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Laparoscopic vs open complete mesocolic excision with central vascular ligation for right-sided colon cancer

Mehmet Ali Koc, MD[a], Suleyman Utku Celik, MD[a,b], Volkan Guner, MD[a], Cihangir Akyol, MD[a,*]

Abstract

Complete mesocolic excision (CME) is being performed more frequently and has recently become an established oncologic surgical method for right hemicolectomy. Despite its advantages, such as its association with early mobilization, a short hospital stay, early bowel movement, mild postoperative pain, and good cosmesis, CME is technically demanding and carries the risk of severe complications. This study aims to compare the clinical, pathological, and oncological results of open and laparoscopic right hemicolectomy with CME.

The data of 76 patients who underwent right hemicolectomy with CME and high vascular ligation were reviewed retrospectively. The patients were divided into 2 groups according to whether the open or laparoscopic technique was used.

Thirty-two patients underwent open right hemicolectomy, and 44 patients underwent laparoscopic right hemicolectomy. The 2 groups were similar in age, sex, American Society of Anesthesiologists class, abdominal surgical history, tumor localization, and operation time. No significant differences were found regarding the specimen length, tumor size, harvested lymph nodes, number of metastatic lymph nodes, or tumor grade. According to the Clavien–Dindo classification system, the laparoscopic group had significantly fewer complications than did the open group (11.4% vs 31.2%; $P=.04$). The open group had a longer postoperative hospital stay than did the laparoscopic hemicolectomy group (9.9 ± 4.7 vs 7.2 ± 3.1 days; $P=.002$). In addition, the groups were similar with respect to disease-free survival ($P=.14$) and overall survival ($P=.06$).The data in this study demonstrated that no differences exist between the open and laparoscopic techniques concerning pathological and oncological results. However, significantly fewer complications and a shorter length of hospital stay were observed in the laparoscopic group than in the open group. Laparoscopic right hemicolectomy with CME and central vascular ligation is a safe and feasible surgical procedure and should be considered the standard technique for right-sided colon cancer.

Abbreviations: ASA = American Society of Anesthesiologists, CME = complete mesocolic excision, CVL = central vascular ligation, DFS = disease-free survival, OS = overall survival, TME = total mesorectal excision.

Keywords: complete mesocolic excision, laparoscopic, right hemicolectomy, survival

1. Introduction

Colorectal cancer is the 3rd most common cancer in men and the second most common cancer in women globally.[1] The survival rate of patients with colorectal cancer has increased as interdisciplinary and multimodal approaches have emerged. Surgery, which is the main component of the multimodal approach, has a large impact on patient survival. Dissection along the embryological planes between the visceral and parietal peritoneal leaves with appropriate harvest of lymph nodes has become important, especially in both colon and rectal cancer surgeries. Thus, Hohenberger et al[2] described the complete mesocolic excision (CME)-central vascular ligation (CVL) technique for treating colon cancer and showed that it decreases the local recurrence rate and improves survival.

The CME-CVL technique has been described primarily for open surgery. Although it is a challenging technique that involves the main vascular trunk dissection, it has been increasingly performed laparoscopically owing to surgeons having gained experience in performing minimally invasive colorectal surgery.[3] Thus, the advantages of minimally invasive surgery such as the decreased need for analgesia, the lower risk of wound infection, the early return of bowel function, and a shortened

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[a] Department of General Surgery, Ankara University School of Medicine, [b] Department of General Surgery, Gulhane Training and Research Hospital, Ankara, Turkey.

[*] Correspondence: Cihangir Akyol, Ankara University School of Medicine, Ibn-i Sina Hospital, Ankara, Turkey (e-mail: cihangirakyol@gmail.com).

