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Comparison of conventional right colectomy and complete mesocolic excision technique—case–control analysis of short-term results

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Summary
Introduction The long-term oncologic advantages of complete mesocolic excision (CME) with central vascular ligation and extended lymphadenectomy in right-sided colon cancer have been emphasized in several studies, without compromise of perioperative morbidity or mortality; however, prospective randomized data are scarce.
Methods We performed a single-center non-randomized case–control study comparing conventional non-CME right colectomies (nCME) and complete mesocolic excision (CME) procedures during the period from January 2019 to December 2020. Perioperative morbidity, length of hospital stay (LOHS), operative time, and lymph node yield were analyzed.
Results A total of 131 patients underwent surgery for right-sided colon cancer, with 28 (21%) in the CME group and 103 (79%) in the conventional group. Operative time was significantly longer in the CME group ($p<0.001$) compared to conventional procedures. The duration of hospitalization was statistically similar ($p=0.226$), no difference was observed in 30-day morbidity ($p=0.166$), and the majority of complications in both groups were grades 0–2 (CME: 82%; nCME: 91%). There were no 30-day mortalities. The lymph node yield in CME was significantly higher compared to the conventional surgery ($p=0.041$).
Conclusion Complete mesocolic excision (CME) for right-sided colon cancer is safe without increasing complications or hospital stay, with an acceptable increase in operative time. The significant increase in lymph node yield enables better staging and may lead to improved long-term oncologic outcomes.

Keywords Colonic neoplasms · Perioperative morbidity · Lymph node excision · Central vascular ligation · Survival

Abbreviations

ASA	American Society of Anesthesiologists
BMI	Body mass index
CME	Complete mesocolic excision
CVL	Central vascular ligation
DFS	Disease-free survival
LOHS	Length of hospital stay
ROC	Receiver operating characteristic
TME	Total mesorectal excision
UICC	Union for International Cancer Control

Introduction

The concept of complete mesocolic (CME) excision in right-sided colon cancer—introduced by Hohenberger in 2009—follows similar principles and aspects to the total mesorectal excision (TME) in rectal cancer, with sharp dissection in the avascular plane between the visceral fascia of the mesocolon and the parietal fascia of the retroperitoneum. Guided by the embryologic anatomic plane, the surgical specimen is removed together with the lymphatic, vascular, and fat tissue of the mesocolon [1]; thus, the tumor can be removed as one unit with its arterial blood supply, draining vessels, and regional lymph nodes, while the

Data availability The datasets generated during and/or analyzed in this study are available from the corresponding author upon reasonable request.

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central ligation of supplying vessels enables a larger area of mesocolon and more lymph nodes to be removed [2]. Overall, it is a more radical procedure compared to conventional surgery, with a longer specimen, larger area of mesocolon excised, and a higher number of lymph nodes harvested [3].

The CME procedure is technically more challenging compared to conventional right hemicolectomy, with a potential risk of injury to the superior mesenteric vein (SMV) and its tributaries. Although oncologic evidence is gathering in favor of CME, and some guidelines—like the German S3 guideline—recommend it [26], it is still not widely considered routine practice [4, 5].

Our study was aimed to prospectively analyze the potential risks and short-term results of CME right colectomies compared to the conventional technique during a 2-year period.

Methods

Study design

We performed a single-center, non-randomized case–control observational study of patients undergoing elective right hemicolectomy between January 2019 and December 2020. All patients had endoscopically and histologically confirmed UICC clinical stage I–III right-sided colon cancer or dysplastic adenoma and underwent CME or conventional surgery (nCME) performed by the same group of experienced surgeons. Tumor location in the cecum, ascending colon, and proximal part of the transverse colon were considered appropriate for inclusion criteria, patients with known metastatic disease were excluded. CME procedures were performed by only two out of four surgeons trained in the technique, while conventional surgery was performed by all four physicians. All surgeons had an annual caseload of at least 40 major colorectal cases per year.

