

COMMENTS TO REVIEWERS:

Manuscript NO: 81997

Title: **A comprehensive review on small common bile duct stones**

Andrzej S Tarnawski, DSc, MD, PhD

Editor-in-Chief,

World Journal of Gastroenterology

Dear Dr. Tarnawski,

Thank you very much for inviting us to resubmit our manuscript, ‘A comprehensive review on small common bile duct stones (Manuscript NO: 81997).’ The reviewers and editor provided excellent suggestions and guidance, and we have revised the manuscript according to their suggestions. We believe that the reviewers’ suggestions have helped us to substantially improve the quality of the manuscript.

We sincerely hope that the concerns raised by the reviewers and editor have been sufficiently addressed and would like to request that the revised manuscript be considered for publication in the *World Journal of Gastroenterology*.

Respectfully yours,

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RESPONSE TO REVIEWER #1:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This study by Sakue Masuda(MD, MS) and colleagues is very meaningful and useful. The authors have reviewed the treatment progress of small common bile duct stones, especially about EPBD and EST. However, I may ask a few questions about this manuscript.

1. As the title "A comprehensive review on small common bile duct stones" said, would you please demonstrate some research outcomes of laparoscopic/ choledochoscopic treatment on small common bile duct stones.

Response: Thank you for this pertinent comment. We have now added the following text to page 13 line 4 – page 14 line 5:

"CBD stones complicated with cholecystolithiasis

In the general population, CBD stones complicated with cholecystolithiasis commonly occurs. The established gold standard for the treatment of symptomatic cholecystolithiasis is laparoscopic cholecystectomy (LC), but the treatment option for CBD stones is yet to be clarified. CBD stones complicated with cholecystolithiasis can be treated with two-session minimally invasive and one-session feasible strategies. The former requires pre- or post-LC ERCP, whereas the latter requires LC plus intraoperative laparoscopic CBD exploration (LCBDE) or LC with intraoperative ERCP [44]. As per efficacy, morbidity, or mortality endoscopic and surgical techniques for extracting these stones are equally suitable [45]. However, one-session procedures usually result in a shorter hospital stay [15]. Moreover, a recent meta-analysis has demonstrated that the one-session procedure has a higher success rate than the two-session procedure [46].

For one-session procedures, many surgeons prefer the less invasive and less complicated transcystectomy approach, however, bile duct incision is recommended for dilated CBD, large diameter and multiple stones, impacted stones, and stones with

intrahepatic localization [47,48]. It is recommended to start with transcystectomy and move unto exploration by bile duct incision if difficult [44,49]. Laparoscopic stone removal can be performed fluoroscopically or cholangioscopically. The use of a flexible cholangioscope is the most preferred method because of its accuracy and direct visual control. However, one-session procedure requires advanced laparoscopic techniques, a long learning curve, and specialized equipment, and these qualities may not exist in all treatment facilities [50-52]. ESGE recommends that transcystic or transductal exploration of the common bile duct is a safe and effective technique for removal of CBD stones in patients undergoing laparoscopic cholecystectomy, provided that local expertise and resources are adequate^[15]. It is of note that results of surgical treatment of CBD stones, which are generally excellent in published reports, are usually from laparoscopic centers of excellence, however, there are hardly reports by less experienced surgeons. Therefore, the ESGE does not clearly state whether one-session or two-session procedure should be preferred.

There are no recent reports on laparoscopic surgery for small CBD stones, however, Huang et al., in their report on laparoscopic surgery for small CBD with CBD stones^[53], indicated that it is safe and feasible for small CBD patients to perform LCBDE. ”

2.If possible, Would you please add a new table about the incidence and treatments of short-term and long-term complications of EPBD/EST; 3. In “Abstract”, line

Response: We have now added a new table as “Table 1”.

3, In “Abstract”, line 3, change the word “Indications” to “indications”.

Response: We have now corrected the above point.

4.At page 12, line 8, please change the abbreviation ”ESBE” to “ESBD”.

Response: We have now corrected the above point.

RESPONSE TO REVIEWER #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This review analyze the pros and cons of EPBD and EST for CBD small stones retrieval comprehensively, combined guidelines with updated literatures.

