Prospective Cohort Study

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Surgical quality assessment for the prospective study of oncologic outcomes after laparoscopic modified complete mesocolic excision for nonmetastatic right colon cancer (PIONEER study)

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Background: The modified complete mesocolic excision (mCME) procedure for right-sided colon cancer is a tailored approach based on the original complete mesocolic excision (CME) methodology. Limited studies evaluated the safety and feasibility of laparoscopic mCME using objective surgical quality assessments in patients with right colon cancer. The objectives of the PIONEER study were to evaluate oncologic outcomes after laparoscopic mCME and to identify optimal clinically relevant endpoints and values for standardizing laparoscopic right colon cancer surgery based on short-term outcomes of procedures performed by expert laparoscopic surgeons.

Materials and methods: This is an ongoing prospective, multi-institutional, single-arm study conducted at five tertiary colorectal cancer centers in South Korea. Study registrants included 250 patients scheduled for laparoscopic mCME with right-sided colon adenocarcinoma (from the appendix to the proximal half of the transverse colon). The primary endpoint was 3-year disease-free survival. Secondary outcomes included 3-year overall survival, incidence of morbidity in the first 4 weeks postoperatively, completeness of mCME, central radicality, and distribution of metastatic lymph nodes. Survival data will be available after the final follow-up date (June 2024).

Results: The postoperative complication rate was 12.9%, with a major complication rate of 2.7%. In 87% of patients, central radicality was achieved with dissection at or beyond the level of complete exposure of the superior mesenteric vein. Mesocolic plane resection with an intact mesocolon was achieved in 75.9% of patients, as assessed through photographs. Metastatic lymph node distribution varied by tumor location and extent. Seven optimal clinically relevant endpoints and values were identified based on the analysis of complications in low-risk patients.

Conclusions: Laparoscopic mCME for right-sided colon cancer produced favorable short-term postoperative outcomes. The identified optimal clinically relevant endpoints and values can serve as a reference for evaluating surgical performance of this procedure.

Keywords: modified complete mesocolic excision, right-sided colon cancer, short-term outcomes, standardized surgery

Introduction

The introduction of complete mesocolic excision (CME) significantly improved oncologic outcomes after colon cancer surgery[1,2]. The CME approach emphasizes sharp dissection along embryologic planes, allowing removal of the tumor and its mesentery as a unit, reducing the risk of cancer cell leakage and central lymph node (LN) removal[1].

Nevertheless, the original CME procedure is uniform and does not consider tumor location or extent, which increases the risk of intraoperative vascular injury during minimally invasive surgery because of complete kocherization and extensive extramesocolic LN dissection[3,4]. Additionally, the original procedure does not clearly define ranges for central and longitudinal radicality in relation to tumor characteristics and does not emphasize the importance of achieving a safe radial margin (RM), which is a strong predictor of superior oncologic outcomes[5,6].

There are no universal standards for right-sided colon cancer resection. Surgical approaches vary between countries and institutions, ranging from the Japanese D3 dissection to a modified

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form of CME, which is widely used in real-world settings to accommodate the specific characteristics of each patient's tumor[7,8]. The modified CME (mCME) approach for right-sided colon cancer is based on the original CME principles but uses a tailored approach. It accounts for tumor location and stage, resulting in an adequate RM, tailored lymphadenectomy, selective extramesocolic LN dissection, and tailored mesocolon and ileal mesentery resection[8].

We initiated the PIONEER study to evaluate oncologic outcomes after laparoscopic mCME in right-sided colon cancer. Here, we describe short-term outcomes and the highest achievable quality of this surgery by assessing patient-centered outcome indicators in low-risk patients who underwent laparoscopic mCME in high-volume colorectal centers.

HIGHLIGHTS

- Laparoscopic modified complete mesocolic excision for right-sided colon cancer produces favorable short-term postoperative outcomes, as assessed by objective surgical quality indicators.
- Optimal clinically relevant endpoints and values have been identified for evaluating surgical performance of laparoscopic modified complete mesocolic excision.
- These endpoints and values can be used as a reference to assess the success and quality of the procedure.

Materials and methods

Study design and patients

The PIONEER study is an ongoing prospective, multi-institutional, single-arm study conducted at five tertiary colorectal cancer centers in South Korea and registered in the Research Registry under the UIN www.researchregistry.com. The protocol was reported previously[9]. Patients scheduled for laparoscopic mCME of right-sided colon adenocarcinoma (from the appendix to the proximal half of the transverse colon) were eligible for this study. The inclusion criteria were age >19 years, American Society of Anesthesiologists (ASA) physical status class I–III, and no preoperative treatment. The exclusion criteria were emergency operation (e.g. for perforation or malignant colonic obstruction); distant metastasis on preoperative imaging; hereditary colon cancer; any other malignancy in the previous 5 years (except basal cell carcinoma, skin squamous cell carcinoma, or cured cervical carcinoma in situ); simultaneous multiple primary colorectal cancers; pregnancy or breastfeeding; unsuitable for laparoscopic surgery (e.g. extensive adhesions from prior surgery, unable to tolerate pneumoperitoneum); and refusal to provide informed consent.

