

CHAPTER 6

Surgical treatment: complete mesocolic lymphatic excision

Complete mesocolic excision is a precise embryologic dissection that includes the visceral and parietal peritoneal layers and preserves the mesocolon with its peritoneal envelope and colonic fascia in a manner similar to total mesorectal resection (TME).¹ It is a complete oncological resection, which includes the colon and the peritoneal embryological envelope, with the perineural and lymphovascular structures of the mesenchyme. According to Patrón Uriburu,² two types of visceral fascia must be distinguished: the colonic fascia, which is the fusion of Toldt's fascia and the colon, and the mesocolic fascia, the fusion of Toldt's fascia and the mesocolon. There is also a parietal fascia known as the retroperitoneal fascia or Toldt's fascia that covers the retroperitoneum. The fusion plane of the visceral and parietal fascia is the dissection site. The concept includes an anatomical, embryological and oncological dissection, with resection of both the lymphovascular-neural structures of the mesocolon and the retroperitoneum. Since there is no interconnection between the two, the preservation of the fascia is essential to prevent the dissemination of tumor cells. This situation only occurs in tumors with invasion \geq T3. Like the mesorectum, the mesocolon is currently considered an associated but distinct organ from the colon. There are some differences between the right and left mesocolon, such as the existing peritoneal windows on the right side (e.g. duodenal window) and the greater thickness of fat on the left side. The concept of partial or total, right or left mesocolectomy is supported by some authors.³⁻⁵

The literature reports a slightly better prognosis in right-sided stage II tumors, given the high prevalence of microsatellite instability-high (MSI-H) in them, while stage III tumors have a worse prognosis. Likewise, some studies have reported lower DFS in right-sided tumors that received chemotherapy and in metastatic tumors, compared to left-sided tumors. In the 1990s, rectal cancer had a poor prognosis due to a high rate of local recurrence. In 1988, Heald et al.¹ introduced the concept of total mesorectal excision (TME) based on a dissection that follows the anatomical and embryological planes. TME provides a surgical specimen with intact coverage not only of the tumor but also of the mesorectal fat with its lymphatics and nodes. It has also been shown that results have improved with standardization, so that rectal cancer surgery has experienced a significant reduction in recurrence and an improvement in OS.

In 2009, Hohenberger et al.⁶ reported improved outcomes in patients with right-sided tumors undergoing complete mesocolon excision (CME) using the same principles as TME. Thus, a new concept for right colectomy was introduced based on 3 main aspects: 1) dissection of the embryological planes to completely remove the envelope containing the mesocolon with the tumor-related lymph nodes, 2) central vascular ligation to remove the major tumor-related lymph nodes in a central direction, and 3) resection of a sufficient length of colon to remove pericolic lymph nodes. Figure 6.1 shows the different groups of lymph nodes that may be affected.

The goals of CME are to reduce local recurrence and improve survival. The rationale is that lymph nodes follow the distribution of arteries and negative lymph node count correlates with survival. Furthermore, the ratio of the number of metastatic nodes to the total lymph node count, known as lymph node ratio (LNR), has been shown to be an even better prognostic factor than the rate of affected lymph nodes (pN stage) alone.⁷

Some studies have questioned the minimum number of 12 lymph nodes removed to define an oncologically successful surgery, particularly in the presence of an adequate resection with a good lymph node count, so it is

difficult to define a limit number of lymph nodes to be resected based on the quality of the surgery.⁸

Some studies have failed to demonstrate that performing high ligations without removing the entire mesocolon ensures a greater number of lymph nodes and improves survival. Others have argued that metastatic lymph nodes outside the resection territory would behave as distant metastases and that the extent of resection would have no influence on survival and would be associated with a poor oncological outcome.⁸⁻¹⁰

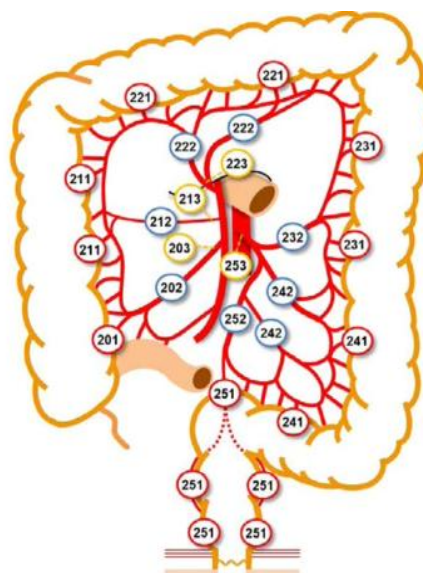


Figure 6.1. Lymph node groups according to the Japanese Colon Cancer Society.

