

Point-by-Point Responses

Dear editor,

It is a very good opportunity for us to submit our manuscript to *World Journal of Gastroenterology (WJG)*, and we are very grateful for the opinions of the reviewers and editorial board. We have made several modifications to this manuscript, which are summarized in a point-to-point manner as follows:

QUESTION 1: "Dear Sir I read with great interest your manuscript. I believe it is well written with a solid methodology. Its conclusions are logical and well presented Main limitations (relatively small number of GC cases and unknown nodal status) are acknowledge in the manuscript. I recommend its publication. "

RESPONSE 1: We thank a lot for the encouragement from the reviewer.

QUESTION 2: For manuscripts submitted by non-native speakers of English, please provided language certificate by professional English language editing companies. Please provide language certificate letter by professional English language editing companies (Classification of manuscript language quality evaluation is B).

RESPONSE 2: The reviewer gives this manuscript a "grade A" for its language quality. If the editorial service thinks it still needs a further improvement in English language usage (as the authors are all non-native English speakers, even though, before submitted it to WJG, they asked a visiting U.S. surgeon to polish the English of this manuscript), the authors would be very willing to do so.

QUESTION 3: Author names (unabbreviated) should be given first as first name, middle name (acronym, with no period) and family (sur)name, and typed in bold with the first letter capitalized, with a hyphen included between the syllables of Chinese names, **followed by the complete name of the affiliated institution, city, province/state, postcode and country typed in non-bold.**

RESPONSE 3: We added the postcode for the institution of each author and followed the style from the editorial service.

QUESTION 4: (Author contributions) The format of this section will be as follows: Author contributions: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; Wang CL, Liang L and Fu JF wrote the paper.

RESPONSE 4: We modified this part following the style from the editorial service:

Mao YY, Wei FQ and Liu H designed the research; Yu TN, Mao YY, Wei FQ and Liu H performed the research; Yu TN and Liu H analyzed the data; Yu TN, Mao YY, Wei FQ and Liu H wrote the paper.

QUESTION 5: you need to provide the grant application form(s) or certificate of funding agency for every grant, or we will delete the part of "**Supported by...**".

RESPONSE 5: The certification for the grant (LQ17H030003) is uploaded.

QUESTION 6: (Background) This section should clearly describe the rationale for the study. It should end with a statement of the specific study hypothesis. Please write your research background. No more than 100 words.

RESPONSE 6: The part of "Background" is rewritten as follows (54 words):

According to the latest American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) manuals, cystic duct cancer (CC) is categorized as a type of gallbladder cancer (GC), which had the worst prognosis among all types of biliary cancers. We hypothesized that this categorization could be verified by using taxonomic methods.

QUESTION 7: (Aim) (no more than 20 words) The purpose of the study should be stated clearly, with no or minimal background information, following the format of: "To investigate/study/determine..."

RESPONSE 7: The part of "Aim" is rewritten as follows (10 words): To investigate the

categorization of CC based on population-level data.

QUESTION 8: (Keywords) Please list 5-10 key words for each paper, which reflect the content of the study. 5~10 key words. Please don't include abbreviations in the key words

RESPONSE 8: The updated keywords were Cystic duct cancer, Gallbladder cancer, Extrahepatic cholangiocarcinoma, Surgical management, Taxonomy, Categorization.

QUESTION 9: (Core Tip) Please write a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments. The purpose of the Core Tip is to attract readers' interest for reading the full version of your article and increasing the impact of your article in your field of study. 70~100 words, please **supplement**.

RESPONSE 9: The part of "Core Tip" is rewritten as follows (73 words): In the latest AJCC and UICC manuals, cystic duct cancer is categorized as a type of gallbladder cancer, yet not verified by direct epidemiological evidence in previous researches. Our study used taxonomic methods to analyze population-based big data, including Fisher's discriminant, binary logistics and artificial neuron network models. By using these three models, our study proved that cystic duct cancer is better to be deemed and treated as a kind of extrahepatic cholangiocarcinoma.

QUESTION 10: (Audio core tip)

Please offer the audio core tip, the requirement are as follows:

In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article.

Please submit audio files according to the following specifications:

Acceptable file formats: .mp3, .wav, or .aiff

Maximum file size: 10 MB

To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

RESPONSE 10: Yu TN, the first author, recorded this audio.

QUESTION 11: (Reference) The author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces[1].
e.g.

Cystic duct cancer (CC) is a rare type of biliary cancer which arises in the conjunction between the gallbladder and the extraheptic bile duct[1].

RESPONSE 11: The references were formatted as required.

QUESTION 12: ARTICLE HIGHLIGHTS do not copy the main text

RESPONSE 12: This part was written as follows:

(1) ***Research background***

According to the current guidelines, cystic duct cancer (CC) is categorized as a type of gallbladder cancer (GC), which has the worst prognosis among all types of biliary cancers.

(2) ***Research motivation***

In previous researches, no direct epidemiological evidence verified that CC is more similar to GC, rather than extrahepatic cholangiocarcinoma (EC).

(3) ***Research objectives***

This study aimed to investigate the categorization of CC based on population-level data.

(4) ***Research methods***

We used three taxonomic methods for analysis, including Fisher's discriminant, binary logistics and artificial neuron network models.

(5) ***Research results***

T staging system of perihilar cholangiocarcinoma (a type of EC) better discriminated CC prognosis than GC. By the three taxonomic models, the majority (75.0%-77.8%) of CC cases were categorized as EC.

(6) ***Research conclusions***

Our study suggested that CC should be categorized as a type of EC, not GC.

(7) ***Research perspectives***

Aggressive surgical attitude might be considered in CC cases, to see whether long-term prognosis could be immensely improved like the situation in EC. Future studies with larger sample size are needed.

QUESTION 13: Please check and confirm that there are no repeated references! Please add PubMed citation numbers (PMID NOT PMCID) 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.

RESPONSE 13: We have checked that there are no repeated references, and formatted all the references according to the “Guidelines for Manuscript Preparation and Submission: Retrospective Study” of Baishideng Publishing Group

QUESTION 14: Main text. The main text contains Introduction, Materials and methods, Results, Discussion, and Article highlights (Research background, Research motivation, Research objectives, Research methods, Research results, Research conclusions, and Research perspectives), Acknowledgments, and References.

RESPONSE 14: Main text were formatted as required.

QUESTION 15: Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as “Manuscript No. -Figures.ppt” on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.

RESPONSE 15: The file “Manuscript No. 50847 -Figures.ppt” was uploaded.

QUESTION 16: (Table 1 to 3) Please don't include abbreviations in the title of the figure/table. Please explain all the abbreviations in the figure/table legends: full name (abbreviation). Please explain all the abbreviations of each figure/table under each piece of figure/table legends.

RESPONSE 16: The titles of three table 1 were rewritten. Abbreviations were also listed.

QUESTION 17: Statistical significance is expressed as $aP < 0.05$, $bP < 0.01$ ($P > 0.05$ usually does

not need to be denoted). If there are other series of P values, $cP < 0.05$ and $dP < 0.01$ are used, and a third series of P values is expressed as $eP < 0.05$ and $fP < 0.01$.

RESPONSE 17: Statistical significance was modified.

QUESTION 18: Please put supplementary materials into another file named as “xxxxx-Supplementary material.pdf”

RESPONSE 18: A pdf file “Supplementary table 1-Supplementary material” was created.

Thank you again for the suggestions. Looking forward to hearing from you.

Sincerely,

Hui Liu, PhD (lhui2010@zju.edu.cn)

Zhejiang Provincial Key Laboratory of Laparoscopic Technology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, 310016, Zhejiang Province, China.