

Split, March 29th, 2021

Dear Editor,

Thank you for taking our work into consideration for publishing in your highly regarded journal. Please find attached our point-by-point response to the Reviewers' comments and accordingly revised manuscript entitled "Is there a higher percentage of undetected osteopenia and osteoporosis among patients with ulcerative colitis in Saudi Arabia?". We have carefully considered all Reviewers' suggestions and remarks. We found their comments constructive, justified and very helpful for improvement the quality of our manuscript.

We hope that you will find our answers to the Reviewers' comments satisfactory and that the revised paper in the new form will be acceptable for publication in the World Journal of Gastroenterology.

Sincerely,

Assistant Professor Mislav Radić

Responses to Reviewers' comments:

Reviewer No. 1

Ad 1

Reviewer: The letter written by Ivna Olic Akrapovic et al. has some interesting comments on the paper of Ewid M et al., which could help clarify a couple of issues in Ewid M et al.'s paper. In the letter, the authors concluded "Only by including both screening methods, we could accurately measure whether UC cohort has lower risk of osteopenia/osteoporosis than CD cohort". This conclusion, however, appears to be an overstatement because it is still not clear how combination of two methods can "accurately measure" the risk of osteopenia. Since the authors had emphasized the importance of TBS as a complementary tool for evaluating risk of fractures in IBD patients, it could be better to say "By including both screening methods, we could make better predictions about whether UC cohort has lower risk of osteoporotic fractures than CD cohort."

Answer: Suggestion accepted. We have rephrased the sentence according to suggestion.

Reviewer No. 2

Ad 1

Reviewer: In this letter, the authors suggested the use of trabecular bone score (TBS) to further facilitate discrimination of patients harboring at a higher risk of fracture in addition to Bone mineral density (BMD) base on the article in WJG (Ewid et al 2020). The authors posed a question as to whether mesalamine was responsible for a lower risk of fractures in UC relative to CD cohort, and suspected the results of (Ewid et al 2020) by lack of apparent correlation between the steroid uasage and BMD. Given that TBS is a

independent indicator for susceptibility of the bone fracture, it is reasonable to assume that BMD combined with TBS is useful for predicting patients prone to osteoporosis and/or osteopenia. The reviewer wonders why the authors did not ask whether the biological therapy such as anti-TNF- α had no correlation with BMD in (Ewid et al 2020), as anti-TNF- α therapy halted the bone loss (or BMD) (Gulyas et al. Clin Rheumat 39. 165-175, 2020).

Answer: Suggestion accepted. We have quoted suggested reference.

Reviewer No. 3

Ad 1

Reviewer: The authors suggest that the usage of trabecular bone score (TBS) for the evaluation of osteopenia/osteoporosis in IBD patients. In the first place, it seems that the study by Ewid et al. has several issues. The study by Ewid et al had small number of enrolled patients, in particular, ulcerative colitis patients. In addition, the disease duration of UC and CD was not shown in that study. However, your suggestion is worth considering for the evaluation of osteopenia/osteoporosis in IBD patients although the measurement method using TBS is not common.

Answer: Suggestion accepted. We have underlined that TBS is not a common method in routine clinical practice.

Reviewer No. 4

Ad 1

Reviewer: This letter should be accepted to discuss the points submitted in the original manuscript.