Editorial

Complete mesocolic excision (CME) with central vessel ligation (CVL): a new standard in colon cancer surgery

Simon J.A. Buczacki[1,2], R. Justin Davies[1]

[1]Cambridge Colorectal Unit, Addenbrooke's Hospital, Cambridge University Hospitals NHS Trust, Cambridge Biomedical Campus, Hills Road, Cambridge, CB2 0QQ, UK; [2]Cancer Research UK Cambridge Institute, Li Ka Shing Centre, Robinson Way, Cambridge, CB2 0RE, UK

Correspondence to: Mr. R. Justin Davies. Addenbrooke's Hospital, Cambridge University NHS Trust, Cambridge Biomedical Campus, Hills Road, Cambridge, CB2 0QQ, UK. Email: justin.davies@addenbrookes.nhs.uk.

Abstract: The new surgical technique of complete mesocolic excision (CME) with central vessel ligation (CVL) has been reported to lead to improvements in oncological outcomes for patients with colon cancer. Here we discuss a recent large-scale retrospective report by Bertelsen *et al*. that provides compelling evidence to support previously smaller and/or less well designed studies and confirms CME surgery to be oncologically superior to the traditional approach. This Danish study importantly demonstrates an approximately 10% improvement in four-year disease free survival with CME surgery for all patients with stage I-III colon cancer. These data are the first to also show that relatively small surgical advances can still lead to major improvements in cancer survival.

Keywords: Colon cancer; surgery; complete mesocolic excision (CME)

Submitted Feb 04, 2015. Accepted for publication Feb 06, 2015.
doi: 10.3978/j.issn.2224-4778.2015.03.02
View this article at: http://dx.doi.org/10.3978/j.issn.2224-4778.2015.03.02

The seminal work of Richard 'Bill' Heald in the 1980s paved the way for improvements in both local recurrence and cancer-free survival rates for patients with non-metastatic rectal cancer from 20-45% (1) to <3% (2). The approach Heald used was fundamentally anatomical in origin. Rather than performing a close rectal dissection he removed en bloc the draining lymph nodes from the rectum by performing a total mesorectal excision (TME). Although oncological improvements have been seen for patients with colon cancer these have been far less dramatic than with rectal cancer and it is difficult to attribute these to better quality colonic surgery, rather these appear to be as a consequence of improvements in adjuvant therapies. Indeed, the recent focus in colonic cancer surgery outcomes has been driven in the main by the introduction of laparoscopic resections together with its associated improvements in morbidity and length of stay. More recently, several groups have asked whether improvements in colon cancer resection technique can lead to similar improvements in patient survival and local recurrence as were seen with the introduction of TME. These new approaches have, in the main, utilised a more radical approach with meticulous dissection along anatomical planes, an extensive lymphadenectomy and ligation of feeding vessels at their origins. Small volume reports inspired by data from the pioneers of the technique in Erlangen, Germany (3) have demonstrated that these operations, coined complete mesocolic excision (CME) with central vessel ligation (CVL), can be performed safely and appear to lead to improvements in patient disease-free survival and local recurrence (4,5). To-date a large scale randomised control trial comparing CME with CVL to traditional surgery has yet to be performed and is argued by some as unfeasible not least as a consequence of surgical equipoise. At the end of last year a significant report was published by Claus Anders Bertelsen in the December issue of *Lancet Oncology* detailing a large retrospective study on outcomes following CME and CVL in comparison to standard surgery (6).

Bertelsen's work is a further study that convincingly demonstrates that CME, in European hands, improves survival for all non-metastatic stages of colon cancer (I-III). The study performed between 2008 and 2011 involved

four centres. One centre performed CME and the three others non-CME. Data was collected retrospectively for stage I-III, colonic resections involving 364 patients in the experimental arm and 1,031 in the control group. For all stages of colon cancer operated on, 4-year disease-free survival was improved by approximately 10% in patients undergoing CME. These improvements were most marked for stage I and II disease. On regression analysis CME was found to be an independent predictive factor for disease free survival for all stages analysed.

From a demographic perspective the two groups were generally well matched. The CME group had a larger proportion of extended right hemicolectomies performed than non-CME and predictably there were a larger proportion of open operations in the CME group although still almost 50% of CME resections were laparoscopic. Although larger numbers of lymph nodes were identified in the CME resections there was no evidence of stage migration. A larger proportion of patients in the CME group with stage II disease received chemotherapy; however this was not found to be an independent predictive factor for disease free survival on regression analysis. It does however remain to be determined whether the results presented are entirely attributable to the CME technique or related to institutional differences. No historical data, for example, are provided showing equivalence in outcomes in a pre-CME era between the four centres. The authors acknowledge a further potential minor confounder in relation to the use of methylene blue injection to improve pathological yields of lymph nodes in the CME group. The fact that stage migration was not observed suggests that this minor confounder, even if present, plays only a minor role. No data are also provided in the paper as to complication rates although it has been shown before in other studies that CME is likely as safe as traditional surgery (3). Mortality rates were comparable between the two groups.

