

Dear Editor,

We greatly appreciate the Editorial Board's consideration of our manuscript "Residual common bile duct stones on direct peroral cholangioscopy using ultraslim endoscope" for publication in *World Journal of Gastroenterology* pending revisions as recommended by the Reviewer. We are encouraged that you are willing to consider a revised paper.

We appreciate the careful review and believe the paper has been further improved after addressing the excellent points raised. We hope you will now consider it suitable for publication in *World Journal of Gastroenterology*.

Sincerely,

Yung-Kuan Tsou, MD,

Department of Gastroenterology and Hepatology, Division of Digestive Therapeutic Endoscopy, Chang Gung Memorial Hospital & Chang Gung University College of Medicine,

5, Fu-Shin Street, Kweishan, Taoyuan 333, Taiwan.

**Tel.:** +886-3-3281200 ext. 8108

**Fax:** +886-3-3272236

E-Mail: [flying3454@xuite.net](mailto:flying3454@xuite.net)

## **Answers to Reviewer 1**

1. More information should be given about the population these 22 patients were retrieved from. For example: how many patients were excluded because of the various exclusion criteria? (1) patients younger than 20 years, pregnant, or critically ill; (2) patients with concomitant gallbladder stones; (3) patients with CBD diameters of less than 10 mm. How many ERCPs were performed in total for bile duct stones in the institution during the study period?

**Ans:** The study was originally designed to include patients without GB stones or without GB to avoid the factor of “migrated GB stones” (so that we could sure that the stones seen on POC were residual stones not migrated GB stones). The study enrolled patients of the two endoscopists, Dr. Lin CH and Dr. Tsou YK because only the two endoscopists were experienced in POC. Therefore, there were a total of 92 patients met the inclusion criteria during the study period. The case number of the patients excluded was as the follows.

- (1) patients younger than 20 years (n = 0), pregnant (n = 0), or critically ill (n = 5)
- (2) patients with concomitant gallbladder stones ( n = 42)
- (3) patients with CBD diameters of less than 10 mm (n = 9)
- (4) patients refused to participate in the study (n = 14)

Finally, a total of 22 patients were enrolled in this study (page 6, line 11-22)

There were 9 ERCP endoscopists in our institution during the study period, and a total of 436 patients with bile duct stones (including IHD stones) undergone ERCP during the study period.

2. Only patients with bile duct stones confirmed before index ERC with radiological methods were included. However, many patients will have only ultrasound before the ERCP, and ultrasound generally detects only a minority of bile duct stones. Therefore, results may have been biased and can not be extrapolated to the entire population with bile duct stones.

**Ans:** Because we consider the ERCP is a therapeutic tool only, we routinely performed CT scans and/or MRCP (or less commonly, EUS) for a patient with suspected CBD stones and/or biliary tree infection (based on clinical symptoms, serum biochemistries, and abdominal ultrasound) in whom there was no CBD stone documented on abdominal ultrasound. Yet, the reviewer did point out a very important viewpoint which we did not mention in the text—the study results cannot be extrapolated to the entire population with bile duct stones. Since we enrolled only patients without GB or without GB stone, our study results can only be applied to this subgroup of patients with CBD stones. We

has added this interpretation to our paper. (page 12, line 23-25 and page 13, line 1-2)

3. Unfortunately the authors did not perform intraductal ultrasound in their 22 patients simultaneously. That would have allowed comparison of the two methods.

**Ans.:** IDUS has not been available in our institution.

4. The authors should give information about % damage of the cholangioscope during the procedure

**Ans.:** The damage rate of the cholangioscope (an ultraslim endoscope) was 0% during the study period. (add in page 10, line 3-4)

5. Probably the authors do not want to suggest performance of peroral cholangioscopy in all patients after ercp and stone removal. They should give suggestions in the Discussion which high risk patients for residual stones should have the procedure.

**Ans.:** This was an observation study. Just as we mentioned in the last paragraph of Results session in this manuscript, the case number was too small to obtain statistic significance between patients with (n = 5) and without (n = 17) residual CBD stones. However, we found that recurrent CBD stones as an indication for index ERC, prior choledocholithotomy, and fragmented stones during stones retrieval on the index ERC were more frequently observed in patients with residual stones. We suggest patients with these characteristics may have POC to detect residual stones. (page 13, line 2-6)

6. The authors should give information about follow up in their 22 patients concerning recurrent stones after index ercp. How long was this follow up period?

**Ans.:** The patients were followed up every 6 months or when there were symptoms/signs suggested of recurrent stones. There were 4 patients had recurrent CBD stones during follow-up (17.5 ± 4.9 months) which were documented on ERC. (page 10, line 13-16)

#### **Answers to Reviewer 2:**

1. Abstract part is too lengthy and should be summarize more concisely.

**Ans:** Abstract has been condensed according to suggestion.

2. As the author mentioned on the discussion part (P12, line 19), The clinical significance of the residual tiny stones is unclear. Although this paper is focused on short-term results of peroral choledochoscopy, the author should summarize the recurrence rates of CBD stone after conventional techniques in the previous reports not only endoscopic but also laparoscopic CBD exploration. A Table might be helpful for the readers of this journal.

**Ans:** The recurrent stones rate was 3.2% in a series of laparoscopic CBD exploration with a median duration of follow-up 20.1 months (range, 1-62 months). (Surg Endosc. 1998 Jan;12(1):23-9). In this study, we focus on “residual stones” after ERC not “recurrent stones” after ERC. Therefore, in the literature search, we cannot find any paper dealing with “residual stones” after laparoscopic CBD exploration.

3. Figure 2: Peumobilia in the CBD is less visible in this photo. The author should indicate the CBD by small arrow-heads.

**Ans:** a small arrow-head is added to indicate CBD.

### **Answers to Reviewer 3:**

1. Introduction The authors mention endoscopic ultrasound as a method for diagnosing residual stones. Is there any role for MRC? The sequence of words should be corrected in the sentence in the line 10

**Ans:** To the best of our knowledge, there has been no study dealing with MRC for examination of residual CBD stones after a negative balloon-occluded cholangiogram.

2. Materials and methods Did the authors examine post-ERC amylases to exclude the irritation of pancreas?

**Ans:** None of our patients developed abdominal pain after ERC and POC. Therefore, we did not check serum amylase level after ERC/POC according to the consensus for definition of post-ERCP pancreatitis (Cotton et al. Endoscopic sphincterotomy complications and their management: An attempt at consensus. *Gastrointest Endosc* 1991; **37**: 383–933)

3. Results The results in text (page 10, all three paragraphs) are the same as the results in Tables 1,2,3. The authors should omit double

**Ans:** The text and tables are two different parts of a paper, and we have tried to avoid double.