Complete mesocolic excision and central vascular ligation for colon cancer: Principle, anatomy, surgical technique, and outcomes

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ABSTRACT

Classic colon cancer surgery refers to a wide resection of the tumor-bearing segment and the lymphatics draining along the named artery. The concept of TME has been applied to colon cancer and complete mesocolic excision (CME) in conjunction with central vascular ligation (CVL) has been introduced as the surgical treatment for colon cancer. Here, we discuss appropriate CME procedure with regard to the oncologic backgrounds, essential components, applied anatomy, laparoscopic technique, short-term, and oncologic outcomes. The introduction of CME has improved oncologic outcomes greatly in patients with colon cancer. The improved outcomes with CME can be attributed to underlying sound oncologic principles such as dissection through the proper plane of mesocolic excision, central vascular ligation, and sufficient length of proximal and distal margins. Thereby, CME technique can achieve en bloc removal of the diseased lesion with the increased amount of the colonic mesentery even though the length of for both bowel and mesentery resection remains a matter of debate. CME is a technically demanding operation thus, comprehensive understanding of the applied vascular anatomy is essential for successful CME. Favorable outcomes of open CME have been replicated with a laparoscopic approach. In future perspective, incorporating a structured education program on minimally invasive (laparoscopy or robot) CME would be beneficial.

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Abbreviations: CME, complete mesocolic excision; CVL, central vascular ligation;
SMA, superior mesenteric artery; SMV, superior mesenteric vein; IMA, inferior mesenteric artery; IMV, inferior mesenteric vein.
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1. Introduction

Colorectal cancer is the third most commonly diagnosed cancer in men (10.0% of the total cases) and the second in women (9.2% of the total cases) with 1,360,000 newly diagnosed patients, worldwide [1]. In the United States, it is estimated that 96,830 new cases of colon cancer and 40,000 new cases of rectal cancer in 2014 and proportion of colon cancer comprised over 70% when compared with rectal cancer [2]. Treatment for colon cancer varies by tumor location and stage at diagnosis and, surgery in combination with selective use of adjuvant chemotherapy are main modalities for localized colon cancer.

Rectal cancer surgery has been revolutionized after introduction of total mesorectal excision (TME) by Heald et al. [3] TME removes the rectum and mesorectum as one intact unit by sharp dissection along the mesorectal fascia and the concept of TME has been applied to colon cancer surgery. Hohenberger et al. [4] firstly described complete mesocolic excision (CME) in conjunction with central vascular ligation (CVL) and emphasized the sharp dissection along the mesocolic plane with true central ligation of the main arteries and veins at their roots. The authors analyzed data of 1329 patients undergoing R0 resection for colon cancer. After the application of the concept of CME, local recurrence rate decreased from 6.5% to 3.6% and 5year cancer related survival rate increased from 82.1% to 89.1% [4]. The concept of CME was further supported by pathologic study. West et al. [5] compared CME specimens with specimens of standard surgery and observed that CME surgery removed greater area of mesentery and achieved higher resection rates through the mesocolic plane when compared with standard surgeries. The Danish Colorectal Cancer Group showed that CME surgery yielded better 4year disease-free survival rates when compared to conventional non-CME surgery for patients with stage I–III colon cancer [6].

Japanese D3 lymphadenectomy has been performed in many Asian countries which is based on similar principles to CME with CVL. According to the Japanese Society for Cancer of the Colon and Rectum, D2 lymphadenectomy is defined as removal of D1 lymph nodes (epicolic, paracolic) and D2 nodes (intermediate), and D3 lymphadenectomy as removal of D3 nodes (main) at the root in addition to D1and D2 nodes [7]. When comparing D3 specimens with CME specimens, both specimens showed higher rates of the mesocolic plane surgery and long distances from the high vascular tie to the bowel wall [8].

