

Answering Reviewers

Dear Editor,

First of all, thank you for considering our manuscript for publication in the World Journal of Gastroenterology. This manuscript has been revised as suggested in the Editor's file and peer review report. All the revisions have been mentioned below and highlighted in the updated version of the manuscript. Minor language polishing, text editing and grammar checks have been performed.

All the authors reviewed the peer review report for detailed discussion and possible revision of the manuscript as suggested by the reviewers. The individual response to the reviewer's report is mentioned below. We sincerely hope that reviewers would kindly accept our explanations and revisions for publication of this manuscript.

Review report 1 (Reviewer's code: 00053888)

All the authors were very pleased by the comments of the reviewer. In view of this report no further revision was required.

Review report 2 (Reviewer's code: 01559599)

This review report was concerned about perforation, which is a lethal AE of EPLBD in relation to distal bile duct stricture. Reviewer was questioning whether patients with distal bile duct stricture have been excluded as its presence may be related with serious adverse events and duct clearance rates. Authors thoroughly reviewed the inclusion and exclusion criteria and reviewed the actual database again.

We can confirm that none of the patients treated with large balloon sphincteroplasty had distal bile duct stricture. This has been included in the exclusion criteria now. Roux-en-Y or billroth procedure was not an exclusion criteria and has been amended.

We are a high volume tertiary referral centre with very experienced operators and acknowledge the morbidity and mortality associated with EPLBD in relation to distal bile duct stricture based on published data (reference 28). We avoid performing large volume balloon dilatation in presence of distal bile duct stricture due to related serious adverse events including mortality.

Secondly, reviewer was interested about low rate of pancreatitis with EPLBD. There are many patient-related and procedure related risk factors for post ERCP pancreatitis. Detailed description of individual risk factors for post ERCP pancreatitis is beyond the scope this manuscript. Authors believe that all concerned readers would have basic knowledge about risk factors for post ERCP pancreatitis.

This is one of the principal emphases of this study that in our experience EPLBD was not associated with significantly increased risk of post ERCP pancreatitis. Peri-procedural optimization of patients is our standard practice to prevent post ERCP pancreatitis. This includes providing adequate intravenous hydration, prescribing rectal diclofenac and keeping a low threshold for placement of pancreatic stents for contrast injection and wire cannulation of pancreatic duct. These preventive measures along with rich high volume experience are probably the principal factors for a very low rate of post ERCP pancreatitis. This has been included in the discussion part now. We hope that reviewer would kindly be satisfied with our explanations in this regard.

Review report 3 (Reviewer's code: 00503834)

Authors sincerely noted the comments of the reviewer. Reviewer was not clear about the definition of the post ERCP Pancreatitis. We have mentioned in the discussion section that "Pancreatitis was defined according to the consensus criteria described elsewhere". Authors strongly believe that all concerned readers would be well aware of the consensus criteria of post ERCP pancreatitis and probably does not need further explanation apart from mentioning of "consensus criteria".

Certainly, there are patients-related and procedure-related risk factors for post ERCP pancreatitis. We believe that readers would be well aware of the risk factors of post ERCP pancreatitis. Individual discussion of these risk factors is beyond the scope of this manuscript.

Difficult biliary cannulation, wire cannulation and contrast injections of pancreatic duct are among procedure-related risk factors for post ERCP pancreatitis. Our post ERCP pancreatitis rate was less than 1%, which indicates probably very occasional happening of procedure related risk factors. Particularly, in an observation study it would be very challenging to prove that post ERCP pancreatitis happened specifically to a patient or procedure related factor. Hence, further exploration of two cases of pancreatitis among this large cohort would probably not provide any more meaningful answers.

Peri-procedural optimization of patients is our standard practice to prevent post ERCP pancreatitis. This includes providing adequate intravenous hydration, prescribing rectal diclofenac and keeping a low threshold for placement of pancreatic stents for contrast injection and wire cannulation of pancreatic duct. These preventive measures along with rich high volume

experience are probably the principal factors for a very low rate of post ERCP pancreatitis. This has been addressed in the revised manuscript.

Furthermore, reviewer questioned why some large CBD stone could be removed with EST only and other need large balloon dilation. Even more some need POC together with EHL.

Our study is unique in view of complexity of stone disease, which is probably in context of referral population in view of status of tertiary referral centre. All patients in our study in addition to standard endoscopic techniques for stone removal had large balloon sphincteroplasty at index ERCP (1st ERCP at our centre). This indicates complexity of stone disease, as standard techniques could not clear the duct. Even POC together with EHL could not result in duct clearance in some patients at the index ERCP which emphasis the complex nature of the stone disease in our cohort. We have revised the manuscript mentioning predictors of failed duct clearance at the index ERCP.

