

Dear Editor-in-Chief and Reviewers,

We are thankful to you and the reviewers for the insightful critic and comments. We also thank you for giving us the opportunity for resubmission after revision to the manuscript. This is a revised submission of our manuscript. We have enhanced the manuscript accordingly and enclosed below is the point-to-point response with the changes made highlighted in yellow as per the journal's requirements.

Yours sincerely,

Corresponding author

Reviewer #1:

1. The sample size is too small to evaluating OS or PFS, especially for open group. Furthermore, there was no open surgery after 2020 in this study. The reliability of this part is relatively poor.

Response: Thank you. You are right that our sample size is small and limits the interpretation of long-term oncological outcomes. However, we still included the OS and DFS to allow readers to have an understanding of the long term outcomes of these patients in our cohort. In view of your suggestion, we have added the following in our limitations: "Long-term oncological outcomes such as OS and DFS may also not be conclusive or representative of other cohorts, especially for the oMVR group, with a small sample size of 12 only."

2. In subgroup analysis, the patients in robotic group with more complicated lesions had better 3-year survival. How to explain this? Although, robotic surgery could be more precise in suture and dissection.

Response: Yes, it was interesting that the 3-year survival was superior in the robotic compared to the laparoscopic MVR group. This was actually explained in our discussion: "With the theoretical benefits of robotic surgery over laparoscopic surgery, it is postulated that long-term survival will be higher, and recurrence will be lower in the robotic group. This was supported by our study which showed superior 3-year OS and 3-year RFS in robotic MVR compared with laparoscopic MVR". However, 5-year OS and 5-year DFS were similar between robotic and laparoscopic MVR groups. Hence, we also described this in our discussion: "We postulate that robotic surgery may improve long-term survival with more precise dissection and adequacy of resection, and also by reducing short-term complications with downstream long-term complications (e.g. inadvertent ureteric injury requiring need for repeat surgeries). Nevertheless, the overall evidence regarding the superiority of robotic surgery over laparoscopic in rectal cancer remains equivocal and this needs to be validated."

3. The morbidity of postoperative complication for open group is too high. e.g. Ileus (66.7%), SSI (50%). Try to explain this in the discussion.

Response: Thank you for raising up this point. We have also supplemented our results and included the extent of resection in the oMVR group: "Of the patients who underwent oMVR, two cases had bilateral PLND, two cases had sacrectomy and three cases had vertical rectus abdominis myocutaneous (VRAM) flap reconstruction", which may explain the high incidence of post-operative complications. Please refer to our results and discussion for the additional information.

We agree that the morbidity is high. However, our open MVR cohort only included 12 patients. There were 8 patients with ileus, and 6 patients with SSI. Definitive conclusion should not be made based on the percentage alone in view of the small

sample size of open MVR. Nevertheless, we still agree that morbidity is high, but is concordant with literature which stated post-operative morbidity of up to 80% [8].

Reviewer #2:

Thank you for reviewing our manuscript with your detailed comments. Please see below for our point-to-point response to your comments.

1. Title. the title reflects the main subject/hypothesis of the manuscript.

Response: Thank you.

2. Abstract. The Methods and Results sections are too long. The Core Tip section should be focused on the message of the manuscript, non just on summarizing the main results.

Response: Thank you. We have modified the core tip section. For the methods section, we have truncated the part on institutional board review since this was more described in detail in the title page (page 2), and have also removed certain components on study variables and outcomes since these were also described in the results.

3. Key Words. I suggest to include “Multivisceral resection”, as a key word

Response: Thank you. We have added this as a keyword.

4. Background. The manuscript adequately describes the background, present status and significance of this study. However, this section could be shortened. The paragraph about colorectal cancer screening in Singapore may be removed.

Response: Thank you. We have shortened the manuscript and removed the section about colorectal screening in Singapore as per your suggestion.

5. Methods. No information is provided on the preoperative diagnostic work-up. How did the authors diagnosed cT4b rectal tumors ? did the patients have an appropriate preoperative staging with magnetic resonance imaging and/or endoscopic ultrasound ? were all the patients peroperatively diagnosed with cT4b tumors confirmed as pT4b by postoperative pathological examination ? how many patients were preoperatively diagnosed with cT1-3 stage tumors and found to have T4b stage as an unexpected intraoperative/pathological finding ? Were patients discussed in multidisciplinary tumor boards ? The treatment guidelines adopted at the authors' institution for locally advanced rectal tumors has to be summarized. The authors state that patients with systemic metastases with non-resectable disease were excluded and were referred for palliative chemotherapy with or without radiotherapy. Did any patient become resectable after CT +/- RT ? were any of such patients included in the study ? please, specify.

Response: We have added in the pre-operative workup under Section 2.2 Treatment protocol. cT4b rectal tumours were diagnosed based on magnetic resonance imaging of the rectum. Endoscopic ultrasound was not performed.

Regarding your question on how many patients were preoperatively diagnosed with cT1-3 stage tumors and found to have T4b stage as an unexpected intraoperative/pathological finding, we are unable to comment as this study only included patients with cT4b tumors. cT1-3 tumours were not analysed.

