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INVITED REVIEW

The Concept of Complete Mesocolic Excision

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ABSTRACT

Complete mesocolic excision (CME) was introduced into the literature in 2009 for standardization of colon cancer surgery, which had not been established until then, in reality. Based on surgical anatomy and embryology, this concept of oncologic surgery for colon cancer included strict preservation of the mesocolic fascia on either side of the colon by sharp dissection of the interfaces, together with central dissection of the regional lymph nodes by a central ligation of the feeding arteries. CME should be applied to all cancers at any site within the colon. There is clear evidence that CME surgery achieves a higher lymph node yield, a higher quality of plane preservation, a greater distance from the tumor to the central resection line and longer vascular pedicles. In most meta-analyses, the rate of intraoperative bleeding is slightly higher, mainly due to venous bleeding from the branches of Henle's loop, compared to "conventional" surgery. Postoperative complications occur at a similar or slightly higher rate. Postoperative mortality is not increased. There is increasing evidence that long-term oncologic outcome is better with CME. CME has not been implemented in all centers because of a steep learning curve due to the need for full understanding of the anatomical and embryologic background and adequate experience of handling the central intestinal vessels; thus the experience of the surgeon is critical.

Keywords: Complete mesocolic excision, concept, implementation

Introduction

In 2009, we presented the concept of complete mesocolic excision (CME) and put it up for discussion as an alternative to conventional and mostly non-standardized surgery for coloncancer, which was being performed in most institutions globally at that time.[1] This proposition was supported by oncologic outcome figures, which differed markedly from most survival and local recurrence rates published in the literature, at that time. Overall survival data may have been similar, but the difference was more pronounced in advanced or more complex case groups, such as stage 3 disease, T4-tumors and emergencies. In this context, 5-year-survival with stage 3 disease varied from 38.5% to 74%.[2,3]

This was not the first concept presented for improving outcomes in colon cancer surgery and several other reports including above average oncologic long term outcome figures above had been published previously.

Is the Concept of "Complete Mesocolic Excision" Really a New One?

For several decades, Turnbull et al.'s[4] "no-touch isolation technique" was accepted as a major progress in colon cancer surgery. The philosophy was that all the vessels (lymphatics, arteries and veins) supplying or draining the tumor had to be divided ahead of any mobilization or other manipulations of the tumor-bearing colon. Thus, dissemination of tumor cells should be avoided and prognosis improved. This concept resulted from analysis of different outcome figures, when comparing Turnbull's[5] results with those of his colleagues who had mainly used conventional surgery, at the Cleveland Clinics.[4,5] Applying the no-touch isolation technique, 5-years survival was 68.85% for all patients operated for cure, compared to 52.13% with conventional surgery, and 56.84% and 28.06%, respectively, for stage 3 disease. Finally, the illustrations in the publications clearly showed that "conventional surgery", as practiced by Turnbull's et al.[4], only included the pericolic lymph nodes. However, even Turnbull[5] performed just a "high tie", exposing the vascular pedicles by encircling them with the index finger. Then, a clamp was set and the vessels divided afterwards. An appreciable amount of tissue, together with the central lymph nodes, was left behind. The separation of the planes was mainly achieved by blunt finger dissection. The technique performed by Turnbull was accurately reproduced in a video made by Jagelman in the

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1990s, who was a resident of Turnbull and who performed a right hemicolectomy demonstrating the procedure performed by Turnbull, in detail. Finally, Turnbull did not consider the concept of strict plane preservation, and he never did perform a true central vascular tie, at least not for right sided or transverse colon cancer.

Enker et al.[6] had already published enhanced survival from his personal experience in 1979. He called his approach to colon cancer surgery "wide anatomic resection". He described his technique in detail in 1978.[7] In this article, he mainly referred to the supplying arteries to be divided in relation to the site of the tumor, to include all regional lymph nodes. According to his sketches, illustrating the extent of colonic resection and the division of the supplying arteries, his practice in this regard did not differ from ours with CME. For splenic flexure and left sided transverse colon cancer, he even resected more bowel, always including the ascending colon. However, from his wording he did not describe the plane or fascia principle, describing the "adhesions" as "ligaments" to be divided, and he did not give further technical description about how he prepared and dissected the vessels centrally or the extent of dissection. He also called his technique for transecting the arteries "high tie". In this article, he also questioned the feasibility of Turnbull's[5] procedure in every patient.

In the Concord Hospital in Sidney, a dedicated colorectal unit was formed in 1980.[8] From that time on, the group around Bokey et al.[8] changed the technique for operating on colon cancer. They mobilized the colon along the embryologic planes and specifically preserved the posterior mesocolic fascia, as an important principle. Furthermore, they took down the greater omentum from the transverse colon following the interface, predefined if necessary. In this regard, they followed the principles of CME fully. However, there is no mention of a true central tie with exposure of the origin of the colic main arteries in their technical descriptions. They even say that they performed just a high tie. This is supported by their approach to left sided colon cancer, with the following: "The root of the inferior mesenteric artery was not touched, but this vessel was divided after the exit of the left ascending colic artery". Obviously, they always left the central nodes of the main feeding arteries. This is supported by their outcome figures. In their publication in 2003, overall survival of Dukes' C patients was just 43.0%, although they did not separate the results of the two different periods reported. In their paper published in 2015, 5-year survival in stage 3 disease was now 66.3%, but the median lymph node count was no more than 15, compared to 28 in all Erlangen series.[9,10]

Japanese surgeons began to standardize the surgery of colorectal cancer early.[11,12]

In 2012, Kontake et al.[13] published a rate of five-year, overall survival in stage 3 colon cancer of up to 73.0%, for patients operated between 1974 and 2002. Japanese surgeons meticulously performed early dissection of the feeding vessels, did not include the adjoining vascular arcades resulting in shorter bowel length and did not focus on the importance of plane preservation. Nevertheless, their survival figures were excellent. Thus, there had been several technical descriptions approaching the concept of CME without fully capturing the complete concept and they quickly accepted CME as a comprehensive concept.

