Obesity Facts

Research Article

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Obesity and Clinical Characteristics of Inflammatory Bowel Disease

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Keywords
Inflammatory bowel disease · Overweight · Obesity · Clinical characteristics · Biologics

Abstract

Introduction: The frequency of obesity and possible correlations with characteristics and outcome of inflammatory bowel disease (IBD) are undefined. Primary aim was to assess the body mass index (BMI) distribution in IBD patients in follow-up. Secondary aim was to compare clinical characteristics and course of IBD in normal weight versus overweight or obese patients. ***Methods:*** Adult IBD patients in regular follow-up were prospectively enrolled and BMI was recorded during outpatient visits. Comparisons were assessed by the Student *t*-test, Mann-Whitney U test and Chi-square test, as appropriate. ***Results:*** In the 300 IBD patients enrolled (150 Crohn's disease [CD], 150 ulcerative colitis [UC]), BMI distribution included: 16 (5.3%) underweight, 170 (56.7%) normal weight, 92 (30.7%) overweight, 22 (7.3%) obese patients. For the secondary aim, the 16 underweight patients were excluded, thus leaving 284 patients for the analysis (141 [49.6%] CD; 143 [50.4%] UC). Among these, 114 (40.2%) were overweight/obese and 170 (59.8%) normal weight. CD group included 89 (63.1%) normal weight and 52 (36.9%) overweight/obese patients. Perianal disease and refractoriness to biologics were more frequent in overweight/obese than normal weight CD patients (9 [10.1%] vs. 12 [23%], $p = 0.03$; 0 [0%] vs. 4 [23.4%], $p = 0.01$). In UC group, there were 81 (56.6%) normal weight and 62 (63.4%) overweight or obese patients. ***Conclusion:*** In IBD patients in follow-up, the proportion of underweight patients is low. Overweight and obese CD patients showed a higher frequency of perianal disease and refractoriness to biologics. BMI may influence phenotype and responsiveness to biologics in CD.

Introduction

Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the gastrointestinal tract, limited to the colon in ulcerative colitis (UC) but not in Crohn's disease (CD) [1]. In IBD, malnutrition may occur in subgroups of patients [2]. IBD-dedicated gastroenterologists are well trained in identifying and treating malnutrition. This condition recognizes different underlying pathophysiological mechanisms, such as decreased food intake, gut malabsorption, loss of proteins and nutrients in the stools and a hypercatabolic metabolism due to chronic inflammation [2]. Malnutrition has been extensively investigated in underweight IBD patients, representing a marker of severe clinical outcome [2]. Recently, attention has been focused on the role of diet in IBD course [3].

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Overweight and obesity also may be associated with malnutrition, whose impact in IBD patients has been less extensively investigated [4–11]. Obesity is a pathological condition whose pathogenesis relies on disproportion of energy intake and consumption. Obesity is defined according to the body mass index (BMI), an easy and costless diagnostic tool (values ≥30 kg/m^2, overweight from 25 to 29 kg/m^2) [8]. Due to its easy quantitative evaluation without interobserver variations, BMI indeed currently represents the more widely used marker of obesity in clinical practice, trials and in studies involving large study populations [9]. BMI has also been reported as a predictor of patients' risk and outcome [10].

The prevalence of these two conditions is rapidly increasing, being almost tripled worldwide, due to changes in lifestyle and diet, known potential risk factors for both IBD and obesity [11]. Recently, a large, 10-year population-level database reported that obesity rates in IBD significantly increased from 19.7% to 30.1% ($p < 0.0001$) [12]. Independent epidemiological studies reported a prevalence of 15–40% of obesity in IBD patients [13, 14].

Whether obesity may represent a risk factor for developing IBD is not established, as the few data at this regard are conflicting. More recently, weight gain in IBD patients may occur in relation to a significant optimization of treatment, possibly leading to obesity in predisposed individual with erroneous lifestyle [7]. However, the frequency of obese versus non-obese or underweight IBD patients is not defined.

A comparable clinical outcome in obese versus non-obese IBD patients has currently been suggested, although with conflicting findings [15–18]. Whether obesity in IBD may influence the responsiveness to biologic treatments and the need of immunomodulators or surgery is also not known.

