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Date: 29 April 2024

Dear Prof. Tarnawski,

The comments you have kindly provided to improve our submitted manuscript entitled **“Diagnostic delay in inflammatory bowel diseases in a German population”**.

We would like to thank the reviewers for the valuable comments, which have been very fruitful for the refinement of the manuscript. The entire manuscript was thoroughly revised according to the reviewers' comments. A detailed point-by-point response is attached below. We assume that this revision has substantially improved the quality of the manuscript and hope that the reviewers will agree with our changes to the manuscript.

The study was not financially supported. All authors have contributed significantly in writing the manuscript and are in agreement with the content. The content has not been published or is under consideration for publication elsewhere and will not be sent to another journal until a decision is made concerning publication by World Journal of Gastroenterology.

Thank you in advance for your endeavours.

Yours sincerely, on behalf of all authors,



Dr. med. Anja Schirbel



Dr. med. Elisabeth Blüthner

Point-by-point Response

Reviewer: 1

The authors investigated an interesting topic and pointed out the crucial role of doctors in it. Relevant research can help medical institutions propose a series of improvement measures for early detection of related diseases.

Response:

We thank the reviewer for his time and the very positive feedback on the manuscript.

Reviewer: 2

The incidence of inflammatory bowel disease is increasing year by year, and the problem of delayed diagnosis of IBD is a prominent problem regardless of geography. This study is a 10-year retrospective study of delayed diagnosis in German IBD patients, and found some risk factors for delayed diagnosis, which are related to both "Patient waiting time" and "Physician time to diagnosis". Relative risk factors for Crohn's disease and ulcerative colitis are also different. Although due to regional differences, ethnic differences, differences in medical systems, and differences in doctors' perception of diagnostic criteria in different regions, this study is still a guide and reference for gastroenterologists around the world. It is recommended that this article be published, which will provide guidance and reference for doctors in different medical systems in the timely diagnosis of inflammatory bowel disease.

Response:

We do appreciate the good comments of the reviewer, followed the specific annotations and tried to answer the specific questions within the revised text, respectively.

1) Lack of clarity on the presentation of results and conclusions, such as what are the risk factors for delayed diagnosis? What are the protective factors that reduce waiting time? The expressions in the abstract, results, and discussions are inconsistent, and it is easy to misunderstand.

Response:

We appreciate this encouraging comment and have edited the abstract and results to make the statements more precise and consistent.

2) Some of the results are puzzling, such as why there is a difference between CD and UC "Physician time to diagnosis" when they are doctors who have the same knowledge of IBD. Why does "a positive family history for UC" delay a doctor's diagnosis? It is better to have a discussion and a reasonable explanation.

Response:

This is an interesting concern. We agree with the reviewer that some results might be surprising. Multiple studies demonstrated a diagnostic delay in CD patients in comparison to UC patients but have not put in effort into the impact of the different time intervals [1–4]. Of note, Nguyen and colleagues published a comprehensive statistical analysis of factors that influence time to diagnosis and disease outcome [5]. Interestingly, the published data was in accordance with our results. The patient waiting time in CD vs. UC patients (1.0 vs. 0.7 months; $p=0.541$) almost equals whereas the physician diagnostic time was significantly prolonged in CD patients (1.1 vs. 3.5 months, $p<0.001$). Symptom variance of patients with CD compared to patients with UC, overlap of functional disease complaints as well as frequent involvement of proximal small bowel might be the reason for these results. We debated these points extensively in the discussion of our paper (page 15 - 17, line 316 – 367).

3) The conclusions in the abstract do not cover the main outcomes of the article, and only patients with CD are mentioned, but not UC patients.

Response:

Thank you for this critical comment. In the revised version of our manuscript, we followed this recommendation and reworded the abstract. By now, the revised statements in the results match better with our mentioned conclusions in the abstract.