Laparoscopic surgery for colon cancer has clear short-term advantages such as less postoperative pain, lower wound infection, and earlier recovery when compared with conventional laparotomy [9]. The oncologic safety of laparoscopic surgery has been also confirmed in large randomized clinical trials [10–12]. However, applying laparoscopy to CME for colon cancer is difficult, mainly due to vascular dissection and splenic flexure mobilization [13]. Accordingly, there is skepticism as to whether favorable outcomes of open CME can be reproduced with laparoscopic CME [14–17]. In a recent randomized trial, laparoscopic D3 lymphadenectomy for colon cancer showed short-term surgical safety and clinical benefits when compared to open surgery [18] and growing number of papers encourage the use of laparoscopic CME for colon cancer [16,19–21]. Here, we discuss appropriate CME procedure with regard to the oncologic backgrounds, essential components, applied anatomy, laparoscopic technique, short-term, and oncologic outcomes.

2. Surgical principle of colon cancer

2.1. Oncologic background of CME

Metastasis refers to is the secondary tumor growths at a distance site from a primary tumor site. The routes of metastases include lymphatic, hematogenous, disseminated metastasis, and direct invasion to adjacent organs. To date, there are two hypothesis when metastasis develops [22]. One hypothesis is that metastasis is mainly driven by primary tumor cancer progression thus cancer metastases occur stepwise pattern. Thus, CME improves outcomes by removing the mesocolon as one package and high ligation of the tumor-feeding vessels. The other hypothesis is that metastasis develops independently and progresses simultaneously [23]. Thus, lymph node metastasis reflects the advanced tumor nature and extended lymphadenectomy will not improve outcomes. Based on this, some authors are skeptic over the use of CME for colon cancer [24]. However, current principle of colon cancer surgery is en bloc resection of the primary tumor with regional lymph nodes and all grossly suspected or involved lesions should be removed during operation.

The number of lymph nodes retrieved reflects the extent of lymphadenectomy and the increased number of nodes is related to favorable survival [25]. CME surgery increased the number of nodes retrieved compared with non-CME surgery [5,26,27]. Improved outcomes after CME can be explained partly by the concept of stage migration [28]. A sufficient lymph node examination enables accurate nodal staging and prognostication. However, the numbers of nodes are affected by diverse clinicopathological factors such as
gender, tumor location, histologic grade, specimen length, or histologic immune response [29]. Ogino et al. [30] demonstrated enhanced tumor immune reaction was associated with favorable survival independent of lymph node count. Thus, it would be overestimating that increased nodal count, itself, after CME surgery improves survival. We believe that increased lymph node count may be a byproduct during CME and ultimately, improved outcomes can be achieved by en bloc resection of a primary tumor and mesocolon as one package while preserving visceral and retroperitoneal mesocolon fascia. CME surgery removes more mesocolon tissues compared with non-CME surgery [5,27]. Theoretically, more lymph nodes harboring isolated tumor cell or micrometastasis (tumor deposits <2 mm) can be cleared by CME surgery. The presence of occult metastasis in regional lymph nodes is associated with an increased risk of recurrence and poor survival in node-negative colorectal cancer [31]. Baskaranathan et al. [32] observed that 9.25% of patients had free cancer cells on the peritoneal surface and the presence of free cancer cells correlates poor cancer-specific survival in colorectal cancer. CME removes greater area of mesentery while preserving mesocolon integrity [5,27]. Thus, CME may remove more free tumor cells on peritoneal surface and reduce potential sources of disease recurrence.

### 2.2. Essential components of CME

To date, the detailed surgical treatment for colon cancer is still different among the nations and surgeons [4,8,27,33,34]. In Japan, lymph nodes in the mesocolon are grouped based on their locations and D3 lymphadenectomy, which removes principal lymph nodes along the major artery, is recommended for clinically node-negative disease [7]. D3 lymphadenectomy for colon cancer is a widely accepted surgical procedure in Asian countries, including Korea and China as well as Japan [35] and systematic regional lymphadenectomy has been performed for therapeutic purpose rather than staging. Although there is some differences of the extent of surgery between CME and D3 lymphadenectomy, we believe that these two surgical techniques share common characteristics with regard to excellent oncologic outcomes [4,5,8,21,36].

The original CME technique emphasized meticulous dissection between the mesocolon and retroperitoneum along the Toldt’s fascia and retrieval of the specimen as one unbreached mesocolon package. The CME surgery should be performed with techniques of central vascular ligation (CVL) to clear all locoregional lymph nodes. In addition, adequate proximal and distal margins should be obtained (Table 1).

