

COMPLETE MESOCOLIC EXCISION AND RIGHT HEMICOLECTOMY

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In order to understand the term complete mesocolic excision, the knowledge of anatomy is crucial. In the classical literature, mesenteric organ is described as fragmented and discontinuous. Total mesorectal excision (TME) has become the "gold standard" for the surgical management of rectal cancer. In describing it, Heald provided an anatomical basis for surgery. Similar description was needed for colon cancer surgery. According to the modern anatomical studies, fibers of Toldt's fascia form a plane between the apposed portions of the mesocolon and the underlying retroperitoneum. The demonstration of mesocolic continuity, combined with the presence of Toldt's fascia, interposed between the apposed portions of the mesocolon and the retroperitoneum, rationalize planar dissection in colonic resection. By addressing these anatomical features, the mobilization of the entire colon and mesocolon (which remain intact) can be performed. Hohenberger et al. used the concept of TME for colon cancer surgery and in 2009 introduced the term complete mesocolic excision (CME). The concept for CME is the consequent surgical separation by sharp dissection of the visceral fascia layer from the parietal one resulting in complete mobilization of the entire mesocolon covered by an intact visceral fascial layer, ensuring safe exposure and tie of the supplying arteries at their origin. With this technique, survival rate increased. In comparison to open CME, laparoscopic CME has comparable results. Complete mesocolic excision seems to offer a survival benefit and better local control, but none of this is proved by randomized controlled trials. *Acta Medica Medianae* 2015;54(1):107-114.

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Introduction

In order to understand the term complete mesocolic excision, the knowledge of anatomy is crucial. Until recently, surgery of the colon was based on anatomic descriptions of Sir Frederick Treves. He delivered his case series of 100 cadaveric dissections at the Royal College of Surgeons in England and noted that there was neither an ascending nor a descending mesocolon in approximately 50% of cadavers (1). Treves' descriptions of the mesocolon laid the foundation for anatomic teaching. Traditionally, the small intestinal mesentery, transverse and sigmoid mesocolon all terminate or attach at their insertions into the posterior abdominal wall. The right and left mesocolon are described as vestigial or absent, and confined to the posterior aspect of the right and left

colon. So, in classical literature mesenteric organ is fragmented and discontinuous (2). Earlier in 1879, Carl Toldt identified a distinct fascial plane between the mesocolon and the underlying retroperitoneum, formed by the fusion of the visceral peritoneum of the mesocolon with the parietal peritoneum of the retroperitoneum (Toldt's fascia). These findings provided a rationalization of the surgical, embryological and anatomical approaches to the mesocolon. Despite this, Toldt's fascia and the mesocolon continue to receive minor mentioning in anatomic textbooks (3).

Anatomical basis

Total mesorectal excision (TME) has become the "gold standard" for the surgical management of rectal cancer. In describing TME, Heald et al. provided an anatomical basis for surgery. Similar description was needed for colon cancer surgery (3). In 2012 Culligan et al. published a study with the aim to characterize mesocolic anatomy in patients undergoing mesocolic excision of the entire colon (4). Continuity between the right and transverse mesocolon and left mesocolon was

evident in all cases. In all 109 patients mesocolic fat was prominent around the major blood vessels creating an adipovascular pedicle. In all cases, the mesosigmoid was continuous with the left mesocolon which was fully adherent to the retroperitoneum above and the mesorectum below. In all patients, the fibres of Toldt's fascia formed a plane between the apposed portions of the mesocolon and the underlying retroperitoneum. The demonstration of mesocolic continuity, combined with the presence of Toldt's fascia, interposed between the apposed portions of the mesocolon and the retroperitoneum, rationalize planar dissection in colonic resection. By addressing these anatomical features through mesofascial separation, the entire colon and mesocolon can be mobilized intact (4). The same author gave description of microscopic structure of mesocolon and associated fascia which was consistent from ileocecal to mesorectal level. A surface mesothelium and underlying connective tissue is evident throughout. Fibrous septae separate adipocyte lobules. Where opposed to retroperitoneum, two mesothelial layers separate mesocolon and underlying retroperitoneum. A connective tissue layer occurs between these (ie, Toldt's fascia). After surgical separation of mesocolon and fascia both remained contiguous, the fascia remained in situ and the retroperitoneum undisturbed (5). According to the authors from China (6, the potential surgical plane formed between the mesocolon and the underlying retroperitoneum is easy to find. By a sharp dissection following the areolar tissue ('angel's hair') and complete mobilization of the entire mesocolon, the intact fascias is clearly seen, covering the posterior mesocolon (visceral fascia layer) and the retroperitoneal organs. No vascular, lymphatic, or nerve distribution is evident in this plane. The mesocolon is covered by the visceral fascia and peritoneum from both sides like an envelope (6). Where the mesentery is opposed to the retroperitoneum, it remains separated from its true connective tissue layer (Toldt's fascia). Importantly, a further mesothelial cell layer lies beneath Toldt's fascia and lines the true retroperitoneum. As a result, the colon and associated mesentery never become "secondarily" retroperitoneal structures. Clarification of mesenteric anatomy permits approach to surgical nomenclature in colon resections respecting mesocolic plane and avoiding intramesocolic plane and muscularis propria plane surgery (7).