Multiple authors advocate establishing CME as the standard of care for right-sided colon tumors, based on existing evidence of a potentially better oncologic outcome, with the same morbidity and mortality as traditional colectomy. This is due to better lymph node dissection, which could include remote lymph nodes and those located in major arteries, such as the superior mesenteric artery.^{11,12}

Nicholas West, a digestive pathologist and Hohenberger defined the morphology or morphometry of the specimen consisting of 4 components:^{7,13}

1. Distance between the tumor and the highest vascular ligation.
2. Distance between the colon wall and the highest vascular ligation.
3. Length of the removed intestine.
4. Surface of the mesocolon.

This was the conclusion of a retrospective study that demonstrated a 27% advantage in 5-year survival for patients with stage III colon cancer resected by mesocolon plane dissection.¹³

Many studies have shown that colon cancer survival is related to the number of lymph nodes removed. Chen et al.¹⁴ reported that resection of 15 or more nodes increased survival by 11 months in stage I patients, 54 months in stage II patients, and 21 months in stage III patients, so they concluded that it is necessary to remove at least 15 nodes in right-sided colon tumors. Chen said, "I would recommend surgeons to remember that the number of nodes makes a difference"

Prandi et al.¹⁵ demonstrated a direct relationship between the number of lymph nodes removed and survival, which was even higher in stage II (pN0). Swanson et al.¹⁶ demonstrated that the prognosis of T3N0 tumors is dependent on the number of nodes examined. Le Voyer et al.¹⁷ demonstrated that not only the number of nodes is important, but even the number of negative nodes is related to the prognosis.

Kataoka et al.¹⁸ argue that right-sided colon cancer has higher *skip metastasis* rates than left-sided colon cancer, confirming the previous finding by Nagasaki et al.¹⁹ of greater central lymph node involvement in right-sided tumors. In their study of 4034 patients with stage III colon cancer (1618 right and 2416 left), they concluded that there are significant differences in the pattern of lymph node invasion and prognosis between both sides of the colon, suggesting that laterality might define the surgical approach. Patients with right-sided colon cancer compared with those with left-sided colon cancer had greater L3 lymph node involvement (8.5 vs. 3.7%) and greater discontinuous lymph node spread between levels (13.7 vs. 9%). In multivariate analysis, L3 lymph node invasion was associated with worse OS in left-sided colon cancer but not in right-sided colon cancer.

Nagasaki et al.¹⁹ identified for D1, D2 and D3 an incidence of lymph node involvement of 67, 27.4 and 5.6% and a 5-year DFS of 82.8, 65.4 and 52%, respectively, with a highly significant difference. Multivariate analysis demonstrated that D2 lymph node involvement was an independent prognostic factor for recurrence-free survival. The 5-year recurrence-free survival between pN1 patients with D1 vs. D2+D3 was significantly different (84.4 vs. 71.5%) and a similar trend was presented by pN2 patients (72 vs. 53%), concluding that the high survival in stage III, even in patients with D2 and D3, would justify standard central vascular ligation for advanced colon cancer.

A study conducted at a low-volume center in Italy has shown that CME is feasible and safe and results in higher lymph node counts and longer specimen length, without increasing surgical time or morbidity.²⁰

Between 2006 and 2015, 461 cases of stage III pN1 colon cancer were retrospectively reviewed at a center in Taiwan, where patients with lymph node metastasis accounted for 13.2%. Patients with discontinuous lymph node metastasis tended to have a higher proportion of right colon cancer, a lower number of positive lymph nodes, and a lower LNR, with a higher average body mass index. Liver recurrences were more prevalent in the discontinuous metastasis group ($p = 0.028$). The presence of discontinuous metastasis was a negative prognostic factor for 5-year recurrence-free survival (51.4 vs. 68.7%; $p = 0.002$) and 5-year OS (66.4 vs. 80.4%; $p = 0.024$). Subgroup analysis revealed the significance of recurrence-free survival ($p = 0.001$) and OS ($p = 0.011$) in cases with discontinuous metastases with pN1 disease. They conclude that discontinuous lymph node metastases are an independent negative prognostic factor in cases of stage III colon cancer with pN1 disease.²¹

The concept of surgical dissection by embryologic and fascial planes allows the resection of an intact mesocolon containing lymph nodes, a key point of CME. This approach would allow not only the recovery of lymph nodes but also the reduction of the dissemination of neoplastic cells.⁶ In addition, a better OS and prognosis of patients with intact mesocolon and stage III have been demonstrated.⁷