All patients were discussed in multidisciplinary tumour board pre-operatively and post-operatively regarding the role of neoadjuvant chemoradiotherapy based on the patient's demographics and co-morbidities. For patients who underwent emergency surgery, only post-operative discussion was made due to the nature of presentation. We have summarised the guidelines for the treatment of locally advanced rectal tumours.

Regarding your question on whether patients with non-resectable disease and systemic metastases, none of the patients were able to undergo MVR after CT +/- RT. We have also added this in our methodology.

6. Results. No information are provided on the use of preoperative radiotherapy, that is a mainstay of treatment in locally advanced rectal tumors. Analogously, no information is provided on the distance from the tumors to the anal verge. Please, specify how many all-stage rectal tumor patients were treated during the study period. The study population is not described with sufficient details. It appears that patients diagnosed with a) cT4b primary rectal cancer; b) locally recurrent rectal cancer; and c) stage 4 disease with resectable systemic metastases who underwent MVR were included in the study. I presume that "patients diagnosed with stage 4 disease with resectable systemic metastases" refers to patients with cT4b primary rectal cancer AND resectable systemic metastases", but this point is absolutely not clear in the text. The following information are not clear in the text and tables (and have to be provided): - How many patients with primary locally advanced rectal tumor vs. recurrent rectal tumor were included - How many patients with resectable distant metastases were included - Which surgical procedures were performed to resect distant metastases. Were distant metastases resected before, after or at the same time as multivisceral pelvic resections?

Response: Thank you for this comment. We agree that pre-operative radiotherapy is an important aspect in treatment of LARC. We have added this information in Table 1. Unfortunately, we did not have any data on the distance of the tumour from the anal verge.

There were 579 patients with rectal cancer who underwent surgery during this study period, with approximately 60 cases of patients per year. We have included this in our methodology.

Yes, you are right that patients diagnosed with stage 4 disease with resectable systemic metastases refers to patients with cT4b primary rectal cancer and resectable systemic metastases. We have paraphrased this statement for better clarity.

There were 3 patients with recurrent rectal tumour. None of the patients had distant metastases. We have included the required information in our results.

7. Discussion. The Discussion section is too long. It appears to be about 50% of the manuscript text. The main weakness of the present paper is the small number of cases: 46 patients in 9 years. That is 5 patients per year, on average, meaning that the authors' institution is not a large volume surgical unit for locally advanced rectal tumors. Also, the study population was divided in even smaller sub-categories: open (n=12), laparoscopic (n=13), and robotic (n=21). These small numbers limit the clinical significance of the present study.

Response: Thank you for the comment. We have shortened our discussion and removed areas which are less relevant (e.g. on patients who underwent emergency oMVR). However, we added into our discussion the reasons for high post-operative ileus and SSI as suggested by reviewer 1.

We agree that sample size is small for patients with cT4b rectal cancer who underwent MVR and hence, this was included in our limitations. Unfortunately, while we cannot overcome this limitation, it is promising to know that the outcomes of miMVR are good even with such a small sample size. Robotic MVR can also be safely performed for complex surgeries with similar post-operative complications compared to laparoscopic MVR. We have made the changes in the limitations and conclusion to emphasise on this point.

8. Illustrations and tables. Figures are of sufficient, good quality and appropriately illustrative. Tables are not (see my comments at points 5, 6, and 7)

Response: Thank you. Please see our response to points 5,6,7 above. For additional information required, we have included this in the results and modified the tables.

9. Biostatistics. Does the manuscript meet the requirements of biostatistics? NA

Response: Thank you.

10. Units. Does the manuscript meet the requirements of use of SI units? it does

Response: Thank you.

11. References. Literature references are appropriate.

Response: Thank you.

12. Quality of manuscript organization and presentation. The style, language and grammar are appropriate? Regarding manuscript organization and presentation, please see my comments at points 5, 6, and 7

Response: Thank you. Please see our response to points 5,6,7 above.

13. Research methods and reporting. The authors have prepared their manuscripts according to STROBE Statement

Response: Thank you.

14. Ethics statements. It appears that the manuscript meets the requirements of ethics.

Response: Thank you. Yes, institutional review board approval was obtained for this study with informed consent from patients included.

Editorial Office's comments:

Scientific Editor's comments:

Thank you for the comments on the scientific quality of our manuscript. We have replied in detail with a point-to-point response above.

Specific comments:

1. Please provide the filled conflict-of-interest disclosure form.

Response: We have filled and attached the conflict-of-interest disclosure form for all of the authors.

(2) Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A,B, arrows, etc. With respect to the reference to the Figure, please verify if it is an original image created for the manuscript, if not, please provide the source of the picture and the proof that the Figure has been authorized by the previous publisher or copyright owner to allow it to be redistributed. All legends are incorrectly formatted and require a general title and explanation for each figure. Such as Figure 1 title. A: ; B: ; C: .

Response: We have provided the figures in the form of PPT. However, the texts are unable to be edited as the texts are autogenerated by the software during statistical analysis.

(3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text (and directly before the References).

Response: We have added in the “Article Highlights” section.

(4) Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: We have modified our tables to suit the formatting requirements.

Company Editor-in-Chief’s comments:

I recommend the manuscript to be published in the World Journal of Gastrointestinal Surgery.

Response: Thank you for the comment and we hope this manuscript will benefit readers.