On the basis of these findings, the primary aim of the present prospective study was to describe the BMI distribution in IBD patients in regular follow-up. Secondary aim was to compare, in the same cohort of patients, characteristics of IBD in normal weight versus overweight or obese patients. The frequency of immunomodulatory use and effectiveness, of IBD-related surgery and hospitalizations was also compared between normal weight and overweight/obese patients.

Methods

Study Protocol

In a prospective study, all patients referring to our tertiary IBD center from September 2022 to January 2023 were enrolled. Diagnosis of IBD was made according to standard criteria, in agreement with current European guidelines [19, 20]. UC and CD were defined according to the Montreal classification [21]. During a scheduled outpatient IBD visit, BMI was prospectively recorded. For each patient, clinical characteristics of IBD were retrospectively collected from medical records.

Study Population

Patients were enrolled according to the following inclusion criteria: (1) well-defined diagnosis of IBD [20, 21]; (2) age ≥18 years; (3) regular follow-up at our referral IBD center (≥2 visits/year). Exclusion criteria were (1) incomplete data in clinical records; (2) low compliance. Demographic and clinical characteristics of enrolled patients were already reported in clinical records of our referral center. For each patient, these data were retrospectively reported in a database, including: age, gender, BMI, smoking status (yes/no/ex), IBD type (CD, UC), IBD duration (years), UC extent (proctitis, E1, left-sided colitis, E2, extensive colitis, E3) [21], CD location (ileum, L1, colon, L2, ileo-colon, L3, upper, L4) [21], behavior (non-stricturing, non-penetrating, B1, stricturing, B2, penetrating, B3) [21], perianal disease (PD) (yes/no), IBD-related surgery (yes/no), extraintestinal manifestations (yes/no, type), prior treatment with systemic and low absorbable steroids, thiopurines, methotrexate or biologics for IBD (yes/no, type, duration, adverse events). During the scheduled outpatient visit at enrollment, the following biochemical parameters were collected: hemoglobin (g/dL), leukocytes (cells/μg), platelets (cells/μg), iron (μg/dL), ferritin (ng/mL), albumin (g/dL), total cholesterol (mg/dL), triglycerides (mg/dL), cobalamin (pg/mL), folate (ng/mL). Responsiveness to immunosuppressors (ISS) (azathioprine, 6-mercaptopurine, methotrexate) or biologics (infliximab, adalimumab, certolizumab pegol, biosimilars, vedolizumab, ustekinumab) was defined according to current European guidelines [22, 23]. For the subgroup of patients with prior use of biologics, data were also separately considered according to primary failure, secondary failure, and/or adverse events.

BMI Assessment

For the primary aim of the study, the BMI of each IBD patient was prospectively recorded both in clinical records and in the abovementioned database. At the end of the study, patients were subgrouped according to the standard BMI definition [8, 9]: underweight (BMI <18.5 kg/m^2), normal weight (BMI ≥18.5 kg/m^2 and <25 kg/m^2), overweight (BMI ≥25 kg/m^2 and <30 kg/m^2), and obese (BMI ≥30 kg/m^2). As only 1 patient with UC showed a BMI >35 and none >40, obese patients were not categorized according to obesity severity.

Whether clinical responsiveness and adverse events using ISS or biologics in IBD differ in overweight or obese versus normal weight patients represented the secondary

Table 1. Distribution of clinical characteristics of Crohn's disease (CD) and, separately, of ulcerative colitis (UC) patients, subgrouped according to the body mass index (BMI)