Sample size

A total of 131 patients enrolled were divided into CME and conventional right hemicolectomy (nCME) groups according to the procedure chosen and performed. The preferred procedure (CME or nCME) was up to the surgeons' discretion based on clinical decision, where both could be done in an open or laparoscopic fashion.

Surgical technique

Conventional right hemicolectomies were performed in open and laparoscopic fashion.

For cecum and ascending colon lesions, the division of the ileocolic vessels in conventional surgery was at the level of the descending part of the duodenum, dissection of the mesocolon was carried out through the flaccid mesocolic window, and right and middle colic vessels were divided at the level of transverse mesocolon transection in the mid third. In right flexure and proximal transverse tumors, the dissection plane was extended to the distal third of the transverse colon. Figures 1 and 2 show the intraoperative

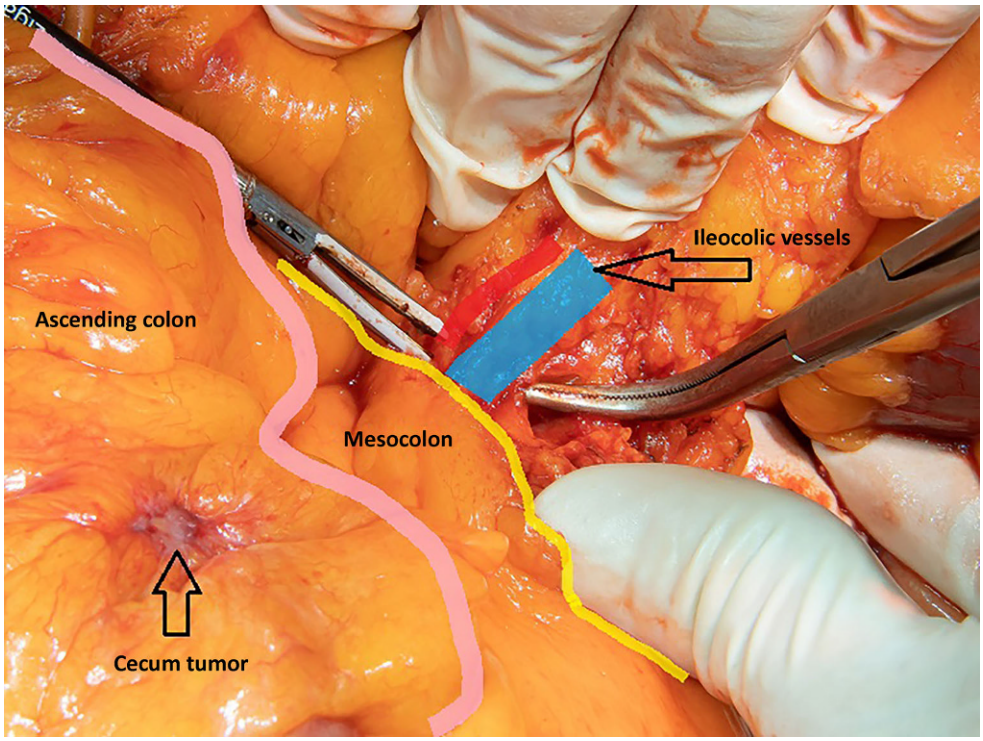

Fig. 1 Intraoperative field in an open conventional non-complete mesocolic excision right colectomy. *Arrows* indicate the ileocolic vessels, the right mesocolon, the cecum, and the ascending colon. *Blue band* indicates the ileocolic vein, *red band* shows the ileocolic artery