#### 2.2.1. The plane of mesocolic excision

The plane of mesocolic excision is classified into: (1) a muscular propria plane means a poor plane of surgery; (2) an intramesocolic plane means a moderate plane of surgery; and (3) a mesocolic plane means a good plane of surgery [26]. The rate of mesocolic surgery was higher after CME surgery (89%) compared with non-CME surgery (47%) [27]. West et al. [37] demonstrated that a mesocolic plane of surgery improved survival in stage III colon cancer. A mesocolic plane surgery produces a good-quality specimen which shows a good bulk of mesocolon with a smooth surface with no or only minor visceral fascia defects. Thus, the primary tumor with its vasculatures and lymphatics is removed uninjured. Poor quality surgery such as a muscularis propria plane surgery inevitably produces defective specimen and it is likely to result in tumor cell spillage through major or multiple defects of the specimen or leave a remnant disease. Recently, a number of investigators studied the anatomy and multi-layered fascial structures of mesocolon and raised issues of standardization of nomenclature [38–47]. Mike and Kano [43] proposed that the concept of a fusion fascia which is formed by fusion of the peritoneum and the mesentery after intestinal rotation during the fetal period. Accordingly, the authors suggested that current nomenclatures of fascial structures such as the visceral peritoneum (fascia) and the parietal peritoneum (fascia) need to be replaced with the fusion fascia of the colon and the deep subperitoneal fascia, respectively. In addition, appropriate dissection plane should be between the fusion fascia of the colon (Toldt’s fascia) and the deep subperitoneal fascia. Culligan et al. [41] investigated histologic and electron microscopic structures of the mesocolon. In the ascending, descending, and apposed sigmoid mesocolons, the mesocolonic layered structures were surface mesothelium, mesocolon, deep mesothelium, Toldt’s fascia, retroperitoneal mesothelium, and retroperitoneum (from dorsal to ventral side). Thus, Culligan et al. [39] described that i.e. during left colectomy, surgical dissection plane can be either between the mesocolon and Toldt’s fascia (mesofascial separation) or between the Toldt’s fascia and retroperitoneum (retrofascial separation). These nomenclatures are not familiar to most surgeons however, to be popularized the CME principle, the surgical anatomy of the mesocolon and proper dissection plane need to be re-scrutinized in future studies.

#### 2.2.2. Central vascular ligation

Apical (central or D3) lymph node metastasis has been reported 0–11.1% in patients with right-sided colon cancer (the cecum, ascending colon, and hepatic flexure) [48,49]. The incidence of metastatic lymph nodes at the origin of the inferior mesenteric artery has been reported to 0.3–8.6% in patients with left-sided colon and rectal cancer [50]. Skip metastasis from epicolic node (pericolic or D1) to main node (apical or D3) has been reported 0.8%–2% [51–54]. CME surgery increased the distance between tumor to high tie and bowel to high tie [5,26,27]. Central ligation of main supplying vessels reduces a risk of residual metastatic lymph nodes and enables accurate staging and prognostication. Kotake et al. [55] observed that and D3 lymphadenectomy for T3 and T4 colon cancer was superior to D2 lymphadenectomy in terms of overall survival. Survival benefit was also seen in patients without lymph node metastasis. They postulated that removal of micrometastasis in the main nodes may improve survival.

#### 2.2.3. Length of proximal and distal margins

Unlike mesocolic plane and central ligation, there is no objective boundaries for proximal and distal resection margins. Mesocolic fat is more prominent around major vessels and that creates a bulky vascular pedicle [38]. Although there is some difference, CME technique favors the 10 cm-rule for proximal and distal margins [54]. Epicolic and paracolic nodes metastases occur along the marginal artery and thereafter tumor spreads to the intermediate and apical lymph nodes along the main supplying artery [49]. Thus, sufficient proximal and distal margins are needed to remove the mesocolon containing lymph nodes and thereby improve oncologic outcomes. Interestingly, the bowel lengths appear to be sufficient even in non-CME surgery in the actual reported data. West et al. [5] reported that mean length of large bowel for right-sided colon cancer was 26.5 cm after CME and 18.3 cm after non-CME surgery. For left-sided colon cancer, mean length was 39.2 cm after CME and 26 cm after non-CME surgery. The length of bowel resected and the amount of mesocolon containing lymph nodes are closely interrelated, thus it is difficult to assess direct impact of bowel length on outcomes. However, it may be valuable to rescrutinize the traditional 10 cm-rule for proximal and distal margins and investigate optimal small bowel and colonic lengths for colon cancer in this...
3. Vascular anatomy and lymphatic system