Finally, Søndenaa et al.[14] from Bergen in Norway was able to achieve a broad consensus amongst an international board of surgeons, most being early adopters of CME surgery.

Key Features and Characteristics of CME

At the beginning of this millennium, there was still a broad variation of oncologic outcome figures following "conventional" curative colon cancer resections. The overall survival data may have been quite similar. However, the results of more complex cases, such as T4-tumors, nodal positive cancer and emergencies differed enormously. Furthermore, the risk of local recurrence was underestimated; it was at least as high as in rectal cancer.

These differences were indicative of the missing standardization of "conventional" colon cancer surgery, at that time. Of course, there were guidelines available in many countries. They included the extent of lymph node dissection and of colonic resection or the recommendation of an en-bloc resection, if adjacent structures or organs were fixed or invaded. However, the recommendations for lymph node dissection, for example, may have described the lymph node stations to be removed but did not give detailed instructions nor of to perform a central dissection adequately. A "high tie" was the common practice adopted at that time. A true central tie of the feeding arteries, flush with the arteries at their points where they arose was not really described or even followed outside of Japan, and the importance of preserving the integrity of the surgical planes was not explicitly mentioned.

The CME concept was frequently only associated with a right, and eventually extended, hemicolectomy. It is correct that on the right side the anatomical conditions are more complex than with the left colon. However, basically the same principles are also applied for the rest of the colon. Furthermore, it is not always realized that CME includes a radical regional lymph node dissection with a central tie of the feeding arteries. We have operated emergencies, such as complete obstructions and perforations, in the same way as

elective cases. Only the decision concerning an anastomosis depended on the sequelae of these complications, mainly on the degree of a diffuse peritonitis, so that in half of the cases an anastomosis was omitted.

CME surgery is based on precise anatomical and sharp dissection along the interface of the embryologic adhesions between the intra-abdominal organs, covered by a continuously running mesenteric fascia and the parietal fascia, which also covers the retroperitoneal organs and the large vessels, namely the aorta and the vena cava (Figure 1). This interface was described by Toldt[15] as the "white line". As frequently, but nevertheless wrongly, indicated, he never described this phenomenon as a fascia. Finally, these two fasciae join at the vascular confluence of the hepatic veins and the vena cava and at the origin of the celiac axis and the superior and inferior mesenteric artery.

Depending on the organ which the mesenteric fascia is covering, it is termed the mesocolic and mesorectal fascia, but also the mesopancreatic fascia, where it extends to the pancreas, and so on. The second step after mobilization of the abdominal organs from the parietal fascia is to take down the adhesions of these mesenteric fasciae fixing, for example the greater omentum to the transverse colon or the mesoduodenum from the ascending mesocolic fascia, to get access to the superior mesenteric vein and artery behind. The dissection along these interfaces is achieved by sharp dissection, at all times, applying permanent traction and counter-traction.

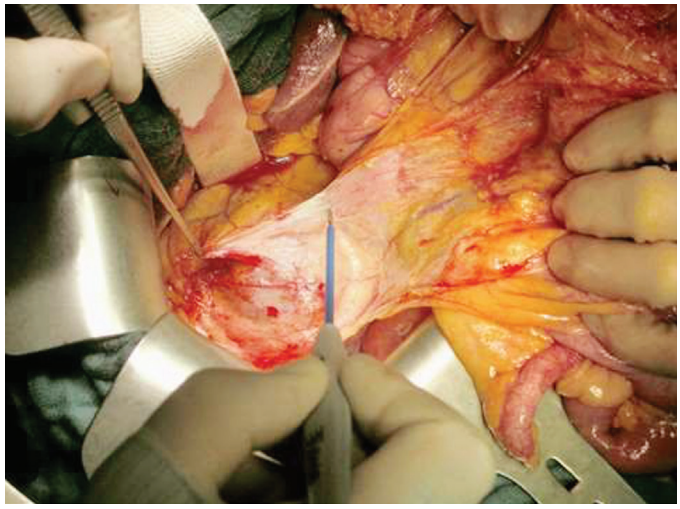

Figure 1. The interface between the parietal fascia on the left-hand side and the mesenteric fascia is divided by sharp dissection with the tip of the cautery. It presents as a white line, as described by Thold[15], already (which can be seen here, too, adjacent caudally to the tip of the cautery). The mesenteric fascia on the right side is covering as a continuously running plane the abdominal organs including the duodenum, next to the cautery. The following steps after complete mobilization will isolate the mesoduodenum from the ascending mesocolon, to get access to the central mesenteric vessels

Only recently anatomists have realized these conditions and interrelations[16] and the respective nomenclature is not yet officially accepted. Finally, the application of CME needs profound knowledge and understanding of these conditions.

During these dissections of the fasciae, the preservation of its integrity is of profound importance. West et al.[17] from Leeds have categorized the quality of specimens related to the integrity or laceration of the mesocolic fascia, which covered the resected colon on either side. They defined "mesocolic plane" as the optimum, an "intermesenteric plane" and a "muscularis propria plane" as the worst case. This has a tremendous impact on survival of the patients. Independent of any other feature and related only to the quality of specimen retrieval, the survive rate in the long run will be reduced by 50% with a stage 3 disease in case of a muscularis propria plane dissection.[17]

Following these principles, the colon and even the entire bowel including the duodenum with the pancreatic head, for right sided cancer is mobilized in such a way that even in very obese patients the tumor bearing colon can be brought forward in front of the abdominal wall, allowing unhindered access to the central vessels feeding the tumor. The compartment involved can now be easily twisted, and will be lying right in front of one's eyes, in a very superficial position. All the central vessels, namely the superior mesenteric vein and artery, will now be safely accessible for right sided cancer. This is essential for the second step of CME, which is the complete clearing of the regional lymph nodes, including the most central ones by a central tie of the arteries feeding the tumor, flush with the central vessels they are arising from. The Japanese term "D3-dissection" is more or less equivalent to our "central tie" procedure.