This Danish study is important not only for its size and convincing collection of data but also for the questions it raises in relation to the aetiology of the oncological improvements seen. It has been argued by some that CME with CVL is no different from good quality colon cancer surgery (7). In the Far East, although not having used the same nomenclature, similar approaches described as D3 lymphadenectomies, have been used for some time as standard of care in stage II and III disease (8). Furthermore, comparing oncological outcomes following an eastern style D3 lymphadenectomy and CME are essentially equivalent (9). It is also unclear through which mechanism CME achieves its benefit i.e., Halsted or Cady-Fisher like mechanisms (10). It appears that stage migration is unlikely to be a predominant mechanism for the apparent benefits with CME and therefore the role of the super-high pedicle ligation also remains uncertain. The importance of sharp dissection, paying particular attention to not disturbing peritoneal planes as with TME appears to be of utmost importance. Many clinical and scientific questions are raised by the data surrounding CME and with time the various components will likely become stratified according to their relative importance.

Evidently, and based on this important study, CME-type surgery provides an important advance for improving outcomes for patients with stage I-III colon cancer. In perspective, the oncological improvements seen with CME surgery exceed those shown to be attributable to adjuvant chemotherapy. Although these data presented are of a lower evidence level than a formal RCT the authors are quick to point that currently a RCT would be near impossible to perform. There have been several other large retrospective and prospective non-randomised studies looking at CME-type surgery. In addition there have been two recent systematic reviews similarly concluding that CME surgery is likely oncologically superior to standard surgery and doesn't appear to carry an increased morbidity (11,12). There is therefore a reasonable weight of evidence in support of accepting CME as standard of care despite a RCT having not taken place. Several important questions however remain in relation to its application, driven in part by the lack of understanding of the mechanism of the apparent effect. These include the necessity of CVL with CME, complication rates compared to standard surgery and whether a laparoscopic approach is as good as open when applying CME principles. Some of these questions could be addressed by a suitably organised RCT. It appears that CME-type surgery is here to stay and it follows that standardisation, training and nomenclature need to be internationally agreed upon. With time we may find that this radical form of surgery is not necessary for all patients but at present we feel that the principles of CME should be embraced by the surgical community.

Acknowledgements

Disclosure: The authors declare no conflict of interest.

References

1. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision

for rectal cancer. Lancet 1993;341:457-60.
2. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet 1986;1:1479-82.
3. Hohenberger W, Weber K, Matzel K, et al. Standardized surgery for colonic cancer: complete mesocolic excision and central ligation--technical notes and outcome. Colorectal Dis 2009;11:354-64; discussion 364-5.
4. Eiholm S, Ovesen H. Total mesocolic excision versus traditional resection in right-sided colon cancer - method and increased lymph node harvest. Dan Med Bull 2010;57:A4224.
5. Bertelsen CA, Bols B, Ingeholm P, et al. Can the quality of colonic surgery be improved by standardization of surgical technique with complete mesocolic excision? Colorectal Dis 2011;13:1123-9.
6. Bertelsen CA, Neuenschwander AU, Jansen JE, et al. Disease-free survival after complete mesocolic excision compared with conventional colon cancer surgery: a retrospective, population-based study. Lancet Oncol 2015;16:161-8.
7. Hogan AM, Winter DC. Mesocolic plane surgery: just plain surgery? Colorectal Dis 2009;11:430-1.
8. General rules for clinical and pathological studies on cancer of the colon, rectum and anus. Part I. Clinical classification. Japanese Research Society for Cancer of the Colon and Rectum. Jpn J Surg 1983;13:557-73.
9. West NP, Kobayashi H, Takahashi K, et al. Understanding optimal colonic cancer surgery: comparison of Japanese D3 resection and European complete mesocolic excision with central vascular ligation. J Clin Oncol 2012;30:1763-9.
10. Buczacki SJ, Davies RJ. Colon resection: is standard technique adequate? Surg Oncol Clin N Am 2014;23:25-34.
11. Killeen S, Mannion M, Devaney A, et al. Complete mesocolic resection and extended lymphadenectomy for colon cancer: a systematic review. Colorectal Dis 2014;16:577-94.
12. Kontovounisios C, Kinross J, Tan E, et al. Complete mesocolic excision in colorectal cancer: a systematic review. Colorectal Dis 2015;17:7-16.

Cite this article as: Buczacki SJ, Davies RJ. Complete mesocolic excision (CME) with central vessel ligation (CVL): a new standard in colon cancer surgery. Transl Gastrointest Cancer 2015;4(3):182-184. doi: 10.3978/j.issn.2224-4778.2015.03.02