The institutional review board of each participating center (five tertiary hospitals) in South Korea approved the study protocol and all amendments. The published manuscript explicitly provides detailed information regarding ethical approval[9]. All participants provided written informed consent to acquire and use their anonymized clinical data. All investigators followed the tenets of the Declaration of Helsinki. This study has been reported in line with the strengthening the reporting of cohort, cross-sectional and case–control studies in surgery (STROCSS) criteria[10].

Surgical quality assessment

To ensure surgical quality, we selected only surgeons with considerable expertise for participation in the study. Each surgeon independently performed ≥ 50 laparoscopic mCME procedures in the previous 3 years. Additionally, each surgeon was required to pass a blinded review of previous videotaped procedures. Potential participating surgeons provided videos of three laparoscopic mCMEs performed in the past 3 months to the Research Council, which selected two videos for blinded peer review by three experts. If all experts approved the videos, the surgeon was accepted for this study.

This study requested the mandatory submission of photo documents for all cases. These include either one photograph of the surgical field after the completion of the dissection to display the central radicality of lymphadenectomy (central vessel ligation) or photographs of the front and back sides of the unfixed, unopened specimen to evaluate the quality of mesocolic excision and tissue morphometry. These photographs were uploaded to an electronic database for central review of central radicality and macroscopic specimen quality by a study-specific committee. The level of central radicality was categorized according to the extent of lymphadenectomy of the central LNs: IA, lymphadenectomy around the origin of the colic artery, with complete exposure of the superior mesenteric vein (SMV) and superior mesenteric artery (SMA) adventitia; IB, lymphadenectomy around the origin of the colic artery, with complete exposure of the SMV and partial exposure of the SMA adventitia; II, lymphadenectomy around the origin of the colic artery, with complete SMV exposure; III, lymphadenectomy around the origin of the colic artery, with partial SMV exposure; and IV, lymphadenectomy around the origin of the colic artery, without SMV exposure.

Using photographs of the anterior and posterior aspects of fresh specimens, the study-specific committee categorized the plane of dissection into three groups, according to West's classification: grade A, mesocolic plane; grade B, intramesocolic plane; and grade C, muscularis propria plane[11,12].

Surgical procedure

The surgeon first explored the abdominal cavity to look for distant metastasis. Laparoscopic mCME was performed in a lateral-to-medial or medial-to-lateral manner, according to the surgeon's preference. mCME was performed by separating the visceral fascia from the parietal fascia by sharp dissection and ligating the supplying vessels at their origin in a tailored fashion, depending on the location and extent of the primary tumor. Differences between the original CME and mCME were described previously[8,9].

To secure the RM, complete kocherization was performed if the tumor was infiltrating or adhering to the duodenum or perinephric fat. If the tumor was locally advanced, the entire prerenal soft tissue behind Gerota's fascia was cleared, especially for tumors growing posteriorly. After completing mesocolon mobilization, central vascular ligation and mesocolon dissection were performed. The level of central radicality was determined by the surgeon based on preoperative and intraoperative findings regarding tumor invasion depth and LN metastasis. After identifying the root of the middle colic artery, only the right branch of this artery was ligated for tumors in the cecum or ascending

colon. The root itself was ligated for tumors at other sites. The distal ileum and transverse colon lengths were determined by the extent of mesenteric dissection, according to the location and extent of the primary tumor. The anastomosis method varied according to each center's standard procedure.

Postoperative protocols followed each hospital's policies. All adverse events were closely observed and treated. Hospital discharge criteria included pain controlled with oral analgesics, tolerating a soft diet, and no evidence of infection-related complications.

Outcomes

The primary endpoint of the PIONEER study was 3-year disease-free survival (DFS), defined as the time from surgery until the first objective documentation of recurrence or all-cause death. As the last date for DFS data collection will be June 2024, this outcome will be reported later. Threeyear overall survival will also be reported after June 2024.