This procedure was always performed in our department by a lateral to medial approach. Some surgeons prefer the opposite way, exposing the superior mesenteric vein first. This is also the preferred approach of laparoscopic surgeons, some of whom are able to perform CME surgery the same way as we had described. We have never ligated the bowel to either side of the tumor as this maneuver may just disturb the integrity of the colonic fasciae.

In summary, "conventional surgery" for colon cancer was never defined in detail and it included a broad spectrum of variation. Furthermore, CME aims to create a specimen with perfect integrity of the mesosolic fascia on either side of the mesentery, as well complete clearing of the regional lymph nodes, including the most central ones, by a central tie of the feeding arteries flush with the central vessels they arise from. Such specimens should be achieved not just sometimes, but in at least 90% of all operations.

Feasibility of CME in Laparoscopic and Robotic Surgery

The introduction of CME and the evolution of laparoscopic surgery for colon cancer were almost coincidental. This had a degree of negative impact on the acceptance of CME, mainly in Europe, at least in the beginning, and in those departments were the introduction of laparoscopic surgery had first priority. Moreover, strictly following the principles of CME with a laparoscopic operation may be very challenging, both for less experienced surgeons and when operating on obese patients. The feasibility of laparoscopic CME was tested early in South East Asia, not least because there the mean body mass index (BMI) is between 19 and 23 kg/m^2 compared to about 27 kg/m^2 in Middle Europe. Most randomized trials or clinical studies, comparing open versus laparoscopic surgery, were initiated in South East Asia.

Since then, quite a lot of randomized trials and comparative studies have been published on this subject. Recent reviews reveal that in the laparoscopic cohorts operative time is longer, while blood loss and wound infections rates were significantly less and time to flatus, oral feeding, and length of hospital stay were significantly shorter. The 1-, 3-, and 5-year overall survival rates were better, or at least not inferior, in the laparoscopically operated cohorts compared to the open procedure.

Although there are some publications exclusively analyzing T4-tumors and transverse colon cancer, in most studies these entities were excluded or under-represented and the median BMI was mostly below 24 kg/m^2.[18,19] Similar results were achieved, in the meanwhile, by robotic surgery.[20]

Finally, as a result of all these studies it can be concluded that laparoscopic CME surgery of right and left sided cancer may be at least equivalent to open surgery, in terms of outcomes. However, these results are not completely applicable to any patient and to any site along the colon. Patients with a higher BMI and more complex tumors, such as transverse colon tumors including both flexures and locally very advanced cancer, are not yet adequately investigated and should be selected carefully for an eventual laparoscopic approach.

Extent of Colonic Resection

The length of colonic resection for cancer is mainly dependent on the pericolic extent of lymphatic spread of lymph node metastasis and the pattern of arterial blood supply of the colon. As positive lymph nodes are very rarely found beyond a distance of 10 cm to either side of the tumor, this extent of resection would be sufficient. This approach is common practice in Japan (Figure 2). To clear the entire area of possibly involved lymphs we, however, always included the adjacent arterial arcade (Figure 3), as shown in an example with a splenic flexure carcinoma.

With a coecal carcinoma, this will include lymph nodes along the right branch of the middle colic artery, or even the lymph nodes along the right colic artery if there is a suspicion of involvement, even if this is rare. This principle results in a right hemicolectomy for a tumor at that site (Figure 4), an extended right hemicolectomy for hepatic flexure cancer (Figure 5) and a subtotal colectomy for splenic flexure carcinomas (Figure 3).

For cancer of the sigmoid or the descending colon, the distal resection has to be extended to the upper rectal third, because with these tumors the inferior mesenteric artery has to be divided centrally and the pericolic artery may be missing along the distal sigmoid (Sudeck's point) (Figure 6).

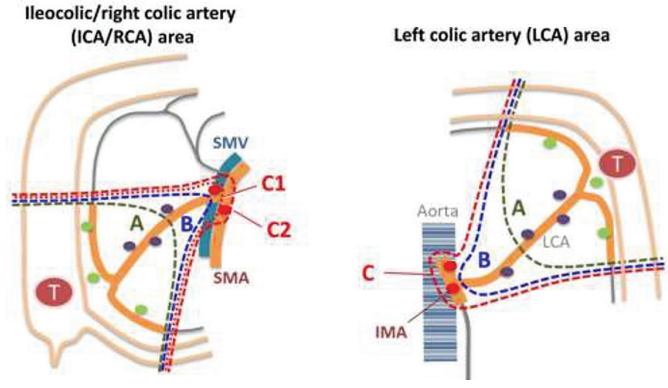

Figure 2. The Japanese Guidelines recommend an ileocecal resection for a cecal carcinoma and a segmental resection for a carcinoma close to the splenic flexure (however, with a central tie of the feeding arteries in case of an advanced tumor)[21]

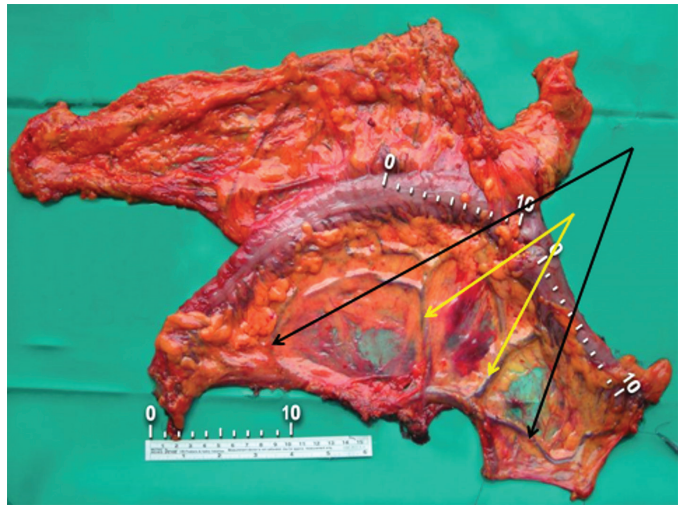

Figure 3. Specimen of a carcinoma right at the splenic flexure. To clear all possibly involved lymph nodes, the vascular arcades to either side (black arrows) of the two main feeding vessels (yellow arrows) are also included into the dissection resulting in a longer specimen. All feeding arteries were ligated, centrally. In Japan, only the two main feeding arteries would be transected