Hohenberger et al.⁶ studied 1329 patients with colon cancer and compared two groups, one operated on between 1978 and 1984 without CME vs. another operated on between 1995 and 2002 with CME. Local recurrence was 6.5 vs. 3.6% and DFS was 82 vs. 89%. The Danish registry shows a high complication rate after CME. Berthelesen et al.²² reported a significantly higher rate of superior mesenteric vein injury comparing CME with conventional surgery (1.7 vs. 0.2%), although the 90-day mortality was 6.2 vs. 4.9%, respectively. Intraoperative injuries, including superior mesenteric and splenic vein injury, were more

common in the CME group (9.1 vs. 3.6%), as were sepsis and respiratory failure. This correlates with data from an Israeli study of 304 colectomies with a 10-year rate of superior mesenteric vein injury of 1.6%.²³

Pelz et al.²⁴ reported a high rate of reinterventions (19%), with 5.5% postoperative complications, 1% anastomotic dehiscence, and 0.5% mortality.

In a multicenter randomized controlled trial (COLD trial), 100 patients (43 D2 and 56 D3) were studied. There was no mortality and morbidity at 30 days was 47 and 48%, respectively. The average number of lymph nodes removed was 26.6 and 27.8. 5% presented metastasis in D3 and it was never the only affected level. Positive N was more frequent in D3 (46 vs. 26%). It is concluded that D3 dissection is feasible and provides better lymph node staging.¹¹

In another multicenter study of 17 hospitals in China (RELARC), 995 patients operated on between 2016 and 2019 (495 with CME and 500 with D2 dissection) were analyzed. There was no mortality and postoperative complications were 20% and 22%, respectively ($p = NS$), with more severe complications (Dindo III-IV) in the CME group (1 vs. 3%). Intraoperative complications were also more frequent in the CME group (3 vs. 1%). Central lymph node metastases were detected in 3% of D3 dissections, with no isolated central lymph node metastases found. Although CME may increase the risk of intraoperative vascular injury, it appears to be generally safe and feasible among experienced surgeons.²⁵ The low number of positive central nodes in D3 and the high rate of incomplete mesocolon might provide uncertain clues as to whether D3+CME dissection is actually superior given that the Chinese study found a better lymph node harvest in D2 dissections. Table 6.1 shows a comparison of the data found in the COLD and RELARC trials.

In 2022, a systematic review evaluated the definitions and steps of D3 lymphadenectomy and CME for right radical colectomy, concluding that the only universally accepted step is high arterial ligation, while there is great heterogeneity in the other steps and definitions.²⁶

Table 6.1. Comparative analysis between the results of the COLD and RELARC trials.

Trial	COLD TRIAL		RELARC TRIAL	
	D2	D3	D2	D3
LD				
N	43	56	500	495
BMI	27	27	23	23
N	27	28	23	26
D3+	0	7%	0	3%

LD: lymphadenectomy. BMI: body mass index.

A 2021 meta-analysis of 27 studies with 19,989 patients found a higher rate of postoperative adverse events in the CME group, with no differences in anastomotic leaks or perioperative complications. CME had higher lymph node harvesting, longer length of removed colon and mesocolon, and positive effects on overall survival and 3-year disease-free survival, with decreased local and distant recurrence. It concluded that, despite limited evidence, CME improves oncologic outcome, albeit with a higher rate of adverse events.²⁷ In another meta-analysis, 7 articles out of 714 articles with a total of 1368 patients were included, comparing D2 and D3 lymphadenectomies. D3 was found to improve outcomes in terms of blood loss, lymph node

salvage, and 5-year overall survival. There were no differences in operative time, anastomotic dehiscence, wound infection, general morbidity, hospital stay, mortality, duration of resected colon, and 3-year overall disease-free survival. This review suggests that D3 lymphadenectomy is superior to D2, although it recommends careful consideration of this conclusion given the limited evidence available and the need for further randomized controlled trials.²⁸ As mentioned above, the rate of central lymph node metastasis varies from 0 to 18%, which would support the determination of CME+CVL as the gold standard. Studies have shown that when there is N3 involvement, N1 and N2 are also positive. Furthermore, there is variation in the rate of central lymph node metastasis between different segments of the right colon, being found in 0% of the cecum tumors, 4% of the ascending colon and 8% of the right transverse colon.²²

The international prospective study of 4000 patients at 36 institutions, *Cohort for Optimal Bowel Resection Extent and Central Radicality for Colon Cancer or T-Rex*, is ongoing and will provide fundamental information on the distribution of the pattern of lymphatic metastases.²⁹

In a recent Italian multicenter randomized controlled trial, including 258 patients from 9 centers, the number of lymph nodes retrieved was significantly higher after CME (25 vs. 20%). There were no differences in intra- or postoperative complications, mortality, and duration of surgery, with a shorter hospital stay for the CME group. Survival rates are pending. To date, CME in right-sided colon cancer operated on at referral centers has been shown to be safe and feasible and does not increase perioperative complications. It also documented that the quality of surgery and lymph node recovery are higher after CME.³⁰

According to SEER, in 83,000 patients the 5-year DFS for all stages was greater than 80%, except for Stage IV (48%).³¹ In a study from the National Cancer Database, 379,785 patients had an OS at 3 and 5 years of 61% and 51%, respectively.³² Yu et al.³³ documented a 5-year DFS of 68% with standard colectomy (92.8% in EI, 85% in EII, 64.9% in EIII, and 11.2% in EIV). The 3- and 5-year survival rates reported by the CME studies were 89.6 and 82.8%, higher than those reported for conventional right colectomies.

