

Dear Prof. Lian-Sheng Ma, Editors, and Reviewers,

Thank you for your letter and for the comments concerning our manuscript entitled “Artificial Intelligence in Gastroenterology and Hepatology: Status and Challenges” (Manuscript NO.: 62695, Review). Those comments are valuable and helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have provided a comprehensive response to all comments made by the reviewers point by point in the following pages. The revised portions are marked in red in the revised manuscript. The important changes made in the manuscript are as follows:

- Some other platforms such as R and MATLAB have been cited in the manuscript.
- Some latest and valuable references have been cited in the manuscript.
- Some typographical errors such as “opochs” and “Ieee” have been corrected as “epochs” and “IEEE”, respectively.
- The approved grant application forms have been uploaded as a file (62695-Approved Grant Application Forms) in the revision process.
- The original figure documents have been uploaded as a file (62695-Image File) in the revision process.

We deeply appreciate your consideration of our manuscript, and thanks for the editors and reviewers’ constructive advice. If you have any questions, please don’t hesitate to contact me at the address below. Looking forward to receiving your feedback soon. Thank you very much!

Best regards,

Jia-Sheng Cao, MD,

ESMO member.

Department of General Surgery, Sir Run-Run Shaw Hospital, Zhejiang University.

Email: blackcao@zju.edu.cn;

Xiu-Jun Cai (Correspondence author), MD, PhD,

FACS, FRCS, IHPBA member, ELSA member.

Department of General Surgery, Sir Run-Run Shaw Hospital, Zhejiang University.

Email: srrsh_cxj@zju.edu.cn;

Tel: 86 571 86006617; Fax: 86 571 86044817

Lian-Sheng Ma, Science Editor, Company Editor-in-Chief, Editorial Office
Remarks to Authors

Comments (Brief comments): *"We are pleased to inform you that, after preview by the Editorial Office and peer review, as well as CrossCheck and Google plagiarism detection, we believe that the academic quality, language quality, and ethics of your manuscript (Manuscript NO.: 62695, Review) basically meet the publishing requirements of the World Journal of Gastroenterology. As such, we have made the preliminary decision that it is acceptable for publication after your appropriate revision. Upon our receipt of your revised manuscript, we will send it for re-review. We will then make a final decision on whether to accept the manuscript or not, based on the reviewers' comments, the quality of the revised manuscript, and the relevant documents. Please follow the steps outlined below to revise your manuscript to meet the requirements for final acceptance and publication."*

Response: Thank you very much for your remarks. We have modified our manuscript based on those suggestions and comments by editors and reviewers. We believe that the quality of our manuscript has been significantly improved. Point-by-point responses to each editor and reviewer's comments are as follows.

Reviewer Comments to Authors

Reviewer #1

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Comments (Brief comments): *"The authors are dealing with the Artificial Intelligence in gastroenterology and hepatology. In this paper, Cao et al. conduct a comprehensive review of the AI applications in endoscopy, radiology, pathology for accurate diagnosis, treatment, and prognosis. In addition, the authors introduce AI technologies for data processing and the definition, learning and validation of AI models. Finally, they discuss the current limitations and future considerations of AI applications in the areas of gastroenterology and hepatology."*

Response: Thank you very much for your remarks. We have modified our manuscript based on your suggestions and comments, and we believe that the quality of our manuscript has been significantly improved.

Comments (Q1): *"The authors cite Python as an appropriate language for data analysis and AI applications. It would be interesting to cite some other platforms/languages, such as R or Matlab that offer a successful environment for AI."*

Response: Thanks for your suggestions. We are very sorry for our negligence of not describing other platforms/languages such as R Studio or MATLAB, which offer a successful environment for AI. Therefore, we have made revision in the manuscript. For example, in Data process part of METHODS IN DL, we have added *"Other different programming languages such as R Studio (<http://www.r-project.org>) or MATLAB software (University of New Mexico, New Mexico) also offer a successful environment for AI, and they provide similar approaches to address specific tasks."*. And we also have added *"Although several programming tools such as Python, R Studio, and MATLAB vary among themselves, they provide similar options and algorithms to adjust the parameters based on specific tasks."* in Modeling part of METHODS IN DL.