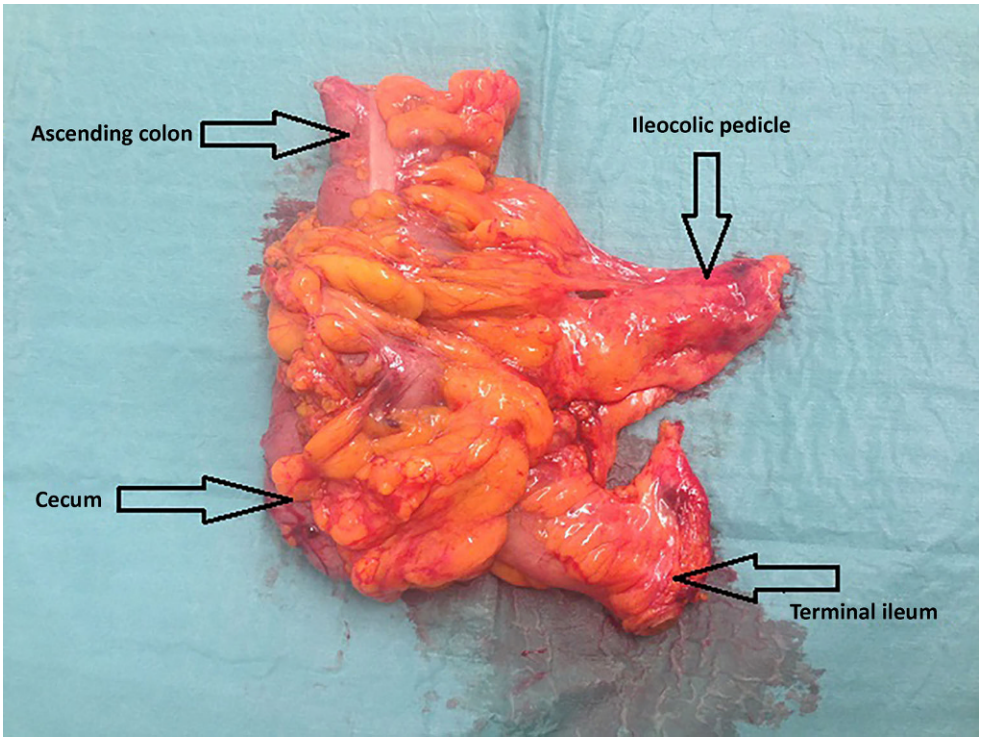

Fig. 2 Surgical specimen after conventional non-complete mesocolic excision right colectomy. *Arrows* indicate the ileocolic pedicle, the terminal ileum, the cecum, and the ascending colon

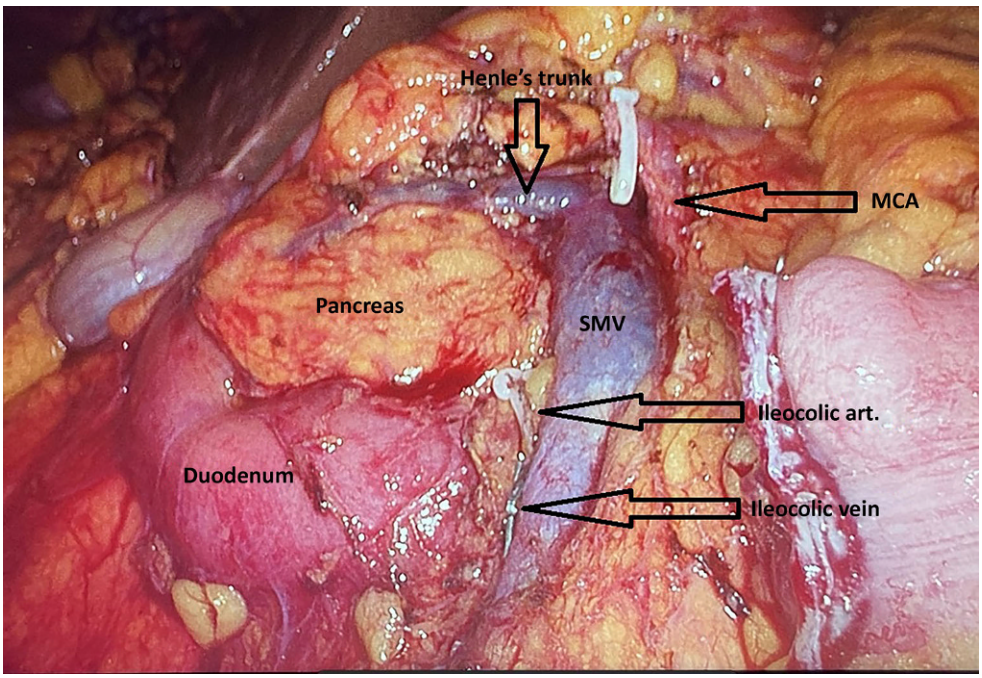

Fig. 3 Intraoperative field in CME right colectomy. *Arrows* indicate the duodenum, pancreas, ileocolic vessels, SMV, middle colic artery, and Henle's-trunk

field and a surgical specimen after conventional right colectomy in cecal tumor.

