

ANSWERING REVIEWERS



August 14, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4586-review.doc).

Title: Endoscopic papillary large balloon dilation in patients with perampullary diverticula

Author: Kook Hyun Kim, Tae Nyeun Kim

Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

We really appreciate your comprehensive review of this article. We fully agree with the reviewers' detailed comments. We have made some corrections and clarifications in the manuscript after going over the reviewers' comments. The changes are summarized below:

- 1) **Reviewers' comments:** In the abstract, "CBD >10mm" is the inclusion criterium, in the methods "CBD stone >10mm". Please clarify

Corrections: "CBD \geq 10mm" was changed into "common bile duct **stones** (\geq 10 mm)"

- 2) **Reviewers' comments:** Figure 1: For the purpose of the study, it would be more illustrative to show an example of balloon dilatation at the edge or within a diverticulum

Corrections: The previous endoscopic images and cholangiograms (Figure 1) were replaced into other patient's illustrations, where major papilla is located inside the diverticulum. Therefore, detailed legends were changed accordingly.

- 3) **Reviewers' comments:** Table 3 and 4: Please explain the subtypes in the table or use the description "papilla within diverticulum", papilla at edge of diverticulum" or "papilla outside

diverticulum”.

Corrections: In the Table 3, 4 and 6, description of subtypes such as type 1, type 2 and type 3 was clarified as followings: Type 1 is defined as when major papilla is located inside the diverticulum, Type 2, in the margin of the diverticulum and Type 3, outside the diverticulum

4) Reviewers' main comments

4-1) **Reviewer's comments (38617):** EPLBD with and without ES should be separately evaluated in this study, and the authors should make some discussions on the difference between EPLBD with and without ES....

4-2) **Reviewer's comments (35978):** Were there differences in outcome between patients who had balloon dilatation alone or sphincterotomy followed by balloon dilatation? The necessity of sphincterotomy before balloon dilatation might be discussed.

4-3) **Reviewer's comments (39316):** There is a major -study design- drawback that does not allow the publication of the study. EPLBD with or without limited ES are two quiet different interventions, and there is a strong possibility that the study results are influenced by this inappropriate combination.

Corrections: As the reviewers indicated, EPLBD with and without ES according to the presence of PAD were separately evaluated in this study. However, there was no significant difference between two groups. And the necessity of ES prior to EPLBD was discussed in the manuscript. The details are described as followings:

(I) We further analyzed our data and described the results of clinical outcomes and complications between EPLBD-ES and EPLBD+ES according to the presence of PAD. Those results are presented in the Table 2 and 5, and they are described in the abstract of page 2 and in the results of page 6. In addition, two additional references (References 21 and 22) are incorporated in the reference of page 15.

At page 2 (Abstract),

a) Overall stone removal rates, complete stone removal rates in the first session and the use of mechanical lithotripsy

were not significantly different between EPLBD+ES and EPLBD alone in patients with PAD [96.6% vs 97.1%; 72.9% vs 88.2%; and 5.1% vs 0%, respectively].

b) No significant differences with respect to the rates of pancreatitis, perforation, and bleeding were observed between EPLBD+ES and EPLBD alone in the PAD group [3.4% vs 14.7%, $p = 0.095$; 0% vs 0%; and 3.4% vs 8.8%, $p = 0.351$, respectively].

At page 6 (RESULTS),

a) When the PAD and Non-PAD groups were further divided by EPLBD+ES or EPLBD-ES, no significant differences with respect to overall stone removal rates, stone removal rates in the first session or needs for mechanical lithotripsy were observed [57/59 (96.6%) vs 33/34 (97.1%), $p = 1.000$; 43/59 (72.9%) vs 30/34 (88.2%), $p = 0.016$; and 3/59 (5.1%) vs 0 (0%), $p = 0.297$, respectively] (Table 2).

b) When complications of EPLBD with or without ES were compared in the PAD group, the rates of pancreatitis, perforation, and bleeding were not found to differ significantly [2/59 (3.4%) vs 5/34 (14.7%), $p = 0.095$; 0% vs 0%; and 2/59 (3.4%) vs 3/34 (8.8%), $p = 0.351$, respectively].

(II) We made some discussions about difference between EPLBD+ES and EPLBD alone in patients the PAD. The explanation or opinions about our findings are carefully presented in the second paragraph of page 8 and in the first paragraph of page 9.

At page 8,

a) Furthermore, when EPLBD alone was performed, bile duct stones were successfully removed without mechanical lithotripsy in the PAD group. However, when EPLBD+ES was applied, mechanical lithotripsy was required for three patients (5.1%) in the PAD group, although this did not represent a significant difference.

b) These findings suggest that EPLBD-ES could be an appropriate technique for CBD stone retrieval in the presence of PAD, as long as safety is guaranteed.

At page 9,

a) Although the pathogenesis of pancreatitis following EPLBD is not clear, it is suggested that ES prior to EPLBD could prevent potential injury of the main pancreatic duct, because ES can steer the direction of balloon dilation toward the CBD and minimize the pressure overload on the pancreatic orifice^[8,20,20-2]. However, the recent studies have

proposed that EPLBD alone can be an alternative for the removal of large stones^[20-22].

b) The relatively high percentage of older patients in this study might be associated with the observed lower incidence of pancreatitis^[21]. In particular, it has been suggested that longstanding CBD stones can cause gradual bile duct dilation, and subsequently, a patulous ampullary orifice^[22]. In a recent study, a very low incidence of pancreatitis (1.4%) was observed following EPLBD in patients with recurrent CBD stones after ES, which is similar to the pathophysiology of the process of patulous ampulla^[27].

We hope the revised manuscript will better meet the requirements from reviewers.

Thank you again for your constructive review and comments.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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