The secondary endpoints reported here are the incidence of morbidity during the first 4 weeks postoperatively, including anastomotic leak, postoperative bleeding, wound infection, ileus, chyle leakage, pulmonary infection, deep surgical site infection, and other adverse events. Complications were graded using the Clavien–Dindo classification; grades I–II were considered minor complications, and grades III–IV were considered major complications[13]. Intraoperative complications, defined as unexpected surgical adverse events (e.g. iatrogenic bowel, blood vessel, or other organ injury; and severe bleeding), were recorded. Vascular injury was defined as a laceration or transection of the branches or main trunk of the SMA and vein (i.e. ileocolic vessels, right colic vessels, mid-colic vessels, and gastrocolic trunk of Henle, SMA, and SMV). Intraoperative bleeding was defined as blood loss of greater than 200 ml during surgery. Postoperative bleeding was defined as the presence of bloody drainage of greater than 100 ml within 1 h or a total drainage of 300 ml within 24 h after surgery, with a drainage fluid to serum hematocrit ratio of greater than or equal to 50%[12].

mCME completeness was assessed by reviewing the resected surgical specimen, primarily by surgeons at each center and secondarily by central reviewers based on specimen photographs. Central radicality was assessed by reviewing the operative field after specimen removal, primarily by surgeons at each center and secondarily by central reviewers based on intraoperative photographs. Metastatic LN distribution was assessed by categorizing LNs retrieved from resected surgical specimens based on the Japanese Classification of Colorectal Carcinoma[14]. These analyses of trial safety were prespecified.

RM was defined according to National Comprehensive Cancer Network guidelines[15] as the distance between the edge of the mesentery or retroperitoneal surface and the deepest point of tumor infiltration. Only the mesenteric margin was considered when assessing the proximal transverse colon. RM assessment included both tumor-bearing LNs and direct tumor extension. The specimen's surface was first marked with ink, after which the specimen was opened along the antimesenteric side of the colon and then fixed in formalin. The most deeply invaded tumor site was sectioned, and colorectal pathologists evaluated the RM according to a standardized protocol. If an enlarged LN or tumor deposit was visible near the RM surface, assessment was performed without dissecting the LNs.

Tissue morphometry was assessed using ImageScope version 10 (Aperio, Vista) on photographs of the resected surgical specimens[2,16]. The mesentery was positioned flat without stretching. Distance from the tumor to the closest bowel wall and the HVT, length of the large and small bowel, and area of resected mesentery were quantified.

We selected seven optimal clinically relevant endpoints, most of which were similar to those reported in previous colorectal surgery benchmark studies[17,18]. They included overall postoperative complications, major complications, mesentery area, mCME quality, LN yield, RM less than 1 mm, central radicality.

Statistical analysis

Sample size was calculated based on the reported 3-year DFS after CME for right-sided colon cancer of ~80%[19,20]. Our null hypothesis was a 3-year DFS after laparoscopic mCME for right-sided colon cancer of greater than or equal to 88%. Using the Clopper–Pearson method with an exact P-value of 0.025 and a power of 90%, we calculated that 225 patients were required. To allow a dropout rate of ~10%, our target enrollment was 250 patients.

Categorical variables were presented as numbers (percentages) and continuous variables as median [interquartile range (IQR)]. To determine optimal relevant endpoints, we considered only low-risk patients, defined as an absence of previous major abdominal surgery, associated surgical procedures, diabetes mellitus, cardiopathy, renal insufficiency, anticoagulation, or cT4a tumors ($n = 162$). We first calculated the median with IQR for each individual center, and then derived cut-offs for optimal relevant endpoints from the 75th percentile (for values indicating worse outcome) or 25th percentile (for good outcome indicators) of each participating center. All statistical tests were performed using SPSS software version 24.0 (SPSS).

Results

Baseline characteristics

Between August 2019 and May 2021, 250 patients meeting inclusion criteria were registered in this study (Fig. 1). Two subsequently declined to participate. Peritoneal dissemination was observed intraoperatively in five patients, who underwent non-curative surgery. Protocol deviations (failure to submit the three required photographs) occurred in two patients. Overall, 239 surgical field photographs and 225 pairs of specimen photographs were collected and analyzed. Thus, 241 patients were included in the analyses.

The final patient cohort had a median age of 67 years and median BMI of 23.9 kg/m^2; 51.5% were male (Table 1). Preoperative comorbidity was present in 84.7% of patients (ASA class ≥ 2), and 13.3% had previous abdominal surgery. The tumor location was the ascending colon in 61% of patients.

Operative and pathologic outcomes

Median operative time was 158 min, and median estimated blood loss was 30 ml (Table 2). Combined multiorgan resection was performed in 6.6% of patients (most frequently cholecystectomy). Middle colic artery root ligation was performed in 27.8% of patients. There were no conversions to open surgery, and median postoperative hospital stay was 6 days.

