

Peer Review File

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Reviewer Comments

General comments:

- the study is based on the subjective perception of patients on feeling abdominal distension. This method is affected by many factors; pain threshold, expressive ability of patients, social and educational level of patients (which is not mentioned in demographics),...etc. Abdominal distension evaluation should be combined, subjective, and objective (like audible intestinal sounds, the passage of flatus, and defecation) not solely dependent of patient perception. Please explain!

Reply: Firstly, thanks to you for your review. As defined by Lacy et al. (PMID:32246999) in their article, abdominal bloating is the subjective sensation of gassiness, trapped gas, or a feeling of pressure or being distended without obvious visible distension. Patients also describe a sense of fullness or pressure, which can occur anywhere in the abdomen (epigastric, mid, lower or throughout). Abdominal distension is the objective physical manifestation of an increase in abdominal girth. Patients commonly describe how they look “like a balloon” or “like I’ m pregnan” . We refer to this article without distinguishing too clearly between bloating and abdominal distention. In addition, Our study defined abdominal distension as a subjective sensation of gassiness, trapped gas, or a feeling of pressure or being distended without obviously visible distension. The follow-up study was based on this definition

- Some terms need to be updated: Elevated body mass index—not a proper term. It should be replaced by other terms like overweight or obese patients.

Reply: We are sorry for using improper term and we have modified the original text and marked it in red colour.

Changes in the text: “A previous study revealed that factors for ileus post-cystectomy include obesity and older age” (page 3, lines 48).

- Line 81: 35 patients occurred in abdominal distension after surgery?! What is that sentence supposed to mean ?! Need to rephrase it!

Reply: We apologize for our inaccurate description and we have changed this as “Postoperative abdominal distension occurred in 35 patients”.

Changes in the text: “Postoperative abdominal distension occurred in 35 patients.” (page 5, lines 89-90)

Special comments:

Methods:

- Exclusion criteria: authors excluded those with preoperative intestinal lesions, and I agree with them. However, they include those with a history of abdominal surgery which has a direct impact on postoperative abdominal distension. That will introduce a selection bias. Explain, please?!

Reply: We appreciate your thoughtful comments. In this study, some of the patients had a history of abdominal surgery, and reviewing the relevant literature we found that the conclusions on the effect of a history of abdominal surgery on the recovery of intestinal function

in patients after surgery were mixed, for example, Rybakov et al. (PMID:28921903) included a history of abdominal surgery in their study and confirmed it as an independent risk factor in the analysis of risk factors for postoperative intestinal obstruction in colorectal cancer; on the contrary, Law et al. (PMID:15624064) confirmed that patients with a prior history of abdominal surgery were not worse in terms of bowel obstruction, complication rates, etc.; therefore, we included the presence or absence of a patient's history of abdominal surgery in our study analysis and further investigated the role of abdominal surgery history in the occurrence of outcome using univariate/multivariable logistic regression analysis.

- Authors didn't mention the version of the program they used for statistical analysis.

Reply: We are sorry for the vague description and we have further clarified the version of the statistical analysis program in the text.

Changes in the text: "In this study, R x64 4.1.2 statistical software was used to process the data." (page 4, lines 78)

Results:

- Table (1): Authors should mention the P(value) of each criterion between 2 arms of the baseline characteristics to know if there were significant differences between 2 arms in their demographics with potential impact on postoperative outcome; abdominal distension. The graph is not enough though!

Reply: Thank you for your valued advice. We have added the p-values of the variables in the baseline characteristics to Table (1). Besides, we described the results briefly in the original text.

Changes in the text: "No significant differences were found between the two groups in terms of demographics such as age and gender" (page 5, lines 90-91) and Table (1).

- Since abdominal distension is a subjective diagnosis, so social status should be analyzed in demographics as it affects the expression ability of patients.

Reply: Thank you for your valued advice. We further investigated the educational level of the patients and divided them into the group with completed high school and the group without completed high school for analysis, and the results showed that there was no statistical difference in the educational level of the two groups.

Changes in the text: Table (1).

- According to ERAS cystectomy protocol (Cerantola, Yannick et al. 2013); nasogastric tube shouldn't be used either pre or intraoperatively. If it's needed, early removal is advisable. So preoperative stomach tube insertion is not advisable anymore to enhance postoperative GIT recovery time. There is much literature found out there is no association between implementation of ERAS protocol items including (Nasogastric tube insertion) and incidence of postoperative ileus. I don't know why preoperative stomach tube insertion was done in some patients (n=38)?!

Reply: The routine use of stomach tube insertion after radical cystectomy has declined over the past 20 years, but it is still left in place in some large centers, such as the Peking University First Hospital team's study titled "Laparoscopic Radical Cystectomy With Extracorporeal Neobladder: Our Initial Experience" (PMID:30468754), gastrointestinal decompression is routinely left in place before surgery; not only because it can aspirate fluid and gas from the

gastrointestinal tract to facilitate intraoperative exposure of the field of view, but also to reduce intestinal pressure after surgery and facilitate anastomotic recovery; more importantly, the placement of a gastric tube can prevent some fatal complications. For example, there was a case of postoperative intestinal obstruction in our center, but a fatal aspiration occurred before nasogastric tube could be placed.

- Where is Charlson comorbidity index for both arms. Is there difference?

