

## Editorial: visceral fat as a predictor of post-operative recurrence of Crohn's disease

An argument could be made for visceral fat being one of the first biomarkers of Crohn's disease (CD). Hypertrophied mesenteric, or "creeping", fat encasing affected intestine was reported in the seminal publication describing CD from Oppenheimer and Crohn in 1932.<sup>1</sup> Once thought almost incompatible with the diagnosis, the incidence of obesity in CD has risen dramatically over the last two decades.<sup>2,3</sup> The increasing incidence of CD occurring in parallel with the obesity epidemic has again raised interest in studying the interaction of mesenteric fat and IBD. In place of body mass index (BMI) measurements, body composition analysis has revealed the association of visceral fat with disease activity, complications and post-operative outcomes in CD.<sup>4-6</sup>

Holt and colleagues performed a post hoc analysis in 44 of 174 patients from the POCER study to determine whether pre-operative image-based body composition parameters were associated with post-operative CD recurrence.<sup>7</sup> Disease recurrence at 18 months following surgery, defined by a Rutgeerts' score of I2 or greater, was compared to fat and skeletal muscle area measurements at the L3-L4 level derived from CT and MR studies using the SliceOmatic body composition analysis platform (Tomovision, Montreal, QC, Canada). The authors found that an increased visceral fat area, adjusted for overall body height and gender (visceral adipose tissue/height index) was associated with endoscopic disease recurrence (RR: 2.1, 95% CI: 1.5-3.0). Highlighting the value of more granular body composition data, BMI was not correlated with endoscopic recurrence ( $P=.614$ ). These results agree with other work showing standardised visceral fat measurement (but not BMI) to be correlated with poor CD outcomes.<sup>4-6</sup>

Is visceral fat quantification positioned to become a clinically useful predictor of CD recurrence? At present, more work is needed to determine the best use, if any, of body composition for improving post-operative prognostic accuracy. The degree of visceral fat may be influenced by several factors, including corticosteroid exposure, prior abdominal surgery, stricturing or penetrating complications and Crohn's disease activity itself. The authors recognised this and did report that high-risk patients (prior surgery, smokers), steroid users and post-operative treatment intensity did not differ by endoscopic recurrence status, albeit using univariate analysis. The VHI cut-off value of >1.5 times the gender mean demonstrated a sensitivity and specificity of 100% (82%-100%) and 29% (12%-51%), respectively, for identifying disease recurrence. While visceral fat measures alone

may be insufficient to guide therapeutic escalation, it may still make a meaningful contribution to models predicting future CD recurrence.

Perhaps more valuable than exploring its potential as a biomarker, this study adds to mounting evidence evaluating the association between visceral fat and intestinal inflammation. Visceral fat adipocytes have increased expression of several inflammatory cytokines including TNF- $\alpha$ , IL-1 and IL-6.<sup>8</sup> Adipocyte inflammatory expression profiles occur not only at hypertrophied fat surrounding diseased bowel but also in the distant omental mesentery. Human observations showing increased translocation of luminal bacteria to the mesenteric fat of subjects with Crohn's disease compared to unaffected patients.<sup>9</sup> Questions remain whether visceral fat proliferation and activity is a contributing cause, or alternatively result, of intestinal inflammation. Nonetheless, continued exploration of the interaction between visceral fat and disease course is likely to provide important insight into the pathophysiology of Crohn's disease.

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## Editorial: visceral fat as a predictor of post-operative recurrence of Crohn's disease—Authors' reply

We are grateful to Drs Stidham and Waljee for their appraisal<sup>1</sup> of our work examining visceral adiposity as a predictor of post-operative Crohn's disease recurrence.<sup>2</sup> We agree that the study findings raise two issues: the role of body composition as a biomarker in Crohn's disease, and the association of visceral fat with intestinal inflammation.

As medical treatments for Crohn's disease multiply, it is important that post-operative prophylaxis is appropriately targeted to ensure optimum results while avoiding unnecessary adverse effects and cost. A personalised approach may entail risk stratification and prediction of response to therapy, by considering patient and disease characteristics. Well-described risk factors include cigarette smoking, prior intestinal resection, absence of preventative treatment, penetrating disease at index surgery, perianal disease, and histological features of granulomas in the resection specimen and myenteric plexitis.<sup>3</sup> Microbial,<sup>4</sup> genetic,<sup>5,6</sup> and perhaps body composition variables may also have a role to play in a composite model. Stidham and Waljee are right to state that further research is required to place body composition analysis in place as a clinical predictor of outcomes in Crohn's disease, but such analysis may be more easily accessible in future as automated segmentation techniques<sup>7,8</sup> develop. Further areas of related research include differentiation of anatomical fat deposits by functional characteristics, and identification of metabolically distinct white and brown adipose tissues.

There are unanswered questions regarding the direction of causality between alterations in visceral fat and inflammation in Crohn's disease. Measurement of intra-abdominal adipose tissue area is a crude descriptor of the functional activity of the visceral adipose tissue compartment, and we welcome further research in this field.

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