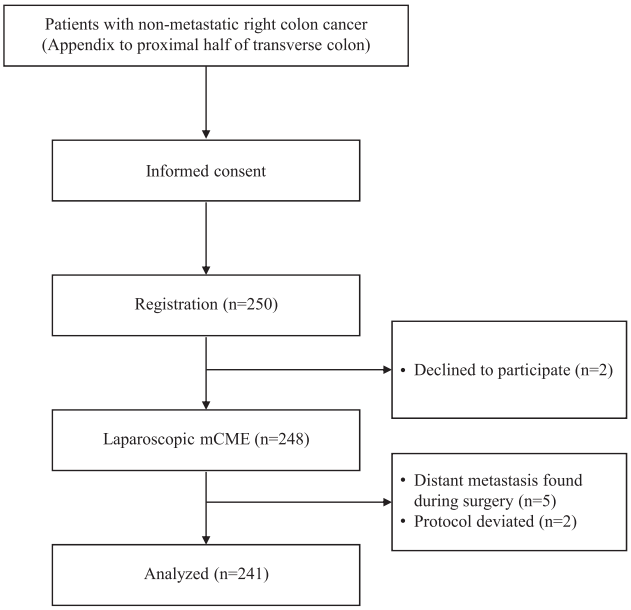

Figure 1. Flow diagram of the study. mCME, modified complete mesocolic excision.

Specimen quality assessment was not possible in 16 patients because of a lack of photographs. The results of the intentions-to-treat analysis were classified as follows: grade C, five patients (2.1%); grade B, 37 patients (15.4%); and grade A, 183 patients (75.9%). No patient had tumor involvement in the proximal or distal resection margin. RM data were available for 197 patients. RM was less than 1 mm in 20 patients (8.3%). Of the 241 patients, 56% had pT3 tumors, and 32% had LN metastasis. The median number of retrieved LNs was 34; less than 12 nodes were retrieved in two patients (0.8%).

Tissue morphometry was assessed in 225 specimens (Table 3). Large bowel length was longer in specimens from the hepatic flexure and proximal transverse colon (288.0 mm) than from the appendix to ascending colon (254.0 mm). This resulted in a wider area of mesentery in the former specimens (20 751.9 mm^2 vs. 15 209.8 mm^2).

Table 1

Baseline clinical characteristics

Characteristics	*N* = 241
Age (years)	67.0 (60.0–75.0)
Sex	
Male	124 (51.5)
Female	117 (48.5)
BMI (kg/m^2)	23.9 (21.9–26.3)
ASA physical status class	
I	37 (15.4)
II	159 (66.0)
III	45 (18.7)
Tumor location	
Appendix	2 (0.8)
Cecum	45 (18.7)
Ascending colon	147 (61.0)
Hepatic flexure	29 (12.0)
Proximal transverse colon	18 (7.5)
Baseline CEA (μg/l)	2.40 (1.44–5.19)
Previous abdominal surgery	32 (13.3)

Data are median (interquartile range) or number (percentage).
ASA, American Society of Anesthesiologists; CEA, carcinogenic embryonic antigen.

Table 2

Operative and pathologic outcomes

Outcomes	N = 241
Duration of operation (min)	158.0 (134.0–184.0)
Blood loss (ml)	30.0 (0.0–100.0)
Blood transfusion during surgery	6 (2.5)
Combined multiorgan resection	16 (6.6)
Middle colic ligation	
Right branch	174 (72.2)
Root	67 (27.8)
Conversion to open surgery	0 (0)
Duration of postoperative hospital stay (days)	6 (5–7)
Quality of specimens	
Grade I	5 (2.1)
Grade II	37 (15.4)
Grade III	183 (75.9)
N/A	16 (6.6)
Tumor size (cm)	4.0 (2.4–5.5)
Resection margin	
Proximal	
Length (cm)	12.0 (8.0–18.0)
Tumor involvement	0 (0)
Distal	
Length (cm)	16.5 (10.6–22.2)
Tumor involvement	0 (0)
Radial margin	
≥ 2 mm	175 (72.6)
1 mm ≤ radial margin < 2 mm	12 (5.0)
< 1 mm	20 (8.3)
N/A	34 (14.1)
pT stage	
pT1	49 (20.3)
pT2	35 (14.5)
pT3	135 (56.0)
pT4a	22 (9.1)
pN stage	
pN0	164 (68.0)
pN1	57 (23.7)
pN2	20 (8.3)
Histology type	
Well differentiated	32 (13.3)
Moderately differentiated	180 (74.4)
Poorly differentiated	21 (8.7)
Mucinous adenocarcinoma	5 (2.1)
Goblet cell	1 (0.4)
N/A	2 (0.8)
Lymphovascular invasion	37 (15.4)
Perineural invasion	46 (19.1)
Total number of retrieved LNs	34 (26–46)
Number of patients with <12 LNs	2 (0.8)

Data are median (interquartile range) or number (percentage).
LN, lymph node; N/A, not available.

