Author’s response to reviews

Title: Risk Factors and Long-term Outcome of Disease Extent Progression in Asian Patients with Ulcerative Colitis: A Retrospective Cohort Study

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Author’s response to reviews:

Dear Editor,

We are most grateful for the time and care the editor and reviewers spent for improving our manuscript.

Please find below the point-by-point responses to your comments.

Yun Qiu, MD, PhD; Ren Mao, MD, PhD

On behalf of the author team

Editor Comments:
STROBE guidelines. In accordance with BioMed Central editorial policies (http://www.biomedcentral.com/submissions/editorial-policies#standards+of+reporting), could you please ensure your manuscript reporting adheres to STROBE guidelines (http://www.strobe-statement.org/) for reporting observational research. This is so your methodology can be fully evaluated and utilised. Can you please include a completed STROBE checklist as an additional file when submitting your revised manuscript.

RE: We have included and submitted a completed STROBE checklist.

Reviewer reports:

Jae Jun Park (Reviewer 1): The aim of this study was to analyze the risk factors of proximal extension of ulcerative colitis and long term outcomes. Authors found that only the baseline extent alone was a risk factor for proximal extension and patients with proximal extension more required therapeutic medication. This paper has been conducted on a relatively large number of subjects and is well written and the results are systematically presented as a whole. However, it is a retrospective study, and it is a limitation of the paper that the findings are not novel compared to existing results.

Several comments are as follows:

1. In the analysis in Table 2, reference variable that is the basis of comparison is lacking. Specify which statistical method was used to perform the univariate analysis. Furthermore, there is only one variable in the multivariate analysis item. Was the multivariate analysis performed based on only one variable?

RE: We appreciate the reviewer’s constructive comment. As per the suggestion, we have added reference variable in the revised Table 2.

We are sorry that we did not make it clear in statistical methods. Regarding univariate and multivariate analysis in the present study, we followed a standard approach for model selection. In the univariable Cox’s PH analysis, a criterion of p ≤ 0.10 was used to identify candidate predictors. We then fitted multivariable models and used a backwards selection procedure to eliminate variables not significant in the multivariate framework. A criterion of p ≤ 0.05 was used for determining which variables to include. The odds ratios [OR] derived from the Cox’s PH models are presented with 95% confidence intervals [CIs] and the respective p-values. A ratio higher than 1.0 implies a higher probability of an event compared with the reference group.

In our study, both disease extent and immunosuppressive agents use were identified as candidate predictors based on a predefined criterion of p ≤ 0.10 in the univariable Cox’s PH analysis. The multivariate analysis was performed based on the above two variables.

We have added this important information in the revised manuscript (see page 9 line 3-10).
2. In the analysis of Table 3, specify the total number of patients for each group. Also, specify the detailed timing of analysis in this table.

RE: The exact number for each group have been provided in the revised Table 3. Time to event was calculated from the date of latest endoscopy evaluation (besides the index endoscopy evaluation at diagnosis) to the date of each event (steroids or IMM use etc.) or censoring (the last follow-up).

3. Specify which statistical method was used in Figure 3

RE: The effect of factors at diagnosis (disease distribution or steroids dependence) on the probability of events (disease progression) was evaluated using time-to-event [survival] methods for censored observations due to the varying length of follow-up. Time to event was calculated from the date of diagnosis to the date of event or censoring. Kaplan–Meier estimates were used to draw the cumulative incidence curves, compared by log-rank tests. We have added the information in revised methods part and in the figure 3 legend as well (see page 9 line 3-10 and page 21 line 6-10).

4. Specify for each analysis group for the first analysis in Figure 4. In Figure 4, specify the timing (from when the analysis was started) of the analysis in each group. Moreover, in statistical analysis section, further specify the statistical calculation method in survival analysis regarding last follow up without event, censoring methods etc.

RE: Time to event was calculated from the date of index endoscopy evaluation to the date of events (steroids or IMM use) or censoring (the last follow-up). Kaplan–Meier estimates were used to draw the cumulative incidence curves, compared by log-rank tests. We have added the information in revised methods part.

5. In general, E3 refers to the extent that is more proximal to the splenic flexure. Authors further classified E3 lesion based on hepatic flexure. Describe further in the discussion section whether
this grouping has clinical significance (Consider quoting a recent article from Dig Dis Sci. 2018 Aug 25. doi: 10.1007/s10620-018-5218-x.).

RE: Thanks for the enlightening suggestion. We quoted the above article and described further in the discussion section of revised manuscript (see page 12 line 19-22 and page 13 line 1-5).

Vineet Ahuja (Reviewer 2):

1. The authors have not commented upon one facet of progressive disease:

How many patients had caecal/periappendiceal patch and was that factor related to progression of the disease?

RE: In the present study, 117 (18.5%) patients had skipped periappendiceal lesions, which was comparable to a previous study (19.4%)1. However, skipped periappendiceal lesion was not a risk factor related to progression of the disease based on the univariate or multivariate analysis in our study. We have added the information in revised manuscript (see page10 line 1-2).

Reference


2. Only 59% of patients were on oral or topical 5ASA's. As 5ASA's are the cornerstone of therapy in UC, what were the possible reasons that only 60% of patients were taking 5ASA's.

RE: We are sorry that we did not make this point clear. In the present study, 59% of patients on oral or topical 5ASA pointed to those patients with monotherapy of 5-ASA. Patients with combined use of 5-ASA and steroid/IMMs were counted in the steroid/IMMs group. We have added this information as table note for Table 1(see revised Table 1).