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EDITORIAL

Complete mesocolic excision: Techniques and outcomes

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Abstract

Complete mesocolic excision (CME) for the treatment of colon cancer was first introduced in the West in 2008. The first aim of this procedure is to remove the afflicted colon and its accessory lymphovascular supply by resecting the colon and mesocolon in an intact envelope of visceral peritoneum, which holds potentially involved lymph nodes. The second component of CME is a central vascular tie to remove completely all lymph nodes in the central (vertical) direction. In its original iteration, CME was performed via laparotomy, although many centers preferentially perform laparoscopic surgery, with its associated benefits and similar oncological outcomes, as the standard treatment for colonic cancer. Here, we present the surgical techniques for CME in open and laparoscopic surgery, as well as the surgical, pathological and oncological outcomes of the procedure that are available to date. Because there are no randomized control trials comparing CME to "standard" colon surgery, the principles underlying CME seem anatomical and logical, and the results published from the Far East, reporting an 80% 5-year survival rate for Stage III cancer, should guide us.

Key words: Colon cancer; Complete mesocolic excision; Laparotomy; Laparoscopic colectomy; Surgical technique; Oncological outcome

Core tip: This review presents the most recent knowledge in the field of complete mesocolic excision (CME) for colon cancer treatment and provides key points in both open and laparoscopic surgical techniques, surgical and pathological outcomes, and oncological outcomes of the procedure. The conclusion makes clear that in the absence of randomized control trials comparing CME to "standard" colon surgery, the principles underlying CME seem anatomical and logical, and the favorable long-term results published from the Far East for Stage III colon cancer disease should guide us in the future.

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INTRODUCTION

The years after the introduction of total mesorectal excision led to a major improvement in the survival rate of rectal cancer. Since its introduction, the five-year survival rate has increased from 45%-50% to 75%, and the local recurrence rate has decreased from 30% to 5%-8%[1]. The technique is based on the principle that dissection in the mesorectal plane produces an intact fascial-lined specimen, which contains all the blood vessels, lymphatic vessels, and lymph nodes through which the tumor may disseminate[2,3].

The embryological planes, however, are not narrowed to the rectum and mesorectal layers but continue to the sigmoid and descending colon on the left side, running behind the pancreas and around the spleen, and include the duodenum with the head of the pancreas, the cecum and ascending colon with the mesenteric root on the right side and the lymphatic drainage accompanying the arteries[4]. Thus, the surgical principles of total mesorectal excision have been extrapolated to colonic resection and complete mesocolic excision (CME), which was introduced by Hohenberger *et al*[4]. However, the principles of CME have not been adopted in a widespread manner[5], and the survival rates for colon cancer now lag behind those of rectal cancer[6].

We aim to describe the technique and the outcomes of the CME procedure. The purpose of the CME is to remove the afflicted colon and its accessory lymphovascular supply by resecting the colon and mesocolon in an intact envelope of visceral peritoneum. The mesocolon is situated within two layers of the visceral fascia[7]. This envelope holds potentially disseminated lymph nodes and, by removing it intact, the risk of cancer cells spilling into the peritoneal cavity is minimized. The second component of CME is a central vascular tie to remove completely all lymph nodes in the central (vertical) direction[8].

SURGICAL TECHNIQUE

Open surgery

In open surgery, a "lateral-to-medial" approach is generally performed. For right-side colon cancers, the dissection commences laterally by identifying the lateral peritoneal fold[9] an embryonic fusion plane that facilitates mesofascial and retrofascial separations. Anatomically and histologically, there is a single fascial layer separating the overlying mesocolon from the underlying retroperitoneum (Toldt's fascia). The dissection continues medially in the mesofascial interface. The mesenteric root up to the origin of the superior mesenteric pedicle is mobilized, and the dissection continues over the duodenum and pancreatic uncinate process to allow complete access to the superior mesenteric vein, as well as to the medially and inferiorly located superior mesenteric artery[10]. In their original description, Hohenberger *et al*[4] added a duodenal kocherization at this point, but that is not routinely performed[4]. Continuing medially, the small intestinal mesentery, ileocecal junction, right colon, right mesocolon and mesenteric confluence are fully mobilized and entirely intact from the underlying fascia and retroperitoneum[11]. The autonomic nervous plexus is identified and preserved[10].

