

Answering Reviewers Letter

Dear editors and reviewers:

Thank you very much for your letter and the comments on our paper entitled “**Colonic pouch confers better bowel function and similar postoperative outcomes compared to straight anastomosis for low rectal cancer**”. We have checked the manuscript and revised it according to the comments and have carefully revised our paper based on the comments of reviewers. The point-to-point responses to the reviewers’ comments are presented below.

We also appreciate our dear reviewers for giving us precious advices, which are important for us to improve the quality of our work.

Reviewer 1# (04965020)

It is my great honor to receive your comments about our paper, and responses are presented below. Thank you very much!

- 1) **These patients only received pre-operative chemotherapy and no radiotherapy.**

In our study, we excluded patients who receiving neoadjuvant chemoradiotherapy before surgery. Thank you!

- 2) **If patient needed post-operative Radiotherapy, these patients are excluded. Of note, CRM +ve rate is not mentioned in their manuscript between the 2 arms and there is no mention of how many patients are excluded for this reason in each arm.**

In our study, R0 resection was performed for all patients with low rectal cancer, which was confirmed by pathological analysis, so CRM for all patients is negative. At the same time, we cannot further calculate the distance of CRM, because pathological analysis did not provide us with a specific number about CRM. Thank you!

- 3) **The colonic pouch arm consists of patients with end to side anastomosis, which is a limitation as they have different functional outcomes.**

I have noticed this problem in analyzing the data. But I have read a paper (PMID:30921049 DOI: 10.1097/SLA.0000000000003249) which demonstrated that, for functional outcomes, side-to-end anastomosis and colonic pouch were similar. Therefore, patients with side-to-end anastomosis were included in our study. Thank you!

- 4) **There is a higher leak rate in the straight anastomosis group and this is going to affect the functional outcome.**

In our study, a higher leak rate in straight anastomosis group was found. But there was no significant difference between two groups ($p=0.74$). I have revised my paper according to your important suggestion. Thank you!

- 5) **The tumor and anastomotic location is different between the 2 groups which again adds to the confounding effect.**

This is a good question. There are some reasons for this question. Firstly, include patients has underwent LAR or ULAR the remaining rectal volume is very small so that it has almost no bowel storage function. Therefore, this effect maybe not affect the primary outcome. Secondly, according to some study, the lower the tumor and

anastomotic location, the worst the intestinal function. But in our study, colonic pouch has better bowel function than straight anastomosis, although colonic pouch group has a lower tumor and anastomosis location, which further confirm that colonic pouch is better in bowel function. Thank you!

- 6) **There is no multivariate analysis or matching to adjust for these confounders.**

Given it being a retrospective study, there are some confounders which maybe affect our outcome. But we have adjusted for these confounders as far as possible. Thank you!

- 7) **The difference noted by the authors are mainly after 6 months which defies conventional understanding that most functional scores are different within the first year between this 2 reconstruction options.**

Liang et al. reported that anorectal function after colonic pouch anastomosis was better than after straight anastomosis at 3 months after operation. A randomized study including 100 patients showed that bowel function following colonic pouch anastomosis was better than that after straight anastomosis, especially during the first 2 postoperative months. However, in our study, better bowel function for colonic pouch occurred in 6 months after operation, which is due to low colorectal or coloanal anastomosis that lead to severe symptoms of rectal stimulation between two groups, especially at 1 month after surgery. As the symptom of rectal stimulation subside, colonic pouch has better bowel function than straight anastomosis. Thank you!

Reviewer 2# (05123258):

**It is my great honor to be highly appraised by the reviewer of this study.
Thank you very much!**

Reviewer 3# (04088775):

It is my great honor to receive your comments about our paper, and responses are presented below. Thank you very much!

- 1) **How were patients allocated to receive pouch versus straight anastomosis surgery? Given that the pouch patients had a significantly lower tumour height and anastomosis height do you believe the groups are equally matched or selection bias may contribute to the results? Was any attempt to statistically evaluate this performed?**

In our study, the decision to construct a colonic pouch was made by the operating. surgeon based on preoperative and intraoperative findings including: 1) Sufficient colon length 2) Adequate pelvic volume 3) Normal colon bulk 4) Patient's physical condition. Include patients has underwent LAR or ULAR the remaining rectal volume is very small so that it has almost no bowel storage function. Therefore, this effect maybe not affect the primary outcome. Secondly, according to some study, the lower the tumor and anastomotic location, the worst the intestinal function. But in our study, colonic pouch has better bowel function than straight anastomosis, although

colonic pouch group has a lower tumor and anastomosis location, which further confirm that colonic pouch is better in bowel function. Given it being a retrospective study, there are some confounders which maybe affect our outcome. But we have adjusted for these confounders as far as possible. Thank you!