CME and CVL procedures were carried out adhering to the "critical view" concept proposed by Strey et al. [24]. In CME and CVL procedures, complete dissection of the central mesocolic lymphatic and fat tissue was carried out around the SMV up to the left margin of the vein, caudally from the ileocolic vessels, and cranially to the level of the middle colic vein and Henle's trunk. The ileocolic vein was divided at its origin from the SMV, the ileocolic artery was divided at the level of the SMV, while the right colic vessels—if present—were divided at their origin. Branches of Henle's trunk were divided immediately above the pancreatic branch, but occasionally division of the whole trunk was deemed technically more appropriate. The MCV and MCA were dissected centrally, and the right branches divided at their origin. Specimens were graded according to the classification suggested by Benz et al. [25] Figs. 3 and 4 show the in-

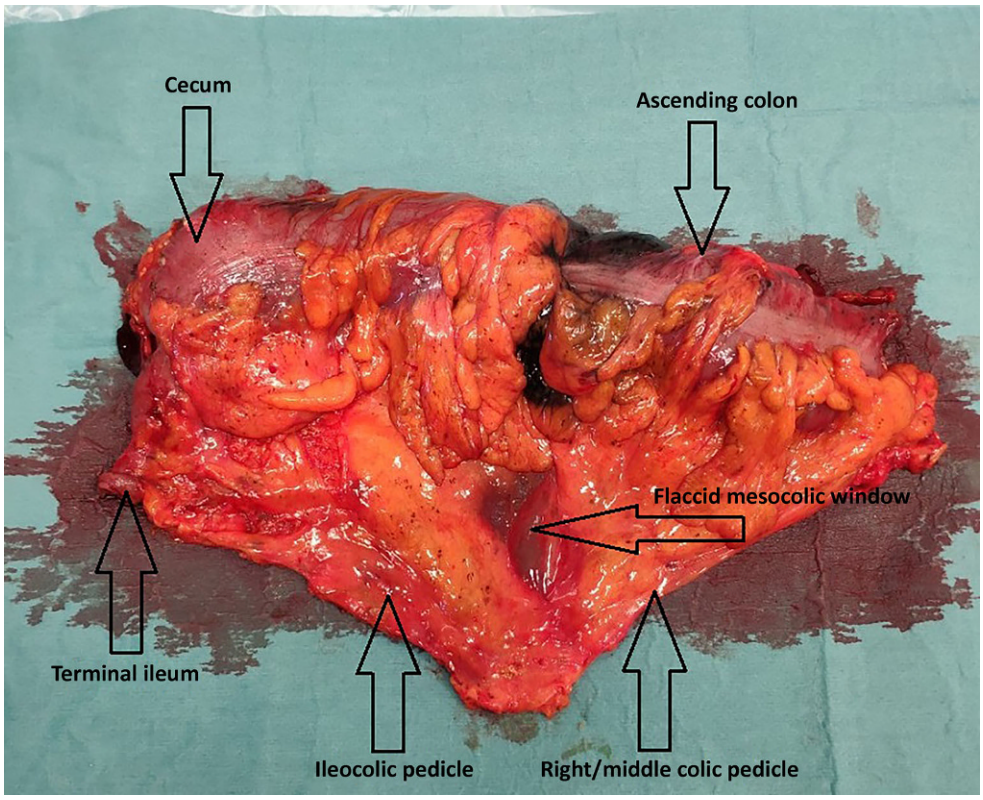

Fig. 4 Surgical specimen after CME right colectomy. *Arrows* indicate ileum, cecum, ascending colon, ileocolic and middle colic pedicles, and the central mesocolic flaccid window