Level of central radicality and distribution of metastatic LNs

Figure 2 shows central radicality levels. Among the 239 patients with photographs for central radicality, 87.0% had an extent of lymphadenectomy for central LNs beyond complete SMV

Table 3

Tissue morphometry measurements according to tumor location

Measurements	Appendix to ascending colon	Hepatic flexure and transverse colon
Tumor to HVT (mm)	113.2 (92.5–136.0)	113.7 (91.9–145.4)
Normal bowel to HVT (mm)	81.5 (67.4–94.9)	72.6 (52.5–88.0)
Area of mesentery (mm^2)	15 209.8 (12 416.6–19 229.9)	20 751.9 (13 920.2–23 624.5)
Length of large bowel (mm)	254.0 (215.0–303.0)	288.0 (242.0–330.0)
Length of small bowel (mm)	70.0 (52.0–97.0)	66.0 (55.0–80.0)

Data are median (interquartile range).
HVT, high vascular tie.

exposure (levels IA–II). Only 2.9% of patients had level IV radicality. The metastatic pattern of central LNs varied according to tumor location and disease extent (Fig. 3). There were no metastatic central LNs at the middle colic artery in patients with appendix to ascending colon cancers. Metastasis occurred most frequently at the middle colic artery in patients with hepatic flexure and proximal transverse colon cancers. Among patients with pT1 or pT2 cancers, one (1.5%) had metastatic LNs at the central middle colic artery. Among patients with pT3 or pT4 tumors, metastasis occurred frequently at the central and intermediate LNs of the ileocolic, right colic, and middle colic arteries. The distribution of metastatic pericolic LNs varied with tumor location. Among tumors in the appendix to ascending colon, metastatic LNs were observed up to 15 cm proximally and 5 cm distally. Among tumors in the hepatic flexure and proximal transverse colon, metastatic LNs were present up to 10 cm proximally and 15 cm distally. Additionally, extramesocolic node dissection was performed in seven cases, revealing no metastatic nodes.

Postoperative morbidity

Intraoperative bleeding occurred in six patients (2.4%) without intraoperative vascular injuries. Postoperative complications within 4 weeks after surgery occurred in 31 (12.9%) of the 241 patients (Table 4). Most complications were minor, occurring in 25 patients (10.4%) and requiring only conservative treatment. Major postoperative complications occurred in six patients (2.5%), including one patient with anastomotic leakage and two with iatrogenic small bowel perforation caused by intraoperative thermal injury.

Optimal clinically relevant endpoints and values

The results of laparoscopic mCME performed in 162 patients with low-risk factors for postoperative complications were used to determine optimal clinically relevant endpoints (Table 5).

Discussion and conclusion

In this study, we present favorable short-term postoperative outcomes of laparoscopic mCME for right-sided colon cancer, as assessed by objective surgical quality indicators. Our findings also indicate that laparoscopic right colon cancer resection can achieve excellent results when performed by experienced surgeons.

CME for right-sided colon cancer is challenging because of the complexity and variability of the central vascular anatomy[3,4]. Originally, CME for right-sided colon cancer was very aggressive and involved complete kocherization and extensive extramesocolic LN dissection, regardless of tumor location or stage[1]. This led to a relatively high risk of serious intraoperative and postoperative complications, especially when performed laparoscopically[3]. Our incidence of overall and major postoperative complications was lower than in previous randomized controlled trials (RCTs), including RELARC, a recent RCT comparing the efficacy and safety of CME versus D2 dissection in laparoscopic right hemicolectomy for right colon cancer[12,21]. Our lower complication rate may be attributed to patient factors,

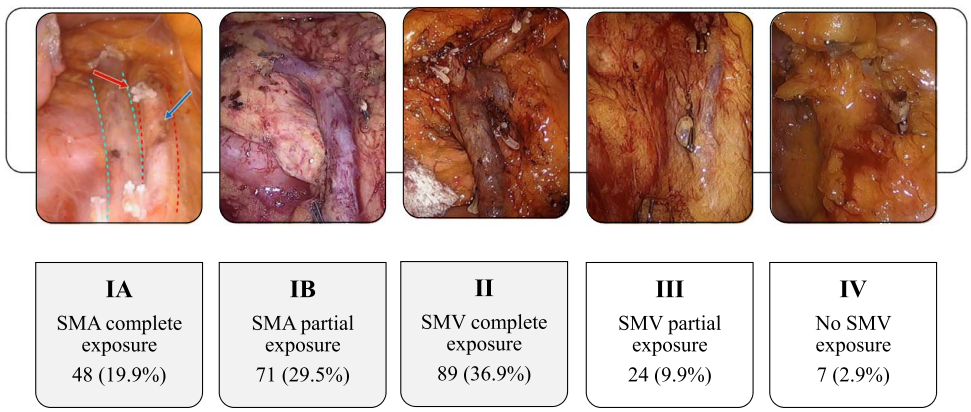

Figure 2. Level of central radicality, evaluated by reviewing photographs of the operative field after lymph node dissection and specimen removal. SMA, superior mesenteric artery; SMV, superior mesenteric vein.

