Response to Reviewers

Date: 12-FEB-2022

To Artificial Intelligence in Gastrointestinal Endoscopy

Manuscript ID number: 03727521

Title of paper: Artificial intelligence in colorectal cancer screening in patients with inflammatory bowel disease

Dear Editor

Thank you for revising our manuscript. We are delighted that the journal has welcomed a revision. Based on the suggestions of the reviewers, we have modified the original manuscript. Our responses regarding the reviewer's concerns and the subsequent modifications made to the manuscript are listed below on a point-by-point basis.

The authors would like to thank the reviewers for their careful and constructive comments.

Sincerely Yours,

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Comments from the Reviewer:

Reviewer 1

1. The abstract should be written more clearly highlighting the major contributions of the paper.

Response: Thank you for the considerations regarding the manuscript. The responses are presented below in a point-by-point basis. As we agree with the mentioned points, we've made the changes in the manuscript. The abstract was changed according to the suggestions.

2. The organization of the Introduction section is very unsatisfactory, and it is very messy and hard to read. Thus, this section needs rewriting in order to make it crisp and the main points of the research methodology should be mentioned clearly. This will help the readers to appreciate the novelty of the research.

Response: Thank you for the suggestion. The Introduction section was simplified and some information about methodology was included.

3. Improve the literature review. Add several pieces of research in 2019 and complete table 1. Moreover, the following references can be used:

- Designing a sustainable closed-loop supply chain network of face masks during the COVID-19 pandemic: Pareto-based algorithms. Journal of Cleaner Production, 130056. EB Tirkolaee, A Goli, P Ghasemi
- Developing a sustainable operational management system using hybrid Shapley value and Multimoora method: case study petrochemical supply chain. Environment, Development and Sustainability, 1-30. Goli, A., Mohammadi, H.
- A Covering Tour Approach for Disaster Relief Locating and Routing with Fuzzy Demand. International Journal of Intelligent Transportation Systems Research, 18(1), 140-152. Goli, A., Malmir, B.
- Sustainable supply chain network design using products' life cycle in the aluminum industry. Environmental Science and Pollution Research, 1-25. Pahlevan, S.M., Hosseini, S.M.S. & Goli, A.
- Hybrid artificial intelligence and robust optimization for a multi-objective product portfolio problem Case study: The dairy products industry. Computers & industrial engineering, 137, 106090.
- A comprehensive model of demand prediction based on hybrid artificial intelligence and metaheuristic algorithms: A case study in dairy industry. Goli, Alireza and Zare, Hasan Khademi and Moghaddam, RezaTavakkoli and Sadeghieh, Ahmad

- An integrated approach based on artificial intelligence and novel meta-heuristic algorithms to predict demand for dairy products: a case study. Network: Computation in Neural Systems, 1-35. A Goli et al.

Response: Thank you for the indications of new articles. Despite being excellent articles, the authors believe that they do not fit in the article in question, in which the focus is the use of AI in CRC screening. We really appreciate your referrals.

4. Improve the conclusion by indicating core achievement in your research, main managerial insights, and some other novel future outlooks.

Response: Thank you. The Conclusion was modified as suggested by the reviewer.

“The use of AI promotes numerous benefits in medicine, especially in the field of digestive endoscopy. Early detection of pre-neoplastic lesions allows for immediate intervention and prevention of progression to more severe forms such as CRC. The benefits for IBD patients go beyond CRC screening and include the identification and characterization of inflammation, recurrence pattern, mucosal healing, and recognition of a worrisome lesions. Future studies related to AI are expected to add clinical information, such as prediction of disease complications as well as models to predict the best drugs to each patient according to the inflammatory profile and response to another therapies. AI also can help in the IBD diagnosis using combinations of symptoms and biomarkers, in addition to genetic and microbiota data, and help in the differentiation between Crohn disease and ulcerative colitis. Despite advances in this area, this technology was not designed to replace human intelligence, rather to improve the detection of lesions. The combination with the expertise of endoscopists is essential for the successful application of AI in clinical practice. Another limitation worth mentioning is that the use of AI is not widely available, but it is expected to be applied in the future for colonoscopy and optical biopsy or endocytoscopy. It is also expected that there will be greater accessibility and availability not only for IBD patients, but also for the general population.”

