

Dear Editors and Reviewers:

We are very grateful for the careful and thorough review given to our manuscript entitled "**Robotic- versus laparoscopic-assisted proctectomy for locally advanced rectal cancer based on propensity score matching: short-term outcomes at a colorectal center in China**" (Manuscript NO. 53038). We have made corrections in the revised manuscript and provided clarifications and additional data to address the reviewers' comments accordingly. The comments are valuable and are responded point by point. All revisions are clearly displayed in the revised manuscript. Thus, our manuscript is improved and we hope it is now be acceptable for publication in World Journal of Gastroenterology Oncology. The main revisions are as flowing:

Responds to the editor's request:

We revised the article step by step according to the editor's suggestions.

Thank you for your kindly suggestions.

Reviewer No: 04028454

Response to Reviewers

Thank you for your kind opinion, which is very helpful to improve the quality of our article.

Reviewer's comment:

1. Comment: First, there are numerous grammar issues. The manuscript needs some editing for presentation in English language. Examples include: line 107 "three" should probably be replaced by "third"; line 126 "is thought considered to be able to " should be edited; line 128 "has" should be "have"; line 129 "with relative" should be edited; line 285 "reports have been reported" should be edited; in Figure 1, should not say "distal gastrectomy" in top box

Authors' response: We have revised these questions and polished the language.

2. Comment: lines 143/144 " The choice is based on the patient's full understanding of the advantages and disadvantages of the two surgical methods". The purpose of this paper is to help understand the advantages and disadvantages of the two methods. What exactly was told to the patients as pros/cons of lap and pros/cons of rob?

Authors' response: We have revised it. What we want to express is the potential merits and demerits of the two surgical methods (RAP and LAP).

3. Comment: lines 154-159 are confusing to me. Patients were excluded who were " (4) totally robotic surgery or totally laparoscopic surgery". Aren't these exactly who should be included? Also, inclusion criteria mentions T4, but "(8) invasion to adjacent organs " is an exclusion criterion. This needs correction. Additionally, "(9) conversion to open laparotomy" is an exclusion criterion? Many authors have shown this to be one of the primary advantages of robotics (fewer conversions). Why is this an exclusion? Why are conversions not mentioned in the body of the work or in Table 2? They should be. Lastly, how many were excluded based on "(10) robotic or laparoscopic equipment failure during operation." How many in each group? Was this early in the experience?

Authors' response: This time, we are comparing the robot or laparoscopic assisted operation. However, the comparison between totally robotic surgery and totally laparoscopic surgery, we will conduct it in the future. The inclusion criteria mentions T4a, not included T4b (invasion to adjacent organs), this have been correction. Indeed, conversion to laparotomy "should not be the exclusion criterion, we included the cases of conversion to open surgery and found that the conversion rate of robot operation group was lower (Table 2). For robotic or laparoscopic equipment failure we didn't meet during rectal operation but during gastric operation in early time, so we removed the exclusion criteria.

4. Comment: lines 165/166: Why was "vascular invasion, and perineural

invasion" included in the PSM? I understand all the patient demographics being used, but why these specific pathologic outcomes? This needs explanation.

Authors' response: At first, we wanted to make the two groups of patients match better. This problem is really ill considered. We moved the vascular invasion and perineural invasion to table 2, and we did PSM and analysis again.

5. Comment: A major issue: "The discharge criteria were as follows: (1) the passing of at least 5 days since surgery" - much of the literature comparing short-term outcomes of robotic and laparoscopic proctectomy show differences during the first 1-4 days postoperatively, including timing of catheter removal, advancement of diet, and discharge. I understand there are differences in LOS based on country, insurance system, cultural differences, hospital policies, etc. This should be described and explained in the discussion.

Authors' response: This has been described and explained in the discussion. In our center, one of the discharge criteria was that the passing of at least 5 days since surgery, this is due to the underdeveloped primary medical treatment in the region of Jiangxi Province and affected by the clinical pathway.

6. Comment: In methods, you should include which robotic system (Si?) is used and which laparoscopic equipment is used. For example, was infrared imaging available and used during either type of procedure? What type of imaging did the lap equipment have (4K?)