It is important to understand vascular anatomy to perform surgically and oncologically safe CME surgery for colon cancer. In particular, minimally invasive approaches such as laparoscopy and robotics have prompted to get a renewed attention on frequent anatomic variations of the branching vessels from the superior mesenteric artery (SMA), superior mesenteric vein (SMV), inferior mesenteric artery (IMA) and inferior mesenteric vein (IMV).

3.1. Artery

The midgut (the entire small intestine to proximal two-thirds of transverse colon) is supplied by the SMA and the hindgut (the distal third of transverse colon to rectum) is supplied by the IMA [59]. The SMA branches off two or three major colonic arteries to the right. The ileocolic artery is constantly present and the right colic artery arising from the SMA is highly variable and present in 0%–63.3% of cadavers [60–62]. The right colic artery may arise from the ileocolic or middle colic artery [63]. The middle colic artery is divided into two branches (right and left). Anatomical variations of the middle colic artery include complete absence in up to 25% of cases and the presence of an accessory (up to 10%) or double middle colic artery [59,64].

Topography of the ileocolic artery and right colic artery toward the SMA is important for vascular ligation for right-sided colon cancer. The ileocolic artery runs anterior to the SMV in 17%–83% of specimens [61–63,65]. The right colic artery, if present, crosses anteriorly in 63%–100% of specimens [61–63,65].

The SMA originates from the ventral side of the abdominal aorta about 3 cm–6.3 cm above the aortic bifurcation [66]. The IMA gives off the left colic artery, 2 to 6 sigmoid branches, and the superior rectal (hemorrhoidal) artery. Sigmoid branches may arise from the left colic artery or superior rectal artery [67].

3.2. Vein

The venous drainage follows the arterial anatomy. Venous blood from the cecum to proximal transverse colon drains into the SMV. Drainage from the distal transverse colon to most part of the rectum is directed to the IMV. Clinically, the venous anatomy of the right colic vein, superior right colic vein, gastrocolic trunk, and the middle colic vein is highly variable and of interest. Understanding of these anatomic variation may prevent inadvertent vein injury during CME for right-sided colon cancer.

Gastrocolic trunk of Henle refers to the confluence of the right gastroepiploic vein, superior right colic vein, and anterior superior pancreaticoduodenal vein [68]. A gastrocolic trunk is present in 46%–70% of individuals [68–70]. Yamaguchi et al. [69] observed that the right colic vein drained into the SMV directly in 56% and...
into the gastrocolic trunk in 44%. The middle colic vein entered into the SMV directly in 84.5% of individuals and into the gastrocolic trunk in 12.1% of specimens. Anomalous drainage of the middle colic vein was observed in two individuals (drainage into the splenic vein and the IMV).

3. Lymphatics

Lymphatics are drained along the course of the arterial anatomy. The colonic wall has an abundant network of lymphatic capillaries that is drained into extramural lymphatics following the arterial supply [59]. Lymph nodes are classified into epicolic, paracolic, intermediate, and main nodes depending on their location. Epicolic nodes are located in the appendices epiploicae. Paracolic nodes are located along the marginal artery. Intermediate nodes are located along the major arterial branches supplying the colon. Main nodes are located at the origin of the SMA or of IMA.

Main nodes are positioned on the ventral side of the SMV and the lymphatic channels run through anteriorly toward the SMA [48]. If the ileocolic artery courses behind the SMV, high ligation at the level of SMV may not jeopardize oncologic principle [54].

