Response letter

World Journal of Clinical Cases

Sep 28, 2020

Dear Editor

We would firstly like to thank the reviewers and editors for donating time and efforts to our manuscript entitled "An Effective Immune-Inflammation Index for Ulcerative Colitis and Activity Assessments". Your comments and those from the reviewers were highly insightful and strengthened the logicality and rationality of our study. Our manuscript has been revised as recommended. Our point-by-point responses to each of the comments of the reviewers are presented as follows. We shall look forward to hearing from you at your earliest convenience.

Yours sincerely

Xiaozhong Yang

Responses to the comments of Reviewer #1:

Specific Comments to Authors: This is a retrospective study with a relevant theme on immune inflammatory indicators to identify disease activity in patients with ulcerative colitis, with a comparison group. In the introduction, the acronym SII is not described. The results could highlight some findings as correlation, were weak, as well as description of relevant data of the ROC curve.

Response: Thanks for the reviewer's suggestions. It's a valuable point indeed. We described the acronym SII clearer and more readable in introduction. In Results, we stated the correlation more clearly and modified our description for better readability.

Responses to the comments of Reviewer #2:

Specific Comments to Authors: The authors aim to report the efficacy of SII, NLR and PLR for patients with UC. However, there are several major concerns with regards to the investigation. Please see below. Major point 1)

Because the study compared only UC patients with healthy controls, the authors were not able to conclude that the makers were useful for confirming UC. The makers were useful for showing only a difference between UC patients and healthy controls. 2) The UC patients were treated with various therapy included immunosuppressant, steroids, and/or monoclonal antibody therapy. The therapies must influence the SII, NLR and PLR. The study should be added the analysis of various therapies for makers. Unfortunately, a study recently reported usefulness of NLR, and PLR for UC treated with anti-TNF (Novel Prognostic Biomarkers of Mucosal Healing in Ulcerative Colitis Patients Treated With Anti-TNF: Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio. Inflamm Bowel Dis. 2020 Mar 31;izaa062. doi: 10.1093/ibd/izaa062.) . I recommend for authors to add the additional analysis to the manuscript using examples from above manuscript.

Response: Thanks for the reviewer's suggestions.

1)As shown in Table 1, hematologic parameters including WBC, PLT, N, L, SII, NLR and PLR in different groups is variable. Our research not only compares the differences in hematological indicators between normal people and UC patients, but also analyzes their diagnostic value for UC, and judges the risk of severe UC. We listed these data in Tables and discussed in Methods and Results.

2) The therapy is an important clinical factor for blood indicators in UC patients. The research mentioned by the reviewer showed that NLR and PLR only have a predictive effect on mucosal healing after anti-TNF treatment.

Because we focused on inflammatory biomarkers in mucosal severity assessment, regardless of the current medication regimen, we analyzed biochemical levels for UC in severe patients. Future research on SII, PLR, and NLR for judging the responsiveness of drug treatment and mucosal healing has been on the agenda, so as to determine whether the treatment should be upgraded. Many thanks for the reviewer's careful review and critical suggestions. These make our paper more readable and logical.

Responses to the comments of Reviewer #3:

Specific Comments to Authors: The authors used a case-control study to study the relationship between white blood cells (WBC), hemoglobin (HB), platelets (PLT), neutrophils (N), lymphocytes (L), monocytes (M), systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) and UC disease status. They found that SII, NLR, and PLR values were higher in patients with UC than controls and were positively correlated with Mayo endoscopic score (MES), extent, degree of ulcerative colitis burden of luminal inflammation (DUBLIN) score and ulcerative colitis endoscopic index of severity (UCEIS). In their references (12&13), platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio predicted mucosal disease severity and neutrophil-to-lymphocyte ratio predicted loss of response to Infliximab in Ulcerative Colitis. The paper is unfortunately lack of novelty.

Response: Thanks for the reviewer's comments and suggestions. Platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio in mucosal disease severity were already reported. However, these previous indexes were not generally accepted criteria for the diagnostic process and potential relapse risk of severe endoscopic disease. We aimed to analyze the abnormal hematological parameters onset which might benefit the early identification

and control of these severe patients. It was established that infiltration and metastasis of malignant tumors are inflammatory-mediated processes and mounting evidence also showed that SII was a novel prognostic predictor in patients with cancer undergoing treatment. Our data currently indicated the increased possibility of early diagnosis of UC and potential risk for severe mucosal lesions, more investigation on predicting treatment response needs to be designed and studied. The reviewer's question is critically important and we'll perform in-depth researches to reveal the possibility.

Responses to the comments of Reviewer #4:

Specific Comments to Authors: Zhang et al has submitted an article with the title of "An Effective Immune-Inflammation Index for Ulcerative Colitis and Activity Assessments". The authors evaluated the hematological indexes in assessing the activity of ulcerative colitis in 172 ulcerative colitis patients. Authors concluded that "systemic immune-inflammation index has importance in confirming ulcerative colitis and identifying its activity". The conclusion is insightful, and could be helpful in clinic application. However, abbreviations (such as "Discussion - GPⅡb/Ⅲa") should be with its full name when it firstly appears in the paper and editing of English language is also recommended.

Response: Greatly appreciate for the reviewer's positive comments of our work and detailed suggestions to improve our paper's quality. All abbreviations and descriptions were checked and corrected. Language was also smoothed thoroughly by language experts. Many thanks for the reviewer's careful review.