

August 7<sup>th</sup>, 2020

**RE: World Journal of Gastroenterology - Manuscript NO.: 56881 - Revisions**

Dear Editor-in-Chief,

We are submitting our revised manuscript entitled “ *Periodontitis combined with smoking increases risk of the ulcerative colitis: A national cohort study*” for consideration of publication in *World Journal of Gastroenterology*.

We appreciate the valuable and insightful comments from the reviewers. We responded to each of the comments made and incorporated all modifications suggested by the reviewers into the revised manuscript. Changes to the revised manuscript have been highlighted (underlined and in blue). Please let us know if you have any further suggestion for changes. I anticipate good response.

Sincerely,

Jaeyoung Chun, MD,

Professor of Internal Medicine, Department of Internal Medicine, Gangnam Severance

Hospital, Yonsei University College of Medicine. 20, Yeonju-ro 63-gil, Gangnam-gu,  
Seoul, 06229, Republic of Korea. [chunjmd@yuhs.ac](mailto:chunjmd@yuhs.ac)

Telephone: +82-2-2019-3310

Fax: +82-2-3463-3882

### **Point-by-Point Response to the Peer-review reports:**

The authors must resolve all issues in the manuscript based on peer-review report(s) and make a point-to point response to the issues raised in the peer-review report(s) which listed below:

#### **Response:**

We thank the reviewer for thoughtful and expert review of our manuscript and for their valuable and insightful comments. We responded to each of the comments made and incorporated all modifications suggested by the reviewers into the revised manuscript. Changes to the revised manuscript have been highlighted ([underlined and in blue](#)).

#### **Reviewer #1:**

**Scientific Quality:** Grade A (Excellent)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** This is a well-designed and well-written up study identifying the relationship between periodontitis and new onset IBD, especially new onset UC, based on national health records. The association that was noted was not very strong and the age-adjusted hazard ratio is only just above 1, indicating a weak

effect that may not be reproducible if the study were to be replicated elsewhere. This should be acknowledged in the Discussion.

**Response:**

Thank you for your comments. As suggested, the following sentence is now included in Discussion of the revised manuscript (page 13): "Taken together, the risk of developing UC increased significantly in patients with periodontitis, [although the relatively low HR for UC in the periodontitis group needs to be evaluated by epidemiologic studies in other countries.](#)"

**Reviewer #2:**

**Scientific Quality:** Grade A (Excellent)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** The manuscript submitted by Kang and cols., aims to elucidate the impact of periodontitis and smoking on ulcerative colitis. The study is based on data from the National Health Insurance service in South Korea and enrolled a significant number of patients (almost 10 million participants). Inclusion or exclusion criteria were described in the text and the results support the conclusion. However, before a final decision is made, some aspects must be addressed.

**Major concerns:**

- Authors must describe in Abstract the means and standard deviation of age and body mass index, as well as the number of individuals from each gender enrolled in the study

**Response:**

Thank you for your comment. Please refer to Abstract of the revised manuscript.

- In introduction, authors must also include the role of environmental factors on the development of IBD. This is of paramount importance as smoking and alcohol consumption are directly associated with higher risks to develop either IBD and periodontitis.

**Response:**

Thank you for your comments. Please refer to Introduction of the revised manuscript (page 6).

- Authors must describe if patients enrolled in the study were under immunomodulatory therapies (corticosteroids, antibiotics, immunobiologicals, etc) during or prior the period of the follow-up?

**Response:**

Thank you for your critical comment. Please refer to the limitations in Discussion of the revised manuscript (page 15). Due to the limitations of claims data, we could not identify the information regarding medication including immunomodulatory agents.