We sincerely hope that reviewer will kindly accept our explanation and revision in this regard.

Suggestion 1

Please provide language certificate letter by professional English language editing companies (Classification of manuscript language quality evaluation is B). For manuscripts submitted by non-native speakers of English, please provided language certificate by professional English language editing companies mentioned in 'The Revision Policies of BPG for Article'.

Response 1: This is not applicable as all the authors are native English speakers

Suggestion 2

Don't forget to submit some files in your revised manuscript [Conflict-of-Interest Statement, Institutional review board statement, Biostatistics statement, Institutional Animal Care and Use Committee Statement, Animal Care and Use Statement, Data sharing statement, Copyright (need signature of all authors in order) and language Certificate (.pdf)]

Response 2: All the relevant files have been provided. Institutional Animal Care and Use Committee statement and language certificate are not applicable.

Suggestion 3

Audio core tip: In order to attract readers to read your full-text article, we request that the author make an audio file describing your final core tip, it is necessary for final acceptance. Please refer to Instruction to authors on our website or attached Format for detailed information.

Response 3: Audio core tip has been provided.

Comment 1: Submit the scientific research process

Response 1: Scientific research process report has been provided separately

批注 [U1]: Please provide one report:

Scientific Research Process

Name of Journal: *World Journal of Gastroenterology*

Manuscript NO:

Manuscript Type:

Title:

Authors:

Correspondence to:

1 What did this study explore?

2 How did the authors perform all experiments?

3 How did the authors process all experimental data?

4 How did the authors deal with the pre-study hypothesis?

5 What are the novel findings of this study?

At last, **sign (handwrite) your name** in the end of file.

Comment 2: Endoscopic Papillary Large Balloon Dilatation with Endoscopic Sphincterotomy is a Safe and Effective Technique for Biliary Stone Removal Independent of Timing and Size of Sphincterotomy – An Academic Hepato-Biliary Centre Experience From United Kingdom

Response 2: Title has been revised to the best possible extent and includes 2 key words.

“Endoscopic Papillary Large Balloon Dilatation with Sphincterotomy is Safe and Effective for Biliary Stone Removal Independent of Timing and Size of Sphincterotomy”

Comment 3: Running title: Supply it. No more than 6 words.

Response 3: Running title has been provided

“Safety and efficacy of EPLBD”

Comment 4: List all author's name List all authors' name

Response 4: All Authors' names have been provided as below along with affiliations and Institution's details.

Aujla, I. Usman; FRCP
Ladep, G. Nimzing; PhD
Dwyer, K. Laura; BSc (Hon)
Hood, V. Stephen; MD, FRCP
Stern, Nicholas; MD, FRCP
Sturgess, Richard; MD, FRCP

批注 [a2]: Title should not appear abbreviation, please correct it, also should not be more than 12 words and including no less than 2 key words.

批注 [a3]: Supply it. No more than 6 words.

批注 [a4]: (Please provide the full name in order here.)

Affiliations: All authors are from the same institution.

Digestive Diseases Unit, Aintree University Hospital, NHS Foundation Trust,
Longmoor Lane, Liverpool, L9 7AL
United Kingdom

Comment 5: Author contributions:

Response 5: Authors' contributions have been provided as mentioned below:

Aujla UI and Sturgess R were responsible for study conception and design; Aujla UI wrote the paper; Ladep NG was responsible for data interpretation and statistical analysis; Dwyer LK and Aujla UI were responsible for data collection; Hood SV, Stern N and Sturgess R critically revised the paper; all authors agreed with content of the manuscript and gave approval of the final version of manuscript.

批注 [a5]: XXX (family name should be put first in full, followed by middle names and first name in abbreviation with first letter in capital) designed research; XXX performed research; XXX contributed new reagents or analytic tools; XXX analyzed data; XXX wrote the paper. An author may list more than one contribution, and more than one author may have contributed to the same aspect.

Comment 6: Institutional review board statement:

Informed consent statement:

Conflict-of-interest statement:

Data sharing statement:

批注 [a6]: You should add some statements.

Response 6: Statements have been provided as below:

Institutional review board statement: Not applicable in view of nature of the study.

Informed consent statement: All endoscopic procedures were performed after obtaining a written informed consent form the patients.

Conflict-of-interest statement: The authors have no disclosures.

Data sharing statement: Being a descriptive study no additional data is available to warrant sharing.

Comment 7: Usman I Aujla,

批注 [a7]: Please add your title, such as MD, PhD, Professor, etc.