Here are some questions about this article.

1. The author defined small stones as less than 10mm in diameter. I recommend to stratify the small stones with two subgroups, less than 5mm and 5-10mm, and analyze respectively Since ESBD or EPBD is not always in need in patients with stones less than 5mm. But on the flip side, EPBD or ESBD will be conducted routinely in 5-10mm stones.

Response: Thank you for this pertinent comment. We have now added the following text to page 5 line 4 – 13:

“There is lack of evidence for the possibility of very small stone extraction without EST or EPBD. It has been reported that if ESWL results in stone fragment size of 3 mm or less, there is a likelihood that the stone will be spontaneously discharged without EST. Therefore, it is possible that stone extraction can be performed without EST or EPBD if the size is less than approximately 3 mm, however, there are no studies that have directly examined this issue [14]. Therefore, in principle, EST and EPBD are recommended for stone extraction of CBD stones, as recommended by the European Society of Gastrointestinal Endoscopy (ESGE) and Japan Gastroenterological Endoscopy Society (JGES) guidelines; however, it is at the endoscopist's discretion whether to perform stone extraction without these procedures for very small stones^[15,16]. ”

2. Some literatures compared the pressure of short term and long term SO between EPBD and EST, which was associated with the recurrence of CBD stones. So relevant contents are suggested to complement.

Response: Thank you for this pertinent comment. We have now added the following text to page 8 line 22 – 26:

"EST causes significant damages to the Oddi sphincter, and post-EST sphincter dysfunction easily occurs [30]. Then, the reflux of intestinal contents such as digestive juices, food residue, and bacteria may increase the risk of biliary tract infection and stone recurrence [31,32]."

3. There were three techniques for small stones less than 10mm, including EST, EPBD, ESBD. The indication for these techniques are supposed to clarified and specified.

Response: Thank you for this pertinent comment.

There is a lack of evidence to establish which of the three is best: EST, EPBD, or ESBD. Therefore, we have stated that "Based on these findings, we consider EPBD in cases of small bile duct stones, bleeding tendency, young age, and even in surgically altered anatomy in which EST is difficult. (on page 8 line 29 - 31)" as a case in which EPBD is considered, and added "Thus, ESBD may be superior to EST in overall efficacy and short- and long-term complications, and ESBD may be recommended over EST in the future; however, (on page 9 line 21 - 23)" and "At this time, it is up to each endoscopist to decide whether to perform ESBD or EST. (on page 9 line 26 - 27)" to the description of ESBD.

4. Distal biliary stricture accompanied by proximal bile duct dilation is a specific situation. How to retrieve stones and what should be selected, EST or EPBD, or ESBD, should be discussed.

Response: Thank you for this pertinent comment. We have now added the following text to page 18 line 21 – page 19 line 13:

"CBS stones complicated with distal biliary stricture

Few reports have been published on CBD stones extraction with distal biliary stricture

[54,55], however, plastic stent(s) [56,57], covered self-expandable metallic stent(s) (cSEMS) [56–58], balloon dilation [59], and surgery [60] have been used for dilating bile duct stenosis. However, balloon dilation carries the risk of bile duct injury. Therefore, when endoscopic stone extraction is performed for CBD stones with benign biliary stricture, it may be advisable to use multiple plastic stents or cSEMS for several months and perform endoscopic stone extraction after bile duct dilation is achieved [61]. Combining them with mechanical lithotripsy may also be useful [54]. Ogura et al. reported that transluminal stone extraction passing through the EUS-TD route, without passing through the distal bile duct might be useful [55]. Reports of CBD stones with malignant biliary stricture are even more scarce, however, the safety of 6-8 mm balloon dilation for malignant biliary stricture has been reported [62]. In malignant biliary stricture with limited prognosis, stenting alone may be sufficient and stone extraction may not be necessary, however, balloon dilation for stone extraction may be considered in cases of short-term stent obstruction.”

Since EST, EPBD, or ESBD are performed on the papillary region, they were not described in this section on distal bile duct stricture.

5. In one sentence, ESBD was typed as ESBE by mistake. Please correct it.

Response: We have now corrected the above point.