Journal of Inflammation Research

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

# Impact of Obesity on the Long-Term Outcomes of Advanced Therapies in IBD: A Real-World Study in Taiwan

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**Purpose:** Obesity has emerged as a factor influencing outcomes in inflammatory bowel disease (IBD), yet its effect on the persistence of advanced biologic therapies, especially in Asian populations, remains unclear. This study evaluates obesity's impact on clinical outcomes and treatment persistence among Taiwanese IBD patients on advanced biologic therapies.

**Methods:** This retrospective cohort study was conducted at Chang Gung Memorial Hospital, Taiwan, involving IBD patients on advanced biologics between October 2015 and October 2024. Patients were categorized by BMI into obesity (≥27 kg/m²) and control (<27 kg/m²) groups. Outcomes included 52-week therapy persistence, infections, IBD-related hospitalizations, surgeries, and flare-ups, with persistence compared across biologic agents.

**Results:** Among 555 IBD patients, 68 were obese. Obese patients had distinct characteristics: higher male prevalence (86.8% vs 65.3%), smoking rates (20.6% vs 7.8%), and comorbidities such as hypertension (30.6% vs 13.6%) and cardiovascular disease (11.8% vs 2.5%). Lab results indicated elevated white blood cells, hemoglobin, albumin, and triglycerides, and lower HDL cholesterol in the obesity group. While overall 52-week persistence rates were similar, Ustekinumab showed a lower persistence in obese patients ($P$ = 0.041).

**Conclusion:** Obesity in Asian IBD patients is linked to specific clinical traits and comorbidities. Although obesity did not affect overall therapy persistence, Ustekinumab's lower persistence among obese patients suggests the need for tailored treatments. Future studies should explore optimal therapies for obese IBD patients.

**Keywords:** inflammatory bowel disease, advanced therapies, drug persistence, overweight, obesity

## Introduction

According to the World Health Organization (WHO), in 2022, approximately 2.5 billion adults aged 18 and older were classified as overweight (25 kg/m² ≤ body mass index (BMI) < 30 kg/m²) or obese (BMI ≥ 30 kg/m²).[1,2] Among this group, an estimated 650 million individuals were classified as obese. By 2014, the global prevalence of obesity had tripled compared to 1975.[3] If current trends persist, obesity rates are projected to reach 21% among women and 18% among men by 2025.[4]

Historically, patients with inflammatory bowel disease (IBD) have been associated with leaner body types, as weight loss and malnutrition were hallmark features of the disease. However, the prevalence of obesity in IBD patients has been

Received: 17 February 2025
Accepted: 29 May 2025
Published: 3 June 2025

increasing, mirroring global trends. A population-based cohort study from Olmsted County, Minnesota, revealed that the proportion of obese IBD patients rose from 12% between 1990 and 1994 to 20% between 2005 and 2010.[5]

Obesity is intricately linked with autoimmunity, elevating the risk of developing inflammatory diseases.[6,7] Adipose tissue, long thought to be metabolically inert, is now recognized as an active endocrine organ that secretes pro- and anti-inflammatory cytokines integral to the pathogenesis of IBD.[8,9] Studies have suggested that obesity influences the clinical course and management of IBD, potentially impacting disease activity, outcomes, and treatment responses.[10–13]

Over recent decades, biologic agents and small molecule therapies have become cornerstone treatments for moderate to severe IBD.[14,15] Given the chronic nature of the disease, maintaining the long-term effectiveness of these therapies is critical to managing symptoms and preventing disease progression. However, the influence of obesity on the persistence and efficacy of these therapies remains poorly understood. Although anti-TNF-α therapies have been the most extensively studied, the findings have been inconsistent. For example, a meta-analysis reported that obesity was associated with higher odds of anti-TNF treatment failure in ulcerative colitis (UC) patients, but not in Crohn's disease (CD) patients.[16] Moreover, most existing studies examining the impact of obesity on biologic therapy in IBD have been conducted in Western populations, while data from Asian cohorts remain limited. Genetic studies have shown that East Asian individuals are more commonly associated with susceptibility loci such as *TNFSF15*, whereas variants prevalent in Western populations—such as *NOD2, ATG16L1*, and *IL23R*—appear to be less relevant in Asian populations.[17,18] In addition, pharmacogenomic markers that predict biologic response in Western cohorts, including those related to TNF-α and IL-23R pathways, may not be directly applicable to Asian populations.[19] Real-world data have also revealed regional differences in treatment adherence and biologic persistence, influenced by sociocultural norms and healthcare system factors.[20] These interethnic differences underscore the need for region-specific research to determine whether findings from Western studies can be generalized to Asian IBD populations, such as those in Taiwan.