After the complete mobilization, the ligation of the supplying vessels follows. Initially, the ileocolic and the right colic vessels (if present) are divided at their origin from the superior mesenteric vessels[4,10,12]. Sharp dissection is then carried out centrally along the superior mesenteric artery, ensuring clearance of all associated lymph nodes[10]. To expose the middle colic vessels, the lesser sac is entered by breaching the omentum caudal to the gastroepiploic arcade[10]. For cecal and ascending colon cancers, only the right branch of the middle colic vessels is divided[4,10,13]. The surgeon needs to be aware of the gastrocolic vein and the loop of Henle because the peri-pancreatic venous vascularity is subject to variability. The transverse mesocolon dissection is continued vertically to meet the dissection along the superior mesenteric vascular pedicle, producing a rectangular specimen with an intact mesocolic envelope containing all central lymph nodes[14]. At that point, the colon is divided at the level of the middle colic vessels[4].

For neoplasms of the hepatic flexure or proximal transverse colon, the lesser sac is entered by dividing the right gastro-epiploic artery and continuing vertically to the transverse colon. The middle colic artery is divided at its origin from the superior mesenteric artery, while the middle colic vein is divided at its junction to the gastrocolic trunk or the superior mesenteric vein[4,9,10,13]. The right gastro-epiploic artery may need to be divided at its origin to allow the retrieval of the peri-pancreatic lymph nodes[4,10]. Some authors[8] advocate for the dissection of the lymph nodes in the lateral 10 cm of the right gastro-epiploic vascular curvature, including the sub-pyloric and over the pancreatic head lymph nodes. For hepatic flexure cancers, the colon is resected near to the splenic flexure[4].

For cancers situated to the left of the middle colic artery, lymph nodes along the inferior aspect of the left pancreas, as well as lymph nodes along the left gastro-epiploic arcade, may be resected[8]. If lymph nodes over the pancreatic head are potentially involved, these nodes should be dissected off the pancreatic head with central ligation of the right gastroepiploic artery. The superior pancreaticoduodenal artery is usually preserved. The surrounding autonomous nervous plexus must be preserved to avoid the risk of functional consequence, *e.g.*, diarrhea[4].

For left colon cancers, the "lateral-to-medial" dissection begins at the lateral peritoneal fold and continues in the mesofascial interface. After the whole mesocolon of the descending and sigmoid colon is dissected, the ureter and the vesicular or ovarian vessels are recognized and left behind. The greater omentum is separated from the transverse colon and the lesser sac is fully exposed, and the two layers of the transverse mesocolon are divided at the lower edge of the pancreas[4]. The splenic flexure is mobilized when needed. For cancers of the descending colon, ligation of the ascending branch of the left colic artery and dissection of the lymph nodes at the origin of the superior mesenteric artery, without damaging the superior hypogastric plexus, is advocated. For cancers located in the middle of the descending colon down to the sigmoid colon, the root of the inferior mesenteric vessels below the pancreas is divided. Colon is divided proximally, between the left transverse colon and the distal descending colon, depending upon the site of the tumor, while transection distally is always in the upper third of the rectum[4,8].