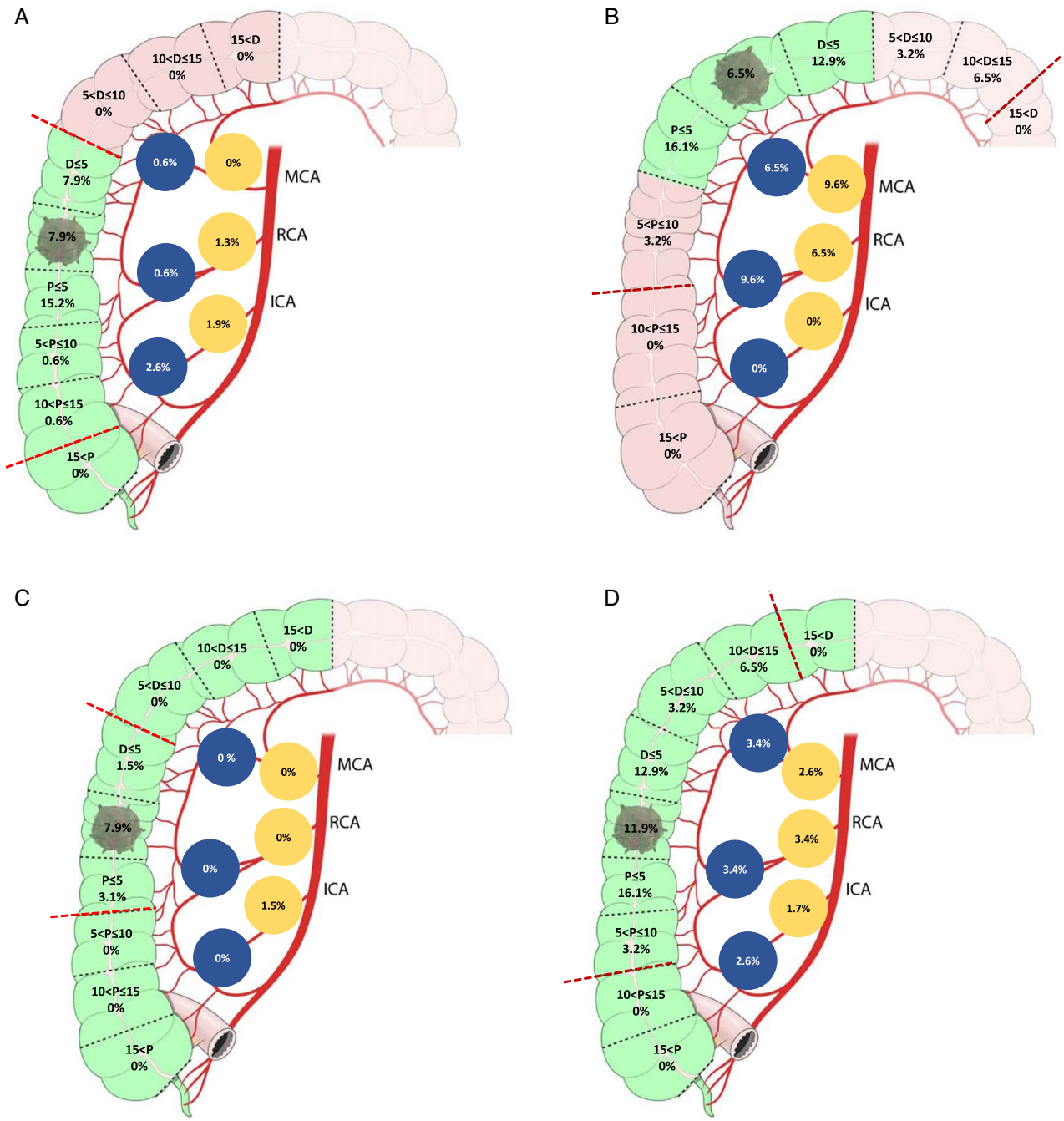

Figure 3. Distribution of lymph node metastasis in right-sided colon cancer. A) Distribution in appendix, cecal, and ascending colon cancers; B) distribution in hepatic flexure and proximal transverse colon cancers; C) distribution in pT1 and pT2 right-sided colon cancers; and D) distribution in pT3 and pT4 right-sided colon cancers. The distance numbers are presented in cm. D, distal to the tumor; ICA, ileocolic artery; MCA, middle colic artery; P, proximal to the tumor; RCA, right colic artery.

such as the lower BMI of our patients. Moreover, all participating centers were tertiary-care hospitals, and all surgeries were performed by experienced specialists. The absence of intraoperative vascular injuries and open conversions further supports the important role of surgical expertise. However, when analyzing only low-risk patients, the overall complication rate was higher than that of the entire study cohort, possibly due to the inclusion of many low-risk patients who developed chyle ascites due to extensive central LN dissection. The number of LNs harvested is an independent risk factor for chyle leakage after right hemicolectomy[22]. Comparing the number of harvested LNs between low-risk patients and other patient groups, surgeries on low-risk patients yielded more LNs (low-risk: other = 37.22:33.61). Furthermore, when comparing central radicality between low-risk and other patients, grade IA radicality was more frequently observed in low-risk patients (low-risk: other =

