

RESPONSE TO REVIEWERS:

We thank the reviewers for their insightful comments. The responses to the reviewers' queries are herewith-

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: COMMENTS TO AUTHORS: Manuscript NO: 81429 Title: EUS guided biliary drainage in surgically altered anatomy : a comprehensive review of various approaches REVIEW: This article is a review of Interventional EUS, particularly biliary drainage, from a bird's eye view. It outlines each method and discusses a recent new approach, EUS-guided gastrojejunostomy bypass (EUS-GJ). However, the explanations of each methodology are limited to concepts, and there are a few descriptions of treatment data that convey the characteristics of the procedure to the reader. In addition, although comparisons between e-ERCP and interventional EUS are often discussed, it seems that e-ERCP reports are biased toward those with poor results. Furthermore, as the author describes, there are different types of SAA, and the results of e-ERCP vary greatly depending on the type of SAA. Please describe the comparison with Interventional EUS according to each of those types. In addition, the contingencies that are more likely to be serious in e-ERCP and Interventional EUS are different: gastrointestinal perforation in e-ERCP and hemorrhage, peritonitis, and stent deviation in Interventional EUS. Please consider weighting according to the type of contingency, not just the rate.

1. The success and complication rate of e-ERCP varies with each technique. Please describe allowing the reader to compare and discuss EUS-BD and e-ERCP for each SAAs: Sleeve gastrectomy, Billroth I gastrectomy, Billroth II reconstruction, Roux-en-Y gastric bypass, and Whipple procedure. (on page 4-5)

Ans: Thank you for your comment. Comparative analysis is given in section on page 9.

2. How often is interventional EUS needed for these SAAs in previous study?: Sleeve gastrectomy, Billroth I gastrectomy, Billroth II reconstruction, Roux-en-Y gastric bypass, and Whipple procedure.

Ans: Thank you for the comment. The need for interventional EUS is likely to be higher with more complex altered anatomies like Roux-en-Y Gastric bypass. However, no previous studies have assess the comparative need based on surgical altered anatomy.

3. Among SAAs, B-II has been reported to have a particularly high incidence of accidental perforation of the gastrointestinal tract. If you can find such literature, consider "If you have difficulty inserting an e-ERCP scope in B-II, I suggest that you switch to Interventional EUS without straining". (on page 4 line 20)

Ans: Thank you for the comment. The change is made as suggested.

4. Roux-en-Y is the one that has the lowest e-ERCP success rate among SAAs. More often than not, e-ERCP in B-II and whipple is not difficult. Roux-en-Y should be properly considered with additional data. (on page 5 line 3)

Ans: Thank you for the comment. Change has been made as suggested.

5. I am not sure what kind of procedure was done in this description. Did Kedia et al. percutaneously create a fistula in the remaining stomach, insert an EUS scope through the fistula, puncture the 2nd portion of duodenal through the remaining stomach with

EUS, and create a second fistula using LAMS? Couldn't they have inserted the EUS scope through the mouth and performed EUS-HGS from the remaining stomach? For this statement, we suggest adding an explanation so that the reader can understand it, or removing it altogether. (on page 6 line 22- page 7 line 1)

Ans: Thank you for the comment. Change has been made as suggested and the line is removed.

6. What kind of cases are they targeting, R-en-Y, B-I, B-II, Sleeve? Please clarify population. (on page 8 line 22, Kedia et al.; on page 9 line 2, Bukuhari et al.)

Ans: Thank you for your comment. Clarification has been done as suggested.

7. The success rate of e-ERCP is too low in the cited references. Are you citing biased citations? Please consider citing papers together that e-ERCP and EDGE consider equivalent. (on page 9 line 5 and line 13)

Ans: Thank you for your comment. Change has been made as suggested.

8. What kind of cases are you targeting, R-en-Y, B-I, B-II, Sleeve? (on page 9 line 10)

Ans: Thank you for your comment. Clarification has been made.

9. I think that "safe" is a mismatch of the results of cited literature, and your conclusions, even though EUS-BD had more incident cases. What is the level of moderate complications? Do they use CTCAE or other criteria? (on page 9 line 18)

Ans: Thank you for your comment. The said clarifications have been made in the text. CTCAE is not used for EUS complications and usually most studies use standard ASGE lexicon for adverse event reporting.

