

Name of journal: World Journal of Gastroenterology
Manuscript NO: 88811
Response to Reviewers

Dear reviewers,

Thank you for the comments on our manuscript entitled "Clinical value of the Toronto IBD Global Endoscopy Reporting (TIGER) score in ulcerative colitis" (NO: 88811). All of these comments were very helpful for revising and improving our paper. We have studied these comments carefully and have made corresponding corrections. The changes in the revised manuscript are highlighted in yellow.

The responses to the reviewers' comments are provided below.

Responses to the comments from Reviewer 1:

Comments:

Well conducted and well written study. In the discussion the following sentence Disk is not the correct word/term : Zittan et al.[11] reported that the TIGER score was positively correlated with faecal calprotectin levels and the inflammatory bowel disease (IBD) Disk. In the discussion ASA should be either 5-ASAs or 5-aminosalicylates.

1. In the discussion the following sentence Disk is not the correct word/term : Zittan et al.[11] reported that the TIGER score was positively correlated with faecal calprotectin levels and the inflammatory bowel disease (IBD) Disk.

Response: Thank you for pointing this out. We again reviewed the original and related literature. This term was proposed firstly in 2017 and the source is "*In conclusion, the IBD Disk is a self-administered adaption of the validated IBD-DI that has the potential to be a valuable tool for assessing IBD-related disability experienced by the patient and promoting discussion on specific issues important to the patient and the health care professional during consultation*"^[1]. The reference cited in our manuscript mentions that "*In conclusion, in this pilot study, the TIGER score demonstrates significant correlation with FC, CRP, and IBD Disk score in Crohn's disease patients, and significant correlation with FC and IBD Disk score in ulcerative colitis patients*"^[2]. We think that the TIGER score should be positively correlated with the IBD Disk score instead of IBD disk, which is a tool actually. Therefore we revised "IBD Disk" to "IBD Disk score".

2. In the discussion ASA should be either 5-ASAs or 5-aminosalicylates.

Response: Thank you for this suggestion. We changed "ASA" to "5-aminosalicylates" or "5-ASAs" (abbreviation) throughout the manuscript including the result, discussion, and tables. The changes are highlighted in yellow.

Responses to the comments from Reviewer 2:

Comments: 1. Are there controversies in this field? What are the most recent and important achievements in the field? In my opinion, answers to these questions should be emphasized. Perhaps, in some cases, novelty of the recent achievements should be highlighted by indicating the year of publication in the text of the manuscript. 2. The results and discussion section is very weak and no emphasis is given on the discussion of the results like why certain effects are coming in to existence and what could be the possible reason behind them? 3. Conclusion: not properly written. 4. Results and conclusion: The section devoted to the explanation of the results suffers from the same problems revealed so far. Your storyline in the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from what one can infer from the empirical results. 5. The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning. A real discussion should also link the findings of the study to theory and/or literature. 6. Spacing, punctuation marks, grammar, and spelling errors should be reviewed thoroughly. I found so many typos throughout the manuscript. 7. English is modest. Therefore, the authors need to improve their writing style. In addition, the whole manuscript needs to be checked by native English speakers.

1. Are there controversies in this field? What are the most recent and important achievements in the field? In my opinion, answers to these questions should be emphasized. Perhaps, in some cases, novelty of the recent achievements should be highlighted by indicating the year of publication in the text of the manuscript.

Response: Thank you for pointing this out. Based on your advice, we amended the relevant sections in the manuscript. About the controversies and the most recent and important achievements, we consulted more literature and emphasized the answers in the introduction that *“Recently, the extent of mucosal inflammation has been emphasised, and the controversy on the accuracy of the UCEIS score and MES has arisen since both tools provide final scores aimed only at the most severely inflamed segment without highlighting the number of segments exhibiting moderate-to-severe inflammation[11, 12]. Endoscopic scores focusing only on the severity during the medical treatment may be flawed because of the presence of segmental remission[13, 14]. Therefore, attempts have been made in the past 10 years to assess disease extent and score the entire colonic mucosa[15, 16]”*. As for the publication year of the recent achievements, we revised and added the publication time of the achievements in the manuscript that *“The UCEIS score, proposed by Travis et al. in 2012” ,“ the MES, created by Schroeder et al. in 1987”* and *“In 2021, Zittan et al.[17] proposed a reliable and useful endoscopic score, the Toronto IBD Global Endoscopic Reporting (TIGER) score”* to make it clearer. The changes are highlighted in yellow in the manuscript.

2. The results and discussion section is very weak and no emphasis is given on the discussion of the results like why certain effects are coming in to existence and what could be the possible reason behind them?

