May 24, 2021

Dear Editors,

On behalf of all the authors, I would like to thank you for your consideration of this paper. In the revised manuscript you will find the changes that we made in response to the Reviewers. In this response to reviewer letter we also indicated how we have dealt with the Reviewers’ comments.

Please find enclosed the edited manuscript in Word format.

Name of Journal: *World Journal of Gastrointestinal Oncology*

Manuscript Type: MINIREVIEW


Riccardo Inchingolo, Fabrizio Acquafredda, Valentina Ferraro, Letizia Laera, Giammarco Surico, Alessia Surgo, Alba Fiorentino, Stefania Marini, Nicola de’ Angelis, Riccardo Memeo, Stavros Spiliopoulos

Invited Manuscript ID: 03358964

Manuscript NO.: 66798

The manuscript has been improved according to the suggestions of reviewer and Editorial Office’s Comments:

Reviewer #1:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** In this study, Inchingolo et al. provided a literature review of the currently available treatment modus operandi and future directions for unresectable HC. Authors list a variety of
non-surgical treatments and associated clinical trials and outcomes. To best of our knowledgeable, there is no similar literature in recent years.

A: Thank you for the consideration of this paper and for your comment.

Unfortunately, the main weakness derives from the lack of detailed visual table, and the newest research. 1. To make it easier for the reader to read quickly and intuitively, I recommend to make a table, which should include the treatment options, clinical trials, number of people included in the study, results, and references. 

A: A table has been added as requested.

2. The references you included in the present study are not the latest, so you need to include more to improve the quality of the research. Or, generate a workflow demonstrating inclusion and exclusion methodology for articles in this review.

A: This is not a systematic review. Anyway, more and latest references have been added.

3. With immunotherapy advances in cancer therapy, recent studies have demonstrated the role of immunotherapy in HCC and cholangiocarcinoma, and there is also a small sample practice in hilar cholangiocarcinoma (PMID: 33722163). I recommend adding a section on immunotherapy and target therapy.

A: A new section has been added.

4. Unfortunately, I don’t see much in this study about the future direction of the no-surgical treatment. In this section you can emphasize, or add a little bit of basic research content that has not been translated into clinical practice.

A: A new section has been added.

5. I recommend to add the following points: 1). Comparison of the efficacy of IRE and other therapeutic modalities 2). RFA + stents compared to RFA alone or stents alone. 3). Advances in the efficacy of multidisciplinary approaches
**Science editor:** 1 Scientific quality: The manuscript describes a review of the non-surgical treatment of hilar cholangiocarcinoma. The topic is within the scope of the WJGO. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The authors provided a literature review of the currently available treatment modus operandi and future directions for unresectable HC. However, the main weakness derives from the lack of detailed visual table, and the newest research. The questions raised by the reviewer should be answered; and (3) Format: There are 2 figures. (4) References: A total of 48 references are cited, including 12 references published in the last 3 years; (5) Self-cited references: There are no self-cited references; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer’s ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJGO. 5 Issues raised: (1) The authors did not provide original pictures. 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; (2) Please obtain permission for the use of picture(s). 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; and (3) The column should be minireviews. 6 Recommendation: Conditional acceptance.

**A:** Thank you for the consideration of this paper and for your comment.
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 Oncology, 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 final acceptance, the author(s) must add a table/figure to the manuscript.

A: Thank you for the consideration of this paper and for your comment.

Finally, we wish to thank the Editors and the Reviewer for their comments that helped us to increase the value of our paper.

Thank you again for publishing our manuscript in the World Journal of Gastrointestinal Oncology.

Sincerely yours,

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