10. Please describe its effectiveness on quality of life and Actives of daily living. (on page 9 line 21)

Ans: Thank you for your comment. The same has been added to the text.

11. You are referring to EUS-like gastric jejunostomy bypass. Readers who are familiar with this technique will understand it, but the reader may have difficulty understanding the text as it is written. (on page 10 line 14)

Ans: Thank you for your comment. The details are mentioned as requested.

Minor

1. How about adding "malignant biliary stricture" and "benign biliary stricture" as keywords? (on page 3 line 10-11)

Ans: Thank you for the comment. The same has been added as suggested.

2. The sentence on page 6 line 19-22 has already been described above. Please delete the duplicate.

Ans: Thank you for the comment. The change is made as suggested.

3. What is the surgical technique? It is important whether the stomach is present or not. (on page 8 line 16)

Ans: Thank you for the comment. Agreed with the assessment and hence details are added as suggested.

4. Is this the result of an attempted internalization in all patients in the PTBD group by Iwashita et al. Or does it include those who did not attempt internalization? (on page 10 line 2)

Ans: Thank you for the comment. The study included internalisation and reported failure despite the same.

5. What is the equal between EUS-BD and PTBD?: success rate, complication rate, ADL, or QOL, etc. (on page 12 line 5)

Ans: Thank you for the comment. Clarification has been made as suggested.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Thanks to the authors for sharing this important topic. There are two suggestions:

1. Too many X-ray images may not be conducive to non-expert readers. Therefore, more illustrations of surgically altered anatomy would be better for them to understand the specific process of the advanced endoscopic procedure and the advantages of EUS-guided biliary drainage.

Ans: The illustrations are added as suggested. The figure legend is given separately.

2. Reference of endoscopic biliary drainage in patients with surgically altered anatomy are not rare. However, less than 30 references are listed in this current manuscript, and about half of them were published 5 years ago. It is recommended to supplement and update these references.

Ans: Thank you for the comment. Changes are made as suggested.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: I read with interest the review and I think that the topic is interesting. However, I consider that could be interesting for general gastroenterologist and not for advanced endoscopist. In general, the paper deals with different advanced techniques in a very superficial manner and is not deep enough to be in the interest of advanced endoscopist. There are many topics ignored in the paper as well as many interesting references (Ex. PTBD vs EUS did not mention at least a couple of RCT comparing these techniques, did not mention papers about EUS-CD vs EUS-HGS, etc).

Ans: Thank you for the comment. The details as missing have been added to the manuscript to make it more comprehensive. While there is data comparing these techniques overall, comparative data in presence of surgically altered anatomy is sparse and hence some topics have not been discussed.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: Thank you for giving me the chance to review this manuscript. I have some concerns.

1. First, I want authors to make the large sections easier to understand.

Ans: Thank you for the comment. The language has been edited to make it more understandable.

2. Could you show the detail of EDGE procedure?

Ans: Thank you for the comment. Details have been added as suggested in page 5, 6 and 7. Illustrations are added for help.

3. What does “LA-ERCP” mean?

Ans: Thank you for the comment. LA-ERCP means Laparoscopy assisted ERCP. Abbreviations have been added to the manuscript.

4. In page nine, the authors mentioned “EUS BD can be safe alternative to enteroscope assisted ERCP in patients with surgically altered anatomy.” However, the authors described “AEs occurred in the EUS-BD group (20% vs. 4%, $P=0.01$) which were of mild/moderate severity” in the same page. What are the detailed contents of the adverse events associated with EUS-BD? The occurrence of pancreatitis should become lower by performing EUS-BD.

Ans: Thank you for the comment. The details are added as requested.

5. What does “EUS-ABS” mean?

Ans: Thank you for the comment. EUS-ABS refers to EUS guided antegrade biliary stenting. Abbreviations have been added to the manuscript.

6. What does “CA” mean?

Ans: CA refers to carcinoma. Abbreviations have been added to the manuscript.

7. What does “RYGB” mean?

Ans: RYGB refers to Roux-en-Y Gastric bypass. Abbreviations have been added to the manuscript.

8. What does “RYHJ” mean?

Ans: RYHJ refers to Roux-en-Y Hepaticojejunostomy. Abbreviations have been added to the manuscript.