18-Nov-2017

Dear editor,

Thank you for the prompt and careful review of our manuscript, which is titled "**Surgical specimen extraction via prophylactic ileostomy procedure: a minimally invasive technique for laparoscopic rectal cancer surgery**" (**Manuscript NO.: 36880**). Per your instructions, we have revised the manuscript according to the editorial and reviewers' comments and resubmit the revised version for your evaluation.

Firstly, our responses to the comments are detailed as follows, and the changes made in the text are indicated in each of the response.

Reviewer#1

Comment 1 *The main concern with this technical detail is a possible cancer cells spread in the abdominal cavity, removing the specimen through the ileostomy site. This is a theoretical risk. In the experience of the Authors, they seem did not find any problem related to intraperitoneal and skin cancer cell spread. However, the risk remains. This point should be addressed in the discussion.*

Response: The single-use incision protectors were used to protect incisions from pollution or cancer cell implantation for both procedures when taking out the surgical specimen via the incision. As the reviewer suggested, we addressed this point in the surgical procedure and discussion part.

Comment 2 *This is retrospective study, with inevitable biases. The surgeons in the initial experience did not have enough confidence with the procedure. When they used the modified technique, for sure, the Authors had more experience. So the small differences in results could be related to the increased experience in laparoscopic colorectal resection, rather than to the modified technique.*

Response: Firstly, our institution is a national cancer hospital. All of three surgeons in this study have been majored in colorectal surgery for more than 20 years. So their operation skills are undisputed. Secondly, we created the consistent surgical standards for both surgical procedures before the study. Last, and the most important is that the two surgical procedures are simultaneous so that the operative skills are well balanced in two groups.

Comment 3 *Schematic drawings describing the modified technique could be useful for an easier understanding by the readers.*

Response: As the reviewer suggested, we described the drawings in the text.

Reviewer#2 *Needs some grammatical corrections since the Summary.*

Response: As the reviewer suggested, we revised the language of our manuscript.

Reviewer#3

Comment 1 *Nevertheless, the use of the ileostomy site as specimen extraction site, has already been described, even as single-port placement site , for example in the field of inflammatory bowel disease other than rectal cancer; and this should be mentioned and referenced.*

Response: Although this procedure has been described in the field of inflammatory bowel disease, surgical specimen extraction via prophylactic ileostomy procedure has not ever been reported in rectal cancer due to the speciality of malignant tumor. However, it is shown that this procedure is safe and feasible according to our results. As the reviewer suggested, we referenced these papers in our paper.

Comment 2 *The authors should also argue about their choice of using a "vertical" incision in the lower abdomen as specimen extraction in the standard group. Several surgeons use horizontal incisions instead, that are supposed to give advantages in terms of pain control and prevention of postoperative incisional hernia, other than offering cosmetic benefits. This should be at least discussed by authors in the discussion section. The theoretical possibility of achieving better outcomes with horizontal lower quadrants incision might mitigate the benefits reported from the "ileostomy extraction" site.*

Response: Experience is acquired through continuous learning and improvement. We have also noticed the advantages of using the horizontal incision. So we have also extracted the surgical specimen via the horizontal incision and surgical scar incision for patients with operation history in the in the lower abdomen in our study. As the reviewer suggested, we mentioned the vertical and horizontal incision simultaneously in our paper.

Comment 3 T*his paper might be probably more appropriate for a surgical journal; in fact, I am not convinced that the topic completely falls into the aim of WJG.*

Response: The World Journal of Gastroenterology (WJG) is an excellent academic journal that publishes review articles and articles describing original research (basic or clinical) in the fields of gastroenterology, hepatology, gastrointestinal surgery, and gastrointestinal endoscopy. In our paper, we introduce an innovative surgical procedure named the 'surgical specimen extraction via prophylactic ileostomy procedure'. So we believe that our manuscript is in line with the magazine's acceptance.

