

Correspond to editors

Dear Editors:

Enclosed please find a revised manuscript entitled “Transanal Natural Orifice Specimen Extraction for laparoscopic low/ultralow anterior resection in rectal cancer”. We thank the reviewers for their careful review and insightful comments. We have performed the additional works that were requested. We believe that we have carefully addressed the concerns. In doing so, the paper has been improved and strengthened. What follows is a response (shown in italics) to reviewers:

reviewer#1 wrote that “1. Grammar and spelling needs to be corrected. 2. For patients with incomplete margins of resection, what was done for these patients? Did they have further resection? What was their outcome? 3. Diagrams of the placement of the purse-string sutures and mechanical stapler would enhance the technical usefulness of this paper.”

1. Grammar and spelling needs to be corrected.

Response: We had invited a native speaker of English to polish our article. The errors in the grammar and spelling have been reduced to the maximum extent in this manuscript.

2. For patients with incomplete margins of resection, what was done for these patients?

Response: The circumferential resection margin was negative in all cases. According to specimen macro assessment of TME, the state of specimen is complete in 18 cases while nearly complete in 3 cases. Three cases with nearly complete is harvested lymph nodes as much as complete group does. We do no more than following-up, and their outcome is not apart from the other group.

3. Diagrams of the placement of the purse-string sutures and mechanical stapler would enhance the technical usefulness of this paper.

Response: We have done that by an additional Fig-E (The anastomosis is put into the anus)

reviewer#2 wrote that : “1) The introduction is too tedious. Would you focus on the purpose of your study. 2) You used inadequate capital letters, please correct these letters. 3) I think you don't need figure F. 4) Please describe the cases of neoadjuvant chemoradiation therapy among your cases. 5) I think you don't need to explain the NOTES in introduction & discussion” .

1 and 2 *The introduction is too tedious. You used inadequate capital letters, please correct these letters.*

Response: We have abbreviated the introduction according to our research topic. What is more, the inadequate capital letters has been revised.

3 *I think you don't need figure F.*

Response: In order to increase coherence of the article, we have provided with an additional Fig-E.

4 *Please describe the cases of neoadjuvant chemoradiation therapy among your cases.*

Response: Three cases in which (TNM) classifications as T3 that were confirmed by endosonography, Magnetic resonance imaging (MRI) and computed tomography (CT) examination, who all had received three cycles of chemotherapy prior to surgery. Radiotherapy followed by resection surgery was conducted as established by national guidelines. The feasibility of the operation was reappraised at two weeks after the treatment. All of three cases had experienced the symptom was reliving and the tumour was downsizing, and with limited side-effects of neoadjuvant chemotherapy.

5 I think you don't need to explain the NOTES in introduction & discussion” .

Response: We think that the NOTES is the trend of mini-surgery in the future, and hold that NOSE may be a bridge of the NOTES and the conventional laparoscopic surgery. As a result, we think that we should be explaining the NOTES in the discussion. Of course, the advice of reviewer is rational, so we deleted the explanation of NOTES from introduction.

reviewer#3 wrote that :“ 1) There is a need of English structure and grammar revision. 2) Please include pre-operative size/stage of tumors studied. 3) In material and methods you mentioned that patients with T4 tumor were excluded in the study and yet in the results such patients underwent postoperative chemotherapy. Please elaborate. 4) Why in all your patients diverting loop ileostomy closure done six months after the operation? Is this standard or were there complications?”

1. There is a need of English structure and grammar revision.

Response: We had invited a native speaker of English to polish our article. The errors in the grammar and spelling have been reduced to the maximum extent in this manuscript.

2. Please include pre-operative size/stage of tumors studied.

Response: We have done it by put additional table in our article (table 1, 3)

3 In material and methods you mentioned that patients with T4 tumor were excluded in the study and yet in the results such patients underwent postoperative chemotherapy. Please elaborate.

Response: superior to surgery, we had appraised the state of tumor by electronic endoscopic colonoscopy, pathology biopsy, endosonography (ERUS), which is called the clinical TNM (cTNM). But when turn to post-surgery, we according to Postoperative pathology Staging TNM (pTNM). So it is no wonder that the result of cTNM and pTNM is differ from each other.