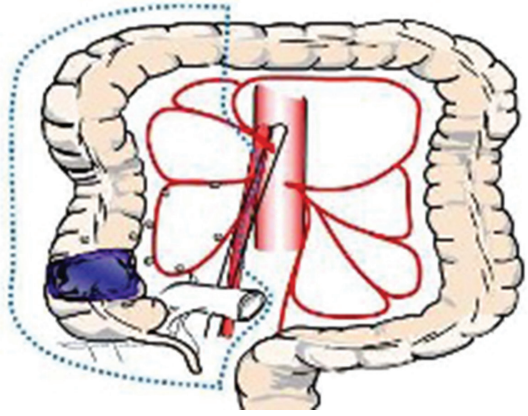

Figure 4. A right sided hemicolectomy is performed for carcinomas of the cecum or the ascending colon

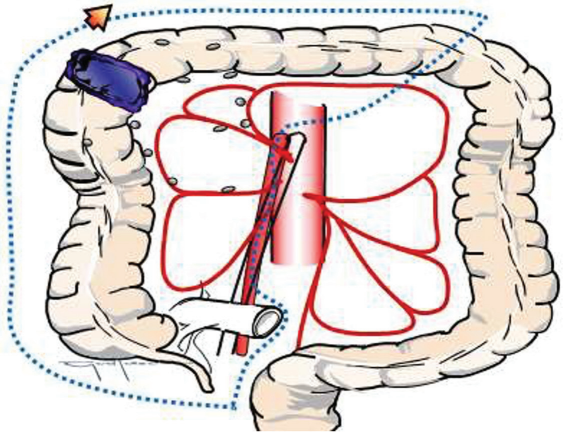

Figure 5. Hepatic flexure carcinomas need a more extended right hemicolectomy with a central tie of the middle colic artery. The arrow close to the tumor is to indicate that the lymph nodes along the right gastroepiploic artery will be not included and need a respective dissection, in addition

Characterisitics of Lymph Node Dissection

The lymphatic spread of a colon cancer follows the arterial blood supply of the colon involved. The venous drainage, which mainly runs parallel to the arteries, is irrelevant in this context. The two sites, were the vein's course is different from the arterial supply are Henle's trunk and the inferior mesenteric vein. With regard to the extent of lymph node dissection, these veins can be ignored.

The eventual involvement of lymph nodes by metastasis cannot be judged just by finger palpation or from its appearance. From clinical experience, suspicious lymph nodes are actually not affected about 50% of the time but, on the other hand, if a lymph node appears to be clear, it will nevertheless be involved about 20% of the time. This raises the question, whether a radical lymph node dissection with a central ligation is always needed or can be omitted in less advanced tumors, as it is common practice in Japan. Of course, it was already practice for T1-tumors with a low-

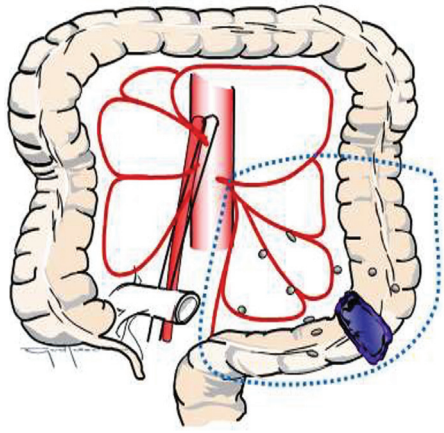

Figure 6. For a tumor of the sigmoid or the descending colon, the distal resection has to be extended to the upper rectal third, because in case of a central tie of the inferior mesenteric artery the arterial perfusion of the distal sigmoid is uncertain, because the continuity of the pericolic artery along this part of the colon may be missing

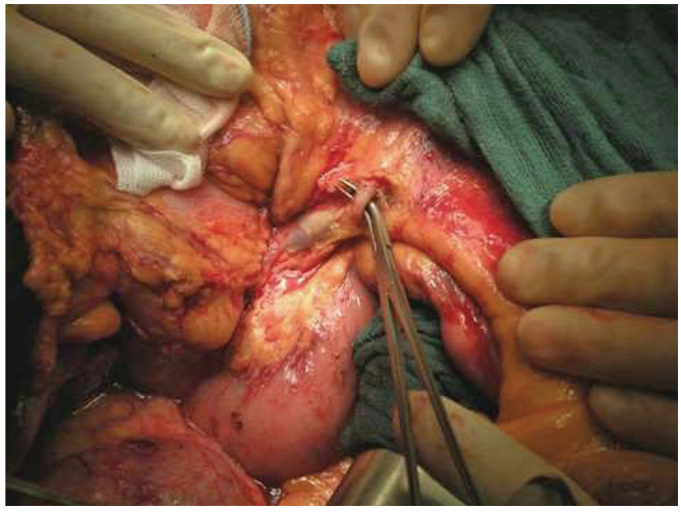

Figure 7. Preparations to cut the right ileocolic artery centrally, which is crossing the superior mesenteric vein from below, quite a common finding. Next, this vessel will be ligated flush with the SMV

risk histology (grading 1,2; L0, <3 cm) to be removed, either endoscopically or by a segmental resection. However, as the risk of lymph node metastasis with a pT1 carcinoma and high-risk features may be 15% or even more, we always performed a radical lymph node dissection. The argument is that in any case a maximum lymph node harvest will be achieved with a very low risk of lymph node metastasis remaining *in situ*. Moreover, the risk of complications in experienced hands will be not increased and there are no functional disadvantages in the long run.[22]

A frequent matter of debate is whether to dissect the most central lymph nodes at all. However, there is a positive correlation between the length of the arterial stump left behind, as determined by a postoperative computed tomography-scan, and the rate of loco-regional recurrence.[23]

In addition, it is still not entirely clear to all surgeons what constitutes a true central tie. Therefore some examples are shown in the Figures 7-9.