Comments (Q2): *“I found the review work with the tables to be very appropriate. It is a good selection of key studies in literature. The work is complete and up to date, however, I would like to recommend some references from 2021: - Chen, H., & Sung, J. J. (2021). Potentials of AI in medical image analysis in Gastroenterology and Hepatology. Journal of Gastroenterology and Hepatology. - Björnsson, E. S., & Kalaitzakis, E. (2021). Recent advances in the treatment of primary sclerosing cholangitis: For Expert Review of Gastroenterology & Hepatology. Expert Review of Gastroenterology & Hepatology. - Zheng, J., Gao, Z., Pu, L., He, M., Fan, J., Wang, S., ... & He, L. (2021). Analysis of Tumor Disease Patterns Based on Medical Big Data. Journal of Medical Imaging and Health Informatics, 11(2), 478-486. - Yu, H., Singh, R., Shin, S. H., & Ho, K. Y. (2021). Artificial intelligence in upper GI endoscopy- current status, challenges and future promise. Journal of Gastroenterology and Hepatology, 36(1), 20-24. - Mori, Y., Neumann, H., Misawa, M., Kudo, S. E., & Bretthauer, M. (2021). Artificial intelligence in colonoscopy: Now on the market. What’s next?. Journal of Gastroenterology and Hepatology. - Akshintala, V. S., & Khashab, M. A. (2021). Artificial intelligence in pancreaticobiliary endoscopy. Journal of Gastroenterology and Hepatology, 36(1), 25-30. - Wu, J., Chen, J., & Cai, J. (2021). Application of Artificial Intelligence in Gastrointestinal Endoscopy. Journal of Clinical Gastroenterology, 55(2), 110-120.”*

Response: Thanks for your suggestions. We are very sorry for our negligence of not including some valuable references in the manuscript. According to the suggestions, we have read the references above and cited some of them.

First, Reference “Chen, H., & Sung, J. J. (2021). Potentials of AI in medical image analysis in Gastroenterology and Hepatology. Journal of Gastroenterology and Hepatology” demonstrates that various AI-image analysis were applied to endoscopy, radiology, and pathology with the increase of maturity of digitalization in the fields of gastroenterology and hepatology. And we have cited it as Reference 10 in the second paragraph of INTRODUCTION.

Second, Reference “Björnsson, E. S., & Kalaitzakis, E. (2021). Recent advances in the treatment of primary sclerosing cholangitis: For Expert Review of Gastroenterology & Hepatology. Expert Review of Gastroenterology & Hepatology.” highlights the advances in primary sclerosing cholangitis regarding both medical and endoscopic biliary therapy. However, we have reviewed the AI-assisted endoscopy for identifying and detecting esophageal and gastric neoplasia, gastrointestinal bleeding, colorectal polyps, and colorectal cancer in the manuscript, and hepatobiliary diseases were not considered due to few articles focusing on endoscopy in the fields of hepatology. Therefore, we would not cite this reference.

Third, Reference “Zheng, J., Gao, Z., Pu, L., He, M., Fan, J., Wang, S., ... & He, L. (2021). Analysis of Tumor Disease Patterns Based on Medical Big Data. Journal of Medical Imaging and Health Informatics, 11(2), 478-486.” concludes that there is a correlation between tumors and smoking, chronic infection, and occupational pathogenic factors after the analysis of medical big data. Because it is not associated with our topics, the reference would not be cited.

Fourth, Reference “Yu, H., Singh, R., Shin, S. H., & Ho, K. Y. (2021). Artificial intelligence in upper GI endoscopy-current status, challenges and future promise. Journal of Gastroenterology and Hepatology, 36(1), 20-24.” is a review article, and it includes the latest studies of AI in upper GI endoscopy. Meanwhile, we have introduced the AI-assisted endoscopy in the fields of gastroenterology, and therefore, this reference would be cited as Reference 16 in the first paragraph of AI IN ENDOSCOPY.

Fifth, Reference “Mori, Y., Neumann, H., Misawa, M., Kudo, S. E., & Bretthauer, M. (2021). Artificial intelligence in colonoscopy: Now on the market. What’s next?. Journal of Gastroenterology and Hepatology.” is a review article, and it includes the latest studies of AI in colonoscopy. Meanwhile, we have introduced the AI-assisted colonoscopy in the fields of gastroenterology, and therefore, this reference would also be cited as Reference 17 in the first paragraph of AI IN ENDOSCOPY.

Sixth, Reference “Akshintala, V. S., & Khashab, M. A. (2021). Artificial intelligence in pancreaticobiliary endoscopy. Journal of Gastroenterology and Hepatology, 36(1), 25-30.” demonstrates the AI-assisted pancreaticobiliary endoscopy in pancreaticobiliary diseases. However, hepatobiliary and pancreatic diseases were not considered due to few articles focusing on endoscopy in these fields. Therefore, we would not cite this reference.