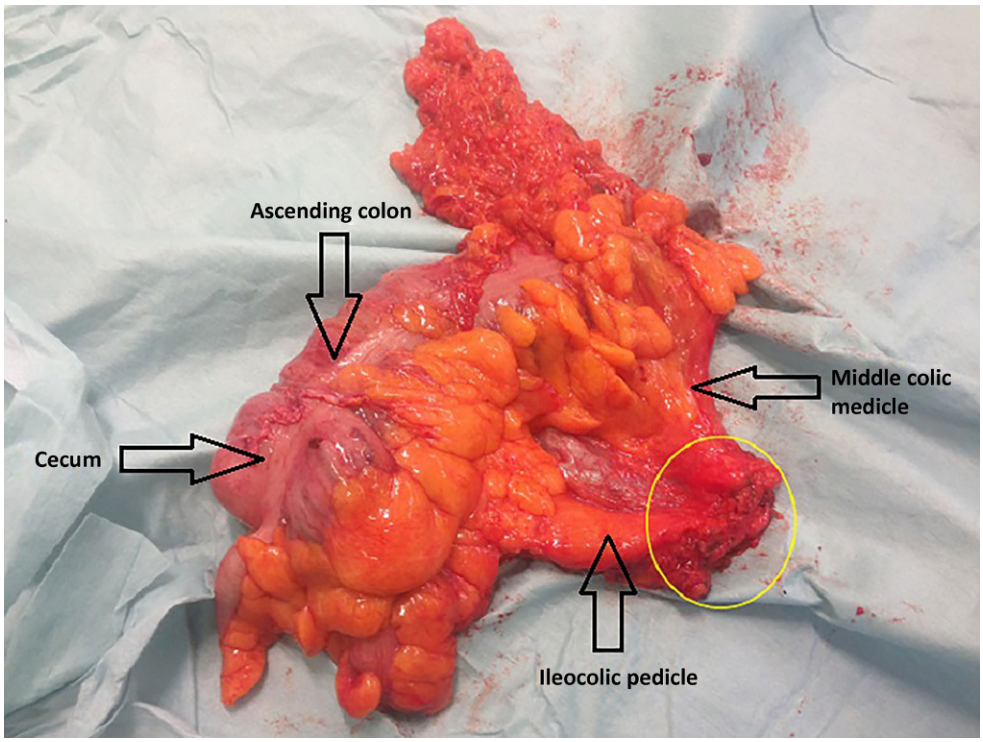

Fig. 5 Central lymphatic region (*outlined*) on a CME right colectomy specimen. *Arrows* indicate the cecum, ascending colon, ileocolic, and middle colic pedicle

traoperative field and the surgical specimen after right colectomy with CME and CVL.

Parameters recorded

Age, gender, body mass index (BMI), ASA status, duration of surgery, length of hospital stay, 30-day morbidity and mortality, and total number of lymph nodes retrieved were collected and compared. Mortality was

represented as death from any cause within 30 days postoperatively, while morbidity was defined as intra- or postoperative complications within the 30-day follow-up. Complication severity was graded according to the Clavien–Dindo classification. Pathologic data collection focused on the number of harvested lymph nodes. The defined minimum lymph node yield in every case was 12, the amount above this value was compared. Our study was aimed at investigating short-term results of CME with central vascular ligation to consider its value, quality, and possible oncologic advantages compared to conventional right colectomies.

Central lymph node involvement was separately investigated in CME specimens. The central lymphatic region was defined as the fat tissue medial to the mesocolic flaccid window of the right mesocolon and the fat around the right colic and middle colic vessels not removed during conventional surgery (Fig. 5).

