

Nov.28, 2019

Jie Wang

Science Editor, Editorial Office

World Journal of Gastroenterology

Dear Professor Wang,

Thank you very much for your letter dated Nov. 27, 2019 regarding our inviting manuscript (Ms 51625) entitled “The influence of bile contamination on the infectious complications of patients who undergo pancreaticoduodenectomy after preoperative biliary drainage”.

We greatly appreciate the comments made by the reviewers, which helped us to improve our manuscript considerably. We revised the manuscript in accordance with each reviewer’s suggestions. Point-by-point responses to these suggestions can be found on the following pages.

We thank the reviewers for their helpful commentary and hope that the revised version of our manuscript is now acceptable for publication in the World Journal of Gastroenterology. We certify that this manuscript is original, has not been published previously, and is not under consideration by another journal.

Thank you for re-considering our manuscript.

Respectfully yours,

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## Response to peer reviewer comments:

We took your suggestions into account during the revision of our manuscript. Please find point-by-point responses to your comments below. All changes that were made to the manuscript are in **underlined**.

### Reviewer 03552376

#### Comments

1. did authors detect the total bilirubin of each patient? Is the level of bilirubin associated with POPF?  
preoperative biliary drainage is associated with bile contamination. in patients with high total bilirubin, did preoperative biliary drainage also relate with bile contamination?

Thank you for this comment. Our database included the total bilirubin of each patient. In response to your suggestion, we re-analyze the association with high bilirubin level and POPF. The 1283 patients (40.5%) with high total bilirubin level ( $1.0\text{g/dl} \leq$ ) were compared with the 1886 patients (59.5%) with normal total bilirubin level ( $1.0\text{g/dl} >$ ) for incidence of all POPF and clinical relevant POPF (Grade B/C). There was no significant difference for all POPF (37.8% vs. 39.5%,  $p=0.55$ ) or clinical relevant POPF (21.4% vs. 20.6%,  $p=0.82$ ) between the patients with high and normal total bilirubin levels. Among the patients with high total bilirubin level ( $1.0\text{g/dl} \leq$ ), 966 patients (81.9%) were received preoperative biliary drainage. There was a significant difference ( $p<0.0001$ ) in rate of bile contamination between the patients with preoperative biliary drainage (34.8%) and the patients without preoperative biliary drainage (6.6%). We incorporated some part of this analysis into the Results section.

2. did bile contamination relate with contamination of pancreatic juice. did the authors detect the bacteria in pancreatic juice?

We agree with your idea that the relation of bile and pancreatic juice contamination is interesting. However, it is technically difficult to test the bacteria in pancreatic juice before or during operation in almost patients. Unfortunately, we could not collect the data of the bacteria in pancreatic juice in this study.

3. the size of pancreatic duct is significantly associated with POPF. the authors did not include the size of pancreatic duct.

Thank you for this thoughtful comment. We understand the size of pancreatic duct is

one of the important factor for POPF and collected the data of duct size. There was a significant difference ( $p<0.0001$ ) in the pancreatic duct size between the patients with clinical relevant POPF ( $2.8\pm0.07$  mm) and the patients without clinical relevant POPF ( $4.01\pm0.04$  mm) in this study.

On the other hand, pancreatic texture (soft or hard pancreas) is also the risk factor for POPF and is strongly related with the size of pancreatic duct. As we consider the pancreatic texture (soft pancreas) and size of pancreatic duct as confounding factor, we selected the soft pancreas as pancreatic factor in this analysis (Table 4).

### **Reviewer 03506087**

#### Comments

1. Congrats for the excellent study based on a national database! The authors retrospectively reviewed data of 4101 patients who underwent PD. Preoperative biliary drainage was performed in 1964 patients. The authors were able to demonstrate a strong correlation between bile contamination and postoperative pancreatic fistula Grade B/C, wound and catheter infection. Overall, this is well-designed, scitifically analyzed, and well-written paper. I have no further comments.

We thank you for these supportive and insightful comments, which encourage us to continue further efforts.

We thank the reviewers for their helpful and insightful comments, and for the careful attention they paid our manuscript.