Laparoscopic surgery

In laparoscopic surgery, a "medial-to-lateral" approach is preferable. In a laparoscopic right hemicolectomy, the mesocolon is incised along the mesenteric axis close to the superior mesenteric vein. The ileocolic vessels are divided as close as possible to the superior mesenteric vein[15]. After exposing the mesocolic interface, a wide separation between the pancreatic head and the transverse colon is achieved. Dissection then proceeds along the superior mesenteric vein, exposing the gastrocolic trunk of Henle. Next, the middle colic artery is identified as it rises from the superior mesenteric artery and is severed at the root of its right branch. This is accompanied by lymph node dissection, taking care to preserve the left branch of the middle colic artery. Simultaneously, the middle colic vein is identified and severed at the root of its right branch. Next, an anterior-to-median approach is performed by dissecting the right side of the greater omentum. The fusion fascia is detached between the omentum and transverse mesocolon and the hepatic flexure is mobilized[16]. The accessory middle colic veins are carefully dissected, accompanied by lymph node dissection, and the transverse mesocolon is dissected below the lower edge of the pancreas, uncovering the superior mesenteric vein. The specimen is extracted by a mini-laparotomy, and an extracorporeal anastomosis is performed[15-17].

In a laparoscopic left hemicolectomy, the procedure starts by retracting the sigmoid mesocolon anteriorly, and the visceral peritoneum on the base of the sigmoid mesocolon is incised at the level of the sacral promontory. The incision continues upward to the ligament of Treitz, and the origin of the inferior mesenteric artery is exposed and divided 1 cm from the aorta. The inferior mesenteric vein is divided below the inferior border of the pancreas. The mesocolic interface is entered and the dissection continues from medial to lateral. Laterally, the sigmoid loop is mobilized by incising along the lateral peritoneal fold. When mobilization of the splenic flexure is required, a medial approach is used. Retracting the transverse colon anteriorly, the root of the transverse mesocolon is dissected onto the body and tail of the pancreas, entering the lesser sac. Then, the dissection moves toward the base of the distal transverse colon and the descending colon. The posterior attachments of these structures are divided. The lateral attachment is freed up to the spleen and the phrenocolic ligament. The splenic flexure is fully mobilized after the omentum is separated from the colon. The distal division of the colon is performed intracorporeally using a linear stapler. The proximal division is performed extracorporeally after dividing the mesocolon up to the chosen site. The specimen is generally extracted through an incision at the level of the umbilicus. Anastomosis is performed intracorporeally using a circular stapler device, which is passed transanally[13,18].

The laparoscopic management of colon cancer close to the flexures and in the transverse colon is still controversial. Many centers use the open approach for these tumors as the standard treatment[19]. Others, for hepatic flexure or proximal colon transverse cancers, perform an extended right hemicolectomy with central ligation of the middle colic and right gastroepiploic vessels, removal of subpyloric lymph nodes, and colon stapling proximal to the splenic flexure[17].

OUTCOMES

To date, the vast number of available studies evaluating CME is retrospective. In a small number of series, CME has been compared to "standard" or "traditional" colon surgery. The problem with "standard" colon surgery is that the surgical technique depends on the individual surgeon and the presence of radical lymph node dissection. It is becoming increasingly evident that differences in oncologic outcomes reported among surgeons are directly related to the differences in the techniques used[18].

Surgical and pathological outcomes

West *et al*[20] reported that specimens from colon cancer resections from Erlangen, Germany, where CME and central venous ligation are routinely applied, are more often in the correct anatomical (mesocolic) plane (92% *vs* 40%, $P < 0.0001$) and have higher number of lymph nodes harvest (median 30 *vs* 18, $P < 0.0001$) compared to standard specimens from Leeds, United Kingdom.

A similar inter-institutional comparison was performed by the same authors[21] among six Danish hospitals where "traditional" surgery was performed and Hillerod Hospital, where surgeons attended a surgical educational training program in CME. As anticipated, the resection specimens from the latter center were characterized by a larger mesenteric surface (144.6 cm^2 *vs* 87.1 cm^2, $P < 0.0001$) and an increased lymph node harvest (median 28 *vs* 18, $P < 0.0001$).

