. The

Table 3. Operative and postoperative data

	Open CME (n = 18)	Laparoscopic CME (n = 17)	p-value
Operative time [minute]	168.83 ± 23.50 (95% CI 168 to 170)	205.17 ± 35.70 (95% CI 188 to 222)	0.01
Blood loss [cc]	353.89 ± 85.70 (95% CI 314 to 393)	224.11 ± 96.51 (95% CI 178 to 270)	< 0.001
Anastomotic technique			0.05
Hand-sewn	15 (83.3%)	14 (82.4%)	
Stapler	3 (16.7%)	3 (17.6%)	
Conversion	-	2	NA
Major vessel bleeding	1 (5.6%)	0	0.32
First passage of flatus [day]	2.34 ± 0.79 (95% CI 1.97 to 2.71)	1.45 ± 0.23 (95% CI 1.34 to 1.56)	< 0.001
First bowel motion [day]	2.79 ± 0.95 (95% CI 2.35 to 3.23)	1.92 ± 0.38 (95% CI 1.74 to 2.1)	0.01
Visual analogue scale	50.12 ± 12.43 (95% CI 44.4 to 55.9)	34.05 ± 7.67 (95% CI 30.4 to 37.7)	< 0.001
Hospital stay [day]	8.89 ± 1.49 (95% CI 8.2 to 9.58)	7 ± 0.93 (95% CI 6.56 to 7.44)	< 0.001
Overall, 30-day complications	7 (39%)	2 (11.8%)	0.07
Ileus	1 (5.6%)	0	
Anastomotic leakage	2 (11.1%)	1 (5.9%)	
Pneumonia	2 (11.1%)	1 (5.9%)	
Wound infection	2 (11.1%)	0	
Post-operative chemotherapy	14 (77.8%)	16 (94.1%)	0.18

CME — complete mesocolic excision

Table 4. Long-term oncological and surgical outcomes

	Open CME (n = 18)	Laparoscopic CME (n = 17)	p-value
Liver metastasis	2 (11.1%)	3 (17.7%)	0.58
Lung metastasis	1 (5.6%)	1 (5.9%)	0.97
Local recurrence	0	1 (5.9%)	0.30
Adhesive obstruction	1 (5.6%)	0	0.32
Incisional hernia	3 (16.7%)	1 (5.9%)	0.32

CME — complete mesocolic excision

median number of lymph node retrieval on several studies of CME and D3 lymphadenectomy range from 18–46 [5, 16–19]. In this study, the mean number of retrieved lymph nodes was 27 ± 5.52 in the laparoscopic group versus 29 ± 5.07 in the open group. The difference between the two groups is not statistically significant. In most reports comparing laparoscopic CME or D3 lymphadenectomy to open approach, there is no superiority of one approach over the other regarding the number of lymph nodes harvested [14, 18, 20]. Yet, this conclusion is not universal. Shin et al. [21], showed a statistically significant lower number of harvested LNs in laparoscopic CME compared to open CME.

The conversion rate in this study (11.8 %) is higher than that of many reports in the literature (1.9–7.6%) [18, 22, 23] as we are still in the learning curve of laparoscopic CME. However, Kim et al. reported a conversion rate of 13.8 % for T4 lesions [20].

There was one case of SMV injury in the open group. Fortunately, this was a minor injury that was repaired immediately without significant blood loss. Although it is rare (1.6%) [24], iatrogenic SMV injury is the most feared complication regarding CME. Surgeons should take great care during dissection or ligation near SMV especially at the origin of a middle colic vein and gastrocolic trunk; otherwise, a catastrophic uncontrollable bleeding or bowel ischemia will supervene.