Statistical analysis

For collecting and organizing the data, Excel 2019 (Microsoft, Redmond, WA, USA) was used. NCSS 2019 Statistical Software (NCSS, LLC; Kaysville, UT, USA) was applied for all analyses. To find the cut-off value (19 lymph nodes) for the number of harvested lymph nodes (above 12), ROC analysis was performed. For a comparison of groups, the chi^2-test was used. Multivariate logistic regression (LR) was applied to find independent factors. Only variables with $p<0.05$ in univariate analysis were introduced for the multivariate test. Age was omitted because of multicollinearity (ASA vs. age, $p<0.001$). $P<0.05$ was considered statistically significant.

Results

A total of 131 patients underwent surgery for right-sided colon cancer during the period from January 2019 to December 2020, with 28 (21%) in the CME group and 103 (79%) in the conventional (non-CME) group. The number of male and female patients in the CME procedure were 12 (43%) and 16 (57%), respectively, while in the standard hemicolectomy group the values were 47 (46%) and 56 (54%), respectively, with no significant difference. The ratio of open to laparoscopic cases in the CME and nCME groups were comparable (laparoscopic CME: 20, open CME: 8; laparoscopic nCME: 70, open nCME: 38, $p=0.664$).

A significant difference in the age parameter was observed between the two groups ($p=0.033$), where patients in the CME surgery group were noticeably younger. The BMI values in the two groups were comparable ($p=0.353$). A significant difference was recorded in ASA status, with a higher number of ASA III patients in the nCME group (35% in nCME vs. 7% in CME; $p=0.004$), while the majority of CME patients were ASA I–II (Table 1).

Table 1 Demographic analysis of patients who underwent either CME or standard right hemicolectomy (nCME) between 2019 and 2020

Parameter	All, *n* (%)	CME, *n* (%)	nCME, *n* (%)	Univariate *p*-value	Multivariate *p*-value
Age (years)					
Mean (SD)	68.3 (9.6)	64.7 (10.9)	69.3 (9.1)	0.033*	–
Gender					
Male	59 (45)	12 (43)	47 (46)	0.794	–
Female	72 (55)	16 (57)	56 (54)		
BMI					
Mean (SD)	27.1 (5.1)	26.3 (4.2)	27.3 (5.4)	0.353	–
ASA					
I or II	93 (71)	26 (93)	67 (65)	0.004*	0.015*
III	38 (29)	2 (7)	36 (35)		

ASA American Society of Anesthesiologists, *BMI* body mass index, *CME* complete mesocolic excision, *nCME* conventional right hemicolectomy
*Statistically significant *p*-value

The operative time was significantly longer in the CME group (149 vs. 100 min, $p<0.001$; Table 2).

Both ASA status and operative time were used for multivariate analysis, in which significant results were observed ($p=0.015$ for ASA and $p<0.001$ for operative time) and both values were identified as independent variables.

The difference in length of hospital stay was not significant ($p=0.226$). The Clavien–Dindo analysis of postoperative morbidity did not reveal a significant difference between CME and nCME groups ($p=0.166$; Table 2), and the majority of postoperative periods (CME: 82% vs. nCME: 91%) in both groups were either uneventful (grade 0) or included grade 1–2 mild complications. There was no 30-day mortality.

Essential calculations were made in relation to harvested lymph nodes, indicating the pathologic and on-

Table 2 Postoperative results of CME and conventional (nCME) surgery in 2019 and 2020

Parameter	All, *n* (%)	CME, *n* (%)	nCME, *n* (%)	Univariate *p*-value	Multivariate *p*-value
Duration of surgery (minutes)					
Mean (SD)	111 (43)	149 (47)	100 (35)	<0.001*	<0.001*
Length of hospital stay (days)					
Mean (SD)	*7.5 (4)*	*8.4 (5.4)*	*7.3 (3.5)*	*0.226*	–
Clavien–Dindo grade					
0–2	117 (89)	23 (82)	94 (91)	0.166	–
3–4	14 (11)	5 (18)	9 (9)		
Harvested lymph nodes (above 12)[a]					
<19	50 (42)	7 (26)	43 (47)	0.041*	0.172
≥19	68 (58)	20 (74)	48 (53)		
Lymph node involvement[a]					
		11 (41)	34 (37)	0.927	–
All patients	131 (100)	28 (21)	103 (79)	–	–