Bertelsen *et al*[15] described how the induction of CME in Hillerod Hospital in 2008 has influence the surgical and pathological outcomes. They reported that the length of the vascular ligation increased from 7.1 to 9.6 cm ($P < 0.0001$), and the mean number of harvested lymph nodes increased from 24.5 to 26.7 (*P* = 0.0095). However, the plane of mesocolic resection, the rate of R0 resection and the risk of complications were equivalent, while the median length of hospitalization increased from 4 to 5 d (*P* = 0.04).

The most recent retrospective population study[22] also reported a statistically significantly greater lymph node harvest in CME compared to non-CME (36.5 *vs* 20.9 *P* < 0.0001) groups of patients. In addition, 82% of the CME group was dissected in the mesocolic plane, compared to 60% of the non-CME group (*P* < 0.0001). The CME group in this population study was also from Hillerod Hospital.

Galizia *et al*[12] reported that the number of the harvested nodes and the length of the vascular ligation were significantly better in the CME group (*P* < 0.01). Moreover, a higher number of tumor deposits were harvested, thus allowing chemotherapy in those newly upstaged patients.

In a systematic review[23], CME resections had a weighted mean R0 rate of 89.9% compared to 86.7% for standard resections.

Interestingly, studies comparing dissection planes in specimens from "standard" and CME resection concluded that the rates of mesocolic and R0 resections were equivalent in the two techniques[15,22], supporting the argument that the majority of trained colorectal surgeons perform mesocolic resection. Thus, CME represents an appealing appellation for an already-practiced technique[24,25].

Oncological outcomes

West *et al*[26] showed that meticulous mesocolic plane surgery is associated with a 15% greater 5-year overall survival rate compared with cases where defects in the mesocolon reached into the mascularis propria.

A Norwegian retrospective study[27], compared colon cancer survival between one hospital that used the CME approach and two other centers that used the "standard" approach. Investigators included only Stage I and II colon cancer for analyses. In the two groups, there were no significance differences between the T stage (*P* = 0.171). The authors observed a better 3-year overall survival rate (88.1% *vs* 79.0%, *P* = 0.003) and disease-free survival rate (82.1% *vs* 74.3%, *P* = 0.026) in the CME group of patients, while the cancer-specific survival rate was 95.2% in the CME group *vs* 90.5% in the standard group (*P* = 0.067). Multivariate Cox regression analysis disclosed age, operative technique and T category as independent prognostic factors for both overall and disease-free survival.

Galizia *et al*[12] compared colon cancer recurrence and survival before and after the introduction of CME in 2008 in the same Italian center. Interestingly, there was no local recurrence in the CME group but there was in 21% of the standard group, while distant metastases occurred with similar frequencies (13.3% and 13.7%, respectively). We should mention, however, that significantly more early stage cancer patients were enrolled in the CME group.

Shin *et al*[18] reported a study of 168 patients with Stage II and Stage III colon cancer treated by laparoscopic CME. A remarkable 89.6% 5-year survival rate was reported.

In the most recent retrospective population study from Demark[22], 364 patients who underwent CME were compared to 1031 patients who were treated with non-CME colectomies. For all patients, the 4-year disease-free survival rate was 85.8% after CME and 75.9% after non-CME surgery (*P* = 0.0010). Multivariable Cox regression analysis showed that CME surgery was a significant, independent, favorable predictive factor for higher disease-free survival rates for all patients (HR = 0.59; 95%CI: 0.42–0.83) and also for patients with UICC Stage II (HR = 0.44; 95%CI: 0.23-0.86) and Stage III disease (HR = 0.64, 95%CI: 0.42-1.00). After propensity score matching, the disease-free survival rate was significantly higher after CME, irrespective of UICC stage, with a 4-year disease-free survival rate of 85.8% after CME and 73.4% after non-CME (*P* = 0.0014). In the same study, overall survival was not significantly higher in the CME group compared to the non-CME group. The authors believe that this may be due to the relatively short follow-up, the improved surgical outcomes for resection of lung and liver recurrences, or advances in chemotherapy for patients with non-resectable recurrences[22].