	Underweight (n = 9)	Normal weight (n = 89)	Overweight (n = 43)	Obese (n = 9)
CD (n = 150)				
CD features, *n* (%)				
A1	1 (11.1)	6 (6.7)	4 (9.3)	0 (0)
A2	6 (66.7)	50 (56.2)	29 (67.4)	4 (44.4)
A3	2 (22.2)	33 (37.1)	10 (23.3)	5 (55.6)
L1	5 (55.6)	62 (69.7)	32 (74.4)	3 (33.3)
L2	0 (0)	8 (9)	3 (7)	1 (11.1)
L3	4 (44.4)	19 (21.3)	8 (18.6)	5 (55.6)
L4	0 (0)	7 (7.9)	1 (2.3)	1 (11.1)
PD	1 (11.1)	9 (10.1)	10 (23.3)	2 (22.2)
B1	1 (11.1)	24 (27)	8 (18.6)	5 (55.6)
B2	6 (66.7)	44 (49.4)	28 (65.1)	4 (44.4)
B3	2 (22.2)	21 (23.6)	7 (16.3)	0 (0)
Age at enrollment, median [range]	41 [23–70][a]	53 [22–86][b]	51.5 [25–74][c]	60 [40–74][d]
CD duration, median [range]	9 [4–36][e]	14 [1–57][f]	17 [4–45][g]	12 [1–31][h]
	Underweight (n = 7)	Normal weight (n = 81)	Overweight (n = 49)	Obese (n = 13)
UC (n = 150)				
UC features, *n* (%)				
Age at diagnosis <18	1 (14.3)	8 (9.9)	2 (4.1)	1 (8.3)
Age at diagnosis >18 and <40	5 (71.4)	47 (58)	22 (44.9)	5 (41.7)
Age at diagnosis >40	1 (14.3)	26 (32.1)	25 (51)	7 (35)
E1	1 (14.2)	11 (13.6)	16 (32.7)	2 (15.4)
E2	3 (42.9)	39 (48.1)	15 (30.6)	4 (30.8)
E3	3 (42.9)	31 (38.3)	18 (36.7)	7 (53.8)
Age at enrollment, median [range]	45 [26–64][i]	47 [20–87][l]	63 [27–83][m]	56 [43–80][n]
UC duration, median [range]	19 [1–30][o]	10 [1–42][p]	14 [2–42][q]	19 [1–40][r]

A1, <18 years; A2, ≥18 and <40 years; A3, ≥40 years; L1, ileum; L2, colon; L3, ileum-colon; L4, upper gastrointestinal tract; B1, non-stricturing-non-penetrating; B2, structuring; B3, penetrating; E1, proctitis; E2, left-sided colitis; E3, pancolitis; PD, perianal disease. *Statistical analysis*: a vs. b, $p = 0.06$; a vs. c, $\mathbf{p = 0.025}$; a vs. d, $\mathbf{p = 0.042}$; b vs. c, $\mathbf{p < 0.00001}$; b vs. d, $p = 0.49$; c vs. d, $\mathbf{p < 0.00001;}$ e vs. f, $p = 0.26$; e vs. g, $\mathbf{p = 0.049}$; e vs. h, $p = 0.58$; f vs. g, $p = 0.11$; f vs. h, $p = 0.64$; g vs. h, $p = 0.18$. i vs. l, $p = 0.69$; i vs. m, $\mathbf{p = 0.015}$; i vs. n, $\mathbf{p = 0.015}$; l vs. m, $\mathbf{p = 0.0001}$; l vs. n, $p = 0.07$; m vs. n, $p = 0.94$; o vs. p, $p = 0.26$; o vs. q, $p = 0.96$; o vs. r, $p = 0.93$; p vs. q, $\mathbf{p = 0.02}$; p vs. r, $p = 0.94$; q vs. r, $p = 0.95$.

aim of the study. Findings were therefore reported in terms of comparison between 2 subgroups of patients: normal weight versus overweight and obese patients grouped together. Moreover, in order to further address this issue, findings were also reported separately when considering underweight, normal weight, overweight or obese patients.

Statistical Analysis

Data were expressed as median (range) for continuous variables and as number (percentage) for categorical variables. Normal distribution of continuous variables was tested by the Kolmogorov-Smirnov test. Comparisons between groups were assessed by the Student's *t* test, the Mann-Whitney U test, and the Chi-squared test as appropriate.

Demographic and clinical characteristics of IBD patients were compared both according to BMI category and by dichotomizing the study population into 2 subgroups: overweight or obese patients (overweight/obese) patients versus normal weight patients. These 2 subgroups were also compared in terms of both previous responsiveness to ISS or biologics and frequency of

adverse events induced by these treatments. All these analyses were reported for the whole IBD group and, separately, for CD and UC groups. For the purpose of the study, data from the underweight IBD patients were also reported and used for comparing the BMI distribution in the tested IBD population, and baseline clinical characteristics of patients.

Statistical significance was considered for all variables in case of $p < 0.05$. Statistical analysis was performed using IBM-SPSS statistical software vers. 26.0.