4 Why in all your patients diverting loop ileostomy closure done six months after the operation? Is this standard or were there complications?”

Response: All of five patients, who underwent coloanal handsewn anastomosis with a diverting ileostomy, had received their ileostomies reversed at three to six months after the operation, based on the diagnosis of free from tumor recurrence and anastomotic stenosis, which is confirmed by electronic endoscopic colonoscopy, barium enema examination, MRI, and CT examination.

reviewer#4 wrote that : “ 1. Preoperative tumor staging should be presented. Tumor height from the anus before and after CRT. 2. How many patients had preoperative CRT? What was response to CRT? Why patients were operated 2 weeks after CRT? Please discuss this point. 3. What means nearly complete TME in 3 cases? 4. Mean operative time, blood loss and mean tumor diameter are different in results and Table 1. 5. How did you protect the region of specimen retrieval? 6. Please provide more information regarding case of anastomotic leak. Did he have ileostomy? Height

and type of anastomosis(hand sewn or mechanical)? 7. What was postoperative management of these patients? Fast track? What were criteria to start meal after the surgery? 8. What was mean follow up time after the surgery? 9. English revision is needed 10. This paper can be interested more in surgical than gastroenterological audience.”

1. Preoperative tumor staging should be presented. Tumor height from the anus before and after CRT.

Response: We have done it by put additional table in our article (table1, 3)

2. How many patients had preoperative CRT? What was response to CRT? Why patients were operated 2 weeks after CRT? Please discuss this point.

Response: Three cases had preoperative CRT. Radiotherapy followed by resection surgery was conducted as established by national guidelines.

After CRT, we reappraised the feasibility of the operation at two weeks after the treatment. All of three cases had experienced the symptom was reliving and the tumour was downsizing, and with limited side-effects of neoadjuvant chemotherapy. But, we usually perform the surgery at 3 to 4 weeks after CRT.

3. What means nearly complete TME in 3 cases?

Response: We have put forward the criterion of mesorectal specimens in our article. Nearly complete Mesorectal specimens is characteristic as intact of mesorectum >5cm, while defect of mesentery >5mm.

4. Mean operative time, blood loss and mean tumor diameter are different in results and Table 1.

Response: This is our blunder applied the standard deviation in Table 1, but applied the mean in the results. We have made them unified.

5. How did you protect the region of specimen retrieval?

Response: After the anus is fully dilated, we used a home-made anus dilator and fine silk traction sutures to evert the anus and expose the rectum, then put a protective bag into anus.

In the premise of protecting vascular nutrition, the region of specimen is fully free in the peritoneal cavity, then retrieval gentle from the anus.

6. Please provide more information regarding case of anastomotic leak. Did he have ileostomy? Height and type of anastomosis(hand sewn or)?

Response: the Case of anastomotic leak was confirmed by stools leaking from a drain. He is a 55 years old man. The Intraoperative Height of anastomosis from anal verge is 5 cm. He underwent the type of mechanical anastomosis without ileostomy. He was treated with nil per oral, decompression of the rectum by transanal drainage, and antibiotic infusion until the leak healed spontaneously. He was discharged on the 15th postoperative day (POD).

7. What was postoperative management of these patients? Fast track? What were criteria to start meal after the surgery?

Response: Most of all patients have received postoperative management on the criteria of fast track, except for six cases with Chronic diseases,such as diabetes and cardiovascular disease.

8. What was mean follow up time after the surgery?

Response: By now, the mean follow up time after the surgery for subject of the study is 14 months.

Certainly, we have collected much new data about the surgery, which may be put into future articles.

We thank the reviewers for their careful reviews and helpful suggestions, which have resulted in a much stronger manuscript that relates better to the literature on rectal cancer surgery. We would welcome the editor's suggestion on how to handle the problem, which will bring the manuscript to the recommended size.

Yours sincerely,

Hua LX

Hlx5522@126.com

Corresponding author:

Zhan WH

E-mail: FH_Han@163.com