

May 18, 2021

Editor-in-Chief, Editorial Office

Re: Manuscript NO: 67486

Title: "Implications of Artificial Intelligence in Inflammatory Bowel Disease: Diagnosis, Prognosis and Treatment Follow up"

Dear Editorial Board and Reviewers,

Thank you for your review of our manuscript, " Implications of Artificial Intelligence in Inflammatory Bowel Disease: Diagnosis, Prognosis and Treatment Follow up"

Below are our point by point responses to the reviewers' comments. We have highlighted all the resultant changes to the manuscript, and tables using blue color and provided a clean copy.

Thank you for the comments and we believe that the edits have strengthened the manuscript.

Please let us know if you have additional questions.

Sincerely,

Motasem Alkhayyat, MD

Reviewer #1: "This is an interesting minireview that aims to IBD and reviewed the current literature of implications of AI in inflammatory bowel disease patients. It is recommended that the content on radiographic diagnostic artificial intelligence for inflammatory bowel disease be added, that the article be fleshed out, or that the title be modified based on what is actually reviewed in this article."

Reply: Thank you for the valuable feedback. The content of radiographic diagnostic artificial intelligence for inflammatory bowel disease has been added to the text.

Reviewer #2: "There is great interest in the usage of AI in various GI diseases including inflammatory bowel disease. For that reason, it is of relevance to try to summarize the present knowledge in a review paper. I think the authors have made a nice attempt in doing so but the manuscript has some shortcomings in its present stand. The introduction sets a rather good background and it is a clear advantage that the authors provide the reader with definitions of some of the central elements included in AI. However, in general I miss a focus on the possible clinical role of the application of AI technology. What does it add sitting in front of an individual patient? Will it change the handling of the patients and if so in what way? It is not enough that a computer can "learn" from big datasets. The developed algorithms must have clinical implications to be useful. In that context it is interesting that AI based on endoscopic imaging can predict histological changes so biopsies may be omitted. This is somewhat contrasting to the fact that histology is an important part of establishing the diagnosis in the sense that IBD has the character of a "syndrome diagnosis" histology being one of the diagnostic criteria. Besides biopsies do have other roles in the evaluation of possible dysplastic changes. Thus, throughout the manuscript I lack a bit more critical attitude in the evaluation of the clinical usefulness of AI. The section "AI and IBD: Disease prediction and diagnosis should be rewritten. It is clearly the weakest part of the manuscript. It should be divided in individual sections describing "Diagnosis" and Prediction of disease relapse. Note that many of the papers mentioned in table 1 describes the use of AI in prediction of disease relapse and NOT its use in diagnosis. The section in its present stand is somewhat misleading in the use of the term "diagnosis" which should be corrected. I think the section would gain by focusing on the potential role of AI in the interpretation of various scans used to evaluate disease (eg CT and MR scans) and in the interpretation on the many images obtained by capsule endoscopy. The use of AI in that context could spare the clinician a lot of time. A minor comment regarding the diagnosis section is that I don't know what is meant by "endocytoscopic observation". The sections on Treatment, follow up and prognosis are clearly the best parts of the manuscript and the tables supports the text nicely. It is of

interest that AI can be used to predict the response to thiopurines better than metabolite measurements. The description of AI in prognosis estimation is also interesting but I think it should be noted that the use of genomics and microbiomics are in a very early state of development and although a focus for research it is still not implementable in daily clinical practice. If the abovementioned comments could be taken into account in a revision of the manuscript I think it would be useful to many readers with an interest in the field"

Reply: Thank you very much for this comprehensive feedback. We have taken it into several points, and resolved each issue separately, points corrected:

1. "in general I miss a focus on the possible clinical role of the application of AI technology. What does it add sitting in front of an individual patient? Will it change the handling of the patients and if so in what way? It is not enough that a computer can "learn" from big datasets. The developed algorithms must have clinical implications to be useful...thus, throughout the manuscript I lack a bit more critical attitude in the evaluation of the clinical usefulness"

> Reply: Thank you very much. We have now included a more detailed critical evaluation for the use of AI as recommended, it is now highlighted under the "introduction" part, page 4, lines 67-80. We have also referenced the ASGE Task Force on Artificial Intelligence which emphasizes on the same point the reviewer had kindly mentioned.

2. "The section "AI and IBD: Disease prediction and diagnosis should be rewritten. It is clearly the weakest part of the manuscript. It should be divided in individual sections describing "Diagnosis" and Prediction of disease relapse. Note that many of the papers mentioned in table 1 describes the use of AI in prediction of disease relapse and NOT its use in diagnosis. The section in its present stand is somewhat misleading in the use of the term "diagnosis" which should be corrected."

>Reply: We highly appreciate this valuable feedback. The title was revised into "AI and image analysis" that includes now 3 subdivisions; ("AI-guided interpretation of radiography", "AI-guided interpretation of endoscopic images and capsule systems", and "AI-guided interpretation of genomics") as recommended.

3. "I think the section would gain by focusing on the potential role of AI in the interpretation of various scans used to evaluate disease (eg CT and MR scans) and in the interpretation on the many images obtained by capsule endoscopy"

>Reply: Thank you very much, we have revised the manuscript to include the section on CT and MR scans, as mentioned in the above point #2.

4. "A minor comment regarding the diagnosis section is that I don't know what is meant by "endoscopic observation""

>Reply: We have changed it into "endoscopic images" as highlighted in the text.

5. "The description of AI in prognosis estimation is also interesting but I think it should be noted that the use of genomics and microbiomics are in a very early state of development and although a focus for research it is still not implementable in daily clinical practice"

>Reply: Thank you for this input. We have mentioned an additional study in the text now under "interpretation of genomics", and we have emphasized on prematurity of this field as kindly mentioned point under the same section as recommended.