

Response Letter

Dear Editor:

Thank you for giving us an opportunity to revise this manuscript (53970). Reviewer comments and your comments are all valuable and very helpful for revising and improving our paper. We have considered these comments carefully during the revision. A point-to-point response to reviewer's and yours comments is listed below. Relevant changes have been made to the manuscript accordingly, and have been highlighted in yellow. These changes will not influence the content and framework of the paper. We appreciate for the editors and reviewers' warm work earnestly. And we hope the revised version of the manuscript will meet with approval.

Once again, thank you very much for your comments and suggestions.

We look forward to hearing from you soon.

Sincerely yours,

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Replies to editor and reviewers

Title: Preliminary experience of hybrid endoscopic submucosal dissection by duodenoscope for recurrent laterally spreading papillary lesions

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Manuscript No: 53970

Replies to reviewers

Reviewer #1:

1. If the procedures and the postinterventional course were completely uneventful, why did the patients stay more than 10 days? What about the postinterventional lab tests? This should be mentioned in the Results section

Response: Hospital stay mentioned in the manuscript includes both preoperative preparation and postoperative hospital stay. In our hospital, preoperative evaluation is usually performed after admission, which might prolong the total hospital stay. In fact, the two patients were both discharged 4 days after endoscopic procedures. Considering the Reviewer's suggestion, we have added the postinterventional lab tests in the Results section. Special thanks to you for your suggestion.

2. The discussion section is very general and should discuss the results of this present study more precisely.

Response: We have re-written this discussion according to the reviewer's suggestion. It is really true as reviewer suggested that we should discuss the results of this present study more precisely.

3. The number of performed procedures is very low. The present study is presented as prospective study. In my opinion this is a technical study or an extended case report. How many patients have been excluded within the last years? and why? Only because they refused this treatment, or have you had other reasons?

Response: It is really true as reviewer suggested that this study should be considered as a technical study. In this study, we enrolled two patients with recurrent laterally spreading

duodenal papillary adenomas between March 2017 and September 2018 in our department. There were 8 recurrence patients excluded within this period: 4 patients underwent pancreatoduodenectomy and/or chemoradiotherapy due to canceration and ductal infiltration. 4 patients underwent endoscopic management using an electric snare or APC ablation for small, locally recurrent adenomas < 1 cm without intraductal growth. The above exclusions have been added in the Materials and Methods section.

Reviewer #2:

1. In Table 1, it is noted that both lesions were completely resected at the time of initial treatment. This means that the horizontal and vertical margins of the specimen were histologically negative. Generally thinking, recurrence means that they were not completely resected, but why they recurred in spite of the complete resection?

Response: Both lesions were indeed *en bloc* resected and complete resected at the time of initial treatment by endoscopic snare papillectomy, as mentioned in Table 1. But they recurred during postoperative follow-up, which indicated that the lesions might not be curative resected. Meanwhile, the histological margins of specimen resected by electric snare might be damaged by electrocoagulation, which made it difficult to determine the histological margins of the lesions accurately.

2. In both lesions, they were evaluated as "clear border", but how was the histological margins? Were they negative? It is not specified in the manuscript nor table.

Response: In fact, the both lesions were evaluated as "clear border" in the preoperative endoscopic evaluation, with no evidence of malignancy such as ulceration and spontaneous bleeding, as mentioned in the first paragraph of the Results section. Meanwhile, the histological margins had already been specified in the manuscript as "Histopathological examination revealed tubulovillous adenoma negative for neoplastic extension **at the horizontal and vertical margins** in both cases (Figures 1 and 2)". Please according to the second paragraph of Results section in the manuscript. Special thanks to you for your suggestion.

3. In Figure 2, it is stated that the tumor was dissected by ESD, but was it not a hybrid ESD?

Response: We are very sorry for our incorrect writing. The tumor was dissected by hybrid ESD. We have revised it in Figure 2. Special thanks to you for your suggestion.

4. In Discussion, it is described that IDUS was performed for the assessment of intraductal growth, however, there was no description about the details of IDUS in the Method and Result.

Response: It is really true as reviewer suggested that IDUS should also be described in the Method and Result. We have added description about the details of IDUS in the Method and Result sections according to the Reviewer's suggestion.

5. "Intrductal" in line 218 and "would" in line 238 are misspelled.

Response: We are very sorry for our incorrect writing. Considering the Reviewer's suggestion, we revised this paper throughout. Special thanks to you for your suggestion.

Replies to Editorial Office's comments

1. The authors need to add more details in the "method" section.

Response: It is really true as editor suggested that this study should be published as a technical paper and we should add more details in the "method" section. We have added more details of patient selection and operative procedures including ERCP and IDUS procedures and postoperative treatments in the "method" section.

2. The discussion section is very general and should discuss the results of this present study more precisely.

Response: We have re-written this discussion according to the Editor's suggestion. It is really true as editor suggested that we should discuss the results of this present study more precisely.

3. The questions raised by the reviewers should be answered.

Response: We have made a point-to-point response to the questions raised by the

reviewers above. Special thanks to you for your suggestion.

4. A total of 15 references are cited, without references published in the last 3 years. The authors need to update the references.

Response: We have updated the references according to the editor's suggestion. Meanwhile, typesetting was corrected.

5. I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response: Original Figures were provided using PPT to ensure that they can be reprocessed by the editor.

6. I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text.

Response: The "article highlights" section was provided at the end of the main text according to the Guidelines and Requirements for Manuscript Revision.

7. Please provide editable Tables

Response: Editable tables were provided using PowerPoint to ensure that they can be reprocessed by the editor.

8. I have changed the manuscript type "prospective study" to "retrospective study".

Response: It is really true as editor suggested that the manuscript type should be a retrospective study. We have changed the associated description in this manuscript. Special thanks to you for your suggestion.