- In discussion, the information concerning a putative protective role of smoking on the risk of developing UC must be addressed more carefully using more recent data. This is a conflicting aspect and needs to be better discussed. Please see: The Impact of Smoking and Smoking Cessation on Disease Outcomes in Ulcerative Colitis: A Nationwide Population-Based Study Aliment Pharmacol Ther. 2019 Sep;50(5):556-567. doi: 10.1111/apt.15390. Epub 2019 Aug 6 Smoking and Inflammatory Bowel Disease: A Comparison of China, India, and the USA. Dig Dis Sci 2018 Oct;63(10):2703-2713.doi: 10.1007/s10620-018-5142-0. Epub 2018 Jun 4. Dose-response Relationship Between Cigarette Smoking and Risk of Ulcerative Colitis: A Nationwide Population-Based Study. J Gastroenterol. 2019 Oct;54(10):881-890. doi: 10.1007/s00535-019-01589-3. Epub 2019 May 15.

**Response:**

Thank you for your critical comments. We have explained the effect of smoking and smoking cessation on the development of UC with references that you suggested in Discussion of the revised manuscript (pages 13-14).

## **Authors' Response to the Editorial Office's comments**

The author must revise the manuscript according to the Editorial Office's comments and suggestions, which listed below:

### **Response:**

Thank you for the comments. As suggested, we responded to each of the comments made and incorporated all modifications into the revised manuscript. Changes to the revised manuscript have been highlighted ([underlined and in blue](#)).

### **(1) Science Editor:**

1. Scientific quality: The manuscript describes a retrospective cohort study of the periodontitis on ulcerative colitis. The topic is within the scope of the WJG.

(1) Classification: Grade A and Grade A;

(2) Summary of the Peer-Review Report: This is a well-designed and well-written up study identifying the relationship between periodontitis and new onset IBD, especially new onset UC, based on national health records. Inclusion or exclusion criteria were described in the text and the results support the conclusion. However, before a final decision is made, some aspects must be addressed.

Authors must describe in Abstract the means and standard deviation of age and body mass index, as well as the number of individuals from each gender enrolled in the study.

**Response:**

Please refer to Abstract of the revised manuscript.

In discussion, the information concerning a putative protective role of smoking on the risk of developing UC must be addressed more carefully using more recent data. The questions raised by the reviewers should be answered;

**Response:**

Please refer to Discussion of the revised manuscript which has been corrected by the reviewer's suggestion.

(3) Format: There are 2 tables and 3 figures. A total of 46 references are cited, including 21 references published in the last 3 years. There are 10 self-citations.

2 Language evaluation: Classification: Grade A and Grade A. A language editing certificate issued by BioMed Proofreading was provided.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the Institutional Review Board Approval Form. Written informed consent was



waived. The authors need to fill out the STROBE checklist with page numbers. No academic misconduct was found in the CrossCheck detection and Bing search.

**Response:**

We already filled out the STROBE checklist at the time of submission. We have uploaded the STROBE checklist with the revised manuscript repeatedly.

4 Supplementary comments: This is an unsolicited manuscript. The study is without financial support. The topic has not previously been published in the WJG. The corresponding author has not published articles in the BPG.

5 Issues raised: (1) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

**Response:**

The original figures are now uploaded as a PowerPoint file with the revised manuscript.

(2) I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text;

**Response:**

Thank you for your comments. Please refer to Article highlight of the revised manuscript (pages 15-16).

(3) please don't include any \*, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters.

**Response:**

Please refer to the revised Tables using superscript numbers for illustration.

Statistical significance is expressed as  $aP < 0.05$ ,  $bP < 0.01$  ( $P > 0.05$  usually does not need to be denoted). If there are other series of P values,  $cP < 0.05$  and  $dP < 0.01$  are used, and a third series of P values is expressed as  $eP < 0.05$  and  $fP < 0.01$ .

**Response:**

As suggested, we have corrected P values in the revised manuscript.

6 Re-Review: Required.

7 Recommendation: Conditionally accepted.

**(2) Editorial Office Director:** I have checked the comments written by the science editor.

**(3) Company Editor-in-Chief:** I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.