Authors' response: This has been described in the methods.

7. Comment: Did you see any difference between the two groups in who was "excluded". Other authors have found that patients with higher BMI, more extensive adhesions, smaller pelvis, bulkier tumors were able to be "included" in the robotic group and were less likely to have conversion in the robotic group. Can you comment on this in your experience? Were your patients more likely to be offered MIS if robotic was

available/chosen?

Authors' response: In our experience, robotic surgery systems have some advantages for patients with higher BMI, more extensive adhesions, smaller pelvis, bulkier tumors. In our center, the patients with the average BMI of 23.19, the proportion of obese patients is relatively small. Most patients prefer robot surgery. But our hospital only has two Da Vinci robotic surgery systems, some patients have limited economic capacity, and a considerable number of people will choose laparoscopic surgery in the end.

8. Comment: Another major issue is with the results. There are quite a few results being presented as significant because they are statistically significant, but I believe many surgeons and readers would question their clinical significance. I wonder if STD would be more meaningful for some of these rather than range, which is what you present. 6cc of EBL difference, 10 cc of drainage output difference over 4 days and 2.4 difference in CRP may be statistically significant, but many readers would question any real clinical significance here. This should be in your discussion. Similarly, the "differences" for catheter and drain removal are presented as significant, but clearly they are not (4 vs 4 and 6 vs 6). Even a 7 minute difference for a 1.5 hour to 6 hour operation is of questionable significance, and this merits conversation in the discussion as well.

Authors' response: We performed PSM again and reanalyzed the results. Indeed, it is true that there are statistical differences in many indicators, but the clinical differences of some indicators are not significant enough. We explained this problem in the discussion. Continuous variables are expressed as mean \pm SD (range) instead of median (Range) in the revised manuscript.

9. Comment: In the discussion, there should be mention of the overall BMI (median, STD) in both groups. Patients range from about 20.5 to about 26. There are essentially no obese patients being operated on during this study. This should be described as it is significant for many readers.

Authors' response: In the discussion, we have added descriptions of BMI. Indeed, there are few obese patients being operated on the present study.

10. Comment: In regard to pelvic drains, are they needed for every case? There is literature suggesting all, some or no patients benefit from pelvic drains. Frankly, I think the conclusions regarding the pelvic drain and foley catheter removal timing is not significant, but if you are going to include it, you should discuss the literature regarding the need / indication for drains for these patients, criteria for removal and when other authors remove drains.

Authors' response: We added this description in the method section. According to Expert consensus on robotic surgery for colorectal cancer (2015 edition), each of our patients undergoing radical resection of rectal cancer needs an indwelling catheter and a pelvic drainage tube. We observed that patients with robotic surgery had less pelvic drainage and shorter indwelling time for pelvic drainage and urinary catheters, which facilitated postoperative activities and accelerated recovery.

11. Comment: In other centers, the foley catheter is routinely removed on POD 2 after these operations. You should include in your discussion results from other centers regarding catheter removal, or, again, remove "difference in foley catheter removal" from your conclusions.

Authors' response: The procedure of catheter removal is very important. Mary's study indicated that urinary catheter removal before 3 days after surgery was related with urinary retention. This is the underlying reason for the average catheter time of 3.5 days in the current study. The optimal time to remove urinary catheter after rectal surgery can refer to the results of an ongoing RCT study (DOI: 10.1186/s13063-019-3210-1).

12. Comment: I don't believe the following is proven by your data: "We also found that the time to remove the urinary catheter was obviously shorter in the RAP group than in the LAP group, which was similar to our previous studies". I also don't think you can state the following conclusion: "This result shows that urinary function is damaged less in

robotic TME thanks to such advantages as three-dimensional stability and high-definition images, easier identification of the pelvic nerve, and flexible instruments that facilitate fine dissection". This is your opinion, but not a conclusion you can make based on your data. There is literature that can be discussed here.

Authors' response: We added discussion to the discussion section. This needs to be confirmed by long-term follow-up of urinary and sexual function.

13. Comment: Why do you not include distal margin, radial margin, or quality of TME in your results? These are common metrics included in this type of reporting and may offer more important data when comparing lap and rob TME. You should include or explain why not included.