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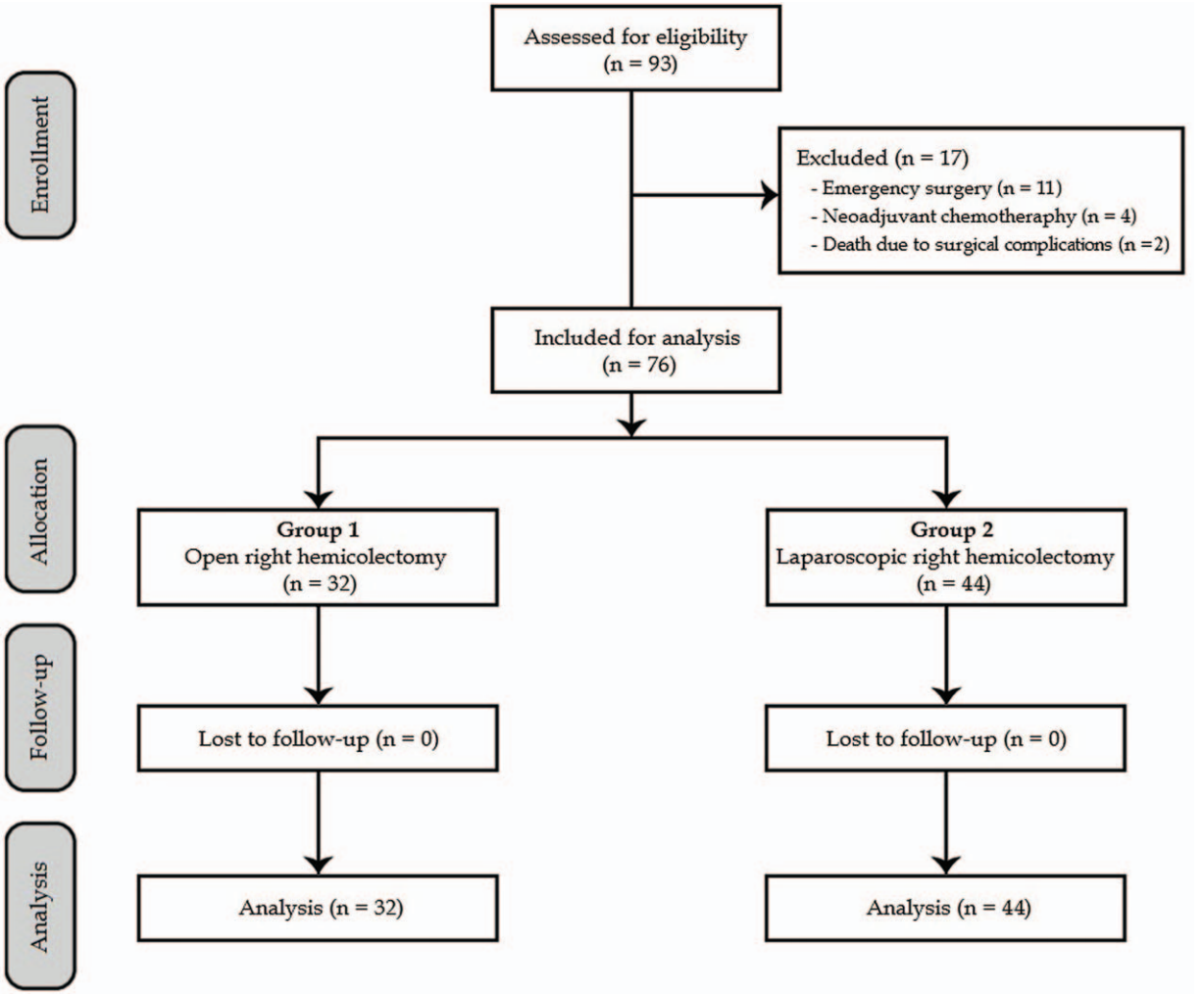

Figure 1. CONSORT flow diagram of the study.

hospital stay, lead to better clinical results. This study aimed to compare the clinical, pathological, and oncological outcomes of open and laparoscopic CME-CVL.

2. Materials and methods

2.1. Study design and population

The study was approved by the Ethics Committee of the Ankara University School of Medicine (approval number: I5-293-20). This study was designed as a single-center retrospective study and involved consecutive patients who had undergone elective open or laparoscopic right hemicolectomy with CME-CVL between January 2015 and December 2019.

Patients older than 18 years and with right-sided colon cancer admitted to Ankara University School of Medicine, Department of General Surgery, and who were followed at least 12 months after surgery were included in the study. Patients who had undergone emergency procedures, those with a history of neoadjuvant chemotherapy, those with inflammatory bowel disease, those with polyposis syndromes, and those who died due to surgery were excluded (Fig. 1).

2.2. Surgical technique

All the surgical procedures were performed by one senior colorectal surgeon (CA) using standard right hemicolectomy with CME-CVL. In the laparoscopic procedures, an inferior-to-superior retroperitoneal approach was used in all dissections with 4-port placement. Extracorporeal resection and side-to-side stapled ileocolic anastomosis were performed from an approximately 4-cm midline umbilical incision. The open procedures were carried out using a midline abdominal incision and the standard lateral-to-medial approach.

