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# Paving the way towards a weight-loss intervention study in obese patients with inflammatory bowel disease

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The incidence of inflammatory bowel diseases (IBD) is rising in parallel with the global obesity epidemic. Contrary to conventional belief, 20–40% of patients with IBD are overweight (body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>), and 10–40% of patients with IBD are obese (BMI  $\geq 30$  kg/m<sup>2</sup>).<sup>1</sup> Despite extensive literature on the predictors of worse clinical course in IBD, no clear risk stratification is implemented in clinical practice, except for the prevention of recurrence of postoperative Crohn's disease (CD), and identification of predictors of poor IBD outcomes remains of major importance.

In the current issue of the *United European Gastroenterology Journal*, Greuter et al. have addressed the impact of obesity on IBD course at a nationwide level.<sup>2</sup> Based on the Swiss IBD cohort, 3075 patients with IBD including 325 obese patients were prospectively followed from 2006 to 2018. Disease activity based on clinical scores (Crohn's disease activity index in CD and the modified Truelove Witts activity index in ulcerative colitis [UC]), C-reactive protein (CRP) and faecal calprotectin levels were assessed at baseline, whereas disease progression defined by CD phenotype and UC disease extent progressions, disease complication, and treatment failure were assessed during follow-up. The authors reported differences in the impact of obesity according to IBD subtype. Obesity was associated with an increased risk of active disease at baseline in patients with CD, but not in those with UC. Additionally, obese patients with CD were at increased risk of complicated disease course compared to normal-weight patients with CD, whereas this association was not observed in patients with UC. Finally, the risk of treatment failure was not affected by obesity in patients with CD and UC. Some limitations need to be acknowledged. Treatment failure was not based on robust markers of disease activity, but on the need for new anti-tumour necrosis factor (TNF) agent, which may be affected by physicians' decisions and exclude patients switching from aminosalicylates to thiopurines. Previous studies reported rapid anti-TNF clearance and low trough levels in obese patients,

but anti-TNF trough levels were not assessed in this study. Endoscopic data were not available but would have helped to better assess disease activity in IBD obese patients, because obesity increased CRP and, potentially, faecal calprotectin levels in non-IBD obese patients.<sup>3</sup> Finally, the absence of an association between obesity and worse UC outcomes may be related to the small sample size.

Nevertheless, this study is of great value compared to the available literature. Most studies assessing the impact of obesity on IBD clinical course were retrospective single-centre studies with a small sample size, limiting the conclusions drawn. A recent prospective cohort study including 1443 obese patients with IBD reported that obesity was associated with an increased risk of persistent disease activity and relapse in patients with CD and UC, in a dose-dependent manner.<sup>4</sup> Additionally, obesity was associated with increased disease activity and worse clinical outcomes in other immune-mediated inflammatory diseases, such as psoriatic arthritis and rheumatoid arthritis.<sup>5</sup>

Therefore, the study by Greuter et al., together with the previously mentioned studies, provides important insights on the impact of obesity in IBD. These findings suggest obesity is an independent risk factor for worse IBD clinical course and this effect may be not only related to higher drug clearance. Indeed, obesity can be considered a low-grade, chronic systemic inflammatory disease, because it leads to an increased release of proinflammatory cytokines, notably TNF.<sup>6</sup> Small randomized controlled trials suggested a beneficial effect of weight-loss intervention on response to anti-TNF in patients with rheumatic inflammatory diseases,<sup>7</sup> but no data are available in patients with IBD. The study by Greuter et al. suggests future clinical trials assessing weight-loss intervention in IBD should be considered.

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