

Reply to Reviewer #1

Comments

In this retrospective study, The Authors investigated the role of fecal calprotectin (FC) in predicting disease flare ups in a cohort of IBD patients. The manuscript is complete and well written, although not sufficiently novel. The topic of the paper falls within the scope of WJG.

We thank the reviewer for these excellent comments. We provide a point by point answer to these comments. We have also modified our manuscript accordingly.

1. The method section in the abstract is too short. This should be more exhaustive, adding the study subjects clinical and demographic characteristics and the inclusion/exclusion criteria.

We thank the reviewer for this comment. We have modified the relevant section in the abstract with a more detailed description of our methodology.

2. I believe the key word “relapse” should be added.

We thank the reviewer for this comment. We have followed his suggestion and added the word “relapse” in the key word section.

3. The introduction section is too long. I suggest moving paragraphs 3 and 4 to the discussion section.

We thank the reviewer for this comment. We have moved a substantial part of the introduction in the discussion section as suggested.

Overall, the present study is interesting as it underscores the utility of FC in clinical practice. However, since many articles (and some are prospective studies) have been recently published (four of them on “Inflamm Bowel dis”), I doubt that the present study would add much to what we already know about this topic.

We thank the reviewer for his/her comments. We acknowledge that there have been similar studies to ours. Nevertheless, our study also has unique features which include the validation on a different population of patients, the identification of distinct cut-off values for prediction of outcomes in regards to prediction of clinical relapse and of ongoing endoscopic activity and the excellent predictive value of combination of FC with CRP to define high-risk IBD patients.

Reply to Reviewer #2

Ileocolonoscopy is the gold standard for the diagnosis and assessment of postoperative recurrence in Crohn's disease (CD). Nevertheless, endoscopy is time-consuming and invasive. A minimally invasive and simple screening test would improve patient adherence to examination and provide greater clinical benefit. A number of fecal biomarkers have been evaluated for their utility for the diagnosis and monitoring of inflammatory bowel disease as alternative tests to endoscopy. Fecal calprotectin (FC) has emerged as a reliable surrogate marker of endoscopic remission in Crohn's disease (CD), which has been mainly evaluated using ileocolonoscopy. The manuscript is well written, but there are more than 750 papers in Pub Med searching for FC and IBD. The manuscript may be interesting if a systematic review and meta-analysis are added.

We thank the reviewer for this comment. We agree that there exists a substantial literature regarding the utility of FC in the management of IBD patients, which emphasizes the significance as well as the complexity of this topic. Nevertheless, the optimal cut-off values and the particular patient subgroups that may benefit the most from FC monitoring still remain to be defined. Thus, we think that our study is of importance for establishing the optimal use of FC in routine clinical practice. In regard to the suggestion for a systematic review and meta-analysis to be added, while we find the idea intriguing we think that it is outside the scope of our present study.

Reply to Reviewer #3

Comments

1. The word endoscopical would usually be written as endoscopic.

We thank the reviewer for this comment. We have replaced the term “endoscopical” throughout the text with “endoscopic” as suggested.

2. The TITLE implies that it is just the fact of measuring FC that predicts outcome.

We thank the reviewer for this comment. We have modified the title accordingly.

3. The results displayed indicated that 39 of 76 patients who had an endoscopic assessment were in mucosal healing. How closely linked was this assessment to the time that the FC was assessed? and/or was FC re-assessed at that time? This is not clear.

We thank the reviewer for this comment. The endoscopic assessment of the patients was performed within 6 months of baseline FC measurement (mean period between FC measurement and endoscopy was 4.1 months). FC was not assessed in the majority (>90%) of patients at that time. We have further clarified this information in the revised manuscript.

4. The use of FC post-resection is a different issue than the use of FC in patients without prior surgery.

We thank the reviewer for this comment. We agree that the use of FC post resection is a separate issue within our patient cohort. Therefore we state in the discussion section that FC measurements should always be considered in the appropriate clinical context, as cut-off values may vary in different patient populations. In fact, our findings support the notion that a lower threshold for endoscopy may be needed in CD patients with post-surgery surveillance as endoscopic recurrence was associated with considerably lower FC values than in surgery-naïve CD patients with inflammatory lesions. We understand that perspective studies with larger number of patients are needed to understand the true value of FC in the postoperative management of CD.

5. Fig 1 appears to have values with SD or SEM in the bars. This is not what is mentioned in the legend

We thank the reviewer for this comment. The graph featured in Figure 1 has been generated with the GraphPad software and column bars represent median values with interquartile range as stated (only the upper part of the interquartile range is depicted for improved clarity of the Figure).

6. Some of the figures (e.g. number 4) don't have an actual legend. these should be reviewed and enhanced

We thank the reviewer for this comment. We have added now actual legends in all Figures as suggested.