4. Preoperative consideration

4.1. Preoperative staging

Preoperative staging modalities include colonoscopy with biopsy, abdominopelvic computed tomography (CT) scan, and/or positron emission tomography. In suspected cases, chest CT scan is performed to rule out thoracic organ metastases. There is still space for improvement in determining T (depth of tumor invasion) and N (nodal involvement) staging by CT scan. A recent meta-analysis showed that sensitivity and specificity of CT was 86% and 78% when differentiating tumor invasion, and 70% and 78% when identifying nodal metastasis [71].

4.2. Indication

D3 dissection is generally recommended in patients with clinical stage II/III disease [2,72]. To date, there is limited evidence with regard to D3 dissection for early-stage colon cancer such as cT2N0 stage. According to the Japanese guideline, D2 dissection as well as D3 are all acceptable in cT2N0 disease. We think that CME with CVL, which is similar to D3 dissection, may be useful even in cT2N0 disease because preoperative imaging still has limited accuracy and D3 dissection can provide more accurate pathologic staging.

Laparoscopic CME takes longer operative time and is technically difficult. Thus, a laparoscopy can be selected as a primary approach when patients have the following clinical features: sufficient hemodynamic stability to tolerate CO₂ pneumoperitoneum, non-emergent settings, or lack of adhesion from prior extensive abdominopelvic surgery. An open approach can be selected when en bloc resection is difficult based on preoperative CT imaging or when patients have a large tumor (larger than 6–8 cm) or extensive infiltrative tumor to the adjacent organs [33].

4.3. Preoperative preparation

Patients with colon cancer do not receive any mechanical bowel preparation and oral antibiotics. Patients are fasted only from midnight the night before the surgery and a glycerin enema is performed once or twice before the surgery. First-generation cephalosporin is used as a prophylactic antibiotic and was administered just before the start of surgery. Postoperative antibiotic treatment is continued for 24–48 h. Low molecular weight heparin is administered for venous thromboprophylaxis, if necessary.

5. Surgical techniques

The concept of CME procedure includes sharp dissection between the visceral and parietal fascia layers with full mobilization of the apposed mesocolon, and central ligation of the supplying and draining vessels at their origin. The CME procedure emphasizes longitudinal (or horizontal) removal, vertical removal, and circumferential removal. The extent of the resection varies by tumor location and we discuss CME surgeries for right-sided and left-sided colon cancers, respectively.

5.1. CME with CVL for right-sided colon cancer

Various laparoscopic and open techniques are introduced in precious literature for performing CME with CVL for right-sided colon cancer. Laparoscopic approach is performed under the same CME principle as for laparotomy. For laparoscopic CME, one 10 mm port is utilized for a camera at the umbilicus and three working ports (the left upper: 5 mm or 12 mm port, left lower: 5 mm port, and right lower quadrants: 5 mm port). Another 5 mm port at the right upper quadrant is utilized in difficult cases. After placement of the trocars, the patient is placed in a Trendelenburg right side up position.

A medial to lateral dissection is advocated in most cases, but when the origin of ileocolic pedicles are not clearly identified, the dissection is alternated with lateral to medial fashion. The detailed procedures of ‘A medial to lateral dissection’ are as follows: The terminal ileum and the ascending colon are dissected off through the embryological plane. Dissection between the mesocolon and Gerota’s fascia continues to the duodenum and head of the pancreas. Once the ileocolic vessels are identified, the mesocolon package containing lymph nodes is cleared along the vessels while exposing the ventral side of the SMV and SMA. The ileocolic vessels are ligated at the root of the SMV and SMA, and the dissection continues cephalad to the right colic vessels, the gastrocolic trunk of Henle, and the middle colic vessels. The right colic vessels, if present, are skeletonized and transected at the root. The gastrocolic trunk has a number of anatomic variations, and careful dissection is necessary to avoid unwanted vascular injury. Unless infiltrated by tumor, the anterior superior pancreateoduodenal vein and right gastroepiploic vein are preserved, and only the right colic and/or superior right colic vein are transected. Then, the middle colic vessels are identified and skeletonized at the roots of the SMA and SMV.

