

## Peer Review File

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### Review comments

#### Reviewer A

General Comment: Thank you for the opportunity to review this paper on a very interesting topic. My comments are as follows.

**Reply:** *Thank you for your comments.*

Comment 1: This study evaluates papers on CME based on an initial independent review by 3 of the authors.

**Reply:** *Yes, that is correct.*

Comment 2: The authors only analysed papers on right sided colorectal resections. Therefore, the title of the paper should state this instead of colorectal cancer in general.

**Reply:** *The title has been edited to accommodate this suggestion. Our new title is “A Narrative Review Complete mesocolic excision in right-sided colonic cancer resections: present paradigm and future directions”.*

*As shown on Page 1, lines 3-4 of our manuscript.*

Comment 3: Many comparative studies on CME include both right and left colorectal resection. Are these mixed studies also excluded for this review?

**Reply:** *Although the majority of the papers included referenced right-sided colorectal resections, some comparative studies included both right and left colorectal resections. To clarify this, an additional sentence has been added under the Methods section: “Where studies reported a mix of both right and left sided resections the data pertaining to right sided resection was still included.”.*

*As shown on Page 7, Paragraph 3 and lines 24-25 of our manuscript.*

Comment 4: The authors mention that CME is inconsistently defined. I disagree. Søndernaa et al. The rationale behind complete mesocolic excision (CME) and a central vascular ligation for colon cancer in open and laparoscopic surgery: proceedings of a consensus conference, Int. J. Colorectal Dis. 29 (4) (2014) 419–428 provides a consensus definition which is almost universally applied.

**Reply:** *The sentence has been amended as follows:*

*“While CME, CVL and D3 have been defined, the terms are sometimes used interchangeably even though they refer to different aspects.” As shown on Page 9, Paragraph 1 and lines 5-6 of our manuscript.*

Comment 5: Similarly, CVL and D3 dissection also have consistent definitions. The issue is not about the definition of these techniques but the confusion between them, meaning CME, CVL, D3 refer to different things but are used interchangeably even when one or more are not performed. This can be clarified in the manuscript.

**Reply:** As stated above, while CME, CVL and D3 have been defined, the terms are sometimes used interchangeably even though they refer to different aspects.

Comment 6: While most of the sections in this review provide an adequately nuanced discussion, the section on Complications can be improved.

Comment 7: For example, the first paragraph on Bleeding cites 4 studies (ref 15, 24,25, 27) where bleeding was a major concern in CME surgery.

Comment 8: Given the large amount of data and considerable variations in technical expertise, individual retrospective studies may not accurately reflect risks of CME (e.g. 8% risk of open conversion from massive bleeding)

**Reply:** Comments 6,7 & 8 are addressed together. We have added a sentence which reads:  
“Nevertheless, given the large amount of data and considerable variations in technical expertise, individual retrospective studies may not accurately reflect the true risks of CME. As shown on Page 16, Paragraph 4 and lines 26-27 of our manuscript.

Comment 9: An early meta-analysis of 12 studies by Wang et al. Safety, quality and effect of complete mesocolic excision vs non-complete mesocolic excision in patients with colon cancer: a systemic review and meta-analysis, *Colorectal Dis.* 19 (11) (2017) 962–972 showed increased intraoperative blood loss with CME. However, of 9 more recent meta-analyses, none showed increased bleeding with CME, and 2 conversely showed reduced operative blood loss with CME vs non-CME (Seow-En I, Chen WT. Complete mesocolic excision with central venous ligation/D3 lymphadenectomy for colon cancer - A comprehensive review of the evidence. *Surg Oncol.* 2022;42:101755). 6 out of these 9 reviews also demonstrated similar length of hospital stay for CME vs non CME.

**Reply:** Thank you for the above information. The content above has been incorporated into the manuscript and reads as:

“However, in a separate study examining blood loss, there was no difference between CME versus conventional surgery for colon cancer (weight mean difference (WMD) 3.50ml, 95% CI -29.13-36.12,  $P=0.0834$ ) (26). An early meta-analysis of 12 studies showed increased intraoperative blood loss with CME (28). However, of 9 more recent meta-analyses, none showed increased bleeding with CME, and 2 conversely showed reduced operative blood loss with CME versus non-CME (29). Also, 6 out of these 9 reviews also demonstrated similar length of hospital stay for CME versus non CME (29)”

As shown on Page 17, Paragraph 1 and lines 5-9 of our manuscript.

Comment 10: I would also urge the authors to reference recent meta-analyses for other complications including anastomotic leak, as well for oncological results.

**Reply:** Results from recent meta-analyses have been included.  
Reference that have been used are shown below and can be found on Pages 33-34, reference numbers 26-28, 32 of our manuscript.

Crane J, Hamed M, Borucki JP, et al. Complete mesocolic excision versus conventional surgery for colon cancer: A systematic review and meta-analysis. *Colorectal Dis.* 2021;23(7):1670-86.

Cuk P, Jawhara M, Al-Najami I, et al. Robot-assisted versus laparoscopic short- and long-term outcomes in complete mesocolic excision for right-sided colonic cancer: a systematic review and meta-analysis. *Tech Coloproctol.* 2022.

Wang C, Gao Z, Shen K, et al. Safety, quality and effect of complete mesocolic excision vs non-complete mesocolic excision in patients with colon cancer: a systemic review and meta-analysis. *Colorectal Dis.* 2017;19(11):962-72.

Seow-En I, Chen WT. Complete mesocolic excision with central venous ligation/D3 lymphadenectomy for colon cancer - A comprehensive review of the evidence. *Surg Oncol.* 2022;42:101755.

Comment 11: While I agree that predictive nomograms may be useful for selecting patients for CME, I am not sure this can be “recommended” as a conclusion of this paper. Instead, studies which evaluate the use of the nomogram in CME should be recommended to better refine patient selection.

**Reply:** *We agree with this statement. The Conclusion of this manuscript now reads as: “A selective approach to CME, balancing survival benefits and quality of life against operative risks, is recommended.” As shown on Page 29, Paragraph 3 and lines 13-14 of our manuscript.*

*Similarly, our Abstract conclusion now reads as “A selective approach to CME, balancing survival benefit and quality of life against operative risks, is recommended.” As shown on Page 4, Paragraph 2 and lines 5-6 of our manuscript.*

#### **Reviewer B**

General Comment: This is very well written paper dealing with very many aspects; like definition, anatomy, surgical technique etc. Authors have collected big number of papers which give proper view on this topic. This subject is very important and new and has big potential to be published

**Reply:** *Thank you for this comment.*