With the increasing reliance on real-world data to evaluate the effectiveness of biologic agents, drug persistence—the duration from treatment initiation to discontinuation—has become a valuable metric.[21] It reflects patient and physician commitment to a treatment, as well as the sustained efficacy and tolerability of a therapy in clinical practice.[22] Against this backdrop, this study aimed to evaluate the 52-week persistence of advanced therapies in obese and non-obese groups among Taiwanese IBD patients, encompassing both CD and UC populations.

# Materials and Methods

## Study Population and Design

This retrospective cohort study was conducted at Chang Gung Memorial Hospital, Linkou, a 4000-bed tertiary referral center in Taiwan. Patients with a confirmed diagnosis of IBD were identified using the database of the Chang Gung Inflammatory Bowel Disease Center. The study period spanned from October 2015 to August 2024. Eligibility criteria required participants to have undergone advanced therapies and to have documented weight and BMI data at the time of enrollment. Patients were excluded if they were pregnant, under the age of 18, or lost to follow-up during the study period. The study population was categorized into two groups based on BMI: the control group (BMI < 27) and the obesity group (BMI ≥ 27), in accordance with cutoff values established by Taiwan's Department of Health.[23] Studies conducted in Asian populations, including Taiwan, have shown that the 95th percentile of BMI for individuals aged 20–29 ranges from 22 to 24 kg/m².[24–26] Since Asians generally have BMI levels 2–3 kg/m² lower than their White counterparts, applying Western BMI standards to Asian populations can underestimate obesity prevalence.[27] Therefore, a BMI of ≥24 kg/m² is recommended as the threshold for overweight, and BMI ≥27 kg/m² is proposed as the threshold for obesity in Asian adults.[23]

## Study Endpoint

The primary endpoint was drug persistence, defined as the duration of biologic therapy up to the 52$^{nd}$ week, measured from the initiation to the discontinuation of treatment. Given the chronic and relapsing nature of IBD, treatment persistence is widely regarded as a composite real-world indicator reflecting sustained efficacy, long-term safety, tolerability, and patient adherence. In Taiwan, National Health Insurance (NHI) reimburses biologic therapy for a maximum of 12 months, after which patients must either discontinue therapy for a mandatory three-month drug-free interval or switch to self-funded treatment, regardless of disease activity.[28,29]

## Biologics Treatment Regimens

Patients in the study received biologics according to NHI reimbursement criteria. Infliximab (IFX) was administered at an induction dose of 5 mg/kg at weeks 0, 2, and 6, followed by maintenance doses every 8 weeks. Adalimumab (ADA) was initiated with 160 mg at week 0, 80 mg at week 2, and 40 mg at week 4, with maintenance doses of 40 mg every two weeks. Vedolizumab (VDZ) was dosed at 300 mg at weeks 0, 2, and 6, with subsequent maintenance doses every 8 weeks. Ustekinumab (UST) was weight-adjusted for induction (260 mg, 390 mg, or 520 mg based on weight ≤55 kg, 55–85 kg, and ≥85 kg, respectively), followed by 90 mg every 12 weeks. Tofacitinib was given orally at an induction dose of 10 mg twice daily for the first 8 weeks, with a maintenance dose of 5 mg twice daily or 11 mg once daily starting from week 9. Dose escalation was defined as any modification involving a shortened dosing interval compared to the standard regimen.

## Data Collection and Definitions

Medical records of eligible participants were reviewed to extract comprehensive clinical and demographic data, including age, gender, smoking status, underlying diseases, and Montreal classification. Disease location or extent in CD and UC was documented alongside the date of the initial biologic dose. Key variables of interest included BMI (measured in kilograms per square meter) and total body weight (measured in kilograms) at the time of biologic initiation. Baseline laboratory parameters, such as white blood cell count, hemoglobin, albumin, and C-reactive protein levels, were collected. Additional biochemical markers, including fasting lipid profiles such as total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), as well as glycated hemoglobin and fasting plasma glucose (FPG), were measured to assess metabolic health.