A rationale for complete mesocolic excision

In 1909, Jamieson and Dobson described the macroscopic arrangement of lymphatic vessels draining the colon, emphasizing that the successful removal of malignant disease depends upon the removal of any affected lymphatic area and proposed principles of radical surgery for colon cancer: resection of the lesion and cleaning of the regional lymph nodes to the vascular roots (8,9).

Survival rates for colon cancer are only slowly improving. The improvement in rectal cancer survival and local recurrence is much more visible. Based on histology and embryology, the total mesorecta excision (TME) technique has successfully reduced the local recurrence rate of rectal cancer. This is achieved using series of measures like the definition of a "holy plane", recommendation of sharp dissection, total mesorectal excision, maintenance of the integrity of the visceral fascia in the specimen, and the pursuit of negative circumferential resection margin (10). Hohenberger et al. translated the concept of TME and in 2009 introduced term complete mesocolic excision (CME) for colon cancer (11). The concept of the surgical approach for CME is the consequent surgical separation by sharp dissection of the visceral fascia layer from the parietal one resulting in complete mobilization of the entire mesocolon covered by an intact visceral fascial layer, ensuring safe exposure and tie of the supplying arteries at their origin. The extent of the surgical procedures is determined by the location of the cancer and the pattern of potential lymphatic spread. If the cancer is located in the right colon then the procedure includes mobilization of the duodenum with the pancreatic head (Kocher manoeuvre) and the mesenteric root up to the origin of the superior mesenteric artery and exposure of superior mesenteric vein. During these preparations the integrity of the mesocolon should be strictly preserved, similar to mesorectal excision for rectal cancer. Hohenberger et al. (11) analyzed prospectively obtained data from 1438 consecutive patients of the Erlangen Registry for Colo-Rectal Carcinoma (ERCRC) with primary tumor manifestation between 1978 and 2002. Groups were divided into three periods, which represented changes in the surgical technique and the introduction of a standardized surgical approach. The primary endpoint was cancer-related survival. Secondary endpoints were: locoregional recurrence, yield of lymph node harvest, postoperative complications and mortality. The median number of examined lymph nodes per patient was 32, ranging from 2 to 169. They assessed the influence of the number of examined lymph nodes on prognosis. In 682 N0-patients the median number of examined lymph nodes was 29 (range 2-106). If <28 lymph nodes were removed, cancer-related 5-year survival was 90.7% (95% CI 87.4-94.0), a lymph node harvest of 28 or more was associated with a statistically different cancer-related 5-year survival rate of 96.3% (95% CI 94.3-98.3, P=0.018). In lymph node positive patients, if 28 or more lymph nodes were removed, cancer related 5-year survival improved from 64.6% (n = 145, 95% CI 56.6-72.6) to 71.7% (n=238, 95% CI 65.8-77.6, P=0.088), but without statistical difference. Locoregional recurrence rate improved over time periods. The 5-year cancer-related survival rate for all patients was 85%. Five-year cancer-related survival rate varied among surgeons depending on their experience.

Since 1978, survival rate increased from 82.1% to 89.1%. In a multivariate analysis, the number of lymph nodes examined (less or more than 28) was identified as independent prognostic factor. Other authors also described the step by step technique of CME and central vessel ligation to ensure an intact mesocolic envelope and removal of all potentially involved lymph nodes for right colon cancers, highlighting the need for careful operative description before widespread adoption (12).