Response 7: Title has been added

Dr Usman I Aujla, FRCP

Comment 8: University Hospital, NHS Foundation Trust, Longmoor Lane, Liverpool, L9 7AL

批注 [a8]: Please provide the Corresponding author's name, title, and detailed address

Response 8: Full details provided as below:

Correspondence to: Dr Usman I Aujla, FRCP
Digestive Diseases Unit,
Aintree University Hospital, NHS Foundation Trust, Longmoor Lane,
Liverpool, United Kingdom
L9 7AL

Email: usman.aujla@nhs.net

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Comment 9: Abstract

批注 [a9]: AIM: No more than 20 words, and start with "To..."
METHODS: no less than 80 words
RESULTS: no less than 120 words
CONCLUSION: no more than 26 words

Key words: 5~10 words
Key words should not appear abbreviation, please correct it.

Should not appear abbreviations when they were used first in this part, please correct it.

Response 9: Abstract has been revised as suggested. It now contains AIM, which is not more than 20 words and starts with "to". Methods and results are in accordance with the desired word count. Conclusion is not more than 26 words. Key words are five and do not appear as abbreviation. Abbreviations have not been used when they appear first in the manuscript.

Comment 10, 11, 12, 13 and 14: $p < 0.000001$), multiple stones [2, range (1-13) vs. 3, range (1-12), $p 0.006$] and dilated CBD (12.4 vs. 18.3mm, $p0.001$)

批注 [a10]: P

批注 [a11]: vs

批注 [a12]: $P < 0.006$, correct?

批注 [a13]: Please modify it as above.

批注 [a14]: $P < 0.001$, correct?

Response 10, 11, 12, 13 and 14: All suggestions have been amended accordingly.

Comment 15: Core tip:

Response 15: Core tip has been provided as desired.

批注 [a15]: Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

Comment 16: Please provide all authors abbreviation names and manuscript title here. *World J Gastroenterol* 2017; In press

Response 16: Authors' abbreviation names and manuscript title have been provided.

批注 [a16]: Please supply it.

Comment 17: INTRODUCTION

Response 17: Abbreviations have not been used when appearing first in the manuscript and all the references are in due order.

批注 [a17]: 1.Should not appear abbreviations when they were used first in this part, please correct it.
2. References' numbers must be in order! Please check the full text and correct them!

Comment 18: %^[1-3].

Response 18: All the references have been modified as suggested.

批注 [a18]: Modify all references like this.

Comment 19: (p=0.046).

Response 19: Amended as suggested

批注 [a19]: P = 0.046 (Please modify)

Comment 20: 81(35.4%) |

Response 20: Amended as suggested

批注 [a20]: 81 (35.4%)

Comment 21: vs.

Response 21: Amended as suggested

批注 [a21]: vs

Comment 22: (p 0.001)

批注 [a22]: Correct?

Response 22: Amended as suggested

Comment 23: &

Response 23: Amended as suggested

Comment 24: *

Response 24: Amended as suggested

Comment 25 and 26: $P < 0.000001$ and dilated bile duct 18.3 mm (9.2-30) mm vs 12.4 mm (5-30), $p < 0.001$.

Response 25 and 26: Amended as suggested

Comment 27: FULL TEXT GUID

Response 27: Manuscript file has already very extensively and precisely explained all these points. This comment was discussed at the author's revision meeting in detail and it was unanimously agreed that all this information has been provided with very sufficient extent and does not need further revision.

Comment 28: References

Response 28: PubMed citation and DOI citation to the reference list have been added. DOI citation of references 6,7 and 8 could not be found.

Comment 29: Please correct references just like reference 1

Response 29: All the references have been amended just like suggested reference 1

批注 [a23]: Change to "and".

批注 [a24]: It's not allowed to occur.

批注 [a25]:

带格式的: 字体: 倾斜

批注 [a26]:

批注 [a27]: Please supply this part.
(1 Research Background

The background, present status and significance of the study should be described in detail.

2 Research motivation

The main topics, the key problems to be solved and the significance of solving these problems for future research in this field should be described in detail.

3 Research objectives

The main objectives, the objectives that were realized, and the significance of realizing these objectives for future research in this field should be described in detail.

4 Research methods

The research methods (*e.g.*, experiments, data analysis, surveys and clinical trials) adopted to realize the objectives as well as the characteristics and novelty of these research methods should be described in detail.

5 Research results

The research findings, their contributions to the research in this field, and the problems that remain to be solved should be described in detail.

6 Research conclusions

The following questions should be briefly answered:

What are the new findings of this study?

What are the new theories this study proposes?

What are the appropriate summarizations of current knowledge that this study provides?

What are the original insights into the current knowledge that this study offers?

What are the new hypotheses this study proposed?

批注 [a28]: Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

Comment 30: $n=$

批注 [a29]: $n=$

Response 30: Amended as suggested