March 04, 2021

World Journal of Gastroenterology (WJG)
Re: "Artificial Intelligence Applications in Inflammatory Bowel Disease: Emerging Technologies and Future Directions"

We are very grateful for the opportunity to respond to the reviewers' and editors' critiques. Please see the revised manuscript with a point-by-point response to the reviewers' comments.

We thank you for considering this manuscript for revision and look forward to your response.

Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Specific Comments to Authors: However, although well written, large parts of this review are very enumerative and at several instances, the author only provide diagnostic performances of the various AI system without providing a rough outline of the study design. The readability and also the educational value of this otherwise nicely executed and important review would be greatly increased if the authors could provide some more details of the studies in the manuscript text. Further, some recent important studies are completely missing. I hence recommend major revision.

RESPONSE:

In this work, Gubatan and co-workers provide a review on applications of artificial intelligence in inflammatory bowel diseases. From the methodology, the authors applied systematic search strategy in PubMed (MEDLINE) and summarize the role of AI in IBD in the following fields: (i) diagnosis and risk prediction, (ii) assessment of disease severity, and (iii) prediction of clinical outcomes in patients with IBD. Overall, the review is well structured and provides a state-of-the art overview on studies in AI in IBD.

Major concerns

1) The entire review is very enumerative and at several instances, only diagnostic performances of the various AI system are given, without providing a rough outline e.g. on the study design and the comparator that the AI system was applied against. The readability and also the educational value of this otherwise nicely executed and important review would be greatly increased if the authors could provide some more details of the studies in the manuscript text.

RESPONSE: Thank you for these excellent suggestions. We have revised Tables 1-3 and added comparators, study design and number of patients in each study included.

Furthermore, we have included a brief description of study design and number of patients in the studies referenced in the body of the manuscript.

Please double check if all relevant publications in the field are indeed included. For example the following important publication is completely missing: Gottlieb et al. Gastroenterology 2020 Oct 21;S0016-5085(20)35283-5.

RESPONSE: Thank you for this suggestion. We have added the above study by Gottlieb et al to our review.

2) References 56 is incomplete/wrongly cited. Please correct to the following: Bossuyt, P., De Hertogh, G., Eelbode, T., Vermeire, S. and Bisschops, R. Computer-Aided Diagnosis With Monochromatic Light Endoscopy for Scoring Histologic Remission in Ulcerative Colitis. Gastroenterology 2021 Jan;160(1):23-25. doi: 10.1053/j.gastro.2020.09.053.

RESPONSE: The reference citation above has been corrected.

Reviewer #2:
Scientific Quality: Grade C (Good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision
Specific Comments to Authors: The review by Gubatan and co-workers gives a good review on the current status of AI in IBD. The manuscript is well written and clear. The literature searching strategy is also clear. It's a bit hard to judge the findings without any descriptions of the cohorts included in the studies. Hoe many patients and controls? Could be included in the tables. A large number of AUCs are presented, but how solid are the findings? Only in one study a validation set is mentioned. Do all the other studies lack validation sets?

RESPONSE: Thank you for these very helpful suggestions. We have revised our Tables 1-3 to include more descriptions regarding study design, number of included IBD patients and controls (when available), as well as which studies included a validation cohort. We have corrected our references according to the journal's requirements and included PMID and DOI.

I miss some overall interpretation of the findings in the different chapters. In the conclusion the authors write that AI has potential and suggest future directions for AI research in IBD, but what is the overall current status for the use of AI in clinical handling of IBD patients. Does AI have a role right now? Page 3, bottom. Have AI really revolutionized anything for clinicians yet or is AI still in its infancy in the clinical context?

RESPONSE: Thank you for these very insightful comments and allow us to clarify.

We have added closing remarks after each section to summarize our major findings: "Taken together, these studies suggest that AI classifiers have high performance in diagnosing or predicting risk of IBD but have some variability with type of AI classifier and modality of data (molecular versus endoscopic)", "These examples highlight the clinical utility, versatility, and performance of AI classifiers in grading the disease activity of IBD patients at the clinical, endoscopic, and histologic level. AI performance may be affected by location of inflammation and may be limited by ability to discriminate between subtle differences", "These studies suggest that AI classifiers may play a role in predicting clinical outcomes and response to specific therapies in patients with IBD. However, future clinical trials are needed to compare the efficacy of AI applications in IBD clinical management versus standard of care before incorporation into real life clinical practice." Finally, we acknowledge the current status of AI in IBD in our conclusion "Currently, the application of AI methods in IBD has been limited to the research setting and has not yet been adopted in real life clinical practice. Furthermore, studies applying AI in the context of colorectal cancer surveillance or prediction in IBD are much needed…"

Some of the references are lack Issue and page numbering.

RESPONSE: We have corrected our references according to the journal's requirements and included PMID and DOI.

Science Editor:

(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: We have included grant information that supported the primary author (JG).

(2) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

RESPONSE: We have revised the references and included missing data including PMID and DOI.

Sincerely,

On behalf of co-authors:
John Gubatan, MD
Sidhartha R. Sinha, MD