

Dear Editor and Reviewers:

Thank you very much for your letter and advice. we appreciate you very much for their positive and constructive comments and suggestions on our manuscript entitled "Laparoscopy-assisted transanal total mesorectal excision for lower rectal cancer: A feasible and innovative technique" (Manuscript ID 58552). Those comments are all valuable and very helpful. We have studied comments carefully and have made correction which we hope meet with approval. Below we provide a point-to-point response to the comments:

Reviewer #1:

1 Clarify precise international indications to perform minimal invasive surgery, minimal surgery and no surgery (size, grading, T, N, distance from the anal margin, distance of anastomosis).

Answer: Thank you for your worthy comment. We agree with the reviewer. We have added international indications on line 19-23 on page 5. And this is also addressed in the Discussion section of the revised manuscript on page 11, line 24-28 and page 12, line 1-2.

According to the literatures many experienced experts have reached the following consensus on indications of Ta-TME surgery: At present, Ta-TME is mainly suitable for malignant tumors requiring accurate anatomy and resection of the middle and lower rectum and mesangial. The indications of Ta-TME for the treatment of malignant rectal tumors should be limited to low and medium rectal cancers, especially low rectal cancers. Ta-TME may be more advantageous for rectal cancer patients with "difficult pelvis", such as male, prostatic hypertrophy, obesity, tumor diameter of > 4 cm, rectal mesangial hypertrophy, lower anterior rectal wall tumor, pelvic stenosis, and unclear tissue plane caused by neoadjuvant radiotherapy. In addition, Ta-TME can sea and sea sphincter resection (ISR) for ultra-low rectal cancer patients. Ta-TME surgery may have indications for the treatment of colorectal benign diseases: (1) large benign tumors of the middle and lower rectum that cannot be removed locally. (2) Inflammatory bowel disease requiring rectal excision. (3) Familial adenomatous polyposis.(4) Radioactive proctitis. The contraindications of Ta-TME are those who have a history of anal stenosis or injury. At present, Ta-TME is not considered for patients with high rectal cancer.

2. Authors should specify that their data are preliminary and that the confirmation by a larger number of cases is mandatory.

Answer : Thank you for your valuable comment and information. Our data are preliminary and need to be confirmed by more cases. We have added line 10-11 on page 12.

3. The authors should clarify the treatment of surgical complications.

Answer: Thank you for your valuable advisement. Five patients had postoperative complications. One patient had anastomotic fracture, followed by Hartmann operation

(The patient developed an anastomotic rupture followed by a pelvic infection. Despite the prophylactic ileostomy, the patient developed proximal colonic retraction, which was followed by Hartman operation.) , and one had intestinal obstruction, which was confirmed by abdominal X-ray on the postoperative day 8, and he was cured by indwelling gastric tube methods. Three patients developed fever within seven days after ta-TME operation, and were diagnosed as pelvic infection. After antibiotic treatment, pelvic infection was cured. We have added line 17-25 on page 8. and line 4-23 on page 11.

Thank you very much for your detailed and earnest comments. I appreciate so much. We have revised them point by point. They are very valuable for us. Thank you.

Reviewer #2:

Comments 1 - Abdominal computed tomography, magnetic resonance imaging (MRI) of the rectum are mentioned twice in the methods.

Answer: Thank you for your worthy comment. We have deleted the part twice in the method on page 5, line 23-25.

Comments 2 - I wonder why all patients had ultrasound (as well as CT) and a barium enema (**as well as colonoscopy**)

Answer: Thank you for your valuable comment. I think our previous wording was not proper, and this part of the previous content was deleted. New content of preoperative examination has been added. All patients underwent a standard clinical examination including rigid proctoscopy, MRI of the rectum and thoracoabdominal computed tomography. Distant metastasis was excluded by imaging examination. We have deleted the part in the method on page 23-25, line 5.

Comments 3 - The mean operation time, mean intraoperative blood loss and mean time to passing of first flatus differ between the abstract and the results section of the manuscript.

Answer: Thank you very much for your detailed and earnest comments. You are right. I apologize for my negligence so much. Revised: Mean operating time was 310.0 min and mean intraoperative blood loss was 69.1 mL. The mean time to passing of first flatus was 3.1 d, mean postoperative hospital stay was 9.2 d. We corrected on page 3, line 20-22.

Comments 4 - I am alarmed to read that 'Patients experiencing unbearable pain were given analgesics.' I wonder whether the authors really mean 'unbearable' or whether this is a mistranslation. I would be concerned that pain was allowed to reach unbearable levels.

Answer: Thank you for your suggestion. We regard the use of painkillers as an intolerable standard. It is also common to use painkillers after routine surgery because the pain is unbearable. We didn't describe it clearly. Since the procedure of taTME required continuous dilation of the anus, our nursing routine used NRS scoring system

to score the postoperative pain. The patient developed 4-7 score pain that was intolerable and required analgesic medication. We added it on page 7, line 25-28 and page 8, line 1-2.

Questions 1 - Have the authors included all patients with rectal cancer seen at their department during this period? If not, now did they decide who should have the taTME procedure?

Answer: Thank you for your valuable comment. **Revised:** The patients included all the patients with low and middle rectal cancer in Aiwen Wu team of our Department, and we selected patients with mid- low rectal cancer, distance 0-8 cm from anal verge [defined by magnetic resonance imaging (MRI)], histological biopsy showing adenocarcinoma stage I-III. The patients were selected to have a detailed understanding of the taTME surgical procedure and risks, have a strong desire to retain the anus and choose the surgical method, and take risks. on page 5, line 25-28.