Response: We appreciate you for pointing out our writing deficiencies. Writing should indeed explain the phenomenons and look for the possible reason. The clinical outcomes and clinical phenomenons do not seem to be easy to explain because of the lack of relevant literature. We consulted more literature and tried to explain the reasons after each part of the results in the discussion. About the finding that *“the TIGER score strongly correlated with the UCEIS score and moderately correlated with MES”*, we emphasized the possible explanation that *“These findings demonstrate a better correlation between the TIGER and UCEIS scores, which we attribute to the better definition and grading of the descriptors in the two scoring systems, such as more detailed scoring criteria for erosions and ulcers[21]”*. As for the finding that *“We discovered that the TIGER and UCEIS scores could distinguish between the different UC severities. Notably, the TIGER score demonstrated optimal diagnostic performance for severe UC.”*, we added the inference that *“This superior performance may be because the TIGER score assesses total bowel segments and considers both inflammation and the extent of UC, whereas the UCEIS score and MES exclude the extent of UC. Interestingly, the extent is one of the dimensions used to evaluate endoscopic severity and can influence the overall severity of UC[22]”* and *“Moreover, a finer categorization and larger scale of the scoring system may be more advantageous and accurate in reflecting inflammatory burden and treatment response[22, 25]. The UCEIS score, ranging from 0 to 8, provides a larger scale and finer gradings of ulcers and bleeding than the MES. Song et al.[26] also demonstrated that the UCEIS score was superior to MES in diagnosing UC severity. Therefore, we infer that the TIGER score can provide a detailed description of the ulcers (size and percentage of surface) and localised inflammation in relation to the bowel segment and a wide range of scores between 0 and 560, resulting in optimal performance when reflecting the overall severity[17]”*. Other revised sections can be found in the manuscript. We have tried to find the possible reasons of every part of the results and the revised contents are highlighted in yellow.

3. Conclusion: not properly written.

Response: Thank you for this suggestion. Our previous conclusions were repetitive and absolute. We have reviewed the literature with similar research directions and taken their methods, results and conclusions into account. Zhang et al.^[3] evaluated DUBLIN, UCEIS score, and the Mayo ES and drew the conclusion that *“This study demonstrates that both the DUBLIN and UCEIS scores outperform the Mayo ES in assessing disease severity and predicting treatment response and clinical outcomes in UC patients”*. Liu et al.^[4] assessed the modified DUBLIN score and got the conclusion that *“Increased DUBLIN and modified DUBLIN scores were conducive to screening serious disease, but only modified DUBLIN scores had the potential to assist in making an upgraded therapeutic”*

schedule". Eventually we revised our conclusion to *"The TIGER score is a useful scoring method that provides an overall intestinal evaluation of endoscopic activity and demonstrates a significant correlation with the UCEIS score, MES, and laboratory indices, particularly CRP levels. Furthermore, the TIGER score may be superior to the UCEIS and MES scoring systems in improving the accuracy of clinical disease severity assessment, guiding therapeutic decision-making to some extent, and predicting short-term clinical outcomes."* to make it more intelligible.

4. Results and conclusion: The section devoted to the explanation of the results suffers from the same problems revealed so far. Your storyline in the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from what one can infer from the empirical results.

Response: As explained in question 2, we have explored and added possible reasons for every part of results that we got from the study. Our storyline in the results section could be followed as the below. The UCEIS and MES score are commonly used in clinics and trials. The TIGER score, a newly proposed endoscopic scoring system, its clinical value remains unclear. Firstly we analyzed the correlation between the TIGER score, UCEIS score and MES with the title of *"Correlations among the TIGER score, UCEIS score, and MES"*. Then we investigated the differentiation and diagnostic capability of the three scores for the disease severity of UC with the title of *"Comparison of the endoscopic scores in different clinical severities"* and *"Comparison of the diagnostic value of the endoscopic scores for patients with severe UC"*. Next, we analyzed the correlation of the three scores with laboratory and clinical parameters, particularly CRP levels, since we thought that the laboratory and clinical parameters could reflect the severity of UC on the other hand with the title of *"Correlations between the three endoscopic scores and laboratory/clinical parameters"*. We then analyzed the predictive potentials of the three scores for treatment with the title of *"The relationship between endoscopic scores and advanced treatment"*, and short-term prognosis (1-year readmission) with the title of *"Relationship between endoscopic scores and 1-year readmission"*. Based on the above results, we concluded that the TIGER score might be superior to the UCEIS and MES scoring systems in improving the accuracy of clinical disease severity assessment, guiding therapeutic decision-making to some extent, and predicting short-term clinical outcomes. Zhang et al.^[3] and Liu et al.^[4] analyzed the clinical value of DUBLIN score and Song et al.^[5] validated that the improved Mayo Endoscopic Score had a higher value for evaluating clinical severity of UC. Based on the above literature, we think that the endoscopic scoring system may contribute to evaluating, treating, and managing patients with UC after validation. We learn from the prior studies that how they draw their conclusions. Our discussion has been revised followed with the story line of the results, and each paragraph in the discussion corresponds to the related result.