Biologic therapy data included prior use of IFX, ADA, VDZ, UST, or TOF, or biologic-naïve status. Details of the current biologic treatment, including the dates of the first and last doses, were documented. Concurrent use of other medications, such as 5-aminosalicylic acid, corticosteroids, and thiopurines, was also recorded. Corticosteroid-free remission was defined as the absence of corticosteroid use for at least 12 weeks prior to reaching the 52nd week of therapy, based on CORE-IBD consensus.[30] Clinical remission was defined as a Mayo score ≤2 with no individual subscore >1 for UC patients or a Crohn's Disease Activity Index (CDAI) score <150 for CD patients, as these criteria are widely used in clinical trials.[31–33]

## Adverse Events and Complications

Clinical outcome data included adverse events such as dose escalation history, drug administration intervals, opportunistic infections, IBD-related hospitalizations, IBD complications, and IBD-related surgeries, as well as episodes of acute flare-ups. Hospitalization was specifically defined as a hospital stay lasting at least three days due to acute IBD flare-ups or complications. Admissions solely for diagnostic evaluations, biologic therapy administration, or conditions unrelated to IBD were excluded. IBD-related complications were carefully documented and included strictures, abscesses, fistulas, and perianal disease. Episodes of acute flare-ups that required emergency room visits or hospitalizations were characterized by symptoms such as persistent diarrhea, bloody stools, severe or prolonged abdominal pain, fever, and other acute IBD-related manifestations. IBD-related abdominal surgeries were comprehensively recorded and included procedures such as surgeries for fistulas or abscesses, intestinal resections, colectomies, proctocolectomies, ileostomies, and colostomies.[34] These data provided a detailed overview of the burden of surgical interventions among the study population.

## Infection Definitions

Infections were assessed as part of the adverse event analysis. Cytomegalovirus (CMV) infection was identified through the detection of viral inclusion bodies in colonic mucosal biopsy samples. *Clostridioides difficile* (*C. difficile*) infection was confirmed by the presence of a positive toxin gene, which is a reliable diagnostic marker. *Clostridium innocuum* (*C. innocuum*) infection was diagnosed based on stool culture results.[35] These detailed definitions ensured the consistency and reliability of infection-related data collection across participants.

## Statistical Analyses

Numerical data were summarized as mean ± standard deviation (SD), while categorical data were expressed as absolute counts and percentages. Comparisons of continuous variables between groups were performed using the Student's *t*-test, and categorical variables were analyzed with either the chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant. Drug persistence was assessed through Kaplan–Meier survival analysis, and comparisons between groups were conducted using the Log rank test. A log-rank p-value of less than 0.05 was considered indicative of statistically significant differences in persistence. All statistical analyses were performed using SPSS software, version 27.0 (IBM Corp., Armonk, NY).

# Results

## Baseline Characteristics and Clinical Outcomes

A total of 555 patients with inflammatory bowel disease (IBD) were included in the study, comprising 222 patients with ulcerative colitis (UC) and 333 with Crohn's disease (CD). Among the cohort, 68 patients (12.3%) were classified as obese (BMI $\geq$ 27 kg/m$^2$), while the remaining 487 patients constituted the control group (BMI < 27 kg/m$^2$). Obese patients exhibited distinct baseline characteristics compared to the control group. Specifically, the obesity group had a higher proportion of males, fewer smokers, and an increased prevalence of comorbidities, including hypertension, cardiovascular disease, and chronic kidney disease.

In CD patients, the obesity group showed less frequent ileocolonic and colonic involvement, with a higher prevalence of terminal ileum involvement. Among UC patients, proctitis and disease confined to the colorectum distal to the splenic flexure were less common in the obesity group. Obese patients also had significantly higher levels of white blood cells, hemoglobin, albumin, high-density lipoprotein cholesterol (HDL-C), and triglycerides. Despite these differences, no significant variations were observed between the obesity and control groups regarding steroid-free remission at 52 weeks, opportunistic infections, IBD-related complications, surgeries, or acute flare-ups. Additional baseline characteristics and clinical outcomes are presented in Table 1.

## Persistence of Advanced Therapies

Among the entire cohort, 420 patients (75.7%) continued advanced therapies for at least one year. This included 51 patients (75%) from the obesity group and 369 patients (75.8%) from the control group. Kaplan–Meier analysis revealed no significant difference in 52-week drug persistence between the two groups (Log-rank P = 0.932, Figure 1a). In the UC subgroup, 155 patients (69.8%) persisted with advanced therapies for one year, comprising 21 obese patients (75%) and 134 control patients (69.1%). Kaplan–Meier analysis again indicated no significant difference between the groups (Log-rank P = 0.669, Figure 1b). Similarly, in the CD subgroup, 265 patients (79.6%) maintained advanced therapies for at least one year, with 30 patients (75%) from the obesity group and 235 patients (80.2%) from the control group. Kaplan–Meier analysis showed no significant difference in drug persistence between the groups (Log-rank P = 0.551, Figure 1c).