To perform CME-CVL in both open and laparoscopic surgeries for right colon cancers, certain protocols are followed. First, the mesocolic fascia is separated from the retroperitoneum by sharp dissection, and the intact mesorectal envelope is preserved. Second, the vascular structures are ligated at their origins (veins at their origin on the superior mesenteric vein and arteries at the level of the superior mesenteric vein) (Fig. 2). The ligation of the ileocolic vessels, right branch of the middle colic artery, gastropancreaticocolic trunk, and right colic artery, if present, at the origin are enough for cecal or ascending colon tumors. However, if the tumor is located at the hepatic flexure or

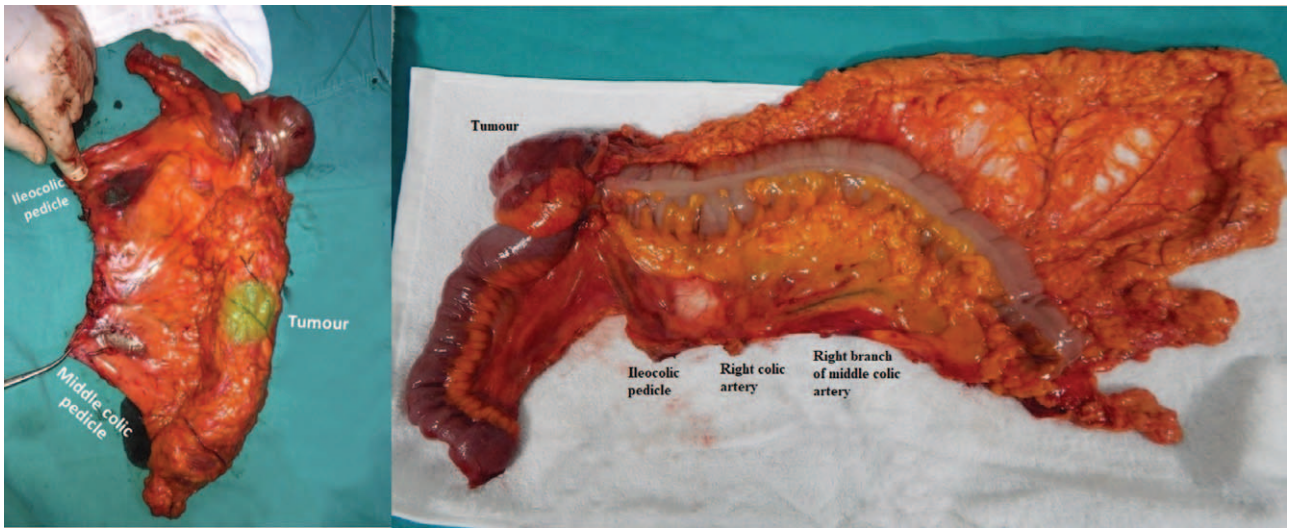

Figure 2. Pathologic specimens after resection. The mesorectal envelope was preserved.

transverse colon, the middle colic artery and vein should also be ligated at the origin. Surgeons must watch, observe, and bear in mind that vascular variations can occur. Awareness of these complex variations may improve the quality of surgery and may prevent devastating complications during right-sided colon resections.[4] It is also important to perform total omentectomy for hepatic flexure and transverse colon tumors, especially to collect the lymph nodes located at the origin of the right gastroepiploic artery.

In the current study, we strictly followed these protocols and ligated the vessels at the level of the superior mesenteric vein (Fig. 3). The Kocher maneuver for the duodenum was performed in the open surgery group, but it was not necessary in the laparoscopic group. However, in both groups, the lymph nodes around the peripancreatic area were harvested. After resection, the specimens were examined by both the surgeon and the pathologist, and the mesocolic fascia was found to be intact in all the specimens.

2.3. Discharge from hospital

The discharge criteria were the presence of normal vital signs, independence in activities of daily living, full tolerance of a soft oral diet, tolerable pain with oral analgesia, and the willingness of the patient to return home.

2.4. Outcomes

Data regarding the patients' demographics, clinicopathological characteristics, operative details, postoperative outcomes, and survival were prospectively obtained from our database. The 30-day postoperative complications were graded according to Clavien–Dindo classification system.[5] The American Joint Committee on Cancer staging system (8th edition) was used for the pathologic staging of the cases.[6]

2.5. Statistical analysis

The descriptive statistics are presented as means ± standard deviations and frequencies (%). The normality of the data for continuous variables was visually assessed using quantile-quantile plots and histograms and was confirmed using the Shapiro–Wilk test. The patients were divided into 2 groups: those who had undergone laparoscopic resection and those who had undergone open resection. Associations between variables were evaluated using Student t test or the Mann–Whitney U test (for continuous variables) and Pearson χ^2 test or Fisher exact test (for categorical variables), where appropriate. Survival curves were prepared according to the Kaplan–Meier method, and disease-specific survival probabilities were compared using log-rank tests. All tests were 2-sided, and P values $<.05$ were considered statistically significant.