There are several studies, some retrospective, showing that prognosis is related to the pattern of lymph node metastasis and that metastases at level 223 (right colic root) are rare. In one study, they occurred in only 1.8% of patients and all those with metastases at level 223 had regional metastases in other lymph node groups.

Furthermore, metastases at this level are the only independent risk factor related to DFS. Metastases at level D3 occur at an advanced stage of the disease in patients with cecal cancer, so CME would be too extensive in most cases for a proximal right colon cancer.³⁴

Park et al.³⁵ reported 6.1% of lymph node metastasis along the right branch of the middle colic artery in cecal cancer.

A retrospective study of 2084 cancers of the cecum and ascending colon demonstrated no benefit from extended mesocolic resection, indicating that there is no need to include the middle colic vessels in their resection.³⁶

A systematic review and meta-analysis of 17 studies indicated that the existing evidence did not demonstrate oncological superiority of standard colectomy compared to CME in terms of survival. The described technique is not inferior in safety and achieves greater lymph node dissection. In addition, it is associated with better OS and DFS at 3 and 5 years.³⁷ Mazzearella et al.³⁸ performed a systematic review and meta-analysis of 30 studies, evaluating 5931 procedures with this technique and concluded that it does not increase the risk of postoperative complications and significantly improves long-term oncological outcome. It suggests that prospective, multicenter, randomized studies should be awaited before considering this procedure as the standard of care.

Therefore, it is not yet conclusive to consider CME with high vascular ligation to be adequate in oncological terms for right-sided colon cancer. In fact, it could be adequate for tumors of the ascending colon or hepatic flexure, while considering it as a standard for those of the cecum could be excessive.

Bertani, from the European Institute of Oncology concludes in his editorial that despite the wonderful videos of the technique available on the web, adoption of CME should be limited to high-volume centers and in licensed programs until it demonstrates its superiority in long-term oncologic outcomes.³⁹

Evidence from the extensive literature that CME may improve survival and oncologic prognosis appears promising. However, to date the quality of the evidence is limited and does not support CME as a standard tactic to replace conventional colectomy.

Although the benefits remain tempting, better designed studies are needed to justify the learning curve, risks and effort required to perform CME, especially when its benefit may be limited to a carefully selected group of patients.

Training

When colon resections performed by general surgeons and trained colorectal surgeons are compared, the latter are found to be associated with significantly better postoperative outcomes, with low perioperative morbidity and mortality rates.^{40,41}

This fact is not exclusive for the performance of CME and D3 dissection.^{42,43} Skill assessments have shown that competence in laparoscopic D3+CME can be achieved after 20 to 30 cases, even in previously trained surgeons. This consideration is critical given that the majority of colorectal procedures are performed by general surgeons and for multiple indications depending on the context.

Surgical protocol or surgeon's report

The surgical procedure should be well documented and include a description of the intraoperative findings: presence of synchronous metastases or macroscopic involvement of mesocolic or mesenteric lymph nodes, tumor location, and involvement of adjacent organs. The type of incision, presence or absence of adhesions, extent of colon and small bowel resection, level of vascular ligation, anastomotic technique, en bloc resection of neighboring organs, and intraoperative assessment of resection margins should also be described. The use of standardized protocols improves documentation. Those currently developed by the American College of Surgeons Commission on Cancer are recommended.

Conclusions and new concepts

In summary, the surgical technique of a colectomy is currently based on two basic concepts:

- A correct anatomical dissection: equivalent to the embryological dissection proposed by Hohenberger, West et al. (complete removal of the mesocolon).
- An adequate oncological dissection: dissection and resection of D2 or D3 lymph nodes, depending on the depth of the tumor and its stage.

Recently, a more integrative concept has been proposed that would unify these criteria: Tumor-Specific Mesocolic Excision (TSME) or Complete Mesocolic Lymph Node Dissection (CMLND). This nomenclature includes a complete individualized removal of the mesocolic lymph nodes, depending on the location of the tumor and the vascular anatomy, which ensures the radicality of the resection, the corresponding lymphadenectomy and the adequate margins.⁴⁴

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