Intraoperative Complications

Even with elective conventional surgery for colon cancer, intraoperative complications are rare. First of all, ureteral injuries are well known. Therefore, even now the ureter is isolated and taped by some surgeons, which necessitates the opening of the covering parietal fascia. This maneuver may increase the risk of postoperative bleeding. As strict CME surgery is performed in the interface between the mesenteric fascia and the parietal fascia, the retroperitoneal organs remain well protected without any need to expose, for example, the ureter. Therefore the risk of ureteral lesions is even lower with CME.

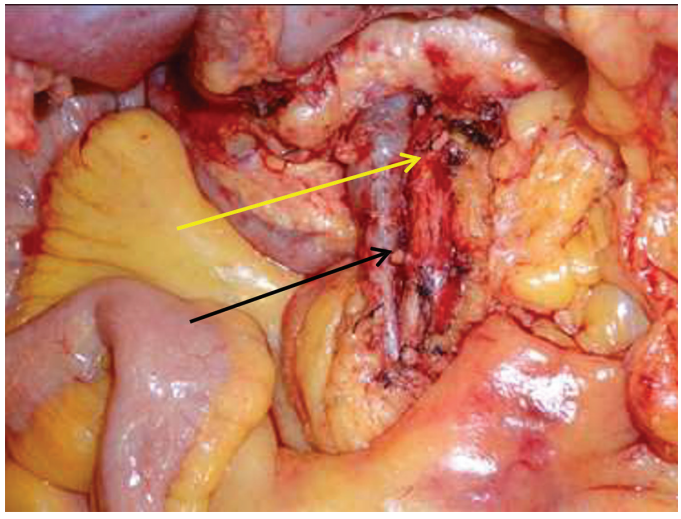

Figure 8. Intraoperative situs after an extended right hemicolectomy for a transverse colon cancer. The middle colic artery (yellow arrow) and the ileocolic artery (black arrow) are divided centrally, each. The stumps are measuring less than 1 cm

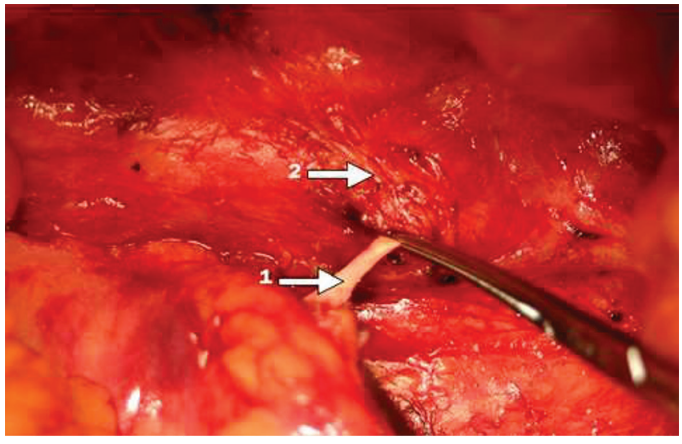

Figure 9. Preparation of the inferior mesenteric artery prior to its transection (arrow 1). The cuff of autonomous nerves covering the artery has been cut peripherally and shaved central-wards. Thus, the entire superior mesenteric plexus (arrow 2) and its function can be preserved with great certainty

Another common intraoperative complication is bleeding from splenic injuries. Its frequency in colorectal surgery is in the range of single figures per thousand. It is, however, much more frequent with transverse colon resections, reaching 3.4%.[24] In more than 90%, these lesions occur during mobilization of the splenic flexure due to splenic tears where the "ligaments" from the colonic flexure are connected to the splenic "capsule" ("Lord's ligaments").[25] These so-called ligaments are simply duplications of the mesenteric fascia which cross the dissection plane during mobilization of the splenic flexure and must be sharply

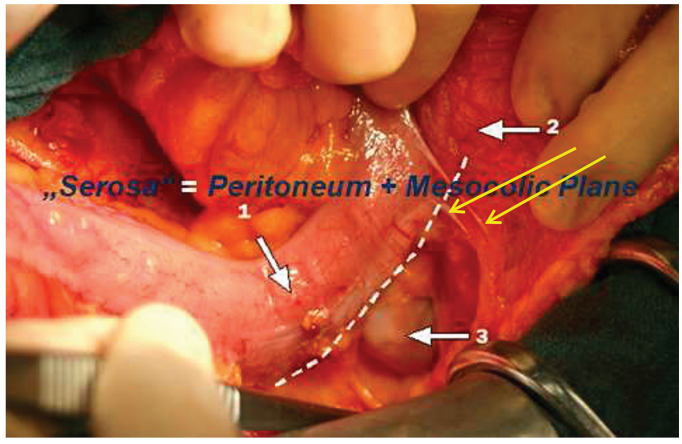

Figure 10. The white dotted line indicates the dissection level between the colonic wall (white arrow 1) and the mesenteric duplications running to the spleen. They have to be divided, sharply (see two yellow arrows). The greater omentum 2) has been taken down, before already. The stomach 3) in the depth of the lesser sac. It should be noted that the so-called serosa includes two layers, the thinned mesocolic fascia and the peritoneum

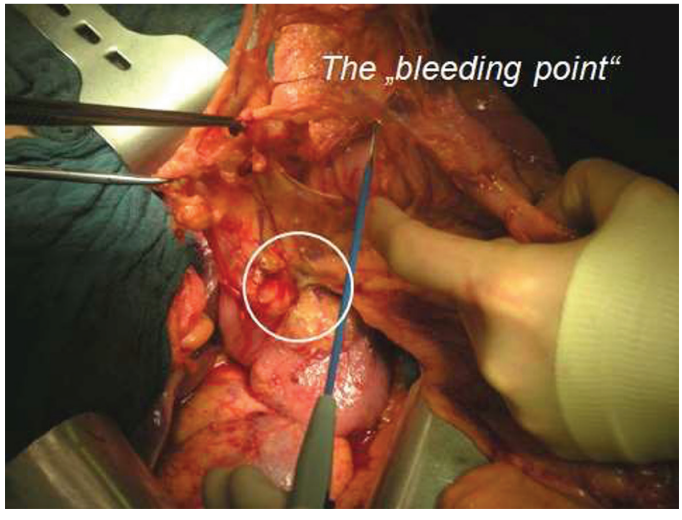

Figure 11. The right superiorcolomic vein is crossing the dissection plane to mobilize the hepatic flexure, completely and finally to expose the superior mesenteric vein. If this confluens is not fully visible but was approached in a funnel like way, instead, in case of an inadvertent bleeding-controlled hemostasis will be difficult

divided right along the colonic wall (Figure 10).

