

Title: Digital Single-Operator Cholangioscopy for Biliary Stricture after Liver Transplantation

Journal: World Journal of Gastrointestinal Oncology

Response to Reviewers' comments

Dear Editor,

We thank you for your careful consideration of our manuscript. We appreciate your response and overall positive initial feedback and made modifications to improve the manuscript. After carefully reviewing the comments made by the Reviewers, we have modified the manuscript to improve the presentation of our results and their discussion, therefore providing a complete context for the research that may be of interest to your readers.

We hope that you will find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us with other questions or concerns regarding the manuscript.

Best regards,
Jian-Yu Hao

Reviewer #1

Comment 1: *What is the author's purpose in classifying DSOC findings into four types? With the exception of two cases of retransplantation, I did not find any impact of this classification on clinical/endoscopic outcomes.*

Response: We thank the Reviewer for the comment. This classification is purely based on our observations during DSOC. At present, it is only observed that type A might have a good short-term prognosis, while type C and D might have a poorer prognosis, but the number of patients is too small to draw any conclusion. Still, this classification could be applied in future studies.

Comment 2: *Nine (47.4%) of the 19 patients underwent ERCP and had plastic stent placement in the common bile duct within three months prior to DSOC. Since stents might cause changes in the mucosa of the biliary tract (such as granulation tissue growth, erosions or ulcers, or biliary infection when they were blocked...), they might have an impact on the findings of DSOC. Should imaging analysis be excluded from these 9 patients? Or at least the authors should describe the effect of stents on DSOC classification.*

Response: We thank the Reviewer. We agree that there might be some impact, but no one has analyzed it before. We suggest that plastic biliary stents may affect the local mucosa (mostly located at the anastomotic site and the upper and lower mucosa of the bile duct), but the effect is unlikely to be diffuse, and the effect on the intrahepatic bile duct should be minimal. Still, it will have to be examined specifically.

Comment 3: *In the conclusion section of the abstract, "Four different visual types in DSOC may help predict patient outcome", which is not supported by the results of this study.*

Response: We thank the Reviewer for the comment. The sentence was deleted from the Abstract's conclusion (page 4).

Comment 4: *Because all patients included in this study underwent whole cadaveric LT, the title of this study should be revised to "Digital Single-Operator Cholangioscopy for Biliary Stricture after Cadaveric Liver Transplantation.*

Response: We thank the Reviewer. The Title was revised according to the suggestion.

Comment 5: *In page 11, the last paragraph, "These five patients all presented with NAS-like imaging in ERCP... The biliary strictures resolved after the extraction of stones and sludge." Based on this result, do the authors recommend that a balloon catheter be used for debridement of biliary strictures in all patients prior to the use of DSOC, as some patients have biliary strictures that resolve after removal of stones and sludge and do not require DSOC. Therefore, the benefit of DSOC (78.9% of patients) in this study would have been reduced.*

Response: We thank the Reviewer for the comment. We consider that for a blind

stone removal of a narrow site, the use of equipment (balloon or stone basket) might damage the bile duct wall, causing a biliary leak. In addition, blind removal of bile duct stones is not necessarily successful. If the patient does have NAS, the damage caused to the biliary wall by the stone removal instrument may mask the true manifestation of the mucosal surface of the biliary wall. Therefore, it is not recommended to blindly clean the bile duct of NAS.

Reviewer #2

Comment 1: Performing DSOC with endoscopic sphincterotomy (ES) for biliary stricture after liver transplantation carries the risk of postoperative reflux cholangitis. From the perspective of long-term prognosis, there may be a risk of worsening the stricture. As described by the authors, DSOC may be a good indication for patients with severe stenosis and difficulty in guidewire insertion, but I think that DSOC with ES should be limited to the indication. In this study, I am concerned that there may be cases in which the stenosis worsens or the management of reflux cholangitis becomes difficult after a mid- to long-term course. DSOC for biliary stricture after liver transplantation seems to have few advantages that outweigh these risks.

Response: We thank the Reviewer for the comment. Using imaging only, including imaging diagnosis of the causes of bile duct stricture after LT, can be very helpful, but some cases are caused by stones or even small tumors in a narrow bile duct, and bile duct expansion and stent implantation cannot solve the fundamental problem in such cases, and they need to be confirmed by DSOC in order to guide the next treatment. After LT, DSOC is not required for every ERCP, but only for the first ERCP or for difficult ERCP, therefore limiting the use of DSOC to selected cases. The treatment effect and recurrence rate of biliary stenosis after LT are better than after 6 months, and DSOC should be used for early diagnosis and treatment ^[1]. Reflux cholangitis is indeed a complication of DSOC, but relevant studies suggest that preoperative antibiotics can significantly reduce the occurrence of reflux cholangitis ^[2]. A longer operative time, longer biliary inflating time, and forceful bile duct irrigation might increase the risk of reflux cholangitis and should be avoided (when possible) during the procedure.

Editors

Comment 1: *Single center study with small sample size. 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.*

Response: The references were revised. There are now no more than 3 references from a same journal.

Comment 2: *Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”.*

Response: The figure legends were verified and were already following that model.

Comment 3: *Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.*

Response: We thank the Reviewer. We now provide the figures in a single PPT file.

Comment 4: *Please 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.*

Response: The Tables were revised accordingly.

Comment 5: *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. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on*

non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable..”.

Response: All figures are original. We added the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

References

1. Sharma S, Gurakar A, Jabbour N. Biliary strictures following liver transplantation: past, present and preventive strategies. *Liver Transpl* 2008; 14: 759-769. doi: 10.1002/lt.21509. PMID: 18508368.
2. Turowski F, Hugle U, Dormann A et al. Diagnostic and therapeutic single-operator cholangiopancreatography with SpyGlassDS: results of a multicenter retrospective cohort study. *Surg Endosc* 2018; 32: 3981-3988. doi: 10.1007/s00464-018-6141-0. PMID: 29532224.