## Drug-Specific Persistence

The persistence of individual therapies was analyzed. Among patients treated with IFX, 30 out of 46 patients (65.2%) achieved 52-week persistence, including 25 control patients (64.1%) and 5 obese patients (71.4%) (Figure 1d). For ADA, 89 of 127 patients (70.1%) continued therapy for one year, with 80 control patients (70.8%) and 9 obese patients (64.3%) achieving persistence (Figure 1e). For VDZ, 150 of 205 patients (73.2%) maintained therapy for at least one year, including 127 control patients (71.8%) and 23 obese patients (82.1%) (Figure 1f). Among UST users, 145 of 165 patients (87.9%) persisted with therapy, including 132 control patients (89.8%) and 13 obese patients (72.2%). Finally, 6 of 12 patients (50%) treated with TOF maintained therapy for one year. Kaplan–Meier analysis identified no significant differences in persistence across therapies between the obesity and control groups, except for UST, where obese patients demonstrated significantly lower 52-week persistence (Log-rank P = 0.041, Figure 1g).

**Table 1** Baseline Characteristics and Clinical Outcomes of Obesity and Control Cohorts

| | Overall (n=555) | Obesity Group[a] (n=68) | Control Group (n=487) | P-value |
|---|---|---|---|---|
| Baseline characteristics | | | | |
| Age at initial dose (mean ± SD years) | 45.9±15.4 | 48.7±15.8 | 45.5±15.3 | 0.096 |
| Gender (male) | 377 (67.9%) | 59 (86.8%) | 318 (65.3%) | <0.001* |
| Body mass index (mean ± SD, kg/m$^2$) | 22.6±4 | 30.1±3.2 | 21.6±2.9 | <0.001* |
| Inflammatory bowel disease (Crohn's disease) | 333 (60%) | 40 (58.8%) | 293 (60.2%) | 0.833 |
| Smoking (%) | 52 (9.4%) | 14 (20.6%) | 38 (7.8%) | <0.001* |
| Underlying disease (%) | | | | |
| Diabetes mellitus | 33 (5.9%) | 7 (10.3%) | 26 (5.3%) | 0.164 |
| Hypertension | 91 (16.4%) | 25 (36.8%) | 66 (13.6%) | 0.001* |
| Atherosclerotic cardiovascular disease | 20 (3.6%) | 8 (11.8%) | 12 (2.5%) | 0.001* |
| Chronic kidney disease | 17 (3.1%) | 5 (7.4%) | 12 (2.5%) | 0.045* |
| Cancer | 24 (4.3%) | 4 (5.9%) | 20 (4.1%) | 0.52 |
| Other autoimmune disease | 71 (12.8%) | 9 (13.2%) | 62 (12.7%) | 0.907 |
| Thromboembolism | 15 (2.7%) | 0 (0%) | 15 (3.1%) | 0.236 |
| Montreal classification (%) | | | | |
| Crohn's disease | 333 | 40 | 293 | |
| L1 | 132 (39.6%) | 28 (70%) | 104 (35.5%) | <0.001* |
| L2 | 44 (13.2%) | 1 (2.5%) | 43 (14.7%) | 0.033* |
| L3 | 144 (43.2%) | 11 (27.5%) | 133 (45.4%) | 0.032* |
| L4 | 115 (34.5%) | 18 (45%) | 97 (33.1%) | 0.138 |
| B1 | 155 (46.5%) | 22 (55%) | 133 (45.4%) | 0.253 |
| B2 | 157 (47.1%) | 18 (45%) | 139 (47.4%) | 0.772 |
| B3 | 63 (18.9%) | 5 (12.5%) | 58 (19.8%) | 0.269 |
| Peri-anal disease | 53 (15.9%) | 3 (7.5%) | 50 (17.1%) | 0.121 |
| Ulcerative colitis | 222 | 28 | 194 | |
| E1 | 25 (11.3%) | 7 (25%) | 18 (9.3%) | 0.023* |
| E2 | 82 (36.9%) | 4 (14.3%) | 78 (40.2%) | 0.008* |
| E3 | 115 (51.8%) | 17 (60.7%) | 98 (50.5%) | 0.313 |
| Combine with biologic therapy (%) | | | | |
| 5-ASA | 362 (65.2%) | 38 (55.9%) | 324 (66.5%) | 0.084 |
| Immunosuppressants | 152 (27.4%) | 13 (19.1%) | 139 (28.5%) | 0.103 |
| Steroid | 329 (59.3%) | 41 (60.3%) | 288 (59.1%) | 0.856 |
| Biologic-naïve | 257 (46.3%) | 33 (48.5%) | 224 (46%) | 0.695 |
| Biologic-experienced (%) | | | | |
| Infliximab | 34 (6.1%) | 5 (7.4%) | 29 (6%) | 0.593 |
| Adalimumab | 144 (25.9%) | 16 (23.5%) | 128 (26.3%) | 0.627 |
| Vedolizumab | 171 (30.8%) | 17 (25%) | 154 (31.6%) | 0.268 |
| Ustekinumab | 67 (12.1%) | 7 (10.3%) | 60 (12.3%) | 0.631 |
| Tofacitinib | 8 (1.4%) | 1 (1.5%) | 7 (1.4%) | 0.999 |
| Current biological agents use (%) | | | | |
| Infliximab | 46 (8.3%) | 7 (10.3%) | 39 (8%) | 0.522 |
| Adalimumab | 127 (22.9%) | 14 (20.6%) | 113 (23.2%) | 0.631 |
| Vedolizumab | 205 (36.9%) | 28 (41.2%) | 177 (36.3%) | 0.439 |
| Ustekinumab | 165 (29.7%) | 18 (26.5%) | 147 (30.2%) | 0.53 |
| Tofacitinib | 12 (2.2%) | 1 (1.5%) | 11 (2.3%) | 0.999 |
| Laboratory test | | | | |
| WBC (1000/μL) | 8.5±3.6 | 10.1±4.7 | 8.3±3.3 | <0.001* |
| Hemoglobulin (g/dL) | 12.3±2.2 | 13.1±2.7 | 12.2±2.2 | 0.015* |
| CRP (mg/L) | 13.2±27.7 | 11.4±22.9 | 13.4±28.3 | 0.577 |

