

## Point-by-point responses to issues raised in the peer-review report

### Reviewer 1# issue

1. Thank you very much for your opinion. I have revised the content by presenting it in chronological order with serial images. Please see manuscript **page 4, line 29<sup>th</sup>-31<sup>st</sup>, page 5, line 2<sup>nd</sup> – 7<sup>th</sup>.**
2. Thank you very much for your opinion. I have done revision and please see manuscript **page 5, line 24<sup>th</sup> -26<sup>th</sup>.**
3. Thank you very much for your opinion. First, owing that patient doesn't have any symptom and the biochemistry studies are all within normal reference, we check the IgG4 level due to the segment of narrow lumen at the distal CBD. In my hospital, it's our routine to check IgG4 value for indeterminate biliary stricture. Secondly, we have done every effort to persuade patient to receive ERCP with/without EUS with cytology brush and/or FNAB, but she is strong-minded to refuse these invasive procedures.
4. Thanks for your opinion. The NET lesion is found incidentally in the microscopic examination and cannot be identified from the surgical specimen. The early adenoCa lesion is located closely to the GB neck. The NET lesion is solitary and not connected to the adenoma.
5. Thanks for your opinion. The initial size of GB polyp measured about 1 cm in diameter on ultrasound. Please see the revised manuscript Figure 2-A. The follow-up frequency of 1 cm GB polyp in my hospital is at 6-12 months interval. The polyp became larger in the first one-year follow-up ultrasound (figure 2-B), so we shortened the frequency to 6 months interval. The polyp grows progressively in the following two times follow-up. Please see revised manuscript figure 2-C & 2-D. Please see **page 5, line 3<sup>rd</sup> – 7<sup>th</sup>.**
6. Thanks for your opinion. We have added the MRCP finding in the paragraph of **page 5, line 7<sup>th</sup>-9<sup>th</sup>**
7. Thanks for your opinion. The intra-operative findings disclosed 1. No evidence of inflammatory process at the peri-GB area 2. CBD looking negative in appearance 3. The outer surface of GB attached to liver bed showed no tumor invasion 4. Partial liver resection has been done with radical cholecystectomy. 5. Section margin of frozen section is negative for malignancy. Please see **page 6, line 7<sup>th</sup> – 10<sup>th</sup>**
8. Thanks for your opinion. We persistently persuade patient to receive ERCP or EUS investigation to elucidate the nature of biliary stricture.

Please see **page 6, line 28<sup>th</sup> -30<sup>th</sup>.**

9. Thanks for your opinion. We have added some discussion about the synchronous CBD & GB cancer. Please refer to the **page 9, line 14<sup>th</sup> to 18<sup>th</sup>.**
10. Thanks for your opinion. We follow the ESGE guidelines and management strategy for those patients with risk GB polyps. Revisions are done and please see **page 9, line 9<sup>th</sup> – 13<sup>th</sup>.**

### **Reviewer 2# issue**

1. Thank you very much for your opinion. The coexistence of GB-NET and GB adenocarcinoma is extremely rare. Most of the coexistent GB carcinoid tumor and adenocarcinoma showed GB-NETs with adenocarcinoma differentiation or adenocarcinoma with carcinoid differentiation and were often associated with cholelithiasis and cholecystitis. However, in this case there is no transitional changes and there was no evident cholecystitis, either. To the best of our knowledge, concomitant but separate NET and cancer in the GB has not been reported.
2. Thank you for your opinion. The original manuscript has been edited by English-speaking expert. The revised manuscript will be sent to the professional English language editing company recommended by BPG editorial office.
3. Thank you for your opinion. Caption revision has been done. Please see manuscript figure legend.