The relevant data were extracted from the database and imported into Statistical Package for the Social Sciences (SPSS), version 16.0 (IBM, Chicago, IL), for analysis. Kaplan–Meier plots were created using GraphPad Prism, version 8.0 (GraphPad Software Inc, CA).

3. Results

During the study period, 93 patients underwent right hemicolectomy for colon cancer by 1 surgeon at our institution. After 17 patients were excluded (11 patients were excluded because they underwent emergency surgery, 4 patients were excluded because they required neoadjuvant chemotherapy, and 2 patients were excluded due to surgical mortality) from the analysis, the final study cohort comprised 76 patients, with a mean age of 65.3 ± 14.0 years (range, 32−93 years). Forty-seven (61.8%) patients were male. Most tumors were located in the cecum (53.9%) and ascending colon (30.3%). Thirty-two (42.1%) patients underwent the open surgery, and 44 (57.9%) underwent the laparoscopic surgery.

Table 1 shows the demographic and clinical characteristics of the patients who underwent right hemicolectomy with CME-CVL for right-sided colon cancer. No differences were found in the demographic characteristics, American Society of Anesthesiologists (ASA) score, history of abdominal surgery, tumor localization, estimated blood loss, or operative time between the patients who underwent laparoscopic surgery and those who underwent open surgery. No patients required intraoperative blood trans-

