

Dear Editors and the Editorial Board,

We are sending the work “Inter- and intraobserver agreement in evaluation of CT enterography in inflammatory bowel disease” (ID#27835) after minor revision before it can be considered for publication in World Journal of Gastroenterology.

We appreciate the suggestions and we have tried to comply the points and issues raised by the Reviewers.

The required adjustments, issues and suggested topics are listed below.

Reviewer 1 Comments:

ABSTRACT

1. The Abstract does not have a background section.
 - *We included a Background section.*

2. The Methods of the Abstract includes results - these should be moved.
 - *We moved it to Results.*

3. The Methods of the ABSTRACT comments on the collection of stool for calprotectin measurements. One assumes that there was no new intervention between the FC measurement and the imaging (or any change in disease activity status). Is this correct?
 - *Yes. We redid the phrase to make it clearer regarding the study population. “Patient inclusion criteria for this study were confirmed inflammatory bowel disease and FC collected less than four months from the date of the CTE, without any clinical or surgical treatment on this interval.”*

4. The Results of the ABSTRACT comments on high FC in those judged to have active disease on imaging. What was the rate of FC elevation in those judged to have no disease activity on imaging?

- *Six (37.5%) out of 16 patients without inflammatory activity in CTE had elevated FC ($p=0.003$). We added this information in the manuscript as suggested by the reviewer 1. We also added the kappa value and reformulated two paragraphs of the discussion as following:*
- *“After a consensus between the radiologists, we found a significant correlation between active inflammatory disease on CTE and high levels of FC ($\kappa = 0.495$, $p=0.001$). Our findings are in line with those of prior studies which demonstrate a good correlation between high levels of FC with endoscopic scores and CTE[16,17]. Arai et al[17] evaluated the correlation between FC, CTE and balloon-assisted enteroscopy in patients with IBD. The authors created a novel CTE score in which 4 imaging variables were evaluated in 5 pre-defined ileal-colonic segments and each variable was scored from 0 to 4 per segment. They showed that the FC levels were well correlated with the CTE score ($r = 0.4018$, $p = 0.0011$).”*
- *“We also found that 85.7% of the patients who were classified as active disease had elevated FC opposite to 37.5% of the patients without active inflammation on CTE who had elevated FC. The FC is a biomarker which reflects the intestinal mucosal damage and using a cut-off point of 250 mcg/g, as in our study, the sensitivity and specificity of detecting active inflammation in IBD are roughly 80%, when compared with endoscopy[16,17,18]. However, some other studies have shown that FC presents a better sensitivity than specificity, which could explain the false positive results[19,20,21,22]. Furthermore, the best area under the curve (AUC) was demonstrated*

in studies which correlated low FC levels with inactive disease[23, 24]. Additionally, other authors have shown that an increase in FC levels may precede the onset of inflammation[25], but in this study we did not follow-up the patients[25]. The combination of these factors may have influenced these discordant results. ”

5. One would expect the inter-observer agreement to be more important in broader contexts, however this was lower than the intra-observer agreement (which was predominantly one individual with much experience)
 - *We have found in our study a higher intra-observer agreement than inter-observer agreement. We have tried to minimize the recall bias of the intra-observer agreement by anonymizing the cases before the readings and the second review was done at least 6 months after the first one, as mentioned in the methods.*

METHODS

6. In expressing the aim of the study (end of METHODS) the word is should be was.
 - *Corrected.*
7. The first part of the METHODS section needs a subheading also.
 - *Corrected.*
8. The METHODS includes results (the number of patients). This should be in the RESULTS section only.
 - *We moved to Results.*

9. The report indicates that 42 of 44 exams were examined twice by the same examiner. This suggests that the intra-observer agreement stated reflected just one individual. This introduces bias that is not acknowledged.

- *We added this as another limitation of the study.*

10. The first part of the statistics analysis section requires correction of English language and correction of spelling (Chi square needs correcting)

- *Corrected.*

RESULTS

11. The authors should review the numbers in the results section: these do not match. Especially the last section of the RESULTS.

- *We reviewed the numbers in the results section.*

12. There are other errors of English language that need correction.

- *The manuscript was reviewed.*

Reviewer 2 Comments:

1. CT enterography is becoming a diagnostic modality for inflammatory bowel disease (IBD) recently due to its easy accessibility, especially for Crohn's disease. Fecal calprotectin is confirmed correlation to the mucosal inflammation of the IBD. Although there probably existing bias for intraobserver agreement because of short duration (only 6 months) and only 2 physicians, this is an interesting study.

- *Thank you. We have tried to minimize the recall bias of the intra-observer agreement by anonymizing the cases before the readings and the second review was done at least 6 months after the first one, as mentioned in the methods.*

RESULTS

2. The interobserver kappa value for localization is mismatch between text (0.636) and table 2 (0.540).

- *Corrected. The correct result was $k=0.540$.*

3. The conclusion in your text should follow discussion instead of acknowledgment.

- *Corrected.*

Sincerely,

On behalf of the authors,

Natally Horvat

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