Seventh, Reference “Wu, J., Chen, J., & Cai, J. (2021). Application of Artificial Intelligence in Gastrointestinal Endoscopy. Journal of Clinical Gastroenterology, 55(2), 110-120.” is also a review article, and it includes the latest studies of AI-assisted endoscopy, including esophagogastroduodenoscopy, capsule endoscopy, and colonoscopy. Meanwhile, we have introduced the AI-assisted endoscopy in the fields of gastroenterology, and therefore, this reference would also be cited as Reference 18 in the first paragraph of AI IN ENDOSCOPY.

Eighth, we have added an extra reference, which introduces an excellent clinical-radiomic model to predict HCC response to first TACE. The sentence “Meanwhile, Chen et al[112] designed an excellent clinical-radiomic model to predict objective response to first TACE based on 595 HCC patients’ CT images, which could assist the selection of HCC patients for TACE.” has been added in the Radiomics part of AI IN RADIOLOGY. Meanwhile, Table 2 has also been updated and updated as a file (62695-Table File) in the revision process.

Comments (Q3): *“The manuscript is very interesting. The motivation and justification are appropriate. The paper is well written in correct English. Now I include some typographical errors: For (several times): opochs read: epochs In refs. 7 and 8, For: Ieee read: IEEE.”*

Response: Thanks for your suggestions. We are very sorry for our mistakes in English. We have corrected “opochs” as “epochs” in Modeling part of METHODS IN DL. And we have also corrected “Ieee” as “IEEE” in References 7 and 8.

Science Editor Comments to Authors

Comments (Q1): *"Scientific quality: The manuscript describes a review of the artificial intelligence in gastroenterology and hepatology. The topic is within the scope of the WJG. (1) Classification: Grade A; (2) Summary of the Peer-Review Report: The authors conduct a comprehensive review of the AI applications in endoscopy, radiology, pathology for accurate diagnosis, treatment, and prognosis. However, some references should be added in it; and (3) Format: There are 3 tables and 2 figures. A total of 149 references are cited, including 113 references published in the last 3 years. There are 3 self-citations, which are related to this review."*

Response: Thank you very much for your comments. We have modified our manuscript according to the Peer-Review Report, and we believe that the quality of our manuscript has been significantly improved.

Comments (Q2): *"Language evaluation: Classification: Grade A."*

Response: Thank you very much for your comments. Two of our authors, Win Topatana and Sarun Juengpanich, are international graduates and English native speakers in our hospital. Additionally, our manuscript was revised and polished by Yun Cai who studies and lives in London for more than 7 years.

Comments (Q3): *"Academic norms and rules: No academic misconduct was found in the Bing search."*

Response: Thank you very much for your comments.

Comments (Q4): *"Supplementary comments: This is an invited manuscript. The study was supported by 3 grants. The topic has not previously been published in the WJG."*

Response: Thank you very much for your comments.

Comments (Q5.1): *"The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy*

of any approval document(s)."

Response: Thank you for your suggestions. We are very sorry for our negligence of not providing the approved grant application forms. And therefore, we have uploaded them as a file (62695-Approved Grant Application Forms) in the revision process.

Comments (Q5.2): *"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."*

Response: Thank you for your suggestions. We are very sorry for our negligence of not providing the original figure documents. Since the figures in this article were created using BioRender, we are unable to provide the figures which ensure that all graphs or arrows or text portions can be reprocessed by the editor. Therefore, we have provided the JPG format in the PowerPoint with modifiable figure legends, and uploaded them as a file (62695-Image File) in the revision process.

Comments (Q5.3): *"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 ×). 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: Thank you for your suggestions. In the manuscript, all pictures in figures are original without reuse, and therefore, the permission is not required.

Comments (Q6): *“Re-Review: Not required. Recommendation: Conditional acceptance.”*

Response: Thank you for your remarks. We have modified our manuscript according to the Peer-Review Report and provided relevant approved grant application forms, and we believe that the quality of our manuscript has been significantly improved.

Company Editor-in-Chief Comments to Authors

Comments (Brief): *"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 Gastroenterology, 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: Thank you very much for your comments. We have revised our manuscript according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors, and we believe that the quality of our manuscript has been significantly improved.