Tumor-specific CME is performed according to the tumor location. For cecal and proximal ascending colon cancers, right hemicolectomy is performed and the right branches of the middle colic artery and vein are ligated. For hepatic flexure and proximal transverse colon cancers, extended right hemicolectomy is performed and the roots of the middle colic artery and vein are ligated. The Kocher maneuver was not performed routinely. Omentectomy is performed just below the gastroepiploic vessels and, unless infiltrated by the tumor, right gastroepiploic vessels are preserved. (Figs. 1 and 2). The mobilized colon is exteriorized through umbilical minilaparotomy and transected with adequate resection margin. Extracorporeal stapled or hand-sewn anastomosis is performed and one closed suction drain is placed.

On the other hand, the basic principle of ‘A lateral to medial dissection’ is initiated retroperitoneal mobilization between embryologic planes of parietal and visceral fascia of mesocolon,
followed by dissection vertically along superior mesenteric vessels ligating ileocolic, right colic and middle colic pedicles. First, the small bowel is retracted to the left, and a retroperitoneal plane is identified and continued laterally using adequate retraction. The embryological avascular plane between the mesocolon and retroperitoneal essential structures such as right ureter, right gonadal vessels and right kidney is developed by sharp dissection. The plane is then extended superiorly below Gerota’s fascia and medially to the retroperitoneal adhesions with the third portion of the duodenum. Maintaining tension during lateral retraction of the cecum resulted in better identification of vascular anatomy, and a peritoneal window was made safely on the mesentery along the flow of the ileocolic pedicles to the superior mesenteric vessels. After clearing of lymph nodes bearing areolar tissue on the SMV, the origin of ileocolic vessels are completely exposed. Ileocolic vessels are then divided and ligated, and the remaining attachment to duodenum is released. Careful sharp dissection along the SMV is continued up to the root of the middle colic vessels. After complete removing lymph node-bearing tissue around the origin of middle colic artery, each branch of middle colic artery is clearly skeletonized. The level of arterial ligation should be performed according to the tumor location. The vein is subsequently ligated in the same manner. For gastrocolic ligament division, caudal retraction of the transverse colon was separated by sharp dissection. Finally, in particular patient, Gerota’s fascia and perinephric fat should be included in the specimen. This procedure is important to evaluate the possibility of circumferential resection margin positivity.

5.2. CME with CVL for left-sided colon cancer

For laparoscopic CME, one 10 mm port is utilized for a camera at the umbilicus and three working ports (the right lower: 5 mm or 12 mm port, right upper: 5 mm port, and left lower quadrants: 5 mm port). Another 5 mm port at the left upper quadrant is utilized in difficult cases. After placement of the trocars, the patient is placed in a Trendelenburg with left side up position. CME procedure is initiated by incising the medial side of the sigmoid mesocolon at the level of the sacral promontory and medial to lateral mobilization is continued through the avascular plane. With adequate traction, the IMA is lifted up and skeletonized with caution not to damage the superior hypogastric plexus around the aortic bifurcation. After complete clearance of lymph nodes around the root of the IMA, the IMA or left colic artery is ligated at the origin depending on the type of procedure planned (left hemicolectomy or anterior resection). The ureter and gonadal vessels are identified with further medial to lateral dissection and preserved. The IMV is lifted up and dissected cephalad to the ligament plane of the duodenum and transverse colon.
of Treitz, and ligated at the lower border of the pancreas. Retroperitoneal space is developed between the mesocolon and Gerota’s fascia. Root of the transverse mesocolon is freed from the lower border of the pancreas and entering the lesser sac by dissection through the ventral side of the pancreas. After completing medial colonic mobilization, the left lateral paracolic attachments are lysed. Dissection continues to the lower pole of the spleen and splenocolic ligament is dissected. Omentectomy is performed just below the gastroepiploic vessels and, unless infiltrated by the tumor, left gastroepiploic vessels are preserved. The embryologic adhesion is cleared up between the stomach and the transverse mesocolon and the lesser sac is identified. Continued dissection to the dorsal and lateral side joins the previously dissected surgical planes.

