
INFLUENCE OF OBESITY ON THE COURSE OF INFLAMMATORY BOWEL DISEASE

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ABSTRACT

One of the leading public health issues of the 21st century is that the prevalence of obesity worldwide has grown to epidemic proportions. The more common inflammatory bowel disease (IBD) suggests that obesity plays a role in the pathogenesis of IBD. Epidemiological data on this issue are still quite contradictory. Similarly, studies examining the impact that obesity may have on the natural history of the disease have yielded inconsistent results. Regardless of its impact on the pathogenesis or natural history of IBD, the growing prevalence of obesity in this population leads to the need for a better understanding of the effect it has on IBD management. The aim of this study is to review scientific publications examining the impact of obesity on the course of inflammatory bowel disease.

Keywords: obesity, inflammatory bowel disease (IBD), Crohn's disease (CD), ulcerative colitis (UC), body mass index (BMI)

INTRODUCTION

The etiology and pathophysiology of inflammatory bowel disease (IBD) are still unclear. The development of IBD is multifactorial, depending on genetic, nutritional, geographical, demographic, and other environmental factors, including lifestyle and medication intake (1–3).

A key factor of growing research interest is the role of body mass index (BMI) and, in particular, obesity in the development of IBD. In fact, many clinicians associate IBD with a low or normal BMI. But this paradigm is beginning to change with the association of obesity with IBD as a result of its pro-inflammatory effect.

Obesity has been associated with the induction of a number of pro-inflammatory mediators, including tumor necrosis factor alpha (TNF- α), interleukin-6 (IL-6), and leptin, which are secreted in increased numbers secondary to adipocyte hypertrophy. This increase in inflammatory mediators may lead to elevated levels of C-reactive protein (CRP) and fecal calprotectin (FCP) (2).

AIM

The aim of this study is to review scientific publications examining the impact of obesity on the course of IBD.

MATERIALS AND METHODS

In the period from 1998 to 2022, in the available databases Scopus, ScienceDirect, Web of Science, PubMed, UpToDate, using keywords in English—obesity, IBD, Crohn's disease, ulcerative colitis, BMI, and inflammation, we have found 7,924 publications, of which 2,830 were review articles, book chapters, and 5,094 publications with research results, abstracts, posters, and other communications.

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RESULTS AND DISCUSSION

The prevalence of obesity worldwide has grown to epidemic proportions and is one of the leading public health problems of the 21st century. Escalating levels of obesity in the IBD population have been documented, parallel to those in the general population. Data from transverse and single-center cohorts suggest that the prevalence of obesity in IBD patients is between 15% and 40% (4), a proportion that increases further in overweight individuals (5–9). In a population group of IBD patients in Olmsted region, Minnesota, the prevalence of overweight and obese patients increased from 24% and 12% in 1990 to 1994, respectively, to 34% and 20% in 2005 to 2010, respectively (10). This trend was confirmed in an analysis of 10,282 participants in a clinical trial with Crohn's disease (CD), which noted that the average BMI at the time of enrollment had increased from 20.8 in 1991 to 27.0 in 2008 (11). These trends are not unique to the adult population, with the percentage of overweight and obese patients having a similar increase in children (12,13).

Chan et al. published a pooled analysis of 5 prospective cohort studies in clinical gastroenterology and hepatology (2). This study included 5 international groups of patients with IBD, which were collected from the study of nutritional and environmental factors. The total pooled cohort analysis included 601,009 patients from 9 countries. An increased risk of developing CD in obese patients (BMI > 30 kg/m²) with a combined adjusted risk ratio (aHR) of 1.34 (95% CI, 1.05–1.71; I² = 0%) compared to those with normal body weight (BMI 18.5–25.0 kg/m²) was established. An increased risk of developing CD in obese patients (BMI > 30 kg/m²) with a combined adjusted risk ratio (aHR) of 1.34 (95% CI, 1.05–1.71; I² = 0%) compared to those with normal body weight (BMI 18.5–25.0 kg/m²) was observed. When the authors specifically assessed patients in early adulthood (aged 18–20 years), there was a 22% increase in the risk of CD for every 5 kg/m² increase in BMI (combined aHR, 1.22; 95% CI, 1.05–1.40; I² = 13.6%). There was no link between obesity and the risk of developing ulcerative colitis (UC).