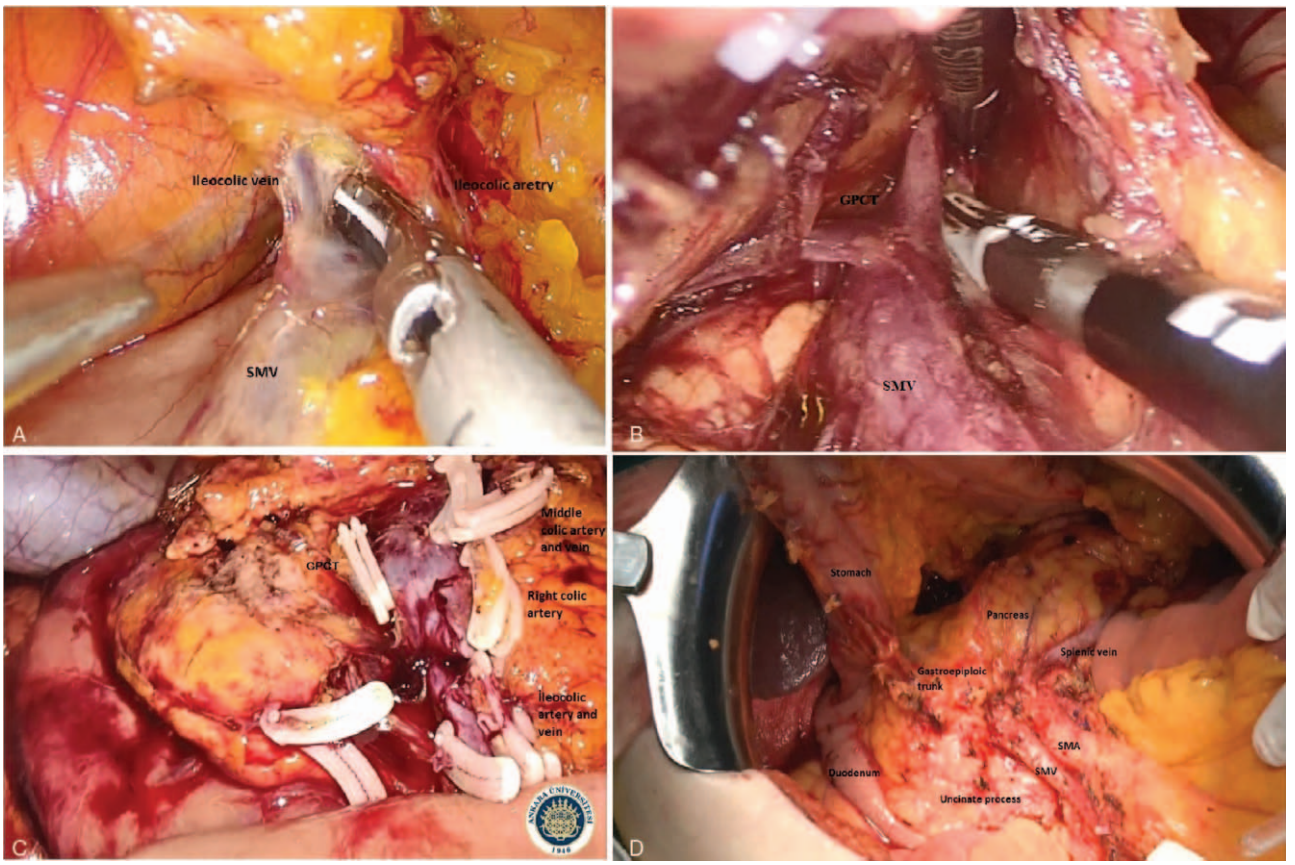

Figure 3. Several pictures of different patients during surgery and after resection was completed. A: Ileocolic pedicle dissection, B: Gastropancreaticocolic trunk, C: The appearance of the stripped SMV, centrally ligated veins, and ligated arteries at the SMV level in the laparoscopic group after resection was completed, D: The appearance of the stripped SMV, centrally ligated veins and arteries in the open group after resection was completed. SMV = superior mesenteric vein.

Table 1

The demographics and clinical characteristics of the 2 groups.

	All (n = 76)	Open (n = 32)	Laparoscopic (n = 44)	*P*
Age (yr)	65.3 ± 14.0	68.0 ± 12.3	63.3 ± 14.9	.40
Sex, n (%)				.18
Female	29 (38.2)	15 (46.9)	14 (31.8)	
Male	47 (61.8)	17 (53.1)	30 (68.2)	
ASA score, n (%)				.66
1–2	55 (72.4)	24 (75.0)	31 (70.5)	
3–4	21 (27.6)	8 (25.0)	13 (29.5)	
Previous abdominal surgery, n (%)				.41
No	56 (73.7)	22 (68.8)	34 (77.3)	
Yes	20 (26.3)	10 (31.3)	10 (22.7)	
Tumor localization, n (%)				.34
Caecum	41 (53.9)	17 (53.1)	24 (54.5)	
Ascending colon	23 (30.3)	10 (31.3)	13 (29.5)	
Hepatic flexura	10 (13.2)	3 (9.4)	7 (15.9)	
Proximal transverse	2 (2.6)	2 (6.3)	–	
Estimated blood loss (mL)	95.0 ± 49.8	104.4 ± 53.3	87.9 ± 46.3	.17
Operative time (min)	217 ± 59	214 ± 63	219 ± 56	.85
Conversion to open, n (%)	–	–	1 (2.3)	

ASA = American Society of Anesthesiologist.

Table 2

Pathology results of the groups.

	Open (n=32)	Laparoscopic (n=44)	P
Pathology, n (%)			.67
Adenocarcinoma	24 (75.0)	31 (70.5)	
Mucinous adenocarcinoma	8 (25.0)	12 (27.3)	
Adenosquamous carcinoma	–	1 (2.3)	
Length of specimen (cm)	36.1±11.9	34.2±8.8	.74
Tumor size (cm)	5.2±2.1	4.6±2.1	.24
Positive resection margin			NS
No	32 (100)	44 (100)	
Yes	0	0	
Closest distance to the tumor (cm)	11.3±5.7	11.6±3.7	.23
Harvested lymph node	25.2±11.6	31.6±16.1	.10
Positive lymph node	3.1±6.3	0.7±1.6	.13
Tumor stage, n (%)			.05
Stage 0-I	3 (9.4)	7 (15.9)	
Stage II	15 (46.9)	24 (54.5)	
Stage III	7 (21.9)	12 (27.3)	
Stage IV	7 (21.9)	1 (2.3)	
Tumor grade, n (%)			.30
Grade 1 (low grade)	–	3 (6.8)	
Grade 2 (moderate grade)	18 (56.3)	25 (56.8)	
Grade 3 (high grade)	14 (43.8)	16 (36.4)	
Perineural invasion, n (%)	5 (15.6)	10 (22.7)	.44
Lymphovascular invasion, n (%)	15 (46.9)	20 (46.1)	.90
Serosal invasion, n (%)	29 (90.6)	37 (84.1)	.32

NS=not significant.

Table 3

Postoperative results of the groups.

