Crohn's disease in remission or simply smouldering?

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The Crohn's disease (CD) activity index (CDAI) has formed the basis for all the major clinic trials in CD over the years since its publication in 1976 [1]. It is, however, beset with problems namely the requirement for a patient symptom diary, the fact that subjective criteria account for 40% of the score and, moreover, the fact that it does not correlate with the inflammatory burden in CD. Thus, the FDA has advised that more objective methods to assess mucosal healing be utilized for future clinical trials in CD.

Calprotectin is a calcium binding protein, constituting 60% of the neutrophil cytosol. Its utility in clinical gastroenterology stems from its ability to non invasively measure the level of intestinal inflammation by acting as a surrogate marker for neutrophil influx into the gut lumen. It has successfully been used to differentiate between irritable bowel syndrome and inflammatory bowel disease (IBD) [2,3], assess treatment response in IBD [4], predict mucosal healing in IBD [3], and predict relapses in quiescent CD [5,6].

In this issue of the *Annals of Gastroenterology*, Scaioli *et al* [7] simultaneously assessed CDAI and fecal calprotectin level from 193 CD patients attending the IBD clinic in Bologna, Italy. Unsurprisingly, there was not a linear relationship between the two values and indeed almost 40% of those in "clinical remission" (CDAI <150) had a fecal calprotectin ≥150 μg/g suggesting subclinical inflammation. Using a logistic regression model, the investigators then analyzed the fecal calprotectin value in those in clinical remission further by assessing the probability of a fecal calprotectin less than or greater than 150 μg/g. They found that for every 10 point increase in the CDAI (in those with CDAI values <150), the odds of a fecal calprotectin ≥150 μg/g of stool increased by 30% and these data were independent of disease location.

Potential criticisms of this data set include the arbitrary choice of a 150 μg/g calprotectin cut off and the lack of mucosal/colonoscopic assessment. With respect to the former, there is a significant swell of data suggesting that clinically significant intestinal inflammation in CD correlates with a fecal calprotectin value around the 250 to 350 mark depending on the assay utilized [5,6,8,9].

This useful data set further supports the notion that a CDAI <150 does not correlate with the absence of intestinal inflammatory activity. Whilst checking fecal calprotectin does better stratify the CDAI, I doubt it will prevent its eventual demise. In my opinion CDAI remains laborious and inaccurate and will continue to be replaced by objective, accurate and prognostic markers including fecal biomarkers, magnetic resonance imaging scores and endoscopic data [10].

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Conflict of Interest: None

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