A few available epidemiological studies on this topic are controversial and further research is needed to elucidate any role that obesity may play in the pathogenesis of IBD (1,14,15). A cohort of more than

300,000 people from the Copenhagen School Health Records Survey was studied to assess the link between BMI between the ages of 7 and 13 and adult IBD. The increase in BMI by 1 in all ages studied was associated with an increased risk of CD, with onset prior to the age of 30 (hazard ratio [HR], 1.2), and inversely associated with the risk of future UC diagnosis at any age (HR, 0.9) (15). In contrast, a large cohort study examining more than 300,000 adults in the European Prospective Investigation into Cancer and Nutrition cohort found no such association between BMI and future risk of CD or UC (1). There is a noticeable difference between these two studies. The first one uses BMI in childhood as a predictor. The second focuses on obesity in adulthood, and examines whether exposure to obesity earlier in life is where the impact really occurs. However, there may be biological plausibility that suggests a causal role in obesity in patients with IBD. However, this remains speculative at best and further research is needed.

In a retrospective review of 581 identified IBD patients, obese patients were less likely to be hospitalized (42.1% vs. 66.0%; $p < .0001$) or undergo surgery (41.1% vs. 61.1%; $p = .005$), compared with normal weight and underweight patients (5). The opposite was true for patients with CD, which implied a higher risk of developing active disease (odds ratio [OR], 1.50; 95% CI, 1.07–2.11) or requiring hospitalization (OR, 2.35; 95% CI, 1.56–3.52) for obese patients (16). A study in one center with 148 patients with CD revealed that those with a BMI greater than 25 had a shorter time to first surgery than those with a BMI of less than 18.5 (24 vs. 252 months; $p = .043$), but the number of operations over time remained the same (6). A retrospective review of 221 patients with CD followed for a median of 14.2 years found a 5% lower risk of surgery with each BMI increase by 1 (HR, 0.95; 95% CI, 0.91–0.99). And there was no difference in the risk of corticosteroid use or hospitalization in future (17). A prospective case-control study did not establish a link between BMI and the risk of surgery or corticosteroid use in the future (7).

The data about UC are scarce and inconsistent. A population cohort of 267 patients with UC demonstrated that with each BMI increase by 1, patients had a 6% higher risk of surgery in the future ($p = .01$) and a 3.4% higher risk of hospitalization ($p = .052$) (17). A retrospective analysis of 1494 IBD patients showed

no association between obesity and the incidence of corticosteroid use, hospitalization, or surgery (8). Other studies have reported either higher levels of surgery in overweight patients or, conversely, a protective effect with a lower proportion of years of active disease in obese patients (9).

Kurnool and colleagues examined 160 UC patients treated with biological agents (18). The authors found that any gradual increase in BMI by 1 was associated with a 4% increase in the risk of treatment failure (adjusted HR, 1.04; 95% CI, 1.00–1.08) for all patients, regardless of the type of the biological preparation used (19). Harper and colleagues showed a 30% increase in the risk of UC exacerbation (HR, 1.30; 95% CI, 1.07–1.58) and a 6% increase in the risk of CD attack (HR, 1.06; 95% CI, 1.02–1.11) with each increasing increase in BMI by 1 (19).

Obesity is clearly becoming a common comorbid condition in the IBD population. As noted above, its clinical significance in the pathogenesis, history, and results of IBD treatment appears to be contradictory among the few studies available. There are several inherent limitations in the current literature that may contribute to this lack of clarity.

First, most of the available data come from retrospective studies measuring BMI in different time frames over the course of the disease. Obesity is a dynamic measurement and undergoes a number of changes during the course of the patient's disease. If obesity affects the results of IBD, it is not clear when this effect is most influential (e.g., the obesity at the time of diagnosis of IBD, the weight gain during the course of the disease, or the presence of obesity years before onset). The retrospective nature of studies and the variable time frames in which obesity is assessed in studies make it difficult to pinpoint the causal relationship. In addition, many studies neglect to consider potential confusing factors, such as smoking, corticosteroid use, or disease activity.

The vast majority of existing studies use BMI as a surrogate measure for obesity. It remains unknown whether BMI is an accurate reflection of fat stores, namely visceral adipose tissue (VAT), especially when one of the main hypotheses supporting the role of obesity in patients with IBD involves the unique metabolic and biochemical properties of VAT compared to subcutaneous adipose tissue (SAT). There

are several studies that suggest that VAT, but not BMI, may have prognostic value in predicting post-operative outcomes and disease recurrence in patients with CD (20, 21). A prospective study showed that the ratio of VAT to SAT was related to CD behavior, as well as future serial fecal calprotectin (FC) and quality of life measurements, although the same is not true for BMI (22). Therefore, BMI is not able to distinguish VAT from SAT and may contribute to the conflicting results observed in the present literature.

CONCLUSION

There is growing evidence that the IBD population is facing an obesity epidemic parallel to that of the general population. This is accompanied by an increasing incidence of IBD, especially in newly developed countries, which raises questions about the role of obesity in the pathogenesis of IBD. There are no reliable epidemiological data, although there are pathophysiologically based theories to support the potential role of obesity in the development of IBD. Similarly, studies on the impact of obesity on the natural history of the disease and the complications associated with IBD are conflicting.

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