Authors' response: We have increased the analysis of distal margins and found that robotic surgery can obtain longer distal margins. However, we did not analyze the circumferential resection margin because our hospital's pathology department has only begun to analyze the circumferential resection margin for some patients' rectal specimens in the past year.

14. Comment: Why did you chose VAS at 24 hours? Why not at 12, 36, 48 or 72 hours? What is your protocol for post-operative pain management for these patients? Is it the same for both groups? Did it change over the 5 years? Do you have morphine milliequivalent usage for these patients?

Authors' response: We have differences in pain management during these 5 years, so we decided to delete the VAS indicator.

15. Comment: LOS was 8 days for both groups. You should include in your discussion what LOS is in other similar studies and discuss why yours was 8, and why you think there is no difference between the two groups. Other groups have found differences.

Authors' response: We added discussion of length of stay in the discussion section. The median hospital stay (8 days) after operation in the current study was similar to Perez's study. In our center, one of the

discharge criteria was that the passing of at least 5 days since surgery, this is due to the underdeveloped primary medical treatment in the region of Jiangxi Province and affected by the clinical pathway. This may be one of the underlying reasons for no significant difference in postoperatively hospital stay between the two groups.

16. Comment: What % of each group was done with intracorporeal anastomosis? Does this matter in regard to postop pain, postop LOS, return of bowel function? This merits presentation in your data and discussion.

Authors' response: The surgical procedures performed in the two groups were similar. After cutting off the lower rectum of the tumor, remove the specimen and place the mushroom head of stapler through the auxiliary incision on the lower abdomen. After closing the incision, the stapler is anastomosed with the mushroom head through the anus. The surgical procedure is described in the method section.

Reviewer No: 02445553

Response to Reviewers

Thank you for your kind opinion, which is very helpful to improve the quality of our article.

Reviewer's comment: This is a large retrospective cohort study, with the inherent problems of that design, which the authors have tried to overcome by a propensity score analysis.

1. Comment: Abstract. The conclusion must be modified. The differences between LAP and RAP are mostly clinically insignificant in spite of statistical significance. The differences are small in the practical situation which should be admitted in the text.

Authors' response: We thank for the suggestion of the reviewer. We have revised the conclusion.

2. Comment: Line 116. Rectal cancer is often symptomatic!

Authors' response: Yes. Rectal cancer is often symptomatic, but during the

early stage, the symptomatic is a disease largely without obvious symptoms

3. Comment: Line 130. Lack of screening is not the only reason for late presentation. Since rectal cancer often is symptomatic, lack of public and professional awareness of the disease is also important.

Authors' response: Lack of public and professional awareness of the disease is also important for patients with diseases at advanced staged. We have revised this part.

4. Comment: Line 147. " and so on". What does that mean - what is included?

Authors' response: We have deleted "and so on, including ECG and other preoperative routine examinations.

5. Comment: Line 152. Measuring the height of the recal tumour by MRI assessment is notoriously uncertain. The authors should report data on the distance from the anal verge (not anal edge) to the lower border of the tumour, measured by rigid sigmoidoscopy during withdrawal.

Authors' response: Yes, the distance measured by rigid sigmoidoscopy during withdrawal. It's our misrepresentation.

6. Comment: Line 156. Why was Hartmann's operation excluded? Line 158. How many operations were converted to open surgery?

Authors' response: We have revised the content. The exclusion standard is that only sigmoidostomy is performed for rectal cancer.

7. 160 - 166. A directed acyclic graph (DAG) would be helpful to clarify the choice of analyses for the PSM.

Authors' response: Figure 1 was displayed the flow chart of patient selection.

8. Lines 242-247. The clinical significance, as mentioned above, of these differences, are very questionable. Concerning removal of drainage and urinary catheters, was the nursing staff blinded for the operative methods?

Authors' response: After reanalysis, variables were expressed as mean (standard deviation, SD) with range. We set out the problem in the conclusion.

9. Lines 279-295. This part of the discussion is mainly a repetition of the introduction and methods and could be considerably shortened.

Authors' response: Yes, we have deleted some of the content.

