

Format for ANSWERING REVIEWERS



March 16, 2015

Dear Editor,

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

Title: Pancreaticobiliary reflux as a high-risk factor for biliary malignancy: clinical features and diagnostic advancements.

Author: Reiji Sugita

Name of Journal: World Journal of Hepatology

ESPS Manuscript NO: 16694-edited

Response to reviewer's comments

R1 (2860712)

- 1 Author should better describe the clinical background of the biliopancreatic reflux (i.e. symptoms at presentation, rate of cholangitis,) and its relationship with the type of reflux.-----Accordingly, I added this information.
- 2 The results obtained using the technique of time-spatial labeling inversion pulse should be described in detail. After all, this paragraf is the core of the work.-----Accordingly, I added this information.
- 3 The text is redundant.-----Accordingly, I have changed the manuscript.

R2 (2733636)

In general, the information in the paper is adequate for an editorial. However, in most instances references and evidence-based information is lacking. It seems most information is only expert opinion.

- 1 The language used in the manuscript should be improved.-----I ask an editing service to brush up my manuscript.
- 2 The authors state that “ can even cause the expression of carcinogenetic substances in the biliary system”. Do they have any reference for this information? A clear explanation is needed.-----Accordingly, I added references.
- 3 “PBR may lead to dilatation of the biliary tree”. What is the evidence behind this stataement? This seems true but the authors sould provide referenec. A reference from 1969 may not provide complete infromation.-----Accordingly, I added references to my manuscript.
- 4 “Pancreatic juice frequently refluxed into the biliary duct in PBM patients, which results in a high incidence of cancer in the biliary tract. Although PBM patients both with and without choledochal cysts

- are at risk for biliary malignancies, both are different in term of the site of malignancy in the biliary tract.” Those information required reference.-----Accordingly, I added references to my manuscript.
- 5 “Pancreaticobiliary maljunction without choledochal cysts” How do those PBM patients without choledochal cysts present in clinical practice? A little more information would do better for the general reader.----I have changed my manuscript according to your suggestion.
 - 6 In there any data regarding the utility of the new magnetic resonance-based method (time-SLIP) to visualize pancreatic juice movement in pancreaticobiliary junction? Or has it only been studied in patients without PBM? what is the future implication of this new imaging technique in management of patients with PBM or pancreaticobiliary reflux?----I have changed my manuscript according to your suggestion.
 - 7 Therapy section needs evidence based information. There are no references.-----Accordingly, I added references to my manuscript.

R3 (2860653)

1The current review seems too brief as a topic, so many important paper were not cited in the review.-----Accordingly, I added references to my manuscript.

2To include more evidence regarding link of biliary/pancreatic hypertension with malignancies development.-----To best my knowledge, unfortunately, I cannot find out relationship with biliary/pancreatic hypertension and malignant development,.

3To include evidence/discussion regarding US as important imaging modality (with illustration) and EUS protocols, including interventional diagnosis, in vivo imaging, novel advancement.-----I added this information and a figure of EUS.

4Pay more attention to discussion of clinical management.----I added clinical management to my manuscript according to your suggestion.

5Surgical issues might be reviewed more extensive (e.g.. statement, however some surgeons propose excision of extrahepatic bile duct together with gallbladder).As well the postoperative rehabilitation.-----I added surgical issue to my manuscript according to your suggestion.

6Discuss US data and questionnaires and molecular biomarkers as a potential for screening and possible measures for prevention.-----I added information about screening and possible measures for prevention to my manuscript.

7Effort to suggest comprehensive algorithms would be appreciated.----I made a figure according to your suggestion.-----I made a chart to understand easily.

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

Sincerely yours,

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