Tumor-specific CME is performed according to the tumor location. For proximal descending colon cancers, the root of the IMA is preserved and the left colic artery and superior rectal artery are ligated at its origin from the IMA. For mid descending and sigmoid colon cancers, the root of the IMA is ligated and the root of the IMV is ligated just below the lower border of the pancreas. The mobilized colon is exteriorized through umbilical minilaparotomy and transected with adequate resection margin. Extracorporeal stapled or hand-sewn anastomosis is performed and one closed suction drain is placed.

5.3. Adjuvant chemotherapy

After recovery from surgery, chemotherapy is recommended for patients with stage II and III disease according to National Comprehensive Cancer Network (NCCN) guidelines [73]. Chemotherapy regimens include fluoropyrimidine (fluorouracil with folinic acid, capecitabine) alone, or in combination with oxaliplatin (FOLFOX). Stage II patients with high-risk pathologic or clinical features (T4, histologic grade 3 or 4, lymphovascular involvement, bowel obstruction, T3 lesions with localized perforation, positive resection margin, or perineural invasion) are candidates for oxaliplatin-containing regimens.

6. Short-term outcomes

During CME for colon cancer, exposure and dissection along the major vascular pedicles for CVL is quite difficult, leading to concerns
over prolonged operative time and increased postoperative complication rates. Mean operative time ranged from 156 min to 178 min [74–76] and operative time of CME is longer compared with non-CME surgery [74,76]. Postoperative morbidity rate ranged from 11% to 28% [4,74–78] but did not differ between CME and non-CME surgery [76,78] (Table 2).

When comparing laparoscopic and open CME, mean operative time after laparoscopic CME ranges from 136 min to 269 min [16,18–21,34,79–83] and most studies reported prolonged operative time in the laparoscopic CME group [18,80,82]. Bae et al. [19] and Huang et al. [83] reported similar operative time between the laparoscopic and open CME groups [19,33,82]. Two studies showed lower morbidity rates in the laparoscopic CME group [18,80]. In addition, shorter time to soft diet [19,80,82] and reduced length of stay [18,19,80] have been reported with laparoscopic CME. Rate of conversion to open CME ranged from 1.9% to 10.4% [16,18,19,33,80,82] in the literature. Recently, Yamamoto et al. [18] performed a randomized controlled trial comparing laparoscopic CME surgery [76,78] (Table 2).

Table 2

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study period</th>
<th>Characteristics</th>
<th>N</th>
<th>Colon cancer</th>
<th>OT (min)</th>
<th>Cx (%)</th>
<th>LN</th>
<th>AC (%)</th>
<th>Survival (%)</th>
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<tr>
<td>Tagliacozzo [76], 1997</td>
<td>Standard (SL) vs. extended (EL) lymphadenectomy</td>
<td>SL:84</td>
<td>SL:145</td>
<td>SL:10</td>
<td>SL:12</td>
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<td>5year-OS = SL:62.8 vs. EL:64.3</td>
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<td>Boley [80], 2003</td>
<td>Non-standardized (NS) vs. standardized surgery (SS)</td>
<td>EL:60</td>
<td>EL:156</td>
<td>EL:12</td>
<td>EL:22</td>
<td>0</td>
<td>5year-CSS = NS:66.4 vs. SS:76.6</td>
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<td>Tentes [78], 2007</td>
<td>Conventional (CS) vs. radical lymph node resection (LND)</td>
<td>Lt</td>
<td>CS:18</td>
<td>LND:11:</td>
<td>NR</td>
<td>5.6</td>
<td>5year-CSS (Stage III) – CS:19 vs. LND:70</td>
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<td>Hohenberger [4], 2009</td>
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<td>1329</td>
<td>Lt</td>
<td>NR</td>
<td>19.7</td>
<td>32</td>
<td>5year-CSS = I:99.1, II:91.4, III:70.2</td>
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<td>Pramatarakis [77], 2010</td>
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<td>115</td>
<td>Lt</td>
<td>NR</td>
<td>14</td>
<td>72</td>
<td>5year-OS = 72.4</td>
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<td>Kamemitsu [75], 2013</td>
<td>D3</td>
<td>370</td>
<td>Lt</td>
<td>165</td>
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<td>5year-OS = I:100, II:94.5, III:85</td>
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<td>Galizia [74], 2014</td>
<td>Non-CME (NCME) vs. CME</td>
<td>NCM:58</td>
<td>NCME:130</td>
<td>CME:12</td>
<td>NCME:15</td>
<td>5</td>
<td>4year-CSS = NCME:74 vs. CME:90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kotake [55], 2014</td>
<td>D2 or D3 for pT3 or pT4 cancer</td>
<td>D2:3425</td>
<td>D2:15</td>
<td>D3:22</td>
<td>D3:66</td>
<td>0</td>
<td>4year-DPS = NCME:75.9 vs. CME:85.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bertelsen [6], 2015</td>
<td>Non-CME (NCME) vs. CME</td>
<td>NCME:1031</td>
<td>R</td>
<td>NR</td>
<td>NCME:21</td>
<td>CME:37</td>
<td>0</td>
<td>4year-DPS = NCME:75.9 vs. CME:85.8</td>
<td></td>
</tr>
</tbody>
</table>