Reviewer 2

This manuscript is a mini review on the application of AI to diseases related to the intestine, mainly the colon. There are no major problems with the description. However, I would like the authors to consider the following points to make easier for readers.

1. As this is a review, even if it is a "mini" review, I would like to see the authors indicate the scope of the search (time range, DB name, etc.) and the criteria for selecting the references.

Response: Thank you for the considerations regarding the manuscript. The responses are presented below in a point-by-point basis. As we agree with the mentioned points, we've made the changes in the manuscript. Data regarding the literature search were included in the end of the Introduction: "An electronic search of the literature was performed using MEDLINE (PubMed) from 2010 to December 2021. Only articles published in English language were included. Keywords used in the search were artificial intelligence, inflammatory bowel disease, ulcerative colitis, Crohn's disease, colorectal cancer."

2. I think it would be easier to understand if the "Introduction" is divided into the purpose of this research and an explanation of AI itself.
Response: Thank you. The Introduction section was modified. We have simplified the Introduction as suggested by other reviewer and added a subsection named "ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING"

3. In addition, I think it would be easier for readers to understand if the case studies are divided into two broad chapters, "Application of AI to colonoscopy using endoscopy" and "Application of AI to patients with inflammatory bowel disease," and then divided into sections for each purpose within each chapter.
Response: We have changed the topics of the article, including the topic "ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING". Also, the topic "Application of Artificial Intelligence in CRC screening in patients with IBD" was put in a subsection of the topic "ARTIFICIAL INTELLIGENCE IN PATIENTS WITH IBD".

4. As the explanation of AI is descriptive, it would be easier to understand by including diagrams.
Response: Thank you for the suggestion. A diagram was included - Figure 1.

5. The phrase "Another advantage of in AI examinations performed "under the eyes"", at the bottom of Page 5, is a little difficult to understand.
Response: Thank you for the correction. We have cut of these words (performed "under the eyes").

6. Whether Reference 2 is a webpage, or a document is not shown. If it is a webpage, please provide the URL and reference date, if it is a paper or article, please provide the source.

Response: Thank you for the correction. The reference was completed (Kulkarni S, Seneviratne N, Baig MS, Khan AHA. Artificial Intelligence in Medicine: Where Are We Now? Acad Radiol. 2020 Jan;27(1):62-70. doi: 10.1016/j.acra.2019.10.001. Epub 2019 Oct 19. PMID: 31636002).

Reviewer 3

This is a mini review. The authors summarize the application of artificial intelligence in gastrointestinal endoscopy and related inflammatory bowel disease and screening for colorectal cancer. Overall, the paper fit the journal well, but major revisions are required before being accepted.

1. Although the title of the article is artificial intelligence in colorectal cancer screening, the related application of artificial intelligence has not been written in depth.

Response: Thank you for the considerations regarding the manuscript. The responses are presented below in a point-by-point basis. As we agree with the mentioned points, we've made the changes in the manuscript. Some information has been added in the manuscript in order to make it clearer and more objective.

2.The length of each section needs to be paid attention to. For example, discussion in section 'APPLICATION OF AI IN GASTROINTESTINAL ENDOSCOPY' has to be simplified. Simplifying the Introduction section is also recommended.

Response: Thank you for the suggestion. Both of the sections were simplified.

3.A section to discuss the disadvantages of traditional medicine and the benefits of AI in gastrointestinal endoscopy is recommended.

Response: Thank you for the suggestion. We have included the suggestion in the text.