To expose this area safely, the dissection in the interface between the descending mesocolic fascia and the parietal fascia in the "retroperitoneum" should be driven forward cranially, as far as possible below the left side of the pancreas, ahead of the splenic mobilization. Then, the left omentum is detached from the left colon in the respective interface. The omentum should not just be divided. Only now can the splenic flexure be taken down. Finally, exactly following the interfaces between the embryologic fasciae by sharp dissection all the time, the safest approach to avoid splenic injuries is achieved. Again, this is one of the principles of CME surgery.

The most serious intraoperative complication is bleeding from major vessels. Above all, this event is the main contributory factor to increased intraoperative complications in reviews and meta-analyses.[26] This risk exists mainly with right-sided hemicolectomy, and injuries result first of all from tears of the branches of Henle's loop and of the superior mesenteric vein. These lesions can mainly be avoided by being well aware of the detailed anatomy of the gastroepiploic-pancreatic-colic trunk. The demonstration in almost all anatomic textbooks with the right colic vein directly entering the superior mesenteric vein is, in reality, a rare variation that will be found in only about 10% of cases. In the rest, the right colic vein joins the venous trunk and crosses the dissection plane (Figure 11), when exposing the hepatic flexure. During this maneuver, the vessel is at risk of being torn.

Finally, the right gastroepiploic vein must be exposed and all vessels joining from the colon must be dived. Sometimes, even the middle colic vein can be part of Henle's loop. To achieve a sufficient overview, extended mobilization along the embryologic fasciae is recommended, prior to the exposure of these branches. Secondly, once they are completely exposed, any traction on the mesocolon by the assistant must be avoided. If, in spite of all these precautions, a tear occurs, the bleeding can frequently be stopped simply by apply a compress. Sometimes a single vascular stitch may be needed but blind stitches should never be applied. All these measures can only be applied if these vessels have been exposed adequately.

As outlined above, these intraoperative complications can be avoided by consequent CME surgery. In the literature, however, intraoperative complications were more frequent with CME surgery compared to the conventional approach.[26,27]

Iatrogenic superior mesenteric vein injury is called the "peril of high ligation"[28] due to an increased risk of intravascular lesions.[29] In a systematic review by Wang et al.[26], above all intraoperative blood loss was higher, which is directly related to all of the potential pitfalls described above.

Postoperative Complications and Mortality

The rate of postoperative complications in the Department of Surgery in Erlangen is listed in Table 1. About 15 years ago, Bowel Cancer Centers were established in Germany and were to be annually certified by the German Cancer Society. Every year, official reports of a predefined data set indicating the outcome figures of all certified centers are published, including details of postoperative complications.[30] These figures are also shown in Table 1. In a way, both can be regarded as reference values.

Table 1. Postoperative complications in Erlangen (1) and in the certified Bowel Cancer Centers in Germany (n=296)[30]

	Erlangen	All German bowel centers (median)	Cancer center variation
Anastomotic leaks	1.8%	4.13%	0-14.3%
Reoperations	3.9%	8.6%	0-30.0%
Morbidity	21.0%	Not announced	Not announced
Mortality	3.3%	2.04%	0-9.52%

Postoperative leaks are the most striking incident in the postoperative course, which have an impact on postoperative overall morbidity and mortality. In Erlangen, the leak rate was below 2% for many years, although emergencies were always included in the reports. Less than 4% needed reoperation and overall morbidity was just over 20%, resulting in an in-hospital mortality of 3.3%.

In the German Bowel Cancer Centers, there was a broad spectrum of postoperative complications. The leak rates, for example, varied from zero to 14.3% in one center. The median rate was 4.13%. A median of 8.6% of the patients had to be re-operated and median postoperative mortality was 2.04%. In the literature, close to 20 reviews and meta-analyses of CME have been published. According to these, and disregarding some separate publications, the rate of anastomotic leaks and of postoperative mortality is not increased when comparing CME with conventional surgery. If in particular cases complication rates associated with CME surgery may differ from these general trends, one has to look at the absolute figures to understand conflicting data.

Oncologic Outcome (Local Recurrence and Survival)

There is a wrong perception that, in contrast to rectal cancer, local recurrence is rare in colon cancer and usually a manifestation of systemic disease.[31] The rate of local

recurrence after colon cancer surgery is at least as high. In the literature published in the first 15 years of this millennium, local recurrence rates between 4% and 15.5% were reported. The risk was even 2.56 times higher with tumors at the hepatic flexure compared to the ascending colon and 2.0 to 4.42 times more frequent with lymph node metastasis compared to N0-cases, depending on the extent of lymph node involvement.[32] In 61.1% of cases, the recurrence was just a local event without peritoneal or retroperitoneal involvement, implying an option of successful R0-resection of these recurrences.

In our department, overall loco-regional recurrence was 3.6% in the period 1995-2002 and increased with more advanced stages. It was 0.9 % in stage 1 and 9.6% in stage 3. With continuing internal quality control, we were able to reduce this rate further, reaching 2.1% in the following period up to 2009. Still, the highest risk is connected to lymph node metastasis, with 5.7% for pN1 and 18.5% for pN2, compared to 1.5% in N0-cases. It is also increased with T4-tumors, being 15.1% compared to 1.2% with T2-tumors. Even with a local recurrence following operation for a former pN2-tumor, further peritoneal or organ metastasis may be missed. This indicates the importance of true central lymph node dissection, which we may not have performed adequately in all cases.