OT, operative time; Cx, postoperative complication; LN, number of lymph node examined; AC, adjuvant chemotherapy; NR, not reported; OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival. *Statistically significant.

8. Conclusions

The introduction of CME has improved oncologic outcomes greatly in patients with colon cancer. The improved outcomes with CME can be attributed to underlying sound oncologic principles such as dissection through the proper plane of mesocolic excision, central vascular ligation, and sufficient length of proximal and distal margins. Thereby, CME technique can achieve en bloc removal of the diseased lesion with the increased amount of the colonic mesentery. CME is a technically demanding operation thus, population-based study (n = 1395) and demonstrated CME is oncologically superior to non-CME surgery in terms of 4year disease-free survival (CME: 85.8% vs. non-CME: 75.9%). Kotake et al. [55] compared D2 and D3 lymphadenectomy for T3 and T4 colon cancer and suggested that D3 lymphadenectomy reduced 18% of relative risk for overall survival. Nagasaki et al. [84] investigated the prognostic impact of lymph node location in patients undergoing CME with CVL for stage III colon cancer. The authors demonstrated that the lymph node location such as pericolic, intermediate, and main lymph nodes was associated with accurate prognostication. In the pathologic N1 group, the recurrence-free survival of patients with pericolic node metastasis (84.4%) was significantly better than that of patients with intermediate or main node metastases (71.5%). Similarly, in the pathologic N2 group, the recurrence-free survival of patients with epicolic node metastasis (72.6%) was significantly favorable than that of patients with intermediate or main node metastasis (53.1%).

When comparing laparoscopic and open CME, similar overall survival (laparoscopy:70.4% vs. open: 67%) [80] and recurrence rates (laparoscopy: 8.6% vs. open: 9.1%) [82], Cho et al. [33] reported similar overall and disease-free survival rates between the minimally invasive approaches (laparoscopy and robot) and open CME. Interestingly, Bae et al. [19] reported a better overall survival rate in the laparoscopic CME group, but numerous multicenter trials have failed to show better oncologic outcomes after laparoscopic colon cancer surgery [11,12,85]. Accordingly, a potential favorable impact of laparoscopic CME on prognosis needs to be further investigated (Table 4).
comprehensive understanding of the applied anatomy is essential for successful CME. Favorable outcomes of open CME have been replicated with a laparoscopic approach. However, the debate about the technical feasibility and optimal extent of surgery regarding CME technique is still ongoing. International prospective observational cohort study for colon cancer surgery, so called T-REX study, is currently underway to establish optimal bowel resection extent and appropriate central lymph node dissection in Japan, Korea, Germany and United Kingdom. The T-REX study will hopefully help to clarify these issues in the future. Finally, incorporating a structured education program on minimally invasive (laparoscopy or robot) CME would be beneficial.
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Conflict of interest
None.

Contributions
Study concept and design: NK Kim, YW Kim, YD Yoon, MS Cho.
Acquisition and interpretation of data: NK Kim, YW Kim, MS Cho, BS Min, KY Lee.
Drafting of the manuscript: NK Kim, YW Kim, YD Yoon, MS Cho, BS Min, KY Lee.
Critical revision of the manuscript: NK Kim, YW Kim, MS Cho, H Hur, BS Min.
All authors have approved the final article.

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