(*Continued*)

**Table 1** (Continued).

| | Overall (n=555) | Obesity Group[a] (n=68) | Control Group (n=487) | P-value |
|---|---|---|---|---|
| Albumin (g/dl) | 3.9±0.6 | 4.1±0.5 | 3.9±0.6 | 0.002* |
| Fasting plasma glucose (mg/dL) | 95±21.3 | 105.2±32.9 | 93.1±18.1 | 0.125 |
| Glycated Hemoglobin (%) | 5.7±0.7 | 6.1±1 | 5.7±0.6 | 0.072 |
| Low density lipoprotein-Cholesterol (mg/dL) | 104.8±37.6 | 102.6±44.2 | 105.3±36.3 | 0.73 |
| High density lipoprotein-Cholesterol (mg/dL) | 52.4±20.4 | 42.1±15 | 54.5±20.7 | 0.004* |
| Triglyceride (mg/dL) | 129.9±77.4 | 171.5±105 | 122.4±69.1 | 0.023* |
| Total Cholesterol (mg/dL) | 180.1±48.8 | 185±67.7 | 179.2±44.7 | 0.565 |
| Clinical outcomes | | | | |
| Dose escalation | 95 (17.1%) | 14 (20.6%) | 81 (16.6%) | 0.417 |
| Clinical remission at 52$^{nd}$ week | 88 (15.9%) | 12 (17.6%) | 76 (15.6%) | 0.616 |
| Steroid-free remission at 52$^{nd}$ week | 118 (21.3%) | 15 (22.1%) | 103 (21.1%) | 0.839 |
| Persistence (weeks) | 54.8±30.6 | 55.2±28.5 | 54.7±30.9 | 0.896 |
| IBD related admission rate | 130 (23.4%) | 14 (20.6%) | 116 (23.8%) | 0.556 |
| IBD related admission (times/year) | 0.6±1.4 | 0.4±1.2 | 0.6±1.5 | 0.382 |
| Opportunistic infection | | | | |
| *Cytomegalovirus* colitis | 17 (3.1%) | 1 (1.5%) | 16 (3.3%) | 0.708 |
| *Clostridioides difficile* | 54 (9.7%) | 5 (7.4%) | 49 (10.1%) | 0.48 |
| *Clostridium innocuum* | 12 (2.2%) | 1 (1.5%) | 11 (2.3%) | 0.999 |
| IBD related complications[b] | 30 (5.4%) | 2 (2.9%) | 28 (5.7%) | 0.564 |
| IBD related surgeries | 29 (5.2%) | 4 (5.9%) | 25 (5.1%) | 0.771 |
| Acute flare-up | 94 (16.9%) | 9 (13.2%) | 85 (17.5%) | 0.385 |

**Note**: We used the Student's *t* test on continuous variable and Chi-square or Fisher's exact test on categorical data. [a]Obesity group included patient with BMI greater than or equal to 27. [b]IBD related complications included fistula, lumen stricture, and intra-abdominal abscess…etc. *P < 0.05.

