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DIPARTIMENTO DI PATOLOGIA E DIAGNOSTICA

UNITÀ OPERATIVA COMPLESSA DI LABORATORIO ANALISI – *Direttore: Prof. Giuseppe Lippi*

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Dear Prof. Editor,

The manuscript entitled “**Procalcitonin in inflammatory bowel disease: drawbacks and opportunities**” [ID: 36922] is resubmitted for publication in **World Journal of Gastroenterology**.

On behalf of all authors, I would like to thank you for the opportunity to respond to the Reviewers’ comments on our manuscript. We found these comments most helpful in improving the manuscript. We have addressed each of the Reviewers’ concerns and have summarized our response in the following point-to-point list of answers to the comments. All changes to the original submission are highlighted throughout the manuscript.

Yours sincerely,

Giuseppe Lippi

Reviewer #1:

The review by Lippi and colleagues deals with the utility of procalcitonin in the diagnosis and management of patients with inflammatory bowel disease. The authors provide a thorough review of the literature dealing with this topic. The manuscript would be improved in the authors provided the following:

- We are really thankful to the referee for the globally favourable comments on our manuscript. Thanks for your efforts to improve our manuscript, it is truly appreciated. Following the referee's suggestions, we have modified and improved the manuscript accordingly.

(i) a discussion in the introduction section as to whether this biomarker is being clinically used or recommended in the diagnosis or management of other inflammatory states; this would be in addition to the information they discuss regarding when procalcitonin is elevated and

- ANSWER: We agree with the Reviewer and kindly appreciate his/her suggestion. We have revised the manuscript accordingly and have added the next paragraph:

“Nevertheless, recent data suggest that procalcitonin measurement may be clinically useful in patients with bacterial meningitis^[10], community-acquired pneumonia^[11], erysipelas^[12], and arthritis^[13]. In all these conditions procalcitonin measurement is now regarded as a first-line screening test for timely identifying bacterial infections and rapidly establishing an antibiotic treatment. Notably, the results of the vast majority of microbiological tests cannot be immediately available, so that the severity of the infection may progress unless a final diagnosis can be made. Procalcitonin has many advantages in this respect, since its measurement may allow identifying infections with minimal host response, is sufficiently specific for discriminating bacterial infections from other severe stimuli that may also induce systemic inflammatory response syndrome, is early present during the course of disease, can be timely and conveniently assayed and, finally, may also provide prognostic information^[4,8].”

(ii) a summarizing paragraph at the end of the section titled "Epidemiological studies on procalcitonin in inflammatory bowel disease" detailing when this biomarker would be useful in managing IBD patients.

- ANSWER: Again, we agree with the Reviewer and kindly appreciate his/her suggestion. We have revised the manuscript accordingly, as follows: *“Taken together, the available published studies suggest that procalcitonin is probably unwarranted for the diagnosis of IBD and/or assessing disease severity, whilst its measurement in patients with suspected infections may enable a timely diagnosis as well as an effective therapeutic monitoring of infective complications in IBD.”*

Reviewer #2:

Dear author, Thank you for your nice review. Unfortunately, due to lack of powerful studies firm recommendation could not be proposed. however, this review could be a start for targeted studies.

- We are really thankful to the referee for the globally favourable comments on our manuscript. No additional actions required.

On behalf of all co-authors, many thanks for this useful review.