Questions 2 - The discussion omits to discuss the major concern about this operation, which is the concern for major complications e.g. ureteric injury. It would be interesting for the authors to describe how their technique avoids the major complications reported in other series. Could the authors improve their discussion?

Answer: Thank you for your constructive suggestion. There is also an attachment that shows the video of the operation. In the methods section, we described the surgical procedures in detail. The abdominal surgery was performed laparoscopically according to TME standard, and no damage to the ureter was found so far. The details of the operation are described on page 6, line 7-28, and page 7, line 1-19.

Questions 3 - the tumor height above the anorectal junction varies from 2cm to 8cm. 8cm seems a very high level to describe as low. We would consider anything at 3cm and lower above the anorectal junction as low. How do the authors confirm tumour height?

Answer: Thank you very much for your detailed and earnest comments. The height of the rectum is defined by the combination of rectal MRI and colonoscopy. TaTME was selected for patients with a distance of 8CM from the anus because of the patient's narrow pelvis and high BMI. We also believe that tumors distance more than 5cm are not suitable for TaTME surgery unless there are adverse factors, such as obesity, pelvic stenosis, and high BMI.

Questions 4 - The authors commented on the quality of the specimens but presented no data. Do they have these data?

Answer: Thank you very much for your detailed comments.

The quality of the specimens was assessed by the surgeon and pathology department. All the specimens were intact and achieved good quality.

We added description on page 7, line 18-19 and page 9, line 10-11.

Questions 5 - Do the authors have the data from the patients for the Wexner scores?

Answer: Thank you for your valuable question. Yes, we have. Our Department has a complete follow-up system for complications, including anal pressure measuring equipment. Most rectal patients are followed up for anal function and urogenital function. Generally speaking, LARS scoring system can better reflect the post-operative function of taTME than Wexner Scores. Therefore, we used LARS scoring system and deleted the content of Wexner. LARS (low anterior resection syndrome) questionnaire was also used. We have added LARS scale to reflect the anal function of TATME after operation on page 7, line 26-28, page 8, line 1 and page 25-26.

Questions 6 - The authors measured post-operative pain. Do they have these data?

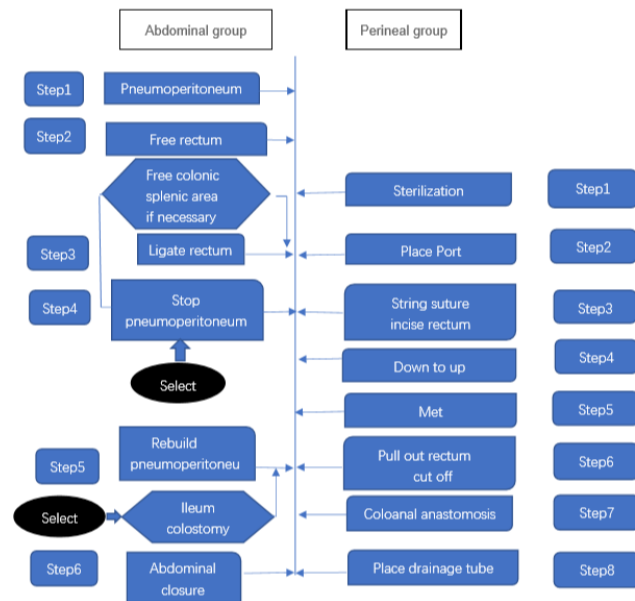
Answer: Thank you for your valuable question. Yes, we have. In Our department, VAR, VRS and NRS scoring scales were routinely used to evaluate the perioperative pain. No patients received prophylactic analgesics after operation. Twenty patients experienced slight anal pain after operation, and only 4 patients received analgesics. Our results show that the postoperative pain of TaTME is within acceptable range

Questions 7 - The discussion mentions 'The laparoscopy-assisted taTME was performed in two groups'. I did not understand what this meant and how the patients were divided into 2 groups. What were the 2 groups? How did they differ?

Answer: Thank you for your worthy comment. In our study the longest duration of Ta-TME surgery in the study was 402 minutes. The main reason is that the operation was performed by a group of doctors in the sequence of intraperitoneal - anal - abdominal operation, and the operating platform was constantly changed. However, theoretically Ta-TME can be performed by both the perineal group and the transanal group at the same time, so it is possible to reduce the operation time. The laparoscopy-assisted taTME was performed in two produce through two surgeon groups. After we adjusted the procedure , the overall operation time was reduced. We didn't make that statement clear, and we've removed it.

Figure 4.

The laparoscopy-assisted Ta-TME was divided into the peritoneal and anal surgery groups. This operation can make full use of the advantages of transabdominal and transanal surgery. Laparoscopic surgery can complete laparoscopic exploration, vascular ligation and lymph node dissection, middle and upper mesentery dissociation, while transanal surgery can complete the lower mesentery migration and specimen removal, and then complete abdominal and transanal anastomosis reconstruction. We have added Figure 4 on page 22.



Thank you very much for your detailed and earnest comments. I appreciate so much. We have revised them point by point. They are very valuable for us. Thank you.

Special thanks to you for your good comments. We hope the manuscript is now acceptable for publication in your journal.

I'm looking forward to hearing from you soon.

Your sincerely, Yingjie Li & Aiwen Wu