1. Can endoscopic disease activity in Crohn’s disease be predicted with non-invasive measures?

Mucosal healing in CD is an important goal of therapy as it has been associated with lower risk of flares, hospitalizations and surgery. This parameter, however, can only be appreciated by colonoscopy which is inconvenient, invasive and expansive. Clinical disease activity scores, such as CDAI and HBI are not reliable predictors of the luminal inflammation and therefore better surrogate measures are needed. In this study, investigators have attempted to develop and validate a new CD activity index based on clinical and laboratory variables using endoscopic disease activity (CDEIS) as the reference standard. Among multiple variables included in the model the following were found to be independently associated with CDEIS: number of liquid stools/day (DBM), CRP, platelet count (Plt), fecal calprotectin (Cal) and mean platelet volume (MPV). The derived score (Utrecht score) was computed based on the formula: DBM x 0.25 + CRP x 0.1 + Plt x 0.01 + Cal x 0.001 – MPV x 0.2 and had a good correlation with CDEIS (r=0.72). The score was then validated in an external cohort with similar results. An index score > 3 had a sensitivity of 84% and specificity of 91% for predicting active disease based on the CDEIS in patients with ileo-colonic disease. Patients with ulcerations had a higher Utrecht score compared to those without.

Comments: Although this may be yet another attempt to develop a more reliable CD activity score, the results of this study are interesting and may have implications for both clinical practice and research. As a major departure from its much maligned predecessors (CDAI and HBI), all but one of the variables in this score are objective and can be easily measured. Several limitations need to be pointed out. The majority of patients in the derivation and validation cohorts were either in remission or had only mildly active disease. Thus it is unclear how this index will perform in patients with moderate or severely active CD. Also, the index did not perform as well in patients with isolated ileal CD compared to those with colonic disease. Although the authors stated that in their estimation the Utrecht was superior in predicting active endoscopic disease compared to fecal calprotectin alone, the results are not reported and I suspect that the difference is not significant. Lastly, in order for this index to have any relevance in practice or research, it has to be further validated in cohorts of patients with active Crohn’s disease before and after therapy.


2. Can fecal calprotectin predict the development of pouchitis after IPAA?

Pouchitis is the most common complication following proctocolectomy with ileal-pouch anal anastomosis (IPAA) in patients with UC with incidences between 20% and 45%. Furthermore, chronic pouchitis can develop in a substantial proportion of these patients and may require immunomodulator therapy. The symptoms of pouchitis are non-specific and cannot be easily differentiated from other
complications such as cuffitis, Crohn’s disease, leaks or irritable pouch syndrome (likely the most common confounder). Although pouchoscopy is very helpful, it is invasive and may require prepping and even sedation. Investigators in this prospective study have evaluated the accuracy of stool calprotectin (CP) and lactoferrin (LF) for the early diagnosis of pouchitis in patients with IPAA. They prospectively collected samples from 60 patients every 2 months following the ileostomy take down. Patients were also regularly surveyed for symptoms using the pouchitis index (PDAI). Symptoms of “pouchitis” triggered an immediate endoscopic examination. Also, all patients had a pouchoscopy 12 months after their ileostomy closure. At the end of follow-up, 10 patients (17%) developed acute pouchitis. In these patients, both CP and LF levels increased significantly up to 2 months preceding the clinical diagnosis of pouchitis. Using ROC curves, the authors determined that a CP value of 56 µg/g had a sensitivity of 100% and specificity of 84%, PPV of 56% and NPV of 100% for pouchitis. A cutoff level for LF of 50 µg/g yielded similar results. There was a good correlation between CP and the overall PDAI score and the endoscopic severity of pouchitis ($r=0.626$ and $0.696$ respectively). However, there was no correlation between CP and LF and symptoms of pouchitis alone. Patients who responded to antibiotic therapy experienced a significant drop in CP and LF values (by about 60%). No other biomarkers including WBC and CRP correlated with the diagnosis of pouchitis.

**Comments**: This study provides further evidence that fecal CP is a useful marker in measuring inflammation in patients with IBD, now expanding to patients with pouchitis. However, until further prospective studies can demonstrate an impact on clinical outcomes of pouchitis from pre-emptive treatment with antibiotics, the role of fecal biomarkers is purely theoretical. At the most, patients with symptoms of pouchitis can be spared an endoscopy if their fecal CP is elevated and proceed directly with treatment. Currently, however, most symptomatic patients are treated empirically with antibiotics with pouchoscopy being reserved to those patients who fail to respond. Further cost-effectiveness studies evaluating the prospective measurement of fecal biomarkers in asymptomatic patients are also needed.