**Abbreviations**: CRP, C-reactive protein; IBD, inflammatory bowel disease; WBC, white blood cell.

## Discussion

Obesity prevalence among IBD patients has been reported to range from 15–40% in Western countries, with a steady increase over time.[36,37] However, studies focusing on Asian populations remain limited. A single-center study in Korea using data from the Asian IBD Registry (1989–2016) addressed this gap by employing a BMI cutoff for stage 2 obesity (BMI ≥ 30 kg/m²) in accordance with the 2018 Korean Society for the Study of Obesity (KSSO) guidelines.[38] This stricter criterion excluded many patients with stage 1 obesity (BMI 25–29.9 kg/m²), resulting in a reported obesity prevalence of only 0.63% among IBD patients. In contrast, our study found that 12.3% of IBD patients were classified as obese (BMI ≥ 27 kg/m²). Despite using a lower cutoff compared to the WHO standard (BMI ≥ 30 kg/m²), our findings closely aligned with Western data. This discrepancy may reflect more recent trends captured by our study, which began in 2015, highlighting a rapid rise in obesity among Asian IBD patients, likely driven by Westernized diets and lifestyles.

Consistent with previous studies, obesity-related comorbidities were more prevalent among obese IBD patients in our cohort.[10] Regarding disease extent, Western studies have generally reported no significant differences in the extent of UC or CD phenotypes between obese and non-obese patients,[34,39] findings echoed by the Korean study.[40] However, in our study, ileal involvement (L1) in CD (70%) and proctitis (B1) in UC (25%) were significantly more common among obese patients (P<0.05). These findings may indicate distinct disease manifestations in obese Asian patients, warranting further research to explore underlying mechanisms. As for disease behavior, we found a predominance of the inflammatory phenotype (B1) in obese CD patients, consistent with previous research.[34,39,41,42]

The pro-inflammatory cytokines and adipokines secreted by adipose tissue are known to influence immune responses, potentially exacerbating disease activity, outcomes, and treatment efficacy in autoimmune diseases, including IBD.[43,44] Obesity has been linked to worse clinical courses and higher comorbidity rates in conditions such as rheumatoid arthritis