Table 4

Postoperative morbidity

Complications	$N=241$
Overall complications	31 (12.9)
Anastomotic leakage	1 (0.4)
Intraoperative bleeding	6 (2.4)
Postoperative bleeding	0 (0.0)
Wound infection	7 (2.9)
Ileus	7 (2.9)
Chyle leakage	11 (4.6)
Intra-abdominal fluid collection	2 (0.8)
Urinary tract infection	1 (0.4)
Iatrogenic small bowel perforation	2 (0.8)
Clavien–Dindo grade	
I, II	25 (10.4)
III	6 (2.5)
IV, V	0 (0)

Data are number (percentage).

23.5%:12.7%). This elucidates the paradox of why patients classified as having a lower surgical risk experience more complications, particularly lymphatic leaks. However, the optimal radicality must be determined when the final report includes oncologic outcomes.

The mCME technique for right-sided colon cancer adheres to the same principles as the original CME procedure but incorporates a more tailored approach based on tumor location and stage. Furthermore, this tailored approach emphasizes achieving an adequate RM to ensure optimal oncologic outcomes[8]. Anatomic variations of the mesocolon and adjacent peritoneum make the concept of RM more complicated in colon cancer than in rectal cancer. Compared to the transverse colon, the cecum, ascending colon, and hepatic flexure colon have a larger interface with the mesocolon. RM less than 1 mm was previously identified as an independent predictor of survival and recurrence in colon cancer[5]. RM was less than 1 mm in 8.3% of our patients. Given that our study was conducted at tertiary referral hospitals where patients often have more aggressive and advanced tumors, this percentage is relatively high, especially when compared to the results of a previous study[6]. Our higher percentage may be attributed to our definition of RM (< 1 mm), whereas the previous study considered only direct involvement of the edge of the RM[6]. Of note, the cecum, ascending colon, and hepatic flexure colon accounted for 91.7% of cases in our study and 90.9% of pT4a cancers. This helps explain why the RM was less than 1 mm in only 0.75% of low-risk patients (excluding cT4a cases).

Table 5

Optimal clinically relevant endpoints and values

Endpoints	Optimal values
Overall complications	≤ 16.4%
Major complications	≤ 5.1%
Area of resected mesentery	
Appendix to ascending colon	≥ 15 057.4 mm^2
Hepatic flexure and transverse colon	≥ 18 312.58 mm^2
Specimen quality (intact mesocolon)	≥ 85.55%
Number of harvested LNs	≥ 31.25
Radial margin <1 mm	≤ 0.75%
Level of central radicality	Grades IA–II

LN, lymph node.

Removal of an intact mesocolon plays an important role in achieving complete oncologic clearance, making grading of the surgical plane essential for assessing surgical quality[11]. Previous studies demonstrated that removing an intact mesocolon in the mesocolic plane is an oncologically superior operation, which is partly why CME is highly recommended worldwide[2,11,23]. In this study, we assessed the quality of mCME by reviewing photographs of the front and back of resected surgical specimens. This allowed evaluation using en-bloc resected fresh specimens instead of sectioned formalin-fixed specimens. Our percentage of intact mesocolic plane was lower than in previous studies evaluating the CME plane of surgery[2,11,24]. We downgraded all specimens with disruption of a thin translucent peritoneal window, which is formed by a bilayer of fused peritoneum with no intervening fat and is often seen in the right mesocolon. Additionally, specimen quality may have been reduced because all operations were performed laparoscopically, with injuries potentially occurring during extraction through the small mini-laparotomy incision. For ascending colon tumors, en-bloc resection of retroperitoneal soft tissue anterior to Gerota's fascia is necessary to secure the RM, which may also have contributed to the lower quality of our study.

Along with emphasizing removal of an intact mesocolon, previous studies emphasized that better oncologic outcomes after CME compared to non-CME are due to more extensive mesentery resection and more harvested LNs[2,11]. In studies comparing Japanese D3 resection (which focuses more on central radicality) to CME, the mesenteric resection area was larger with CME[24]. This difference in mesentery area was influenced by variations in BMI arising from ethnicity differences, while discrepancies attributed to central radicality level were likely to be minimal. However, previous studies did not perform subanalyses of central radicality levels in patients undergoing CME versus non-CME. The absolute area of resected mesentery and number of harvested LNs in the current study were similar to or greater than those reported in previous retrospective studies of Western patients[2,11,24]. Potential survival benefits of the observed mesentery area and LN count will be evaluated when the 3-year DFS outcomes of this study are available.