	Open (n=32)	Laparoscopic (n=44)	P
Clavien-Dindo classification of complications, n (%)			**.04**
No	22 (68.8)	39 (88.6)	
Grade I–II	4 (12.5)	4 (9.1)	
Grade III–IV	6 (18.7)	1 (2.3)	
Type of complications, n (%)			NS
Anastomotic leak	2	–	
Intraabdominal abscess	2	1	
Prolonged postoperative ileus	1	2	
Bleeding	1	–	
Wound infection	2	–	
Urinary infection	–	1	
Pneumonia	1	–	
Myocardial infarction	1	–	
Trocar site hernia	–	1	
Length of hospital stay (d)	9.9±4.7	7.2±3.1	**.002**
30–day readmission, n (%)	6 (18.8)	1 (2.3)	**.02**
30–day reoperation, n (%)	3 (9.4)	1 (2.3)	.20

NS=not significant.

fusions. In the laparoscopic group, conversion to open surgery was required in 1 patient (2.3%) because of difficulties during dissection. As detailed in Table 2, no differences were found between the groups in the pathology results, including the final pathology, length of specimen, tumor size, number of harvested and metastatic lymph nodes, tumor stage, tumor grade, and perineural, lymphovascular, and serosal invasion. To overcome inherent biases such as a tendency to perform open surgery in patients that had stage IV or metastatic disease, a subgroup analysis of patients without stage IV disease was performed. However, the analysis showed similar pathology results.

Overall, the incidence of postoperative complications was significantly lower in the laparoscopic group than in the open group (11.4% vs 31.2%; $P=.04$). Moreover, grade III–IV complications were less common with laparoscopic surgery than with open surgery (2.3% vs 18.7%, respectively). Although the rate of 30-day readmission was lower in the laparoscopic group than in the open group (2.3% vs 18.8%; $P=.02$), the rate of 30-day reoperation was comparable (2.3% vs 9.4%; $P=.67$). Three patients in the open group required reoperation within 30 days for intraabdominal abscess, anastomotic leakage, and postoperative bleeding. Only one patient underwent a reoperation for strangulated trocar site hernia within 30 days after laparoscopic right hemicolectomy. The length of hospital stay was also shorter in the laparoscopic group than in the open group (7.2±3.1 vs 9.9 ±4.7; $P=.002$) (Table 3).

Disease-free survival (DFS) and overall survival (OS) were analyzed after patients with stage IV colon cancer were excluded. The median durations of follow-up in the open and laparoscopic groups were 44.1 and 39.5 months, respectively ($P=.21$). No significant differences were found in either DFS ($P=.14$) or OS ($P=.06$) (Fig. 4). The 5-year DFS and OS were 74.7% and 78.2%, respectively, in the open group and 83.3% and 94.7%, respectively, in the laparoscopic group (Table 4).

4. Discussion

In 2009, Hohenberger et al[2] were the first to show that similar oncological outcomes can be achieved by CME-CVL for right-sided colon cancer using total mesorectal excision (TME) and the holy plane concepts described by Heald for treating rectal cancer. CME has been described primarily for open surgery, and laparoscopic CME has been performed in many centers despite it being technically difficult to perform. However, it took some time for the technique to be adopted. Because CVL has been performed to harvest more lymph nodes and because there are venous variations in the right colon,[4] many surgeons have been performing CME-CVL in open surgery so that they can perform it carefully before proceeding to laparoscopy.

Although CME-CVL has attracted a great deal of attention worldwide, it has not become as common as TME. Because some critics argue that removing lymph nodes is not curative but is a prognostic factor. Additionally, definitive oncological data are lacking, and CME is technically challenging; consequently, there is a higher risk for severe complications in CME-CVL procedure for right sided colon cancer such as severe vascular.[7,8] On the other hand, supporters advocate that CME is a technique following the embryologic planes. Thus, right hemicolectomy can be standardized as is TME, and staging can be conducted more accurately by harvesting more lymph nodes, particularly apical nodes that have a 5% risk of metastasis. Therefore, adjuvant treatments can be optimized in favor of the cancer patient.[7,8]

Considering these advantages, we compared the clinical, pathological, and oncological results of right-sided colon cancer cases treated by a single surgeon using laparoscopic or open complete mesocolic excision and the central vascular ligation technique.