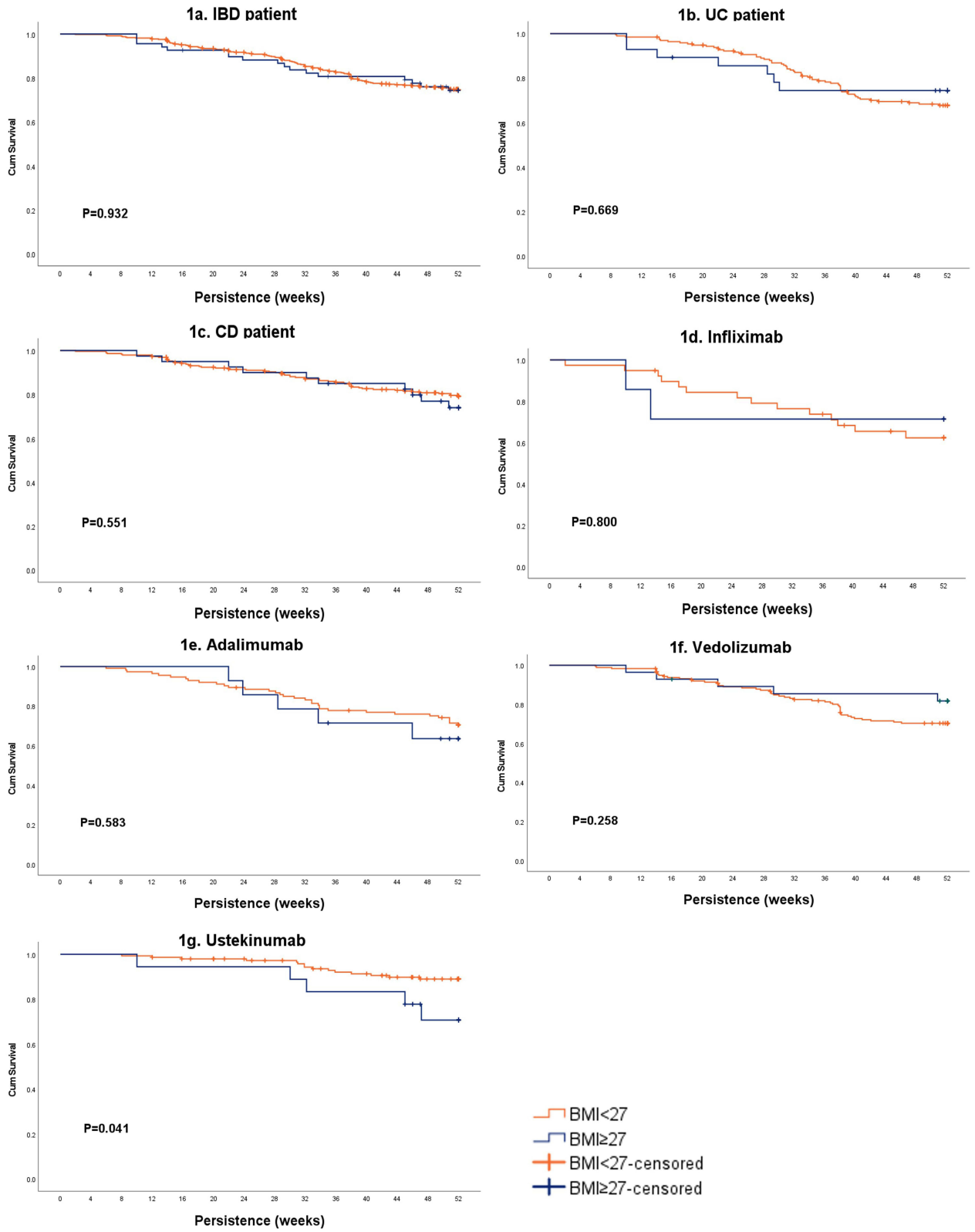


**Figure 1** Kaplan-Meier Survival Curves for 52-Week Persistence of Advanced Biologics in IBD Patients. This figure illustrates Kaplan-Meier survival curves for the 52-week persistence of advanced biologics in IBD patients, with seven panels highlighting different subgroups or treatments. (**a**) Depicts overall persistence among IBD patients, while (**b** and **c**) focus on persistence in UC and CD patients, respectively. (**d**–**g**) Present persistence data for specific biologics: Infliximab, Adalimumab, Vedolizumab, and Ustekinumab, respectively. Of note, within the Ustekinumab subgroup (**g**), the obesity group exhibited significantly lower 52-week drug persistence (Log-rank P = 0.041). **Abbreviations**: CD, Crohn's disease; UC, Ulcerative colitis; IBD, Inflammatory bowel disease.


https://doi.org/10.2147/JIR.S520446

and systemic lupus erythematosus.[43] However, the impact of obesity on IBD outcomes remains inconsistent. Our findings showed no significant differences in clinical outcomes, such as hospitalization rates, surgeries, or opportunistic infections, between obese and non-obese groups. Similarly, a retrospective cohort study found no association between increasing BMI and emergency visits or prednisone use, although higher BMIs (≥35 kg/m²) were correlated with poorer quality of life and elevated CRP levels.[10] Conversely, other studies have identified obesity as a risk factor for early readmissions and disease relapse.[45]

The pharmacokinetics of biologics are significantly influenced by obesity, as an increased volume of distribution and enhanced drug clearance can shorten drug half-life and reduce therapeutic concentrations.[46] This effect may be more pronounced for fixed-dose biologics, such as UST and VDZ, compared to weight-based regimens like IFX. The lack of dose adjustment in fixed-dose therapies may lead to subtherapeutic exposure in obese patients, potentially contributing to reduced treatment persistence.

TNF-α antagonists, crucial for inducing remission in IBD, are particularly affected by these changes, as adipocytes secrete TNF-α, creating an "antigen sink" that sequesters the drug and reduces its efficacy.[10,47] A UK-wide multicenter study reported that obesity was associated with treatment failure and loss of response to IFX at 2–3 years.[48] However, our study found no significant differences in 52-week drug persistence rates between obese and non-obese groups for both IFX (71.4%) and ADA (64.3%). This may reflect the shorter follow-up period of our study, underscoring the need for long-term evaluations to better understand obesity's impact on therapeutic outcomes.