CME complete mesocolic excision, *nCME* conventional right hemicolectomy
[a]Only patients with a final histology of colorectal adenocarcinoma were included ($n=118$)
*Statistically significant *p*-value

cologic difference between CME and the conventional procedure. Thirteen out of 131 patients were excluded from this part of the analysis due to benign tumor status (low-grade or high-grade dysplasia-type adenomas) or malignancy of non-colorectal origin (ovarian cancer metastasis, breast cancer metastasis). To find the cut-off value (19 lymph nodes) for the number of harvested lymph nodes (above 12), ROC analysis was performed. Lymph node yield ($\geq 12+19$) in the CME group was significantly higher than in the conventional group ($p=0.041$), but no statistical significance was observed ($p=0.172$) in multivariate analysis. The ratio of node-positive to node-negative cancers in the CME and non-CME groups was comparable ($p=0.927$). Lymph node involvement in the central lymphatic region was separately recorded in CME patients and only one patient had central involvement of 3+ out of 5 central nodes.

Discussion

Implementation of the CME technique with central vascular ligation (CVL) as a standard procedure for right-sided colon cancers is still a matter of debate. There are concerns of higher morbidity and lengthened hospital stay due to the complexity of the procedure, and the effects on long-term survival are not yet completely clear, although good-quality evidence is gathering that suggests a survival benefit [6, 7].

Nevertheless, with a standardized technique and proper training, most authors in the literature find the CME procedure to be a safe alternative, with morbidity, mortality, and hospital stay not different from conventional right colectomies [8–10].

Recently, three randomized controlled trials have reported short-term results comparing CME with conventional laparoscopic right colectomies. The Chinese RELARC trial reported early safety results, with more intraoperative vascular injuries during CME procedures, but no difference in overall postoperative surgical complications and fewer Clavien–Dindo grade III–IV complications in the CME group [11]. The Italian randomized controlled trial by DiBuono et al. found no difference in postoperative complications, with significantly longer operation durations, higher lymph node yield, and better-quality specimens [12]. The Russian COLD trial also found no differences in short-term outcomes such as postoperative morbidity, hospital stay, and readmission rates, with better specimens and more lymph nodes in the CME group [13].

In our study, in line with most of the available literature, postoperative morbidity and length of hospital stay were not different in the CME and conventional groups, with no 30-day mortality occurring.

The prospectively recorded data came from a fairly large patient population ($n=131$) from a single center, with procedures performed by the same small group of four experienced surgeons within a relatively short period of time (24 months). In our opinion, these factors reduce the heterogeneity of the procedures performed, and contribute to the quality of the comparison, even though the number of CME and conventional procedures were not evenly balanced. This imbalance between the number of CME ($n=28$) and nCME ($n=103$) cases, however, may have had a limiting effect on our study. As the procedure chosen in case of each patient was up to the surgeon's clinical decision, this might be a source of unintentional bias, as some physicians were more likely to choose the conventional procedure over CME.

There was also a difference in the demographics of our study population, with more ASA III and older patients in the conventional (nCME) group. This might have had an impact on the rate of postoperative morbidity, even though the majority of postoperative periods (82% CME, 91% nCME; $p=0.166$) were either uneventful or Clavien–Dindo 1–2. The significant difference in demographics is also probably the result of an unintentional selection bias, with surgeons reluctant to perform a more challenging procedure on frail and older patients. No such selection bias could be observed, however, considering BMI, which is a crucial technical factor in abdominal surgery and in CME procedures especially. It is also worth noting that the CME procedures investigated were performed in a standardized fashion after structured training and proctorship to ensure good-quality surgery and favorable outcomes.

As expected, the surgical time in CME cases was significantly longer compared to conventional right colectomies, but this did not result in higher morbidity or longer hospital stay. Our opinion is that this increase in procedure time is acceptable.

The lymph node yield of the CME right colectomies was also significantly higher in our study. This result coincides with most of the literature, with a generally higher node count compared to most reports [8, 12, 14]. Lymph node involvement in the central lymphatic region was separately recorded in CME patients. In CME specimens, only one patient had central involvement of 3+ out of 5 central nodes, besides having heavy node positivity in the D2 region as well.

