Peer Review File

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Reviewer Comments

In this paper, Zhu et al. explore the role of preoperative biliary drainage (PBD) in their single center cohort of 148 patients. The authors demonstrate an increased incidence of intraabdominal infections with PBD. Furthermore, a drainage to resection interval of more than 2 weeks resulted in increased rates of positive drain cultures.
I'd like to congratulate the authors on their work and the tenacity it takes to maintain and analyze clinical databases and would like to thank them for allowing me to review their data. The paper is overall well-presented and is a valuable addition to the literature as it provides insight into the microbiology and time course that can lead to patients developing complications after PD + PBD. There are some minor concerns I have listed below. Once they have been addressed, I believe the paper is suitable for publication.

General Questions:
Introduction:
- Line 23: "…and short-term group due to PBD duration" should be corrected to "…and short-term group according to PBD duration"
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 1, line 23)

- Line 26: "bacteria" ? "bacterial"
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 1, line 27)

- Line 59: would change to "reduced, which is largely…"
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 2, line 58-59)

- Line 67: "tends to significantly affect multiple organ functions puts patients at higher risk"
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 2, line 67)

- Line 82: "restore the balance of the intestinal flora"
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 2, line 82)

Methods:

- Lines 103 -106: The inclusion of 148/368 patients, ie 40% of patients raises some concern of selection bias. The authors should include the number of patients who were excluded for the various listed reasons

Reply: A total of 220 patients were excluded. Among them, 216 had no preoperative obstructive jaundice, 2 underwent simultaneous hepatic resection, 1 underwent total pancreatectomy, and 1 had incomplete medical records.

Changes in the text: we added the details into Methods and marked it with red. (see Page 3, line 106-109)

- Line 117: …when ENBD failed

Reply: Thank you for the correction.

Changes in the text: we have modified our text as advised and marked it with red. (see Page 3, line 121)

- Line 141: Do all patients independent of their postoperative course get a CT postoperatively?

Reply: Regular contrast-enhanced abdominal CT was used to monitor patients postoperatively. We use CT to assess whether the drainage tube could be removed and the presence or absence of aneurysm in the surgical area.

Changes in the text: None.

- Line 171-72: Do patients with fever, positive cultures and leukocytosis get a CT scan to confirm the presence of an intraabdominal abscess or is the diagnosis of a deep SSI made based on the above criteria only? If so, I would acknowledge the potential for false positives with this approach as this could mean that patients undergoing PBD solely have higher peritoneal fluid cultures in the absence of overt organ space SSI

Reply: We did not use CT scan to make a diagnosis of deep SSI. SSI was diagnosed according to the guidelines. Though patients undergoing PBD solely have higher peritoneal fluid cultures, positive peritoneal fluid cultures alone could not prove the presence of deep SSI.

Changes in the text: None.

Results:

- Line 200: correct to “patients experiencing infectious complications”

Reply: Thank you for the correction.

Changes in the text: we have modified our text as advised and marked it with red. (see Page 5, line 204)

Discussion:

- Lines 308-11: Please clarify the DROP trial here in more detail. The study compared the complications rates of surgery first versus PBD followed by surgery. The study was not sufficiently powered to demonstrate differences in individual morbidities, and only the composite morbidity of ERCP+surgery was elevated compared to surgery alone. For your paper specifically, I would also keep in mind that most of the western centers use ERCP rather than ENBD, which the authors argue

to have a lower complication rate as compared to ERCP.
Reply: The RCT by Van Der Gaag et al. compared preoperative biliary drainage with surgery alone for patients with obstructive jaundice and a bilirubin level less than 250 μmol/L. They found that the rates of serious complications was significantly higher in the biliary-drainage group. The study also showed that preoperative biliary drainage did not necessarily prolong the length of the hospital stay. In this RCT, plastic stents were placed by ERCP. In our study, nasobiliary drains were placed through ERCP in patients receiving ENBD. The essential difference between us is placing plastic stents or nasobiliary drains. We cited the article here because we got a cut-off score of 250 μmol/L from this RCT. We believed that the results of the high-quality article may be instructive for our research.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 8, line 314-319)

- A recent paper drawing from a large North American dataset (PMID: 34538739) asks a very similar question to your data and provides a more up to date view as compared to reference #38 from 2009. Could you compare and contrast notable differences?
Reply: Our data suggested that PBD could increase the incidence of postoperative abdominal infection. But it did not influence 30-day mortality or major morbidity, which was consistent with the recent paper. The main difference between our work is the type of postoperative complication due to PBD. However, we shared a similar opinion that selective PBD should be performed in a group of patients who could benefit from it. Both of our study and the recent paper were aimed to identify this group of patients.
Changes in the text: we have added the finding of the recent paper and marked it with red. (see Page 8, line 303-305)

- Line 399: correct to “selection bias”
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 10, line 406)

- The 2 week mark is an important takeaway from the paper, however, profoundly cholestatic or cholangitic patients do not often allow for a quick turnaround from PBD to the operating room. Can the authors expand on or propose a strategy on how to select patients that can be taken to OR more quickly; which ones warrant delay?
Reply: Thank you for the constructive question. There were large individual differences in patients with obstructive jaundice. In our study, the majority of patients had a TB≤250 μmol/L. Based on data of these patients, we found that drainage duration more than 2 weeks could increase the incidence of infection. At least, patients with TB≤250 μmol/L and no cholangitis were more suitable for surgery within 2 weeks. However, it was inevitable that there was some biases within the results. The conclusion may only be applicable to those patients with mild to moderate jaundice. To answer the question better, the sample size should be expanded. Especially, more patients with preoperative severe jaundice should be included to refine the conclusion. Moreover, the extent of bilirubin decline could be measured and may serve as an indicator of surgical treatment.
Changes in the text: none.

Tables:
Table 1
- Correct “Diabetic Mellitus” to “Diabetes mellitus”
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 16, Table 1)

- Albumin for the total cohort seems to have a wrong decimal point
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 16, Table 1)

- Platelet is missing a “t”
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 16, Table 1)

- Major complications per CD – some are bolded – why?
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 17, Table 1)

Table 2
- List currency for expenses
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 18, Table 2)

Table 3
- Table legend missing to explain range of values provided
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 19, Table 3)

Table 4
- Please provide percentages similar to Table 1 or explain why they aren’t listed
Reply: Thank you for the correction.
Changes in the text: we have modified our text as advised and marked it with red. (see Page 20, Table 4)

Table 5
- Remove decimal from blood loss in short-term
Reply: Thank you for the correction.

Changes in the text: we have modified our text as advised and marked it with red. (see Page 21, Table 5)