Round 1

ANSWERING REVIEWERS

Name of Journal: World Journal of Gastrointestinal Endoscopy

Manuscript Type: ORIGINAL ARTICLE

Manuscript NO.: 75424

Title: ENDOSCOPIC THERAPY USING A SELF-EXPANDABLE METALLIC STENT WITH AN ANTI-MIGRATION SYSTEM FOR POSTORTHOTOPIC LIVER TRANSPLANTATION ANASTOMOTIC BILIARY STRICTURE

Authors: Larissa W Pinheiro, Fernanda P Martins, Mônica LC Contini, Gustavo A Paulo, Angelo P Ferrari, Ermelindo D Libera

REVIEWER'S COMMENTS

Reviewer #1:
Scientific Quality: Grade D (Fair)
Language Quality: Grade A (Priority publishing)
Conclusion: Major revision

Specific Comments to Authors: The manuscript "Efficacy of Endoscopic Therapy Using a Self-Expandable Metallic Stent with an Anti-Migration System for Postorthotopic Liver Transplantation Anastomotic Biliary Stricture" is of great interest as anastomotic (and non anastomotic) biliary strictures are challenge for liver transplant specialists as they require numerous endoscopic treatments. Surprisingly, used as endpoints "The primary study endpoint was the efficacy of the endoscopic treatment of p-OLT ABS using Am-FCSEMS for a 12-month period. Efficacy was evaluated based on ABS resolution. After stent removal, the biliary stricture was considered resolved if there was no stricture observed in cholangiography or a minimum stricture that allowed the passage of a 12-mm inflated extractor balloon without difficulty. Secondary endpoints were technical success (defined as stent placement), adverse effects related to ERCP (bleeding, pancreatitis), and stent dysfunction (migration or obstruction)."; they did not aim at evaluating cholestasis improvement which is key in the treatment of

anastomotic strictures. This should be explained. The authors should also specify how many treatments did the previously treated patients undergo, as this influences outcomes. Did the authors evaluate infection rate?

Answers

Dear Reviewer #1,

We appreciated the comments. The answers are written bellow:

1. The objective of this study was to evaluate the resolution of biliary stricture at the end of follow-up with endoscopic treatment using Am-FCSEMS in patients with p-OLT ABS. Although not the aim, during clinical follow-up, cholestasis improvement was observed based on bilirubin and alanine aminotransferase, as shown in Table 2.
2. The information regarding previous treatments before stent placement is shown in the text and summarized in Table 1: “Among the 14 patients, 8 (57,14%) had already undergone treatment with FCSEMS and/or MPSs, but endoscopic management was considered unsuccessful, with an average number of procedures before inclusion in this study of 2.25 ± 1.04 (range: 1-4). The other 6 patients (42.85%) received Am-FCSEMS as the first treatment.” The results were similar in both groups, however due to the small sample of the study, this hypothesis should not be considered conclusive.
3. The infection rate was not evaluated in this study.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This was a single center prospective case series of the use of self-expandable metallic stents with an antimigration system for the treatment of anastomotic biliary stricture after liver transplantation. The Authors enrolled 14 patients who underwent ERCP with placement of these new

stents: only one patient had endoscopic failure, one year after endoscopy. Moreover, there were three side effects (two pancreatitis and one stent dysfunction). The paper is potentially of interest, in my opinion. There are, however, several points to be discussed. 1. Patients were not homogeneously enrolled. Some of the patients already received endoscopic treatments for anastomotic biliary strictures, whereas other patients were at their first treatment. How can we consider the placement of these SEMS with the antimigration system? As a first line treatment of to be used for refractory strictures? 2. A control group is missing. 3. What type of imaging the patients received in the follow-up to rule out re-appearance of anastomotic biliary stricture? Was it scheduled at fixed time points? 4. I agree with the Authors when they said that multistenting can be demanding (due to the number of ERCP sessions) especially in high volume centers. Can the Authors provide costs of these new stents in order to understand if this technique could be cost-effective? 5. The Authors said that all patients underwent sphincterotomy during SEMS placement with antimigration system. Was it true also for patients with previous endoscopic treatments? 6. The pitfalls of this study should be, in my opinion, discussed more in depth. 7. Were DBD or DCD transplant? Deceased donor or living donor LT? Full or split grafts?

Answers

Dear Reviewer #2,

We appreciated the comments. The answers are written bellow:

1. The design of this study included patients with and without previous endoscopic therapy, regardless of treatment failure. We believe the stents can be used in any group of patients.
2. The study did not include a control group.
3. The patients did not routinely receive imaging during follow-up. Clinical and laboratory follow-up occurred as well as imaging tests were performed when necessary.
4. We do not have this cost evaluated.

5. Yes, you are right. The sphincterotomy was performed on those with native papilla. This sentence was added in the text.
6. We believe that the limitation of this study is related to the fact that it is a retrospective study and related to the small sample, however, it does not preclude important preliminary conclusions.
7. The transplant was from donor brain dead (DBD), deceased donor and full graft. It's written in the text as post orthotopic liver transplantation (p-OLT).