The correlation between the increasing number of lymph nodes retrieved and improvement in long-term survival has long been established in colorectal cancer [15–17], and based on this evidence, current guidelines recommend removal of a minimum of 12 lymph nodes [18].

Besides total lymph node count, the rate of positive lymph nodes is also a strong prognostic marker in colorectal cancer, which makes more extensive lymphadenectomy reasonable [19].

An early retrospective study observed a significant difference in 5-year disease-specific survival between CME and conventional groups in case of node-positive patients who underwent more extended lymphadenectomy (88% in CME vs. 50% in conventional)

[14], and a large retrospective study in 2016 showed an increase in 5-year cancer-related survival especially in stage III colorectal cancer (from 61.7% to 80.9%) with implementation of the CME technique [20]. More recently, another retrospective study also found a significant improvement in 3-year OS and DFS in the CME group compared to the conventional group (93.5% and 91.6%, vs. 85.0% and 80.0%, respectively) [5] in UICC stage II and III disease. More robust evidence came from a large prospective population-based cohort study, which found a 5-year recurrence-free survival of 9.7% vs. 17.9% in CME vs. conventional right colectomy groups, respectively, with the CME procedure having an 8.2% risk reduction potential [21].

It is important to note that in the aforementioned prospective cohort study and a large meta-analysis [22], the beneficial long-term results of the CME procedure and radical lymphadenectomy regarding DFS and recurrence rate were most profound in node-negative UICC stage I and II patients. This suggests that CME and CVL with extended D3 lymphadenectomy may be the recommended procedure for all right colon cancers regardless of clinical suspicion of node involvement, especially considering the relative inaccuracy of preoperative nodal staging [23].

In our study, the ratio of node-positive to node-negative cancers in the CME and non-CME groups was comparable, and the decision to perform extended lymphadenectomy was not predominantly determined by preoperative staging.

This study has certain limitations. As the setup was non-randomized, the selection of patients for CME or conventional surgery was uneven, and ASA III patients were more likely to be selected for conventional surgery. This might have affected postoperative outcomes.

Laparoscopic and open procedures were not differentiated, as the ratio of open to laparoscopic cases in the CME and conventional (nCME) groups was comparable. Nevertheless, this might have increased heterogeneity.

This case–control study however has some considerable strengths. The surgical cases were performed at a single center, with standardized techniques, by a small group of experienced surgeons during a short period of time, which makes comparison of short-term results more reliable. The number of patients enrolled was relatively high ($n=131$) in light of the available literature, and no patients were lost to follow-up.

Conclusion

The present study suggests that the CME technique with CVL and extended lymphadenectomy can be implemented with good short-term outcomes, without increasing perioperative morbidity, mortality, or hospital stay. The increase in procedure duration is significant but acceptable, and higher lymph node yields with the prospect of more precise staging and better oncologic outcomes warrant this extra time invested in both early and locally advanced colon cancers. As data in support of the CME technique are amassing, the long-term oncologic results of the three ongoing randomized controlled trials (COLD, RELARC, and the Italian CME trial) might deliver crucial evidence to evaluate the efficacy of the procedure.

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Author Contribution All authors contributed to the execution of this study. Data collection and analysis was performed by ZD and PM. Data editing and photo-documenting of specimens was performed by DW and GO. Basic statistical analysis was performed by KM, advanced statistics and manuscript revision was performed by BB. Data and study management was done by TM. Data management and writing of the manuscript was done by TSz. Surgical procedures were performed by PM, ZD, TM, and TSz. CME procedures were performed by DZ and TSz.

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Declarations

Conflict of interest T. Sztipits, P. Mészáros, Z. Dubóczki, D. Wettstein, G. Olah, K. Mezo, B. Budai, and T. Mersich declare that they have no competing interests.

Ethical standards The Institutional Ethical Committee and the Hungarian Medical Research Council approved the study.

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