

Dear Editor,

Thanks for your letter and for the reviewers' comments concerning our manuscript entitled "Short- and long-term results of open versus laparoscopic multisegmental resection and anastomosis for synchronous colorectal cancer located in separate segments" (85528). Those comments are all valuable and very helpful for revising and improving our paper. We have carefully taken those comments into consideration in preparing our revision and tried our best to make the point-by-point corresponding responses. The revised portions are highlighted in yellow in the manuscript. The main corrections in the paper and the response to the reviewer's comments are as follows:

Response to the comments:

Reviewer 1:

1. *Where is list of abbreviations?*

**Response:** Thanks for your kind question. Our previous manuscript lacks the description for this content, which we supplemented it.

On page 12, lines 8-15, the following abbreviations were added: "SCRC: Synchronous colorectal cancer; LMRA: Laparoscopic multisegmental resection and anastomosis; OMRA: Open multisegmental resection and anastomosis; LN: lymph node; DFS: Disease-free survival; OS: Overall survival; HR: Hazard ratio; CRC: Colorectal cancer; CA19-9: Carbohydrate antigen 19-9; CEA: Carcinoembryonic antigen; ASA: American Society of Anesthesiologists; CD: Clavien-Dindo; SPSS: Statistical Product and Service Solutions; CI, confidence interval"

2. *Abstract is good but needs some correction as shown.*

**Response:** Thank you very much for pointing out the issue. we have changed the sentence as (On page 3, lines 23-26): "Compared to OMRA patients, LMRA patients exhibited markedly shorter postoperative first exhaust time (2 *vs* 3 d,  $P = 0.001$ ), postoperative first fluid intake time (3 *vs* 4 d,  $P = 0.012$ ), and postoperative hospital stay (9 *vs* 12 d,  $P = 0.002$ )" .

3. *Introduction is good. Materials and methods need some shortage, and I think the cases followed by phone will have defects. In statistical analysis; I think more updated versions of SPSS are available.*

**Response:** Thanks for your kind suggestion. According to your suggestion, SPSS version 26.0 from IBM (Armonk, NY, USA) was re-employed for statistical determinations. we have changed the sentence as (On page 7, lines 14-16.): "Statistical Product and Service Solutions (SPSS) version 26.0 from IBM (Armonk, NY, USA) was used for statistical determinations."

4. *Results are good. Discussion needs some shortage, and correction as seen ( blue underlined). Conclusion is good.*

**Response:** Thanks for your kind suggestion. According to your suggestion, we revised the sentence as ‘the total postoperative complication as well as hospital stay were remarkably better in LMRA patients (On page 10, lines 26 – 28,)’ .

Reviewer 2:

The authors analyze in an interesting manuscript the short-term surgical results and long-term prognosis (5-year OS and DFS) of multisegmental resection and anastomosis for synchronous colorectal adenocarcinomas performed by standar open procedures vs laparoscopic procedures. Some cuestions rise after reading the text.

1. *The study period is too long (2010-2021). It is possible that different surgeons performed the operations and that the clinical protocols were modified during this period. Authors should explain if this fact may have influenced at any extent. When was laparoscopy available at those hospitals?. Did they follow any postoperative ERAS protocol, and when it was implemented?*

**Response:** Thanks very much for your valuable comments. Laparoscopy was available at our hospitals since 2007, the surgeons have skilful mastered laparoscopic colorectal cancer surgery during this period of 2010-2021. Either laparoscopic surgery or open surgery was both performed by experienced surgeons. We did not follow postoperative ERAS protocol. Although the study period is long, it will not affect the results of the study. We hope our description is suitable and address your concerns.

2. *Did postoperative adjuvant chemotherapy was administered?.*

**Response:** Thanks for your kind question. Our previous manuscript lacks the description for this content, which we supplemented it in the results section and Table 1 as (On page 7, lines 27,): “As noted from the table 1, both groups did not differ significantly in age, gender, abdominal surgery history, concomitant diseases, preoperative chemotherapy, CA19-9 and CEA levels, ASA class, postoperative chemotherapy, tumor size, tumor differentiation status, N stage, T stage, and TNM stage.”

3. *The authors should discuss the benefict of performing multisegmental resections vs total or subtotal colectomies.*

**Response:** Thanks very much for your valuable comments. Our previous manuscript lacks the description for this content, which we supplemented it in the discussion section.

On page 9, lines 5-14, under the discussion section, the following sentence was added: “Lee et al[8] retrospectively analyzed the postoperative bowel movements of synchronous colorectal cancer, and found that the mean number of bowel movements in two regional resections group and extensive resection group were 1.9 times and 4.3 times, respectively, there were significant differences between the two groups. You et al[9] compared the bowel function and quality of life between extended resections and segmental colonic resections, the result showed that median daily stool frequency after segmental resections, ileosigmoid anastomosis and ileorectal anastomosis was 2, 4 and 5, respectively, and the overall quality of life was 98.5, 94.9, and 91.2, respectively. As multisegmental resection provides better postoperative defecation function and quality of life and does not increase complications such as anastomotic leakage, this technique is recommended by some researchers” We hope these changes are suitable and address your concerns.

*4. The authors should be more cautious when they conclude that "LMRA has more advantages than OMRA in terms of short-term efficacy, and can achieve the similar long-term oncological results as OMRA". The number of patients included in the analysis is too reduced and the differences found were not statistically significant. They state this clearly in the discussion and conclusions.*

**Response:** Thanks for your kind suggestion. According to your suggestion, we revised the sentence as ‘On the basis of this study, we conclude that LMRA has some short-term advantages compared with OMRA, and is safe and feasible for patients with SCRC located in separate segments.(On page 13, lines 22 – 24,)’ . Furthermore, we further state that limitations of this research in the discussion. ‘as the incidence of SCRC located in separate segments is low, although the sample size in this study is the largest thus far, the number of patients included in the analysis is still small. Therefore, multicenter prospective studies are needed in the future to confirm the advantages of LMRA.(On page 11, lines 28,)’ We hope these changes are suitable and address your concerns.