

Dear Editor:

Please find enclosed our revised manuscript entitled "The optimized timing of using infliximab in perianal fistulizing Crohn's disease" for your consideration for publication in the *World Journal of Gastroenterology*

We thank reviewer for his helpful and careful revisions. We appreciate the overall positive comments of the reviewer and have incorporated his suggestion, which may help us to improve the manuscript. We have addressed the reviewer's concern in the response below.

Reviewer 1 comments:

1. Comment: Abbreviations are not always preceded by full text at the first mention (wk, TNF).

Response: The abbreviation of 'wk' meets the guidelines for manuscript preparation and submission. The abbreviation of 'TNF' had been rewritten into 'tumor necrosis factor (TNF)' in line 112, which was marked in red.

2. Comment: The authors do not mention an important historical fact: fistulizing Crohn's disease was, together with steroid dependance or resistance, the first indication for the use of biological drugs.

Response: We added the historical fact in line 109-111 and marked it in red.

3. Comment: The review mentions only one biological drug, namely Infliximab. A chapter should be added regarding the use of other biological drugs in fistulizing Crohn's disease.

Response: We added a chapter regarding the benefits of other biological drugs after infliximab failure in line 314-323 and marked it in red.

4. Comment: The manuscript would also be enriched with iconographic documentation that would make certain concepts regarding the type of fistulas and their possible persistence or healing.

Response: We added Figure 2 to show healing of a Crohn's disease (CD)-related perianal fistula. Additionally, we also added Figure 1 to show treatment of CD-related perianal fistula with ligation of the intersphincteric fistula tract procedure, and Figure 3 to display a therapeutic strategy of perianal fistulizing CD.

We also thank editors for their thorough and thoughtful review on our manuscript. We have gone through and made edits in format as noted under track changes of our edited document, referring to the format example for opinion review. Revised portion are marked in blue in the manuscript.

Other changes:

1. We added Li-Chao Qiao as a co-author, who participated in the revision of the manuscript.

2. In line 84, we changed 'IFX' into 'infliximab'.

3. In line 172, we changed 'However,' into 'It is the fact that...'

Revised portion are marked in blue in the manuscript.

We hope the revised manuscript is now suitable for publication and will be happy to provide further information or make further revisions if required. Thank you very much for your time and consideration.

Best regards,

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