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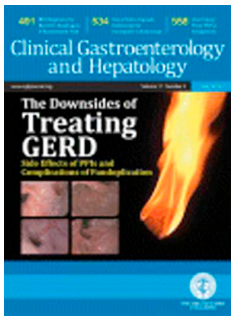

IBS in IBD: A label to stick with caution - authors' reply

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TITLE PAGE

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Abbreviations:

FC	fecal calprotectin
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
UC	ulcerative colitis

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Reply.

We thank Hirten and Colombel for their erudite commentary on our recently published work.[1, 2] The findings of our study highlight the association between irritable bowel syndrome (IBS)-type symptoms, in patients with quiescent inflammatory bowel disease (IBD), and psychological co-morbidity and poor quality of life, and are in keeping with those of another large study from Sweden, reporting that 18% of patients with ulcerative colitis (UC) in deep remission report these symptoms.[3] These studies highlight a hitherto poorly characterized cohort of patients with unmet needs, for which the therapeutic options are limited.

In response to their specific comments, firstly we acknowledged that the use of fecal calprotectin (FC) as an objective measure of inflammatory disease activity is contentious, as is the cut-off used to define disease activity. However, the routine use of ileocolonoscopy and small bowel imaging in a cross-sectional study of 378 patients is impractical and potentially unethical, given that 60% of patients did not have clinically active disease at the time of participation. We used a FC cut-off of ≥250µg/g to define active disease, based on previous studies in this field and expert consensus.[4-6] However, we conducted sensitivity analyses using a cut-off of ≥100µg/g. In these analyses, the proportion of patients with IBS-type symptoms was reduced, but the association between symptoms, psychological co-morbidity and poor quality of life remained. In addition, the mean FC in those with IBS-type symptoms in our primary analysis was <100µg/g in both Crohn's disease and UC.

Secondly, we conceded that describing all patients as suffering from IBS may be misleading, particularly as similar symptoms secondary to other organic complaints such as bile acid malabsorption and small intestinal bacterial overgrowth may be the culprit,[7, 8] particularly in those with previous surgery, and that this may have inflated the prevalence of these symptoms. It may therefore be more accurate to describe these patients as reporting "persistent gastrointestinal (GI) symptoms in the absence of inflammation", rather than "IBS-type symptoms". Indeed, within the same cohort of patients, subsequent analysis of the prevalence and impact of persistent GI symptoms in the absence of inflammation on psychological co-morbidity and quality of life demonstrated similar findings to those described in the present study, irrespective of whether these symptoms met Rome III criteria for IBS.[9]

Thirdly, Hirten and Colombel highlight the potential for misclassification of persistent symptoms in quiescent IBD as IBS, and that treatment of these patients should be tailored to the underlying cause, citing dysregulation of the enteric nervous system and enteric dysmotility, two of the cardinal features of the functional gastrointestinal disorders, as potential targets to therapy. To the best of our knowledge, evidence-based management strategies for these pathophysiologies are lacking in IBD, and it is this exact group of patients that our study successfully seeks to identify and better characterize. Thus, our findings highlight the need for trials of novel therapeutic interventions in these patients, and the requirement of a paradigm-shift in the approach towards their management. In the UK, there has been a recent call from the Health Technology Assessment for a trial of therapies for ongoing diarrhea and abdominal pain in patients with stable UC, which may help to address this deficit in current knowledge.[10]

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