Until the beginning of this millennium, survival from colon cancer had not improved particularly over the 20 years previously, but was always better than the prognosis for rectal cancer. After curative resection with curative intention, overall colon cancer 5-year-survival was approximately 65% to 75% in the early 1980s,[33] but was reported to vary, at 50.4% and 76.6%, respectively, almost twenty years later.[2,8]

Finally, due to the implementation of Heald and Ryall[34] total mesorectal excison, the awareness of the impact of clear resection margins on oncologic outcome,[35] and the progress made with neoadjuvant radiochemotherapy,[36] the prognosis for rectal cancer became better, but there was no progress at all with prognosis following surgery for colon cancer. For these reasons, survival of rectal cancer patients outpaced colon cancer.[37]

At that time, in our department, cancer related 5-year survival of all colon cancer patients operated from 1978 to 1997, R0-resection, stage 1 to 3 was already 85.5%, and 66.9% for stage 3 disease without any adjuvant chemotherapy.[38] In the period from 2003 to 2009, cancer related survival even increased to 90.6% and to 80.9% for stage 3 disease.[10]

When we published our paper introducing the concept of CME[1] in the same issue of colorectal disease, the chief editor at that time, Haboubi[39] stated that "while these advances were being made in rectal cancer surgery, colonic cancer has been left untouched" and called the principle described "a new paradigm". In the meantime, many papers have been published analyzing oncologic outcome following CME surgery. Obviously, with the application of CME, better oncologic outcome figures are now being achieved. However, in some institutions using CME, surgery survival also improved but did not exceed he figures achieved in earlier years.

We suspect that the concept was not followed sufficiently in these cases. Finally, almost all meta-analyses published in recent years have reported a lower rate of loco-regional recurrence and higher survival rates following CME surgery compared to conventional surgery.[40-42]

Quality Management

Every surgeon should know his personal outcome results, which must include the postoperative complications and long-term results, whatever kind of surgery he is practicing. It is not enough to refer to figures presented in the literature.

The principles of a quality circle can easily be transferred to surgical practice. One provides a guideline, follows the single steps and tries to reproduce the course of a CME procedure, for example. The indispensable basis of all of this, however, is prospective documentation of every case without any selection, using proforma with specified items. Pathologists play an important role in this context, because, apart from their histopathological findings, in colorectal cancer surgery they can also deliver objective criteria to qualify a specimen, including eventual tears of the covering mesocolic fascia, the length of the vascular pedicles, the distance of the tumor to the resection level and many others[17,43] (Figure 12). Thus, benchmark data are available, which can also serve as an orientation. From time to time, this data should be collected and analyzed and deviations must be scrutinized and corrected.

In our department a tumor registry had been established since 1969, fulfilling all the aspects mentioned above. In addition, with every operation for a malignancy, the operating surgeon was anonymously documented. There were only three people who knew the encryption. Every surgeon, however, could get insight into his personal results. The follow-up rate of all patients was 98.5%. Eventually, by strict application of the principles of quality management, we were able to improve our results, period by period (Figure 13).

Furthermore, the survival curves of our patients correlated with the operating surgeon were very close. Only the survival rates achieved by the surgeons in training were slightly worse, because their results still included their learning curve (Figure 14).

How to Implement CME Surgery into One's Own Practice

CME-surgery is more complex and technically demanding than total mesorectal excision. Exposing the vessels to be dissected needs some experience with vascular surgery. However, the principles of any current oncologic surgery demand this knowledge and these techniques of vascular surgery. It should be remembered that CME-surgery is oncologic surgery of the large bowel and it is different from the techniques commonly applied in colorectal surgery.

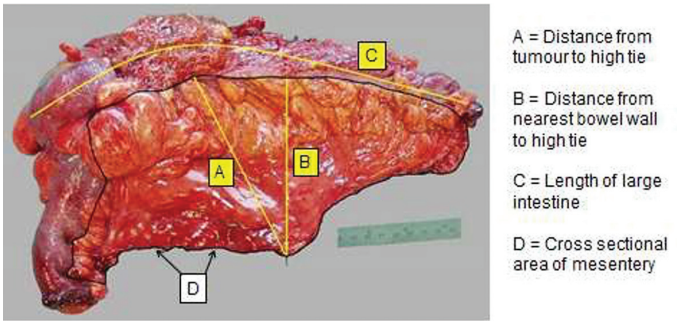

Figure 12. Tissue morphometry, as practiced in the Leeds Institute of Pathology and Molecular Medicine. It is based on photo-documentation of a fresh specimen

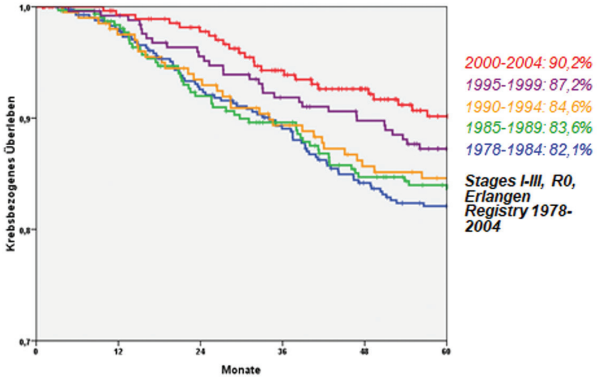

Figure 13. 5-year cancer related survival, achieved in consecutive periods in the Surgical Department of the University in Erlangen