- 2) **Was the LARS questionnaire applied routinely at clinic visits or was this calculated retrospectively?**

Yes, we often provide LARS questionnaire for patients who underwent LAR or ULAR. Thank you!

- 3) **Would you consider your hospital a high-volume center for such surgeries? How many surgeons were approximately completing the procedures - this will affect the external validity of the results.**

Yes, our hospital, whose operation volume for rectal cancer is up to 500 cases every year, is a high-volume center for such surgery.

About 15 surgeons can complete the procedures. Thank you!

- 4) **Were any functional assessments made of the sphincter following both kinds of surgery such as manometry?**

In our study, we often give LARS questionnaire for patients with rectal cancer before surgery. Unfortunately, we do not have anal pressure measuring machine to finish manometry before surgery in our hospital. Thank you!

- 5) **The randomised study by Hallbook that the authors cite has already reported such outcomes. What does the current paper add that has not been previously reported? This should be discussed in the discussion.**

I have revised this discussion in our paper according to your important advice. Compared with randomized study Hallbook, the median tumor height above the anal verge was lower. At the same time, for bowel function, we found the difference is mainly 6 months after surgery rather than after 2 months, which may be due to lower anastomosis. In addition, we further discuss oncological outcome between two groups. Thank you!

Reviewer 4# (05101340):

It is my great honor to receive your comments about our paper, and responses are presented below. Thank you very much!

- 1) **The author should point out the limitations of this study in the discussion section.**

I have revised this discussion in our paper according to your important advice. Firstly, this is retrospective study including only 72 patients, so the conclusion needed to be further confirmed by some prospective studies in the future. Secondly, the pouch patients had a significantly lower tumor height and anastomosis height. But include patients has underwent LAR or ULAR the remaining rectal volume is very small so that it has almost no bowel storage function. Therefore, this effect maybe not affect the primary outcome. At the same time,

according to some study, the lower the tumor and anastomotic location, the worst the intestinal function. But in our study, colonic pouch has better bowel function than straight anastomosis, although colonic pouch group has a lower tumor and anastomosis location, which further confirm that colonic pouch is better in bowel function. Thank you!

- 2) **The author mention that the incidence of anastomotic leakage following colonic pouch construction and straight anastomosis was 11.4% and 16.2%, respectively. The incidence of anastomotic leakage was so high. Why?**

There are many factors affecting anastomotic leakage. The prevalence of anastomotic leakages varies from 5%-19% for colorectal or coloanal anastomosis. Distance from the anorecta junction is an independent predictive risk factor for anastomotic leakage. In our study, the median tumor height above the anal verge was 3.9 cm. Other factors include operation time (>4h), age, operative technique and so on. We have further discussed this question in our paper. Thank you!

- 3) **Most of the references are not the latest. You should included more references which was within 5 years from now.**

I have added some references which was within 5 years from now. Thank you!

- 4) **What is the definition of anterior rectal resection syndrome (ARS), the author should discuss it.**

ARS is a multidimensional bowel dysfunction syndrome consisting of fecal incontinence, urgency, frequent bowel movements, and clustering. We have further discussed this question in our paper. Thank you!

- 5) **Due to the samll size of this study, the conclusion should be downgraded.**

I have point out this limitation in our paper. Thank you!

Science editor:

It is my great honor to receive your comments about our paper, and responses are presented below. Thank you very much!

(1) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

We done as requested and submitted as a single file" 61233-the approved grant application form(s)" on the system. Thank you!

(2) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

We done as requested and submitted as a single PowerPoint file "61233-Figures.PPT" on the system. Thank you!

(3) the author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces;

Thank you for your comment. The suggested changes have been made to the revised manuscript.

(4) for statistical significance, please use superscript letters. Statistical significance is expressed as aP < 0.05, bP < 0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP < 0.05 and dP < 0.01 are used, and a third series of P values is expressed as eP < 0.05 and fP < 0.01.

Thank you for your comment. The suggested changes have been made to the revised manuscript.

Company editor-in-chief:

It is my great honor to receive your comments about our paper, and responses are presented below. Thank you very much!

(1) Before its final acceptance, the author(s) must provide the Chinese version of the ethical approval document.

We done as requested and submitted as a above file on the system.
Thank you!