EDITORIAL OFFICE'S COMMENTS

(1) Science editor:

In this retrospective study, endoscopic treatment of p-olt ABS with Am FCSEMS was safe and effective. It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, please revise your reference list accordingly. The single-center study of small samples has a certain impact on the reliability of the article. Add some disadvantages of this technology in the discussion. Language Quality: Grade B (Minor language polishing) Scientific Quality: Grade D (Fair)

Answers

Dear Science editor,

We appreciated the comments. The answers are written bellow:

1. We reviewed the list of references and don't have more than 3 references from the same journal anymore.
2. We believe that the limitation of this study is related to the fact that it is a retrospective study and related to the number of patients, however, it does not preclude important preliminary conclusions.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Endoscopy, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance,

please upload the primary version (PDF) of the Institutional Review Board's official approval in official language of the authors' country to the system, and the Signed Informed Consent Form(s) or Document(s); for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words). Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Answers

Dear Science editor,

We appreciated the comments. The answers are written bellow:

1. We adapted the documents and files as requested on your observations.
2. The title has been shortened and corrected as well as written in the text.
3. The tables have been corrected and resubmitted.

Sincerely,

Ermelindo Della Libera

Round 2

ANSWERING REVIEWERS

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

Manuscript NO: 75424

Manuscript Type: ORIGINAL ARTICLE

Title: Endoscopic Therapy Using a Self-Expandable Metallic Stent with an Anti-Migration System for Postorthotopic Liver Transplantation Anastomotic Biliary Stricture

Authors: Larissa W Pinheiro, Fernanda P Martins, Mônica LC Contini, Gustavo A Paulo, Angelo P Ferrari, Ermelindo D Libera

REVIEWER'S COMMENTS:

 # 06151472:

Answers provided by the Authors to my previous comments are not detailed, in my opinion. I think that a control group (also a historical group of patients with post-LT biliary strictures) could be of interest, as well as a brief explanation about costs. Nevertheless I did not find any of this information in the revised version of the manuscript. Therefore, my previous comments did not help the improvement of the manuscript, unfortunately."

Answers:

Dear reviewer,

This study has some limitations, such as a small sample size and a retrospective study without a control group from a single center. Presently, there are no studies with control group of patients with post-LT biliary strictures with this type of stent, but we know that future studies, with control group, will indicate more consistent results. Although in our study it wasn't possible to assess costs because it wasn't the objective, it is possible to postulate that since this stent has

a lower migration it could imply lower number of procedures and thus lower costs, but this hypothesis needs to be verified in future studies. The text was modified (in red).

Science Editor's comments:

We are very pleased to receive your revised manuscript (No. 75424). However, after our verification, we found that there are still some issues need to be addressed; ----1. The manuscript has been sent peer-reviewers for re-reviewing. And the reviewer # 05755592 pointed out that "Answers provided by the Authors to my previous comments are not detailed, in my opinion. I think that a control group (also a historical group of patients with post-LT biliary strictures) could be of interest, as well as a brief explanation about costs. Nevertheless I did not find any of this information in the revised version of the manuscript. Therefore, my previous comments did not help the improvement of the manuscript, unfortunately." Please revise the manuscript according to the reviewer's comments, and provide point to point answer to the reviewer; ----2. Please upload the primary version (PDF) of the Institutional Review Board's official approval, prepared in the official language of the authors' country; ----3. Please upload the primary version (PDF) of the Informed Consent Form, prepared in the official language of the authors' country. If there are too many study participants, you can just upload a blank informed consent form; ----4. Please send the revised manuscript to a professional English language editing company to polish the language further. When you submit the subsequent polished manuscript to us, you must provide a language certificate along with it. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240; ----5. Please provide an editable version of Figure 2. In addition, regarding figures and tables, we need to know whether the authors provided the original figures and tables made by author themselves, if not, please provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published. Thank you for your understanding; ----6. Please complete all the revisions based on the version of "7141-75424_Auto_Edited-v1", and upload above mentioned files in a ".zip" file. Finally, please submit your revised version within 7 days.

Answers

Dear Science Editor

We appreciated the comments. The answers are written bellow:

1. This study has some limitations, such as a small sample size and a retrospective study without a control group from a single center. Presently, there are no studies with control group of patients with post-LT biliary strictures with this type of stent, but we know that future studies, with control group, will indicate more consistent results. Although in our study it wasn't possible to assess costs because it wasn't the objective, it is possible to postulate that since this stent has a lower migration it could imply lower number of procedures and thus lower costs, but this hypothesis needs to be verified in future studies. The text was modified (in red).
2. We did upload the primary version (PDF) of the Institutional Review Board's official approval
3. We did upload our blank informed consent form (PDF).
4. The manuscript has been reviewed by a professional in English language.
5. We adapted an editable version of Figure 2 as requested on your observations. All the figures and tables provided were made by the authors themselves.

Sincerely,

Ermelindo Della Libera