Studies on CME

Pramateftakis published his experience with CME and high ligation in right hemicolectomy on 115 patients operated between 1989 and 2008. The 5-year survival rate for patients who completed follow up is 72.4%. The number of lymph nodes harvested was not recorded (13). Bartelsen compared results in two groups, the first before, and second after implementation of CME. A significant increase in the overall length of high tie and the number of excised lymph nodes after CME was observed. For tumors in the caecum, appendix or proximal part of the ascending colon these end-points increased for laparoscopic resection. For those in the hepatic flexure and transverse colon both end-points increased. The high tie and number of lymph nodes harvested after open non-extended right hemicolectomy did not increase. According to the authors, the reason might be that some high volume surgeons had already been performing high ligation as a part of a medial to lateral approach or that there were only a few patients with high tie registered in the control group. In laparoscopic resection, these end-points were increased significantly as a result of the awareness of the principles of CME. Due to the short duration of follow-up, long-term survival data are not available (14). In a recently published study by Italian authors (15), patients with right sided adenocarcinoma treated from 2008-2012 open CME with CVL (central vascular ligation) were compared to patients from historical group treated from 2004-2007. All operations were done by the same group of surgeons. CME group was associated with a significantly higher operation time and intraoperative blood loss, but without the effect to the postoperative course. The number of harvested nodes and tumor deposits were markedly higher in CME than control group. Six (13%) CME patients and 14 (24%) patients in the historical group had tumor recurrence. Interestingly, the local recurrence rate was significantly higher in the historical group. The 1-to 5-year DSS rates were 98, 95, 95, 90, and 90% in the CME group, and 100, 91, 87, 80, and 74% in the historical group, without statistical significance. However, according to the hazard ratio, the estimated relative risk of cancer death in patients undergoing CME with CVL was 40% as that in patients undergoing conventional surgery, corresponding to a 16% increase in the 5-year DSS rate from 74.4 % (95 % CI 68.5–80.3 %) to 90.5%

(95% CI 85.1–95.9%). A significantly better outcome was shown by subgroup analysis in node-positive cancers. The 5-year DSS rate in node-positive colon cancers undergoing CME and classic surgery was 88 and 50% (HR=0.25, 95%CI 0.11–1.02, p=0.05), with a 75% reduced risk of cancer death and nearly a 40% increased survival rate in patients undergoing CME with CVL. Type of surgical operation is an important factor correlated with DSS rate. In a stepwise multivariate analysis tumor recurrence, advanced Dukes' stage, and conventional operation are the best predictors of poor long-term disease-specific survival. In CME group, the 5-year DSS rates in all and node positive patients were 90% and 88%, respectively. Another group of Italian authors (16) analyzed data on 159 patients with right sided cancer staged I-IIIC operated on with the concept of CME and CVL. Morbidity and mortality were 37.7% and 1.9% respectively. Overall and disease free five years survival were 80.5% and 69.8%. Mesocolic plane of surgery was achieved in 64.7% of cases and had an impact on R0 resection rate (98%). CME with CVL significantly improved survival in stage II, IIIA/B and in a subgroup of IIIC patients, with not metastatically involved apical nodes. In the study from Germany (17) on 51 patients with right-sided colon adenocarcinoma treated with open CME with CVL special interest was paid to lymph nodes that would have been presumably left in place during a standard hemicolectomy. The lymph nodes in this segment were separately analyzed. Mean lymph node count in CME specimen was 52.6 (range: 27-171). 35.0% (range: 13.1-65.6%) of the nodes would have been left behind with standard operation. In 3/51 (5.8%) patients the central nodes were positive. In one patient the central nodes were the only metastatic site. UICC stage was influenced in two of the three patients who had central involvement. A group from Korea (18) established modified CME on the basis of original CME for right sided colon cancer and published retrospective study on 773 patients. Five-year overall survival and five year disease-free survival rates were 84% and 82.2%, respectively. These results were comparable with the results of original CME.

Laparoscopy and CME

Laparoscopic colectomy has become a standard procedure for colon cancer based on long-term oncologic outcomes and meta-analysis of multicenter randomized controlled trials (19,20). In 2012 Adamina et al. (21) published results on prospective series of 52 consecutive patients with right colon cancer who underwent laparoscopic CME with high-vessel ligation. All patients had R0 resection with median of 22 lymph nodes retrieved. During the follow-up period of median 38 months, four distant recurrences yielded a median recurrence-free survival of 37 months and a median overall survival of 38 months. During a

median follow-up period 48 (92%) of 52 unselected patients were recurrence free, and only

Table 1. Results of studies on laparoscopic hemicolectomy with CME

Author/ year	Patients number	Op. time minutes	Ly node	Complication rate	Follow up months	LR SR	survival
Feng et al. 2012(22)	35	190 (120-240)	median 19	8.6%	/	/	/
Kang 2014 (23)	128	median 192 (118-363)	median 28	4.5%	median 25.5 (1-52)	0/5.4%	
Bae et al. 2014 (24)	85	median 179 (99-435)	median 27 (8-62)	12.9%	median 58	2.35%/ 9.41	5- year DFS 71.8% 5- year OS 77.8%
Shin et al 2014 (25)	168 right and left colon	mean 196 ±61.2	mean 27.8 (3-76)	5.9%	mean 56.4 (6-81.3)	3.6%/ 8.3%	DFS stageII/III 95.2%/80.9% OS stage II/III 93.9%/84.9%
Mori et al. 2015 (26)	31	mean 269 (165-420)	median 25(12-41)	9.3%	/	/	/
Melich et al. 2014 (27)	81	220 (206-233)	31.3 (27.2-35.4)	3.7%	/	/	/