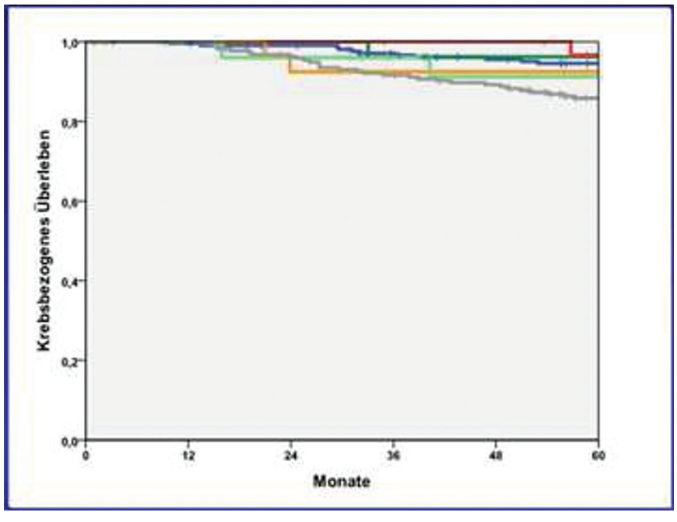

Figure 14. 5-year cancer related survival correlated with the operating surgeons. Each line represents an individual surgeon. They grey line demonstrates the results of all surgeons in training

Strict plane preservation is mandatory and deep and comprehensive knowledge of embryology and anatomy is essential. Therefore, before starting CME, teaching of all these basics and theoretical principles is the first step in implementation. Next, repeated observation of live operations or video-presentations should follow. Only after this can actual operations be performed in the implementing center. Depending on the level of education, a tutor may be needed to assist the surgeon. From personal experience, just one or two surgeons in a department should operate these patients, until the procedure is established. Only then can the technique be adopted by other surgeons.

Even an experienced surgeon has to negotiate a learning curve, as was the case in our team. There is data from Canada analyzing the implementation of laparoscopic right hemicolectomy following the principles of CME. The duration of surgery continued to decrease until the 81st operation. The rate of complications and the yield of lymph nodes were acceptable, from the beginning. However, the range of variations decreased in the same manner as the duration of surgery.[44] Therefore, to recommend a fixed number of CME-operations is unlikely to meet the needs and requirements in all institutions, equally.

The Evidence for Complete Mesocolic Excision

Since 2009, the concept of CME has gained huge interest, worldwide. It is recommended by several national guidelines and the National Comprehensive Cancer Network in the United States, for example.[45] Although some call it the golden standard,[46] others still question its superiority because of limited current evidence[40] and suggest there is a need for randomized trials.

The Web of Science verifies close to 900 peer-reviewed publications referencing the original paper. On the occasion of the twentieth anniversary of colorectal disease, this article was the most frequently cited paper in the history of the journal. Within the last five years, about twenty reviews and meta-analyses have analyzed all papers published on CME reporting outcome data.

There is undisputed agreement that CME achieves a higher lymph node yield, a higher quality of plane preservation and a greater distance from the tumor to the central resection line and longer vascular pedicles, without any relevant functional disadvantages.

Still under debate are eventual intraoperative complications, improvement of postoperative complications, reduction of local recurrence and increased long-term survival.

The review and meta-analysis of Díaz-Vico et al.[41] included 27 publications from 17 countries. The authors conclude that CME improves the quality of the mesocolic resection plane and, more importantly, provides evidence in support of the 3-year DFS and CSS, as well as 3- and 5-year OS benefits of CME, and decreased local and distant recurrence when compared with conventional surgery. Despite the fact that CME is more complex and challenging than conventional surgery, it appears to be a safe and feasible technique in experienced hands. Nevertheless, further high-quality and prospective randomized, multicenter studies encompassing UICC stages 1-3 colon cancer patients would be needed to assess the role of this technique and clarify the potential of CME regarding oncological outcomes in the short and long term before CME can be recommended as the standard of care for primary colon cancer.

Summary and Perspectives

In 1982, Bill Heald published his first paper about total mesorectal excision (TME).[47] Based on the frequency of citations, it took about ten years for this concept to receive broad interest and almost ten more years until it was fully accepted and implemented, worldwide. In the beginning, TME gave rise to the same discussion which occurred some years later about CME. First, that it was not new, then the low local recurrence rates and respective survival rates were questioned, and finally prospective randomized trials were called for before it could be considered the gold standard technique. Compared to TME, the concept of CME is even more complex and technically demanding. Therefore, the resistance was even more pronounced. Nevertheless, it reached wide acceptance within ten years.

The criticism of missing evidence with CME outcome data is just wrong, in our view. The rules of the Canadian Task Force say that a systematic review of prospective cohort studies is consistent with level 2 evidence. In the meanwhile, several such reviews and meta-analyses were performed. The test of this concept by randomized trials is just impossible, as it was with TME. This is because some surgeons are pretending to perform CME-surgery, but do not adhere to the principle fully. The second arm, which would be conventional surgery, is not clearly defined at all. Finally, over the last ten years, even those who disagreed with CME-surgery have adopted surgical techniques which approach the CME-concept. Nevertheless, there are still some open questions. One is the extent of lymph node dissection for cancer of the splenic flexure. Tumors at that site have the worst prognosis compared to the rest of the colon. The concept of CME includes the dissection of the lymph nodes at the inferior edge of the left pancreas and those along the gastroepiploic artery, as well.[48] However, even in our center the 5-year survival of these tumors is just 45%, which indicates that we did not always dissect these additional lymph node stations. Another open question refers to the need of the resection of the adjacent arcades beyond 10 cm to either side of the colon. The T-REX Trial, initiated by Shiozawa et al.[21] from Tokyo, may answer it.

Conclusion

The introduction of TME partially led to a far-reaching centralization of rectal cancer surgery. The same may happen with colon cancer surgery, too. The most challenging task, however, is to test whether, when using quality-controlled CME-surgery, adjuvant chemotherapy will be always needed in lymph node positive cases, if only up to three nodes are involved.[49] The thesis is that these patients will not benefit from adjuvant chemotherapy. Even nowadays, the indication of adjuvant chemotherapy is based on Moertel's trial, published in 1990.[50] The rate of local recurrence in this study was over 20%, which indicates a very poor quality of surgery. Therefore, this 30-year-old dogma may not be valid, if strict CME-surgery is applied.

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