RESPONSE LETTER

Name of journal: *World Journal of Gastroenterology*
ESPS Manuscript NO: 45080
Title: Two-year delay in ulcerative colitis diagnosis is associated with anti-TNFα use

Reviewer's code: 02917331

Dear Reviewers and editor

Thank you for the very kind and insightful comments on the manuscript. We have carefully reviewed the comments and have revised the manuscript accordingly. Our responses are given in a point-by-point manner below. Changes to the manuscript are shown in yellow highlighted text. A "Comments" section was also added according to the retrospective study guideline. We would be very honored if our manuscript is now considered acceptable for publication in the journal.

Sincerely,
Ja-Seol Koo

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Comment 1) One hundred sixty-seven cases were excluded from the analysis. Approximately one quarter of patients were excluded from analysis. This is a crucial bias. The authors should discuss in the limitations.

Response 1) Thank you for your comment. I have inserted additional discussion in the text.

Discussion

There were some limitations in our study. First, it was a retrospective study; therefore, important clinical information, the first day of UC-related symptoms, may have been inaccurate because of recall bias. In addition, nearly one-fourth of patients were excluded from the study because of incomplete medical record data regarding the first day of symptoms. Second, NSAID use, oral contraceptive use, socioeconomic status, and EIM were not investigated. Third, the use of anti-TNFα was increased in the early group than in the delay group when the diagnostic interval was 3 months.

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Comment 2) This study contains multiple analysis. This analysis seems to be multiple testing. Please discuss in the limitations.

Response 2) Thank you for your comment. Our initial hypothesis was that the diagnostic delay for 76th to 100$^{\%}$ percentile of patients (>6.5 months in our study) would be correlated with prognostic factors; however, we did not find any significant results. In addition, our study population has only few cases of UC related surgery that could evaluate the prognosis. Therefore, unlike previous studies, we did not predetermine the criteria for diagnostic delay; instead, we tried to determine the diagnostic delay that affects the prognosis factors. Thus we inevitably used various statistical methods and graphs to evaluate this without the gold standard for prognostic factor and diagnostic delay. All of the above are described in the discussion, if you don't mind, we want to present manuscript without modification. Thank you for your consideration.

Minor Comment 1) In Table 2, 24 months row, total number of patients is different. Please check it.

Response 3) Thank you for your comment. "Clinical remission" line in Table 2 used data from only 467 patients, and this caused a difference in total number. The 467 patients' data showed almost the same diagnostic delay distribution as 551 patients' data. Therefore we added the following statement to the Table legend without Table2 modification.

Table 2. Diagnostic delay and prognosis

The early group was defined as receiving a diagnosis earlier than the diagnostic interval, and the delay group was defined as receiving a later diagnosis. Clinical remission was investigated in 467 patients. And the proportion of the delay group in 467 patients was similar to that of 551 patients: 3 months (42.3%), 6 months (28.2%), 12 months (19%), 18 months (9.6%), and 24 months (7.7%).

Thank you for wonderful comment. I look forward to good results.