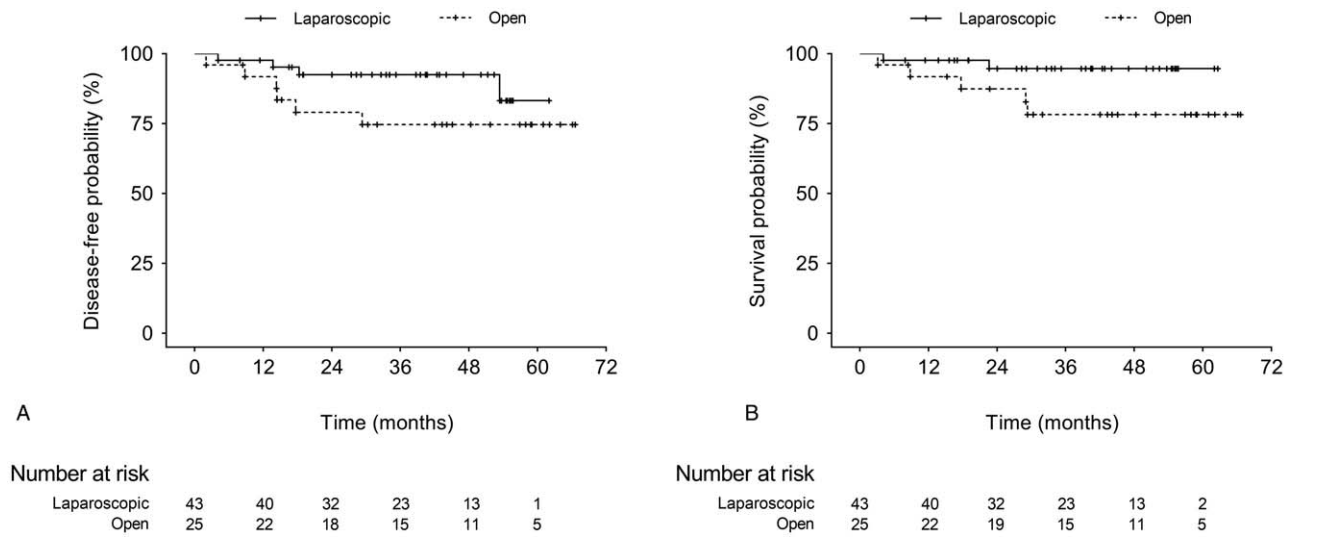

Figure 4. Kaplan–Meier survival probability plots. A: Disease-free survival curves; B: Overall survival curves.

4.1. Clinical outcomes

Because CME is a challenging technique that requires sharp dissection on the main vascular trunks, the operation time is expected to be long. However, in a study by Wang et al,[9] the average operation time for laparoscopic CME was 113.5 ± 34.4 minutes. Adamina et al[10] reported a similar operation time, with an average duration of 136 minutes for laparoscopic CME. Nonetheless, operation times ranging between 175 and 269 minutes for laparoscopic CME and between 159 and 179 minutes for open CME have been reported in several studies.[11–17] In the current study, the laparoscopic and open CME operation times did not differ.[14–16]

The conversion rate can be expected to be high because CME and laparoscopy each have long learning curves. However, in the experienced hands of a surgeon who has completed the learning curve, lower conversion rates should be expected. Although Kim et al[14] reported a conversion rate of 13.8%, this rate has been reported to be between 0% and 6.6% in several studies.[10,11,14–16] In the current study, the conversion rate was 2.3% (1 patient), which is consistent with those reported in the literature.

Previous studies have reported that laparoscopic CME surgery is safe and feasible; it yields good short-term results, including a fast postoperative recovery, a short hospitalization time, few complications, and other advantages.[9] The complication rate with open CME ranges from 12% to 36.4% but that of laparoscopic CME ranges from 4% to 23.3%, and also fewer complications have been reported for laparoscopic surgery in several studies.[11,14–16] As expected, significantly fewer complications were observed in the laparoscopic group than in the open group in the current study (11.4% vs 31.2%; $P = .04$). Similarly, many studies have shown that the length of hospital stay is significantly shorter in the laparoscopy group, which is consistent with our results (7.2 ± 3.1 vs 9.9 ± 4.7 days; $P = .002$).[14–16,18]

Table 4

Disease-free and overall survival of the groups (stage IV patients excluded).

	Open (n = 25)	Laparoscopic (n = 43)	*P*
Disease-free survival (%)			.14
3 yr	74.7	92.5	
5 yr	74.7	83.3	
Overall survival (%)			.06
3 yr	78.2	94.7	
5 yr	78.2	94.7	

4.2. Pathological outcomes

The CME-CVL technique requires sharp dissection following Toldt's line without damaging the mesenteric envelope until the origins of the vessels appear on the superior mesenteric vein. Thus, CVL can be performed, and appropriate lymph node harvesting can be achieved by including the paracolic, intermediate, and apical lymph nodes.[2,9] In the early period of the CME concept, West et al[19] compared the CME specimens from Erlangen with conventional right hemicolectomy specimens from Leeds and found that surgeons in Erlangen removed more of the mesocolon and were more likely to resect in the mesocolic plane than in standard excisions, and a higher lymph node yield was found in their specimens. Therefore, the authors concluded that CME can provide superior specimens. Whether proper resection is performed according to these rules should be checked by tissue morphometry, as described by West et al[20] Since our study was retrospective, the quality of the specimens was unfortunately not evaluated by tissue morphometry. However, the rules described in the surgical technique section were followed very carefully. As a result, no differences were found between groups concerning the specimen length, resection margin positivity, or closest distance to the tumor.