VDZ and UST, both administered as fixed, non-weight-based doses, are newer therapies in the IBD treatment landscape, and limited data exist regarding their efficacy in obese patients.[36] A multicenter study on Crohn's pouchitis found no significant differences in VDZ outcomes based on BMI,[49] while another study linked obesity to lower rates of VDZ discontinuation but no differences in dose escalation.[50] Consistent with these findings, our study observed no significant differences in 1-year VDZ persistence between the groups. Regarding UST, a post hoc analysis of the IM-UNITI study reported no significant differences in clinical remission rates among obese patients over 44 weeks, although lower drug trough levels were observed.[51] This aligns with evidence suggesting that obesity increases drug clearance rates.[52,53] In our study, obese patients demonstrated significantly lower 52-week persistence with UST compared to non-obese patients. While reduced drug levels may not affect short-term clinical remission, they could impair long-term efficacy and contribute to lower persistence. Fixed-dose maintenance regimens, unlike weight-based dosing strategies, may exacerbate this issue, as drug levels may be insufficient in obese patients. Subtherapeutic exposure due to fixed dosing may contribute, other mechanisms—including altered drug metabolism, increased inflammatory burden, immune dysregulation, and a higher prevalence of comorbidities—may also affect long-term treatment outcomes. As a multifactorial endpoint, persistence reflects not only efficacy, but also long-term safety, tolerability, adherence, and healthcare-related factors. These findings underscore the importance of individualized therapeutic strategies—such as therapeutic drug monitoring—to optimize biologic durability in this population.

In summary, while clinical outcomes such as hospitalization, surgery, and infection rates showed no significant differences, our findings suggest that obesity may influence long-term therapeutic outcomes and treatment persistence, particularly with UST. These insights provide valuable guidance for clinicians managing obese IBD patients and underscore the need for further research on personalized treatment strategies in this population.

This study has several limitations. First, it was conducted at a single tertiary referral center, which may introduce selection and referral bias. Second, drug serum levels were not available, limiting pharmacokinetic interpretation. Third, while BMI is a widely used clinical indicator, it may not accurately reflect visceral adiposity. Visceral adipose tissue (VAT) has been increasingly recognized for its metabolic relevance in obese IBD patients[9,54,55] and associated with postoperative outcomes and disease recurrence in CD patients,[56,57] though data in UC remain limited.[58] While imaging-based metrics such as CT or MRI provide more direct and accurate assessments of visceral adiposity, these were not available for our study cohort. As a result, although BMI is commonly used as a proxy for adiposity, its limitations in reflecting VAT and associated disease outcomes should be considered.[59] Fourth, our study was designed to evaluate the overall impact of obesity as a population-level characteristic, rather than to assess it as an independent risk factor. Accordingly, we did not perform multivariable analysis. Lastly, although persistence serves as a practical real-world indicator that reflects sustained efficacy, long-term safety, tolerability, and patient adherence, it does not directly capture

objective clinical outcomes such as symptomatic remission, endoscopic healing, or biomarker response. Moreover, the 52-week observation period—shaped in part by Taiwan's healthcare reimbursement policy—may not fully represent long-term treatment durability. Therefore, future studies with extended follow-up and additional endpoints, including clinical and endoscopic remission, are warranted to better elucidate the impact of obesity on IBD management.

## Conclusion

Obesity in IBD patients was associated with distinct clinical features and lower treatment persistence with UST. These findings suggest that obesity may affect the pharmacologic performance of certain biologics, highlighting the need for personalized treatment approaches. Further studies with pharmacokinetic and clinical outcome data are warranted to optimize long-term management in this population.

## Sample Data Availability Statements

The corresponding author would share the data underlying this article upon reasonable request.

## Compliance with Ethical Standards

This study was approved by the Institutional Review Board (IRB) of the Chang Gung Medical Foundation (approval document No. 202400030B0: "Diagnosis, Treatment, and Prognosis of Inflammatory Bowel Disease"). As a retrospective study, the requirement for written informed consent was waived. All patient data were anonymized prior to analysis to ensure confidentiality. The study was conducted in accordance with the ethical standards of the responsible institutional and national committees, and with the Declaration of Helsinki.

## Acknowledgments

We acknowledge the contributions of the members of the Chang Gung IBD Center. This study was supported by Chang Gung Memorial Hospital, Linkou, Taiwan (CORPG3P0251).

## Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This study was not funded by grants or other financial sponsors. The authors have no financial arrangements for the company whose products are discussed in this manuscript.

## Disclosure

The authors declare that they have no competing interests.

This abstract was presented at the ECCO Congress 2025 as a poster presentation with interim findings. The poster's abstract was published in "Poster Abstracts" in *Journal of Crohn's and Colitis*: https://doi.org/10.1093/ecco-jcc/jjae190.0423.

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