Authors' reply: The Association Between Visceral Adipose Tissue and Stricturing Crohn's Disease Behavior, Fecal Calprotectin and Quality of Life

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We thank Cong Dai et al for their letter, which emphasises the importance of further research into the pathophysiology and clinical significance of visceral adipose tissue (VAT) in Crohn's disease (CD).

It is now well established that VAT is not merely an innocent bystander in CD.[1] The etiology of VAT accumulation in CD is poorly elucidated but is likely to be multifactorial, influenced by genetic factors, gut permeability, microbial translocation, and clinical factors including medications.[2] VAT secretes adipocytokines, both inflammatory (Interleukin-6 and tumor necrosis factor alpha) and anti-inflammatory (adiponectin), which may alter immune responses at the luminal interface. Mesenteric hypertrophy is thought to be a "protective" mechanism in the setting of increased gut permeability associated with chronic inflammation. Although bacterial infiltration is likely to be a key determinate of VAT differentiation, whether VAT acts as a chronic microbial reservoir in CD is unclear.[3] Further research is required to explore the complex interaction between VAT, the mucosal immune system, and the gut microbiome.

In our study, VAT was associated with stricturing CD behavior, prospective disease activity, and quality of life in a disease distribution–dependent manner.[4] Although enticing, further data are required before VAT may be proclaimed as a useful biomarker in clinical practice. Existing studies are conflicting and limited by small sample size, retrospective methodology, and heterogeneous techniques of VAT measurement. VAT may be influenced by multiple factors including age, gender, and prior abdominal surgery. Although not evident in our study, medications may also influence VAT, including anti-tumor necrosis alpha therapy and corticosteroids. A better understanding of VAT in CD will require large prospective and well-phenotyped cohort studies, optimally with evaluation of VAT metrics from diagnosis.

The prospect of future therapies targeting VAT in CD is exciting. Infliximab has been shown to increase circulating adiponectin, which may contribute to the response to induction therapy.[5] On the other hand, VAT volume has also been associated with response to infliximab therapy, with lower VAT volumes associated with higher rates of attainment of mucosal healing in CD.[6] It has also been proposed that mesocolic excision of VAT may reduce the risk of postoperative CD recurrence.[7] Further studies are required not only to understand the bidirectional influence of current therapies on VAT but also to explore potential therapeutic pathways targeting VAT, which may act by potentiating production of anti-inflammatory adipocytokines.

Beyond its impact of CD phenotype, the broader clinical significance of VAT needs to be recognized. Independent of body mass index, VAT accumulation is a strong risk factor for incident cardiovascular and metabolic disease, as it has a distinct metabolic profile to subcutaneous fat.[8] In the quest to ameliorate inflammation in CD, it would be a shame to overlook risk factors for cardiovascular disease, an emergent cause of morbidity in this cohort.[9]

Abbreviations: CD, Crohn's disease; CT, computed tomography; IBD, inflammatory bowel disease; VAT, visceral adipose tissue.

Author contributions: RB, CS, FDB, SPLT, and JMA were involved in the conception and design of the project. RB, CS, SO, CG, SS, AV, AL, FDB, and JMA were involved in data acquisition and management. All authors were involved in analysis and interpretation of research data and drafting and revision of the article. All authors approved the final version of the manuscript.

Conflicts of interest: RB received research support from the Royal Adelaide Hospital Research Foundation through the AR Clarkson Scholarship. RB is mployed by CALHN/TQEH. Grants, research support, and speaker fees from AbbVie, Ferring, Janssen, Shire, Takeda were all paid to this employer for research support. SC is employed by CALHN/TQEH. Grants, research support, and speaker fees from Pfizer, Merck Sharp & Dohme, Janssen, and Shire were all paid to this employer for research support; SC also has a consultancy with Microbiotica. ST is employed by Oxford University Hospitals NHS Foundation Trust and the University of Oxford; he has received grants and research support from AbbVie, IOIBD, Lilly, UCB, Vifor, and Norman Collisson Foundation; he has also received consulting Fees from AbbVie, Allergan, Amgen, Asahi, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Chemocentryx, Cosmo, Enterome, Ferring,

doi: 10.1093/ibd/izy338
Published online 31 October 2018

Giuliani SpA, GSK, Genentech/Roche, Immunocore, Immunometabolism, Janssen, Lilly, MSD, Neovacs, NovoNordisk, Novartis, NPS Pharmaceuticals, Pfizer, Proximagen, Receptos, Shire, Sigmoid Pharma, Takeda, Topivert, UCB, VHsquared,Vifor, and Zeria; he has received speaker fees from AbbVie, Amgen, Biogen, Ferring, and Takeda. JMA is employed by CALHN/RAH. Grants, research support, and speaker and consultancy fees from Abbot, AbbVie, Allergan, Bayer, Celgene, Ferring, Hospira, Janssen, MSD, Orphan, Pfizer, Shire, and Takeda were all paid to this employer for research support.

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