5. The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning. A real discussion should also link the findings of the study to theory and/or literature.

Response: Thank you for pointing this out. We have deleted some details that could not provide much meaning and kept the important details to make the discussion more readable. As explained in question 2, we have consulted more literature, tried to explain the reasons behind our results and linked the findings with other studies. For example, in the discussion of the correlation between TIGER score and laboratory parameters (particularly CRP levels) , we added the explanation that *“Inflammatory biomarkers can exacerbate damage to the epithelial barrier and imbalance of the intestinal mucosal immune system and influence the synthesis of related protein synthesis in UC[32, 33], which may be manifested in endoscopic mucosal inflammation and reflected by the TIGER score since it contains a clear description of mucosal appearance and ulcer conditions and could precisely describe and assess the entire intestine”*. Moreover, to explain that the TIGER score may be a useful indication of escalating treatment, we explained and linked it to other studies that *“Severe endoscopic activity and extensive colitis may represent a severe degree of disease, leading to therapy escalation and poor prognosis[36-38], which could explain why patients with higher TIGER scores were at a higher risk of advanced treatment in this study. Bálint et al.[39] suggested that a scoring system should provide additional information on the localization and extent of the disease and argued that this could guide treatment choices, which is consistent with the above mentioned results”*. For different results, we explained that *“Nevertheless, because of factors including discomfort and complications, total colonoscopic studies included fewer acute severe cases, which might have resulted in different results. Gomes et al.[24] revealed a poor correlation between total colonoscopic findings and clinical manifestations”*. Other revised contents can be found in the manuscript which are highlighted in yellow.

6. Spacing, punctuation marks, grammar, and spelling errors should be reviewed thoroughly. I found so many typos throughout the manuscript.

Response: Thank you for your comments. We apologize for our language mistakes. We carefully edited English language and the typographic errors in the revised manuscript. Additionally, the manuscript was edited by a native-English speaker. We thanked Editage for editing this manuscript.

7. English is modest. Therefore, the authors need to improve their writing style. In addition, the whole manuscript needs to be checked by native English speakers.

Response: Thank you for all your suggestions and we benefit a lot. We will work for our writing style. The manuscript was edited by a native-English

speaker, Green from Editage and a new language certificate could be provided.

We would like to express our great appreciation to the reviewers for the comments on our paper.

If you have any further queries, please do not hesitate to contact us.

Kind regards,

Xue-li Ding

References

1. Ghosh S, Louis E, Beaugerie L, Bossuyt P, Bouguen G, Bourreille A, Ferrante M, Franchimont D, Frost K, Hebuterne X, Marshall JK, O'Shea C, Rosenfeld G, Williams C, Peyrin-Biroulet L. Development of the ibd disk: A visual self-administered tool for assessing disability in inflammatory bowel diseases. *Inflamm Bowel Dis* 2017; 23:333-340 [PMID: 28146002 DOI: 10.1097/mib.0000000000001033]
2. Zittan E, Steinhart AH, Aran H, Milgrom R, Gralnek IM, Zelber-Sagi S, Silverberg MS. The toronto ibd global endoscopic reporting [tiger] score: A single, easy to use endoscopic score for both crohn's disease and ulcerative colitis patients. *J Crohns Colitis* 2022; 16:544-553 [PMID: 34272937 DOI: 10.1093/ecco-jcc/jjab122]
3. Zhang XF, Li P, Ding XL, Chen H, Wang SJ, Jin SB, Guo J, Tian ZB. Comparing the clinical application values of the degree of ulcerative colitis burden of luminal inflammation (dublin) score and ulcerative colitis endoscopic index of severity (uceis) in patients with ulcerative colitis. *Gastroenterol Rep (Oxf)* 2021; 9:533-542 [PMID: 34925850 DOI: 10.1093/gastro/goab026]
4. Liu L, Ouyang H, Su J, Lin Y, Hu Y, Shi H, Xie C. Increased modified dublin scores are associated with serious ulcerative colitis and treatment failure. *Therap Adv Gastroenterol* 2022; 15:17562848221142671 [PMID: 36545387 DOI: 10.1177/17562848221142671]

5.Song Z, Zhang M, Ren Y, Iang B. [improved mayo endoscopic score has a higher value for evaluating clinical severity of ulcerative colitis]. *Nan Fang Yi Ke Da Xue Xue Bao* 2022; 42:997-1005 [PMID: 35869761 DOI: 10.12122/j.issn.1673-4254.2022.07.05]