"The advantages of using AI compared to traditional endoscopy are mainly related to the reduction of costs and risks inherent to the endoscopic procedure, such as polypectomies and histological analysis of lesions not potential for malignancy, in addition to the shorter examination time. Furthermore, studies have already shown the benefits of using AI in all fields of digestive endoscopy. In the esophagus, AI can be applied in the diagnosis of Barrett's esophagus, and in the diagnosis, prognosis and evaluation of response to treatment of esophageal tumors. In the stomach, AI can help in the detection of gastric cancer as well as in the prognosis of patients undergoing chemotherapy. In the lower gastrointestinal tract, its main indication has been in the detection of pre-neoplastic lesions and, more recently, in IBD."

4. Simply citing existing literature such as in Section ‘APPLICATION OF AI IN PATIENTS WITH IBD’is not enough, what are your In-depth comments and discussions?

Response: Thank you for your suggestions. Comments about the importance of AI in IBD were included.

“In the future, the application of AI could revolutionize the entire management of patients with IBD, from predicting the risk of developing the disease to choosing the best therapeutic strategy for each patient. AI can help to create prediction models of disease development risk, based on data such as the presence of genetic and environmental risk factors, as well as characteristics of the intestinal microbiota and the immune response of each individual. Regarding the diagnosis of IBD, AI can assist with algorithms based on the presence of genetic mutations, presence of signs and symptoms, results of biochemical and serological exams, fecal biomarkers, endoscopic and histological characteristics, and presence of changes in radiological exams, in addition to helping to differentiate between ulcerative colitis and Crohn's disease. In the treatment, the application of AI can help in choosing the best therapeutic strategy for each disease phenotype, in addition to helping to choose the best drug for each patient, based on the severity and extent of the disease, presence of disease complications, risk factors of poor prognosis and especially considering the drugs mechanism of action combined with the inflammatory and genetic profile of each patient.”

5.Also, a schematic figure to show AI in screening for colorectal cancer is required. Terms including deep learning, machine learning, AI and some related screening features are recommended to be added in the figure.

Response: Thank you for the suggestion. Figure 2 was added in the manuscript.

Reviewer 4

Thank you for giving me a chance to review this manuscript title Artificial intelligence in colorectal cancer screening in patients with inflammatory bowel disease. In this review, the authors aimed to show the benefits and innovations of AI in the screening of CRC in patients with IBD. My major comments are as following:

1. The paper pays too much attention to the description of phenomena and lacks discussion on mechanism, which may be that the benefits of readers are unsteady and limited. But I believe that after the corresponding modification. It will be a good manuscript.

Response: Thank you for the considerations regarding the manuscript. The responses are presented below in a point-by-point basis. We hope that the changes made based

on the reviewers' suggestions have improved the article, making it clearer and more objective.

2. On page four, second paragraph, "Detection of adenomas during colonoscopy is dependent on the examining endoscopist, with studies reporting a variation of 7%–53% among different physicians[5]. Failure to detect neoplastic lesions can be associated with the development of CRC in the interval between two colonoscopies[4]."The reasons for different doctors' inconsistent diagnosis are diverse, and the description here is inaccurate.

Response: Thank you. The explanation was added in the text.

“The marked difference in this rate has been attributed to the endoscopist's previous experience, the resection technique used and the adequate surveillance of suspicious lesions. Failure to detect neoplastic lesions can be associated with the development of CRC in the interval between two colonoscopies.”

3. On page six, line 20,"This method is known to be more effective in detecting lesions in the right colon because the distal part of the colon, especially the sigmoid colon, may have some blind spots, reducing the efficiency of the CADe system. "Why is the sigmoid colon blind spot?

Response: “The sigmoid colon is not fixed and presents sharp angulation points, such as the sigmoid-descending junction, resulting in increased blind spots with an increased risk of missing lesions, especially small polyps.” This information was added in the manuscript.

3.The reference format is incomplete, such as the references 2 missing content.

Response: Thank you. The references were corrected as the reference 2 (Kulkarni S, Seneviratne N, Baig MS, Khan AHA. Artificial Intelligence in Medicine: Where Are We Now? Acad Radiol. 2020 Jan;27(1):62-70. doi: 10.1016/j.acra.2019.10.001. Epub 2019 Oct 19. PMID: 31636002).