Reply: We particularly appreciate this comment. However, we analyzed information related to gender, age, diabetes mellitus, cardiovascular disease, and hypertension in the two groups at baseline characteristics and did not find significant differences. Therefore, we did not further calculate the Charlson comorbidity index.

- Again, authors should exclude the patients with previous history of abdominal surgery from comparison because its logic to have higher odds of abdominal distension in these subgroups.

Reply: We included the patients with previous history of abdominal surgery in our study analysis and would like to further investigate the role of abdominal surgery history in the occurrence of outcome using univariate/multivariable logistic regression analysis.

- 2nd paragraph of results section should be rephrased!

Reply: We thank the reviewer for noting this point and we have modified the text.

Changes in the text: “Among these, 28 of 56 patients who underwent postoperative water fasting time ≥ 4 days experienced abdominal distension (P-value = $3.3e-09$), 18 of 38 patients who underwent the stomach tube insertion before operation had abdominal distension (P-value = $7.55e-05$), 12 of 29 patients who experienced abdominal surgery before occurred abdominal distension (P-value = 0.008), and 24 of 78 patients who underwent a laparoscopic operation developed abdominal distension (P-value = 0.027), the hypergeometric test indicated the occurrence of these outcomes were not random events (Fig. 1B).” (page 5, lines 101-106)

- Upon which basic, Authors choose cutoff value for postoperative fluid fasting time is 4 hours? why not 3, or 5 hours?!

Reply: We chose an optimal cutoff value of 4 days for the duration of water fasting because we found in our statistical analysis that the most significant differences in the occurrence of the outcome variables between the 2 arms of patients occurred when the cutoff value was 4 days.

- What is your explanation that authors found a significant difference in subgroup of patients (n=24) having laparoscopic approach to get postoperative abdominal distension and the authors didn't find the same difference in subgroup of patients (n=11) managed by robotic approach?

Reply: We think this is because robotic approach provides a clearer field of view with increased magnification, which facilitates precise identification of important tissues such as nerves, blood vessels, and fascia, and it also filters involuntary hand tremors of the operator during operation, reducing the occurrence of bleeding and misinjury during cystectomy. Intraoperative trauma is relatively small, and postoperative gastrointestinal recovery is faster.

- Authors should do subgroup analysis of those who suffered from postoperative intestinal obstruction (Postoperative day number..., paralytic versus ischemic, and their management (conservative vs surgical).

Reply: We appreciate your constructive comments! It is indeed necessary to analyze information about patients with POI. So we performed a subgroup analysis and describe the

results in the text.

Changes in the text: “Among all patients, 7 patients developed POI, all of them had mechanical intestinal obstruction, and the average time of appearance was the 10th postoperative day. One patient died due to aspiration without gastrointestinal decompression, one patient underwent intestinal adhesion release, and the remaining five patients were discharged with gastrointestinal decompression combined with traditional Chinese medicine. The mean number of postoperative hospital days was longer in the patient with intestinal obstruction than in the other patients (16.71 vs. 10.42; $P=0.095$); we considered the difference was not statistically significant because the number of patients was small.” (page 7, lines 134-142)

- Last paragraph of result section, its logic to find the patients who suffered from early abdominal distension that may progress to develop intestinal obstruction. Similarly, its unlikely for those who didn't suffer from early abdominal distension to develop intestinal obstruction. Actually, abdominal distension is an early sign of a potential intestinal obstruction later on. So, I don't get what is the point of this part or even to be tabulated (table 3).

Reply: The last paragraph is to show that the occurrence of abdominal distention after cystectomy significantly increases the length of hospital stay and the occurrence of bowel obstruction, thus increasing the cost, pain, and accidents for the patient. Therefore, we should pay attention to the risk factors associated with abdominal distention in order to reduce the occurrence of abdominal distention.

Discussion:

Line 127; Anticoagulant therapy was not significantly associated with POI either on univariate or multivariate analysis. Check supplementary table 5 in the cited article.

Reply: We are grateful to the reviewer for noting this point and we further verified. We found that in the last paragraph of the original results of the cited literature, the authors describe this sentence: “Regarding the occurrence of paralytic ileus, age at treatment, anticoagulant therapy, OFA, and time to ureteral stent removal were statistically significant in univariable analysis.” But the p-value for anticoagulation therapy is 0.171. We therefore drop the quote from the article and replace the sentence with the following: “Many factors could increase the incidence of POI, including male sex, infection, and increased intravenous fluids.”

Changes in the text: “Many factors could increase the incidence of POI, including male sex, infection, and increased intravenous fluids” (page 7, lines 152)

Conclusion:

The first sentence, the authors proposed the omission of a stomach tube as postoperative management, however, the methodology mentioned that a stomach tube was inserted preoperatively. So, is it preoperative or postoperative insertion?

Reply: We usually leave the stomach tube in place and perform gastrointestinal decompression on the morning of surgery; they are removed after postoperative recovery of gastrointestinal function. Therefore, we changed postoperative to preoperative in the original text, and for high-risk patients, a stomach tube is feasible for high-risk patients and should be removed as soon as possible after recovery of postoperative intestinal function.

Changes in the text: “We recommend that the stomach tube should not be routinely used in the preoperative management of the patient undergoing RC. In addition, we provide a model to

predict the probability of abdominal distention after RC so that physicians can take preventive measures in advance for high-risk patients. A stomach tube is feasible for high-risk patient and should be removed as soon as possible after recovery of postoperative intestinal function.” (page 9, lines 191-197)