10. Lines 301-302. The text about operation time must be Despite the problems listed above transferred to the Methods section.

Authors' response: We have moved the definition of operation time to the method section.

11. Line 350. The summary should be modified according to the comment to the abstract.

Authors' response: We revised the question in the conclusion section. Indeed, we need to pay attention to whether many statistically significant indicators have clinical significance.

12. Fig. 1. The head of the figure is not correct. It tells "distal gastrectomy" instead of "proctectomy".

Authors' response: We have revised figure 1.

Reviewer No: 03004570

Response to Reviewers

Thank you for your kind opinion, which is very helpful to improve the quality of our article.

Reviewer's comment: This retrospective cohort study with relatively larger sample size (screened 945 patients total, allocated 807 patients) indicates that robotic rectal surgery for locally advanced rectal cancer is safe, feasible and associated with less intraoperative blood loss, less volume of pelvic drainage, shorter time to remove the pelvic drainage tube and urinary catheter and may give less damage to normal tissues. Authors used a propensity-score matching analysis to reduce patient selection bias and they benefited from 32 references including two meta-analyses.

1. Comment: 1. In the Figure 1, "945 patients underwent mini-invasive distal gastrectomy" must be corrected as "945 patients underwent mini-invasive proctectomy",

Authors' response: We have revised figure 1.

2. Comment: 2. In the Table 1, "Mlies" should be corrected as "Miles".

Authors' response: We thank the reminder of the reviewer. We have corrected it.

3. Comment: 3. In the Table 2, medians are same in both "Time to remove pelvic drainage tube" between RAP and LAP groups and "Time to remove urinary catheter" similarly. I recommend also adding mean values to the table to highlight significant statistical difference.

Authors' response: Thank you. The variables were shown as mean (standard deviation, SD) with range.

4. Comment: 4. As a general Table format and as an example, I recommend "Median time to liquid diet, days (range)" in place of "Time to liquid diet (M (R), days)".

Authors' response: We thank the suggestion of the reviewer. We have corrected it

Thank you for your careful reading and good comments to our manuscript. We tried our best to improve our manuscript and we hope it is now be acceptable for publication in World Journal of Gastroenterology Oncology.

Sincerely yours,

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Dear Editors and Reviewers:

We are very grateful for the careful and thorough review again for our manuscript entitled “**Robotic- versus laparoscopic-assisted proctectomy for locally advanced rectal cancer based on propensity score matching: short-term outcomes at a colorectal center in China**” (Manuscript NO. 53038). We have made corrections in the revised manuscript and provided clarifications and additional data to address the reviewers’ comments accordingly. The comments are valuable and are responded point by point. Thus, our manuscript is improved and we hope it is now be acceptable for publication in World Journal of Gastroenterology Oncology. The main revisions are as flowing:

Responds to the editor’s request:

We revised the article step by step according to the editor's suggestions.

Thank you for your kindly suggestions.

Reviewer No: 02445553

Reviewer’s comment: Now OK.

Response to Reviewers

Thank you very much.

Reviewer No: 03004570

Response to Reviewers

Thank you for your kind opinion, which is very helpful to improve the quality of our article.

Reviewer’s comment: Corrections of #1, #2 and #4 in my previous letter of evaluation, ok, no problem. But, for Table 2, I think that authors misunderstood the presentation of “Median (range)” and “Mean \pm SD” in a Table. Median value has not standard deviation (SD) statistically. I give below

an example of correct presentation according to data of this manuscript:

Median time to remove pelvic drainage tube, d 6.0 (4.0-29.0) 6.0
(4.0-28.0) 0.036 Median time to remove urinary catheter, d

4.0 (2.0-7.0) 4.0 (2.0-18.0) 0.006 Mean time to remove pelvic drainage tube
± SD, d 7.1 ± 4.2 7.8 ± 4.9 0.000 Mean time to remove

urinary catheter ± SD, d 3.2 ± 1.0 3.8 ± 1.2 0.000

Authors may give median or mean values or both in the Table, according to
their choices.

Authors' response: We thank for the suggestion of the reviewer. We have
corrected it following your advices which expressed as mean ± SD and
median (range).