In a systematic review[23] of 5246 patients, the weighted mean local recurrence rate and the 5-year overall and disease-free survival rates were 4.5%, 58.1% and 77.4%, respectively, with a mean follow-up of 60 months. In the same review of 22 papers on CME, there were overall survival rate (58.7% *vs* 53.5%), disease-free survival rate (77.4% *vs* 66.7%) and local recurrence rate (4.5% *vs* 7.8%) advantages in the CME group.

The improved outcome after CME is likely related to resection in the mesocolic plane[17,19,25] and to high ligation of the tumor-feeding vessels[4,25]. It is unclear which of the two components of CME is more important. We believe that complete removal of an intact mesocolonic envelope (complete mesocolic excision), along with central vascular ligation and apical node dissection, is essential for improving the outcomes.

CONTROVERSIES REGARDING CME

There is a great deal of discussion and debate regarding whether the CME concept is new. The CME technique was introduced in the West in 2008, but Japanese, Chinese, Korean and Taiwanese surgeons have used D3 lymphadenectomy resections for colon cancer for decades. They D3 lymphadenectomy is defined as the dissection of the paracolic, intermediate and central lymph nodes, a procedure equivalent to CME[19].

CME is a more extensive operation than a standard procedure. Originally CME was described as an open procedure[4], although many centers prefer performing laparoscopic surgery, with its associated benefits[28-31] and similar oncological outcomes[8], as the standard treatment for colonic cancer.

A small comparison study between laparoscopic and open CME approaches concluded that laparoscopy offers specimens of similar quality to the open CME approach in terms of lymph node harvest, rate of achievement of an intact mesocolic plane, and distance from high tie to tumor and high tie to nearest bowel wall in proximal right- and left-sided resections. However, for transverse and hepatic flexure tumors, the open CME group had better outcomes in distance from tumor to high tie and nearest bowel wall to high tie compared to the laparoscopic group[13]. Similar oncological results were found in a prospective study from Norway that compared laparoscopic to open CME. The 3-year overall survival rate (80.4% *vs* 88.2%, $P = 0.152$) and disease free survival rate (74.8% *vs* 80.0%, $P = 0.405$) were similar[32].

A recent Korean study comparing the outcome of laparoscopic right to open right CME showed a better 5-year overall survival rate in the laparoscopic group compare with the open group (77.8 *vs* 90.3%, $P = 0.028$) and a similar 5-year disease-free survival rate (71.8% *vs* 83.3%, $P = 0.578$)[33].

For proximal right and left sided tumors, laparoscopic CME can be performed with safety and good oncological outcome. However, for tumors located near the flexures or in the transverse colon, the open approach is still the standard[22].

CME is a longer operation[19,34], which may lead to increased morbidity, but it does reduces the efficiency of an operating theater and influence the health economy[19]. The duration of surgery remains one of the largest obstacles for laparoscopic CME[34]. The operative duration learning curve reveals an initial duration of approximately 250 min, which is more than double the duration reported for a conventional laparoscopic right hemicolectomy performed by experienced laparoscopic surgeons[35].

Even though CME is a more extensive procedure, mortality and complication rates are in acceptable ranges. In a systematic review[22], overall morbidity, 30-d mortality and re-operative intervention for vascular complications were 19.4%, 3.2% and 1.1% respectively and mean blood loss was 150 mL, all comparable to the reported contemporary series for "standard" resections[36,37] However, unusual complications, such as chyle leakage[18], duodenal injury[28] and major vascular injury[38] have been reported.

CONCLUSION

There are no randomized control trials comparing CME to "standard" colon surgery. The concept of CME and the new anatomical characteristics of the mesocolon, as described by Culligan *et al*[5], offer a great opportunity to re-evaluate colon cancer surgery. The principles underlying CME are anatomical and logical, and the results published from the Far East, reporting an 80% 5-year survival rate for Stage Ⅲ disease[18], should guide us.

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