Based on intraoperative photographs, our results showed that experienced surgeons, regardless of tumor status, performed complete lymphadenectomy around the origin of the colic artery and complete SMV exposure (i.e. levels IA–II) in 86.3% of cases. When the final study results are available, analyses evaluating the association between central radicality levels and oncologic outcomes should help establish a standardized central radicality level for right colon cancer surgery.

The metastatic pattern of LNs differed according to tumor location and disease extent. Among metastatic LNs, 5.4% were observed in central LNs, with the majority found in pT3 and pT4 tumors. This is consistent with the results of previous studies reporting that central LN metastasis is significantly associated with T stage. Central LN metastasis occurs in less than or equal to 3.7% of stage T4 colon cancers but rarely in stage T2 or lower cancers[25,26]. Consistent with the results of previous studies, central LN metastasis around the feeding colic artery varied, depending on tumor location. No metastatic LNs were found at the root of the middle colic artery for tumors from the appendix to ascending colon. Conversely, there were no metastatic LNs at the root of the ileocolic artery for tumors located in the hepatic flexure colon and proximal transverse colon. Additionally,

pericolic LN metastasis varied according to tumor location. These LNs were subcategorized in 5 cm intervals from the edge of the primary tumor. Our findings, therefore, suggest that tailored LN dissection may be necessary based on tumor location and disease status, and to avoid missing metastatic central LNs, a certain level of central radicality must be ensured. Detailed analyses of the association between oncological outcomes and these findings will help clarify the appropriate extent of central radicality. Furthermore, we anticipate that analyzing the relationship between regional pericolic node metastatic patterns and oncologic outcomes, in conjunction with the ongoing international T-REX study (NCT02938481), may enable the definition of longitudinal radicality[27].

However, this study has limitations. A primary concern in selecting a nonrandomized trial design was the potential bias in the enrolled population. Maintaining a screening log at every participating institution, complemented by remote and in-person monitoring, aided in managing this bias. Furthermore, designing RCT is problematic in right colon cancer surgery since a standard surgical method has not been established. Comparing all available techniques is difficult because of variations in procedures across different countries and institutions. Thus, an alternative tool was necessary to evaluate laparoscopic mCME for right-sided colon cancer. This is why we emphasized optimal clinically relevant endpoints and values for laparoscopic right colon cancer surgery in low-risk patients when performed by experts, adopting a recently developed standardized methodology[28]. Another study limitation is that all participating centers were located in South Korea, and the characteristics of Asian populations (especially their lower BMI) may differ from those in other regions or races. Lower BMI may be associated with fewer complications and may have facilitated achieving central radicality in this study. However, it is essential to consider specific aspects of surgery that may impact oncologic outcomes, even when dealing with patients with a higher BMI.

The strengths of this study include performing all operations using a standardized laparoscopic procedure by designated laparoscopic experts in high-volume centers and assessing surgical quality using objective indicators. Identifying optimal clinically relevant endpoints and values is expected to provide 'a reference' for the surgical quality of laparoscopic mCME. Surgeons and institutes can compare their results with these values. However, caution is essential in patient selection, and operating centers are important in the outcomes. Claims about favorable results should be while considering these factors, ensuring they are substantiated, contextual, and reflective of the diversity and complexity of surgical procedures and patient profiles. To fully validate our findings, the association between the identified surgical quality assessment indicators and primary outcome of the PIONEER study (3-year DFS) must be confirmed. Until then, our results should be considered preliminary reference points.

In conclusion, when performed by experienced surgeons, laparoscopic mCME for right-sided colon cancer produces favorable short-term postoperative outcomes, as assessed by objective surgical quality indicators. Future analysis of oncologic outcomes will be crucial for determining the optimal results achieved with this technique.

Ethical approval

This study was approved by the Institutional Review Board of Severance Hospital (No. 4-2018-1162).

Consent

Written informed consent was obtained from all patients for the acquisition and use of anonymized clinical data before they were recruited, and all investigators conducted this study in accordance with the tenets of the Declaration of Helsinki. This study was monitored by an independent data and safety monitoring committee.

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Author contribution

S.Y.Y.: conceptualization, data acquisition, data analysis and interpretation, methodology, and writing original draft; M.J.K.: conceptualization and data acquisition; B.-H.K.: conceptualization, data acquisition, and investigation; Y.D.H. and M.S.C.: data acquisition, data analysis and interpretation, and investigation; J.W.P., S.-Y.J., S.H.S., J.S.P.: data acquisition, data analysis, and interpretation; S.Y.P.: conceptualization, data acquisition, data analysis, and interpretation; J.K.: conceptualization, data acquisition, methodology, supervision, and writing review and editing; B.S.M.: conceptualization, data acquisition, funding acquisition, methodology, supervision, validation, and writing review and editing. The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Conflicts of interest disclosure

There are no conflicts of interest.

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Data availability statement

The underlying data for this study is only available upon request.

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