2 of 14 patients with positive lymph nodes experienced recurrence. There were no local recurrences. Results of various studies in laparoscopic CME for right colon cancer are shown in Table 1. In the study comparing 128 laparoscopic CME with 137 patients who underwent open surgery, the number of harvested lymph nodes (27 vs. 28, $p=0.337$) were comparable. The 5-year overall survival rates for the open and laparoscopic group were and 77.8 and 90.3% ($p=0.028$), and the 5-year disease-free survival rates were 71.8 and 83.3% ($p=0.578$), respectively (24). In comparison to open CME, laparoscopic CME has comparable results although in tumors of the distal ascending colon–hepatic flexure–proximal transverse colon showed better lymph node clearance when resected by the open approach compared with laparoscopy. This is shown by the total number of harvested lymph nodes [open 48 (32–56) vs laparoscopic 39 (32–46), $P=0.04$] (28). Duration of surgery remains one of the largest obstacles for laparoscopic CME (27). According to Mori et al. (26), it is significantly shorter in patients with BMI < 22 than in those with BMI > 22 (mean 225 vs. 297min; $P=0.002$), but with no significant differences between highly experienced and less experienced surgeons (mean 250 vs. 282min; $P=0.492$). Lymph node involvement is frequent in colon cancer and it represents the main predictor of long-term survival and recurrence. One in every four node-negative patients experience recurrence after potentially curative resection because of underdiagnosed and/or undertreated nodal disease. According to latest review CME and CVL seem to offer a survival benefit and better local control and is feasible in a laparoscopic setting (29).

Criticizing CME

Studies published so far in the literature have been able to demonstrate that CME and CVL

surgery removes more tissue around the tumor and follows the correct mesocolic plane to achieve maximal lymph node harvesting, which are surrogate end-points. In these studies there is no data on intraoperative complications like serious bleeding, potential complications from larger wound such as incisional hernias or wound infections, late complications and quality of life after such big surgery, lack of data on perioperative oncological managements etc. (30,31). In a recent review that had some limitations according to the authors, overall morbidity rate of CME 19.4% and a 30-day mortality of 3.2%, and the reoperative intervention rate for vascular complications was 1.1% with mean blood loss was 150ml, all of which are comparable with standard resections (31). A multidisciplinary approach is necessary to improve the management of colon cancer. Given the development of chemotherapy and biological therapy, colorectal surgeons should aim to standardize the operative technique for colon cancer. It is essential to determine whether CME surgery poses no additional risk but only clear oncological benefit. At present, there is not enough evidence for the adoption of CME in everyday practice. The question whether complete mesocolic excision is an improvement to the technique practiced currently or whether it is just a new term for what is already practiced remains controversial (32,33).

Conclusion

Studies on CME have demonstrated an increased lymph node harvest, reduced locoregional recurrence and improvement in survival. There is some evidence that the oncological quality of resection is better in CME in comparison to standard surgery. Randomized controlled studies are needed to confirm that CME have benefit for patients with colon cancer.

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Kompletna mezokolična ekscizija i desna hemikolektomija

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Radi boljeg razumevanja termina kompletne mezokolične ekscizije (KME) neophodno je poznavanje anatomije. Prema klasičnoj literaturi mezenterijum je fragmentisan i diskontinuiran organ. Totalna mezorektalna ekscizija (TME) postala je zlatni standard u hirurškom lečenju karcinoma rektuma. U opisu TME Heald je dao anatomske osnovne za operaciju. Prema modernim anatomskim studijama vlakna Toldove fascije formiraju plan između mezokolona i retroperitoneuma. Demonstriranjem kontinuiteta mezokolona u kombinaciji sa Toldovom fascijom koja se nalazi između mezokolona i retroperitoneuma stvoren je osnov za plan resekcije kolona. Na osnovu ovih anatomskih osobina moguća je mobilizacija čitavog kolona i mezokolona koji ostaju intaktni. Hohenberger sa saradnicima je preneo koncept TME na karcinom kolona i uveo termin kompletne mezokolične ekscizije (KME) 2009. godine. Koncept KME podrazumeva hiruršku preparaciju i odvajanje visceralne fascije od parijetalne oštrom disekcijom, čime se kompletno mobilizuje čitav mezokolon a njegova visceralna strana ostaje intaktna. Na ovaj način se bezbedno ekponiraju i podvezuju arterije na njihovom ishodištu. Koristeću ovu tehniku stopa preživljavanja se povećava. U poređenju sa otvorenom KME, laparoskopska KME ima komparabilne rezultate. Utisak je da KME daje benefit u preživljavanju i bolju lokalnu kontrolu bolesti, ali ovo nije potvrđeno randomizovanim kontrolisanim studijama. *Acta Medica Medianae* 2015; 54(1):107-114.

Ključne reči: kompletne mezokolične ekscizije, karcinom kolona, desna hemikolektomija