

Format for ANSWERING REVIEWERS

June 16, 2022



Dear Editor:

Please find enclosed the edited manuscript in Word format (file name: 74757 revised manuscript 2022.6.24. docx).

Title: Screening for Hilar Biliary Invasion in Ampullary Cancer Patients

Author: Tadayuki Takagi, Mitsuru Sugimoto, Rei Suzuki, Naoki Konno, Hiroyuki Asama, Yuki Sato, Hiroki Irie, Jun Nakamura, Mika Takasumi, Minami Hashimoto, Tsunetaka Kato, Ryoichiro Kobashi, Takumi Yanagita, Yuko Hashimoto, Shigeru Marubashi, Takuto Hikichi, and Hiromasa Ohira

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

ESPS Manuscript NO: 74757

The manuscript has been revised according to the reviewers' suggestions:

1 The format has been updated.

2 Revisions have been made according to the reviewers' suggestions.

Reviewer 1: Although false-positive results were obtained with each method, the combination of partial thickening of the bile duct on IDUS and biliary biopsy was useful for diagnosing hilar biliary invasion of ampullary cancer. In addition, it is recommended that hilar biliary biopsy be performed through a catheter to avoid contamination from cancer. However, hilar invasion of ampullary cancer is rare, and hilar investigation might be unnecessary for ampullary cancer patients.

Response: First, we sincerely appreciate your cooperation. We have revised the manuscript according to your comment.

An aim of this study was to clarify the necessity of careful examination of the hilar biliary duct in ampullary cancer patients. It is exactly as you said that hilar investigation might be unnecessary for ampullary cancer patients. This is also an important conclusion. Therefore, we revised the related parts (Lines 76, 105, 110-111, 344, 359-361).

Comment 1: I am not sure how much this is needed in patients with ampullary cancer. Invasion to hilum will be advanced ampullary cancer and might be presenting with other signs and symptoms. Further, large studies are needed to see the timing and

modality if needed for diagnosis of hilar invasion of ampullary cancer.

Response: Thank you for this valuable comment. The points that you raised are limitations. In past reports, hilar invasion of resectable ampullary cancer was not described. Therefore, it is concluded that hilar investigation might be unnecessary in ampullary cancer patients (Lines 264-272). However, a study that involves a large number of patients and hilar invasion cases is desirable (Lines 311-317).

Reviewer 2: The standard surgical treatment for diagnosed ampullary carcinoma is pancreaticoduodenectomy. Intraoperative examination of bile duct margins should be routinely performed to ensure negative margins. This study has certain clinical guiding significance for identifying the occurrence of cholangiocarcinoma at the same time for the earlier local lesions that can be treated by endoscopy. However, due to the complications of pancreatitis, it cannot be used as a routine clinical diagnosis.

Response: First, we sincerely appreciate your cooperation. We have revised the manuscript according to your comment.

As you said, PEP occurred in three patients. In addition, hilar invasion of ampullary cancer is rare. Therefore, hilar investigation cannot be routinely performed for ampullary cancer patients. We added a description of the risk of PEP (Lines 271, 324-325).

Reviewer 3: Nice retrospective study even if the number of patients was not very high. Nice medical work.

Response: First, we sincerely appreciate your cooperation. We are honored by your kind words.

Science Editor: The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade C (A great deal of language polishing)

Scientific Quality: Grade C (Good)

Response: First, we sincerely appreciate that you handled our manuscript.

Company Editor in Chief: I have reviewed the Peer-Review Report, 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.

Response: We sincerely appreciate that you handled our manuscript. We revised the manuscript according to your comments.

Comment 1: 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.

Response: Thank you for checking our figures. We made the PPT figures and added "Copyright ©The Author(s) 2022."

Comment 2: 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. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Response: Thank you for this advice. We revised the tables.

Comment 3: To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thank you for this comment. We used RCA as a reference.

Sincerely,
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