

ROUND 1

RESPONSE TO REVIEWERS' COMMENTS TO AUTHORS

Dear reviewers,

Thank you for considering our paper and for your precious comments.

Hereafter, we provided a point-by-point response to any comment:

REV 1: This is a very interesting paper. Usually we perform a laparoscopic cholecystectomy following ERCP in patients with gallstone and CBD stone. We can perform in one session in operating room like cholecystectomy and CBDE or intraoperative ERCP. However, there are sometimes patients who have difficulty in surgical treatment. This paper would be helpful for surgeon who treat patients with gallstone and CBD stone especially unfit for surgery.

Thank you. We provided minor revisions on language.

REV 2: The authors discussed pure endoscopic treatment of combined cholelithiasis and choledocolithiasis is possible due to the possibility to use together both ERCP and EUS approaches. I suggest that it would be published in the WJG.

Thank you. We corrected few language mistakes.

REV 3: This Letter to the editor is a comment on the management of cholelithiasis with choledocholithiasis. Here below my concern.

Questions and comments to authors:

Although I can understand the clinical implication of EUS-guided cholecystoduodenectomy, it seems to be different from the main theme. The aim of the manuscript review is to provide practical advice and an overview of how to manage patients with “cholelithiasis and choledocholithiasis”. This manuscript’s authors reported the management of patients who had cholelithiasis with choledocholithiasis. As the authors pointed out, EUS-guided cholecystoduodenectomy and lithotripsy is the good treatment to avoid eventually obstruction of the biliary edge of the stent. However, what should treat about the treatment of common bile duct stones? This is only a description of treatment for gallbladder stones or cholecystitis alone, and is not likely to be involved in the main topic.

We appreciated your valuable comments. Bile duct stones are generally treated by standard ERCP and they can be treated in the same session, if necessary. We added a comment in the Letter as you suggested.

REV 4: EUS-guided gallbladder stone removal may be useful for patients who are not suitable for surgery and is a promising treatment in the future.

Thank you. We provided minor language changes.

REV 5: Lorenzo Dioscoridi et al. have advocated that EUS-guided GB drainage (with or without lithotripsy) and ERCP-guided CBD removal can be promising alternative to combination of ERCP and surgical approach. The authors have cited the article written by Dr. Teoh AYB (Teoh AYB, Leung CH, Tam PTH, et al. EUS-guided gallbladder drainage versus laparoscopic cholecystectomy for acute cholecystitis: a propensity score analysis with 1-year follow-up data. *Gastrointest Endosc* 2020.), which showed similar efficacy and long-term outcome of EUS-GBD with lithotripsy in poor surgical candidates compared to LC in good surgical candidates. This result suggests that EUS-GBD with lithotripsy can be a first line treatment even in good surgical candidates. However, I have several major concerns for applying EUS-GBD for good surgical candidates. 1. As Dr. Todd Baron mentioned in editorial (Baron TH. EUS-guided gallbladder drainage is as good as laparoscopic cholecystectomy for symptomatic cholelithiasis: Wait!...what?! *Gastrointest Endosc* 2021;93:584-585.), Dr. Teoh's study is not an apples-to-apples comparison of EUD-GBD with surgery. 2. Dr. Teoh's study included only patients with cholecystitis by gallstones. Gallbladder with cholecystitis can be easily drained via EUS-guidance because of gallbladder distention. On the contrary, gallbladder without cholecystitis is hard to be drained by EUS because of the lack of enlargement and distention of the gallbladder. In such a situation without cholecystitis, special techniques such as a retrievable puncture anchor traction method (Zhang K, Sun S, Guo J, et al. Retrievable puncture anchor traction method for EUS-guided gallbladder drainage: A porcine study. *Gastrointest Endosc* 2018;88:957-63.) are needed. After all, the article by Cianci P, Restini E. "Management of cholelithiasis with choledocholithiasis: Endoscopic and surgical approaches. *World J Gastroenterol* 2021; 27(28): 4536-4554." are discussing about treatment of cholelithiasis with choledocholithiasis, not only cholecystitis. Because the difficulties and procedural risks of EUS-guided GB drainage with lithotripsy for patients with only gallstones is difficult from that for patients with cholecystitis, authors should discuss considering this point.

We appreciated any comment. We do agree that EUS-GBD cannot replace LC in patients fit for surgery. However, the endoscopic perspectives are expanding their indications day by day. We added a discussion on the difficulties of EUS drainage in case of acute cholecystitis and the main limits of the method.

We hope that the paper can be now suitable for publication.

Sincerely,

The Authors

ROUND 2

RESPONSE TO REVIEWERS' COMMENTS TO AUTHORS

Dear reviewers,

Thank you for considering our revised paper.

Hereafter, we provided a point-by-point response to any comment:

REV 1: Thank you for your response to my comments on the peer review. I confirmed a corrected article. The article was corrected adequately.

Thank you for Your precious advices.

REV 2: Dear authors, thank you for your revision. I have one major point to be reconsidered. Regarding this sentence, "The main limitations of EUS-guided gallbladder drainage are still the need of a sufficient loosening of the gallbladder to guarantee a safe puncture and the absence of extraluminal pericholecystic fluid collection." What dose a sufficient loosening of the GB mean? Generally, a distention of the GB is required for safe puncture, especially in using LAMS. When the GB is not sufficiently distended, the GB is easliy moving away from the duodenum during puncture or LAMS insertion. Therefore, cholecystitis is the good candidate for EUS-GBD. On the contrary, the GB without cholecystitis is so much difficlut to be drained endosonographically. Anchor traction method could be a useful tool for this situation. On the other hands, intracystic lithotripsy has a high risk of perforation as the authors mentioned. Therefore, the lithotripsy is usually performed in the second sesion after resolution of cholecystitis by EUS-GBD, not single session. In summary, Galllbladder stones withtout cholecystitis is difficult to be treated using EUS-GBD so far. Evolving the dedicated devices such as anchor traction method should be required in future. Gallbladder stones with cholecystitis can be treated by EUS-GBD with LAMS. However, stone extraction or lithotripsy should be performed in the second session. Therefore, I consider that single-session therapy with EUS and ERCP for GB and CBD stones are difficult so far.

GB loosening is evaluated by the endoscopist during EUS. There is a lack of standardized values but the intracholecystic space must be sufficient to open completely the flair of the stent. We added this point in the paper.

We totally agree with You on the major risks of a single session comprehending both EUS-GB drainage and intraluminal lithotripsy. In the letter, we clarified that we meant associating EUS-GB drainage and standard ERCP for common bile duct stones without intraluminal lithotripsy. Gallbladder stones lithotripsy should be delayed on a later session.

We hope that the paper can be now suitable for publication.

Sincerely,

The Authors