Reviewer#4

Comment 1 *As I mentioned, the feasibility of this procedure is already reported in many previous published paper. For example, laparoscopic total colectomy for*

ulcerative colitis is now reported and the surgical specimens are extracted from the abdomen via prophylactic ileostomy.

Response: As mentioned by the No.3 reviewer, although this procedure has been described in the field of inflammatory bowel disease, surgical specimen extraction via prophylactic ileostomy procedure has not ever been reported in rectal cancer due to the speciality of malignant tumor. Because the tumor implantation and residual tumor are all problems that cannot be neglected. As the reviewer suggested, we referenced relevant papers in our paper.

Comment 2 *Many patient and surgery related factors are compared with statistical analysis and seems to be fair. However, author just compared the disease free survival and overall survival. In this type of report, I feel it would be more important to focus on the type of recurrence. Was there any local recurrence in the surgical site of ileostomy than the control group? I assume that the surgical specimen, especially the cancer, was squeezed out from the small hole of ileostomy site. I am more interested if this procedure creates more local recurrence or spread the cancer cells easily and have more metastasis, and so on. All the factors you are showing are expected data and not surprising, novel.*

Response: In the experimental group, we have emphasized that the ileostomy incision shouldn't be too small so that the specimen is squeezed. When suturing the skin and intestinal wall, the stoma can be constructed to avoid retraction (Figure 1A). The single-use incision protectors were used to protect incisions from pollution or cancer cell implantation for both procedures when taking out the surgical specimen via the incision. We have scanned our database, no patients suffered from local recurrence in the specimen extraction sites in both groups. As the reviewer suggested, we have modified the corresponding contents in text.

Comment 3 *There are 11 patients in total with ASA score 4. Did these patients underwent same kind of surgery? If they are in ASA 4, I assume that it would be very limited surgery.*

Response: We recorded the ASA score based on the descriptions of anesthetists. However, after rechecking the medical records of this 11 patients described by our surgeons, we didn't think that the situations were so terrible. Because all of these patients merely suffered from intestinal obstructions and they had strong surgical intentions. In fact, they underwent same kind of surgery.

Comment 4 *Eight patients had re-operation, why? As the author mentioned, anastomosis leakage is the most critical postoperative complication and this would be the main cause of the re-operation. However, that is the reason why they created ileostomy and they should state the reason of the re-operation even this is not significant difference between the two procedures.*

Response: Three patients underwent reestablishment of stoma because of stoma necrosis, and five patients underwent debridement and suturing procedure because of

incision infection. As the reviewer suggested, we have added the corresponding contents in text.

Comment 5 *Author pointed out that postoperative leakage cannot be prevented by rectal tube. However, there is a meta-analysis (Shigeta et al Surg Endosc. 2016) that rectal tube is effective to prevent the leakage and re-operation. This paper seems to be published after the cited paper.*
Response: These two papers included different studies so the conclusions may be biased. What we wanted to emphasized was that postoperative AL cannot be reliably prevented by placement of a rectal tube only due to the special institutions in our country. So the prophylactic ileostomy procedure was essential. In fact, rectal cancer patients with neoadjuvant chemoradiotherapy are still placed a rectal rube after accept prophylactic ileostomy procedure.

Comment 6 *Are you using the wound protector or surgical ring drape, or any kind of material to protect the wound from the infection or local recurrence? This fact should be stated.*
Response: As above mentioned, the single-use incision protectors were used to protect incisions from pollution or cancer cell implantation for both procedures when taking out the surgical specimen via the incision. As the reviewer suggested, we address this point in the surgical procedure and discussion part.

Secondly, Wang P and Liang JW make equal contributions to this work. So what I would like to emphasize is that both of them should be considered as the co-first authors, and all authors have no conflicts of interest to declare.

Finally, we thank all reviewers again for their positive and constructive comments and suggestions. We hope that these revisions have improved the manuscript and will make it acceptable for publication in ***WJG*.**

If there are any questions, please let us know as soon as possible.

Thank you for your consideration and we are looking forward to your reply.

Sincerely,

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