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<u>Title</u>

Complete mesocolic excision for colon cancer: time for a change in practice?

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Conflicts of interest

The author declared no conflicts of interest.

Complete mesocolic excision (CME) for colon cancer has gained increasing popularity over recent years following publication of the Erlangen experience in 2009.¹ Hohenberger and colleagues standardised their surgical approach for potentially curative disease leading to a reduction in local recurrence (6.5% to 3.6%) and improvement in cancer-related five year survival (82.1% to 89.1%) over a 24 year period. CME is based on similar principles to total mesorectal excision (TME) for rectal cancer, a technique now considered the international gold standard. TME led to significant improvements in outcomes through removal of the tumour in an intact package containing all major routes of dissemination.²

There are three important components to optimal CME surgery. Firstly the specimen should be removed in the mesocolic plane ensuring that the mesocolic fascia and peritoneum remain intact, secondly the supplying vessels should be ligated at their origin, and finally sufficient length of colon should be removed. There is good evidence that integrity of the mesocolic plane is important, with a 15% improvement in five year overall survival reported between the best and worst specimens for all cases, rising to 27% in stage III disease.³ There is a theoretical advantage of a high (D3) versus an intermediate (D2) or low (D1) vascular ligation in that additional central lymph nodes will be removed reducing the chances of residual metastatic disease. However, the size of the effect and population that benefit are not well defined. Whilst the principles of mesocolic plane surgery are relatively well accepted, though not necessarily widely practiced, the concept of high vascular ligation remains hotly debated due to the lack of robust evidence and association with increased morbidity in some studies. In contrast, there is no good evidence that extended length of colon 10 cm beyond the tumour offers any oncological advantage.4

Surgeons from Hillerød, Denmark were convinced by the CME argument at an early stage and implemented CME as standard from June 2008. Independent pathological review soon after standardisation showed that Hillerød specimens were oncologically superior when compared to the other regional hospitals practicing non-CME surgery, with a greater mesocolic plane rate (75% vs. 48%) and distance between the tumour and vascular tie.⁵ Early outcomes suggested that CME in Hillerød was associated with better disease free survival.⁶ Bertelsen and colleagues now report the five year

outcomes for right colon cancer across the Capital region, demonstrating a significant reduction in recurrence of 9.7% in the CME group vs. 17.9% for non-CME surgery in elective potentially curative stage I-III disease.⁷ There is a marked difference in lymph node yield between the CME and non-CME groups (38 vs. 21), often used as a surrogate endpoint of surgical quality. This is unlikely to be explained by central ligation as independent specimen morphometry showed only 11 mm of additional tissue between the bowel wall and high tie with CME surgery.⁵ It more likely reflects the use of ancillary lymph node identification techniques and the increased length of colon resected, with longitudinal nodes not thought to be of great oncological importance.⁴ It is not stated whether apical node involvement was reduced.

There are some key limitations to the current study. The data presented focus purely on right sided cancers, with no long term follow up presented for distal transverse and left sided tumours, unlike the early outcomes study.⁶ It is not clear whether this reflects a failure to replicate the long term benefit of CME in these tumours. It is disappointing that the key determinants of CME quality i.e. mesocolic plane and vascular ligation height have been excluded from the analysis. Whilst assessment of the mesocolic planes is somewhat subjective, it is possible that much if not all of the benefit of CME surgery is derived from simply removing the specimen intact with relatively little if any additional benefit from high ligation. It is conceivable that the benefit of high ligation could be undone by mesocolic disruptions leading to tumour dissemination, therefore in the absence of a robust study with standardised mesocolic plane surgery (backed up by rigorous pathological quality control) comparing high versus intermediate level ligation, the opponents of CME will still argue their case. Despite this the Hillerød group should be widely congratulated. It is enlightening to see a group of committed surgeons with multidisciplinary support transforming their long term oncological outcomes for right sided colon cancer through meticulous CME surgery. Whilst the high versus intermediate ligation question may remain, all teams treating colon cancer should be encouraged refocus on their practice to ensure that long term outcomes improve in line with those reported for rectal cancer.

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