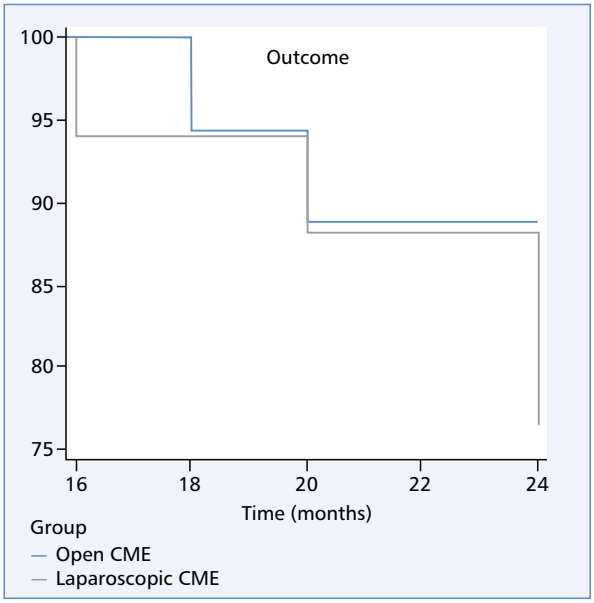

Figure 4. Kaplan Meier curve for survival analysis in the study population; CME — complete mesocolic excision

Table 5. Survival analysis among the study population

	Open CME (n = 18)	Laparoscopic CME (n = 17)	p-value
Death	2 (11.1%)	2 (11.7%)	0.95
Overall survival [months]	23.44	23.29	0.36

CME — complete mesocolic excision

Performing CME via a laparoscopic approach has major advantages regarding short- and long-term surgical outcomes. Patients in the laparoscopic group showed significantly less blood loss, less postoperative pain, enhanced gastrointestinal recovery and shorter hospital stay. These results are supported by many reports and randomized trials [12–14, 19, 25–27]. Regarding long-term surgical complications, adhesive intestinal obstruction occurred in one patient in the open group (5.6%). Three patients in the open CME (16.7%) develop incisional hernia versus one patient in the laparoscopic CME (5.9%). However, in this study, the previous two complications are statistically insignificant between the two groups. On the other hand, patients who underwent open CME had significantly shorter operative times [168.83 ± 23.50 *vs.* 205.17 ± 35.70 (minute); $p < 0.001$]. These results are consistent with the systematic reviews and meta-analyses by Negoi et al. [14] and Chaouch et al. [28]. On the other hand, the present results are inconsistent with those reported by Kim et al. [20] (175 *vs.* 175), Huang et al. [29] (177 *vs.* 194) and Bae et al. [25] (194 *vs.* 179) which show no significant difference between two groups.

The circumferential resection margin (CRM) has traditionally been an important factor for R0 resection and determining the oncologic outcomes of colon cancer surgery. One of the proposed advantages of CME is that sharp dissection in the mesofascial interface enhances the probability of attaining negative CRM which was the scenario in all cases.

In the present study, the recurrence rate was lower in the open group (11.1%) than in the laparoscopic group (17.7%) but with no significant difference. Local recurrence was detected in one case in the laparoscopic group while distant metastasis was detected in three cases of the laparoscopic group and two cases in the open group. The present results are similar to those reported by Sheng et al.[27]. Han et al. [22] and Bae et al. [25]. Also, the present results are consistent with those reported in systematic review and meta-analysis by Negoi et al. [14]. The results are inconsistent with those reported by Shin et al. [21] and systematic reviews and meta-analysis by Chaouch et al. [28] which showed statistically significant lower overall recurrence in the laparoscopic group versus open group.

This study found comparable OS among both groups. The mean OS was 23.29 in the laparoscopic group versus 23.44 in open surgery, p-value = 0.36. The cumulative overall survival probability for all stages at 24 months in the laparoscopic group was 88.2 %, as compared to 88.8% in the open group, with no significant differences being detectable between the two groups. In Negoi et al.'s meta-analysis, including more than one thousand patients, the 3-year OS was reported by four studies. The laparoscopic approach was associated with a statistically significant better 3-year OS [14]. In Sheng et al. study [27], during the follow-up period (median 20.1 ± 4.6 months), the laparoscopic and open groups were similar in terms of local recurrence rate, distant metastasis rate, and short-term survival rate (79.5% *vs.* 77.8%) which is close to these results.

Limitations of this study include recruitment of cases was slow due to low flow of colon cancer cases. This led to a low sample size which can potentially affect the accuracy of results. Moreover, a short period of follow-up in the study may jeopardize the power of this study.

Conclusions

Our study supports the use of laparoscopic CME for right colonic cancer if good surgical expertise is present. It is a feasible and safe procedure with better postoperative short and long-term surgical outcomes and similar pathological and oncological outcomes if compared to the open approach. However, a large number of cases

and a long duration of follow up are needed to better assess survival and oncological outcomes.

Conflict of interest

None.

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