

POINT-BY-POINT RESPONSE

Name of Journal: World Journal of Gastroenterology

Manuscript Title: Inflammatory Bowel Diseases Patients Suffer from Significant Low Levels and Barriers to Physical Activity: Results from the "BE-FIT-IBD" Study.

Manuscript ID: 87571

[REVIEWER 1]

SPECIFIC COMMENTS TO AUTHORS

- 1) In this cross-sectional observational study, the authors investigated physical activity among groups of IBD patients using a self-report questionnaire. Physical activity levels were compared with disease activity and patient demographics. It was found that IBD patients have a fundamentally lower physical activity level, and that this is mainly due to patients' fears that physical activity will worsen their condition. Patients without dyslipidaemia or on biologic therapy also showed better IPAQ scores in moderate activities.
- 2) The study is well-designed and well-presented and has assessed a very important issue. Mild to moderate levels of physical activity appear to be essential for people with chronic inflammatory disease and in no way worsen the condition of patients. The questionnaire used (IPAQ) certainly seems to be suitable for assessing physical activity in IBD patients. I agree with the authors that the discussion of the need for and possibilities of physical activity should be part of the medical visit for patients with IBD. The results of this study should be considered primary results and could certainly form the basis for a larger case-control study. The statistical methods used are appropriate. The visual presentation of the results is appropriate. The use of English is also appropriate.
- 3) One minor comment: at the end of the discussion, it might be worth devoting a short chapter to the biological ways in which exercise can help reduce inflammation. I suggest accepting the manuscript for publication after a minor revision.

RESPONSE TO REVIEWER:

We cordially thank the reviewer for his/her comment on the quality of our review. We thank the Reviewer for the time and effort spent in reviewing our manuscript.

- 1) We thank the reviewer for the efforts in analyzing our work with brilliant attention;
- 2) Thank you very much for the words spent in favor of our work;
- 3) Thank you for this suggestion. As directed by the Reviewer, a paragraph has been added for this purpose. Certainly, this advice has improved the scientific quality of our work. See: *"Moreover, regular PA can pose a valuable strategy for reducing*

inflammatory burden, especially in diseases with inflammatory pathogenesis, such as IBD. Exercise can contribute to the promotion of an anti-inflammatory phenotype in several ways. In fact, at the level of fatty tissue, it can downregulate several pro-inflammatory cytokines such as IL-1, IL-16 and tumour necrosis factor (TNF), and, in addition, it can promote the M2 cytotype of macrophages (i.e., their anti-inflammatory cytotype) and act against oxidative stress [7]. In the context of muscle tissue, moreover, these actions are, to a large extent, repeated [7] with an increase also in peroxisome proliferator-activated receptor γ co-activator 1 α , a molecule that in knockout mice for the same, results in the promotion of IL-6 and TNF [40]. Repeated exercise also appears to induce adaptive changes in the immune system by predisposing to lower neutrophil recruitment [41]. For these reasons, exercise has been repeatedly proposed to counter chronic inflammation [42]. In addition to the above, regular PA can improve vascular endothelial balance by ameliorating oxidative stress and nitric oxide availability [43]."

[REVIEWER 2]

SPECIFIC COMMENTS TO AUTHORS

- 1) This study investigated PA levels and barriers in a southern Italian IBD population. The results suggested that IBD southern Italian patients appeared to be physically inactive and may be exposed to all complications of not performing regular PA. This appeared to be influenced by patients' perceptions of PA's impact on underlining IBD. Emphasis was placed on the use of validated and feasible questionnaires as a strategy to measure patient-reported PA levels and gain an initial understanding of which patients have inadequate PA levels.
- 2) Further studies require multicentre and prospective design to confirm these findings.

RESPONSE TO REVIEWER:

- 1) We thank the reviewer for the efforts in analyzing our work with brilliant attention and the words spent in favor of our work;
- 2) As suggested by the Reviewer we have included space in the discussion of the limitations of our study for this purpose. Certainly, this advice has improved the scientific quality of our work. See: "*In addition, it will be preferable to confirm and strengthen our data even more a multicentre, prospective study design to bring out more differences in population subgroups.*"

[EDITOR IN CHIEF]

SPECIFIC COMMENTS TO AUTHORS

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it,

upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

RESPONSE TO EDITOR IN CHIEF:

We thank the Editor in chief for his comments and to deem our work worthy of publication. We thank you for asking to check our references with Reference Citation Analysis (RCA). We did it. The authors thank the Editor in chief for the time spent and effort in conducting the editing of our work. Thank you.