One of the key aspects of CME surgery is lymph node harvesting. Previously, the number of resected lymph nodes was thought to be of prognostic value. More recently, some studies have also supported this idea and showed that it may affect survival.[7] Hohenberger et al[2] reported that the removal of 28 or more lymph nodes in node-negative patients improves 5-year cancer-related survival. In previous studies, the number of lymph

nodes harvested ranged between 14 and 31 in open CME and ranged between 13 and 28 in laparoscopic CME.[9,11,14–17] In addition, no differences were found regarding the lymph nodes harvested in studies comparing laparoscopic and open CME.[11,14–16] In the current study, the number of lymph nodes harvested were similar between groups (31.6±16.1 in laparoscopic vs 25.2±11.6 in open, $P=.10$). These findings are consistent with those in previous studies, and these numbers are more than sufficient according to the NCCN guidelines.[21] Similarly, no differences were found regarding the metastatic lymph nodes (3.1±6.3 in open vs 0.7±1.6 in laparoscopic, $P=.13$). Moreover, there were no differences between the groups regarding other pathological parameters (tumor size, stage, tumor grade, and lymphovascular invasion). These pathological results showed that the extracted specimens were similar in quality between the groups.

4.3. Oncological outcomes

The CME concept leads to a more standardized surgery, a better dissection plan, and the removal of more lymph nodes, yielding better survival. Hohenberger et al[2] reported a reduction in the local 5-year recurrence rate of colon cancer from 6.5% to 3.6%, and the cancer-related 5-year survival rates in patients resected for cure increased from 82.1% to 89.1%. In several studies, these oncological results have been compared. Compared with non-CME resections, CME resections have been shown to decrease the local 5-year recurrence rate by nearly half in 5 different studies published between 2007 and 2013.[7] According to a review by Croner et al,[22] the 5-year survival was 16% higher for CME surgery than for non-CME surgery. In a prospective study by Storli et al,[18] in which open and laparoscopic CME were compared, the 3-year OS rate was 80.4% for open CME resections and 88.2% for laparoscopic procedures, with cancer-specific survival rates of 89.4% and 94.1%, respectively. Kim et al[14] reported 3-year OS and DFS rates of 79.3% and 75.3%, respectively, for open CME and 94.5% and 82%, respectively, for laparoscopic CME. In another study, the 5-year overall survival rates of the laparoscopic CME and open CME groups were 77.8 and 90.3% ($P=.028$), respectively.[15]

Although some studies have relatively better survival outcomes with laparoscopic CME and others with open CME, a meta-analysis reported that the long-term oncological outcomes were comparable between the laparoscopic and open groups; no differences were found regarding the local and distant recurrence rates, 3- and 5-year overall survival rates and DFS rate.[23] As expected, the OS and DFS rates in our study were comparable with those in the literature. Although there were slightly better results for OS and DFS in the laparoscopic group, no statistically significant differences were found between the open and laparoscopic CME groups.

The study had some limitations, including the nonrandomized retrospective nature of the study and the small number of patients being included from a single institution. In addition, regarding the operation type, laparoscopic or open technique was selected by the surgeon according to the preoperative radiological stage and patient condition, possibly leading to selection bias.

In conclusion, the laparoscopic and open CME outcomes were comparable regarding the pathological and oncological results. Significant advantages of laparoscopic surgery were revealed, such as a lower morbidity and a shorter length of hospital stay. Therefore, laparoscopic CME should be considered a safe, feasible, and standard method for right-sided colon cancer.

Author contributions

Conceptualization: Cihangir Akyol.
Data curation: Mehmet Ali Koc, Suleyman Utku Celik, Volkan Guner.
Formal analysis: Mehmet Ali Koc, Suleyman Utku Celik.
Investigation: Mehmet Ali Koc, Suleyman Utku Celik, Volkan Guner.
Methodology: Mehmet Ali Koc, Suleyman Utku Celik, Cihangir Akyol.
Project administration: Cihangir Akyol.
Resources: Mehmet Ali Koc, Cihangir Akyol.
Software: Suleyman Utku Celik.
Supervision: Cihangir Akyol.
Validation: Mehmet Ali Koc, Suleyman Utku Celik, Volkan Guner, Cihangir Akyol.
Visualization: Mehmet Ali Koc, Suleyman Utku Celik, Cihangir Akyol.
Writing – original draft: Mehmet Ali Koc, Suleyman Utku Celik.
Writing – review & editing: Mehmet Ali Koc, Suleyman Utku Celik, Volkan Guner, Cihangir Akyol.

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