Results

Study Population

BMI Distribution

Overall, BMI was prospectively recorded in 300 Caucasian IBD patients living in Italy (150 with CD and 150 with UC). BMI distribution in the whole group of IBD patients showed that the proportion of underweight (16 [5.3%]) patients was lower than the proportion of normal weight (170 [56.7%]), overweight (92 [30.7%]) ($p < 0.0001$ for both), and that 7.3% of patients were obese ($n = 22$). In the CD subgroup, there were 9 (6%) patients underweight, 89 (59.3%) normal weight, 43 (28.7%) overweight, and 9 (6%) obese. In the tested UC subgroup, 7 (5.7%) patients were underweight, 81 (55%) normal weight, 45 (31%) overweight, and 13 (8.3%) were obese.

When comparing clinical characteristics of the IBD patients enrolled, age at enrollment was significantly lower in CD patients underweight versus overweight (41 [23–70] vs. 51.5 [25–74], $p = 0.025$) and underweight versus obese (41 [23–70] vs. 60 [40–74], $p = 0.042$). The same was observed in both overweight versus normal weight patients and in overweight versus obese patients (51.5 [25–74] vs. 53 [22–86] and 51.5 [25–74] vs. 60 [40–74], $p < 0.00001$ for both). In UC, also the median age at enrollment was significantly lower in UC patients underweight versus overweight and, separately, obese patients (45 [26–64] vs. 63 [27–83] and vs. 56 [43–73], $p = 0.015$ for both) and in normal weight versus overweight patients (47 [20–87] vs. 63 [27–83], $p = 0.0001$). The median IBD duration was significantly lower in underweight versus overweight CD patients (9 [4–36] vs. 17 [4–45], $p = 0.049$) and in normal weight versus overweight UC patients (10 [1–42] vs. 14 [2–42], $p = 0.02$). Additional clinical characteristics (CD and UC site, extent, CD type, age at diagnosis of IBD) of IBD patients are reported subgrouped according to BMI categories in Table 1.

Available biochemical indexes of malnutrition have also been compared among underweight, normal weight, overweight, and obese IBD patients enrolled. Significantly lower hemoglobin levels (g/dL) were observed in underweight (16/16) versus overweight (89/92) and normal weight (169/170) versus overweight (89/92) patients (13.1 [11.7–14.5] vs. 14.4 [10.5–17.5], $p = 0.003$ and 13.8 [10–17.2] vs. 14.4 [10.5–17.5], $p = 0.004$, respectively). Lower ferritin levels (mg/dL) were observed between underweight (12/16) and, separately, normal weight (153/170), overweight (79/92), and obese (19/22) IBD patients (23 [4–139] vs. 60 [5–369], vs. 65 [8–321], vs. 94 [30–231], $p = 0.03$, $p = 0.02$, $p = 0.0009$, respectively). Lower albumin levels (g/dL) were also observed in underweight (7/16) vs. overweight (54/92) and, separately, vs. obese (15/22) patients (3.7 [3.3–4.5] vs. 4.1 [3.2–5.4] and vs. 4.3 [3.6–5.1], $p = 0.04$ for both). Lower cholesterol levels (mg/dL) were also observed between normal weight (126/170) and obese (19/22) patients (161 [47–269] vs. 189 [135–273], $p = 0.003$). Moreover, lower triglycerides levels (mg/dL) between normal weight (123/170) and, separately, overweight (50/92) and obese (20/22) patients (85 [37–251] vs. 119.5 [52–371] and 85 [37–251] vs. 113 [70–390], $p < 0.0001$ and $p = 0.0001$, respectively) were recorded. Additional available biochemical characteristics of the enrolled IBD patients are reported and compared in Table 2 and Figure 1.

Overweight/Obese versus Normal Weight Patients with IBD

For the secondary aim of the study, 284 of these 300 IBD patients were considered for the analysis. This, in order to compare, is the characteristics and outcome of normal weight versus overweight/obese IBD patients, thus excluding the 16 underweight patients.

The population of 284 IBD patients considered in this analysis included 141 [49.6%] patients with CD and 143 [50.4%] with UC. Demographic and clinical characteristics of the IBD population and, separately, of patients with CD and UC are summarized in Table 3.

Clinical Characteristics of Overweight/Obese versus Normal Weight IBD Patients

At enrollment, overweight/obese IBD patients showed a significantly higher median age and IBD duration than normal weight IBD patients ($p < 0.001$ for both) (Table 3). Differently, all the other clinical characteristics of IBD patients considered (gender, age at diagnosis of IBD, prevalence of previous IBD-related surgery, surgical complications and smoking habits) did not significantly differ between the 2 groups (Table 3).

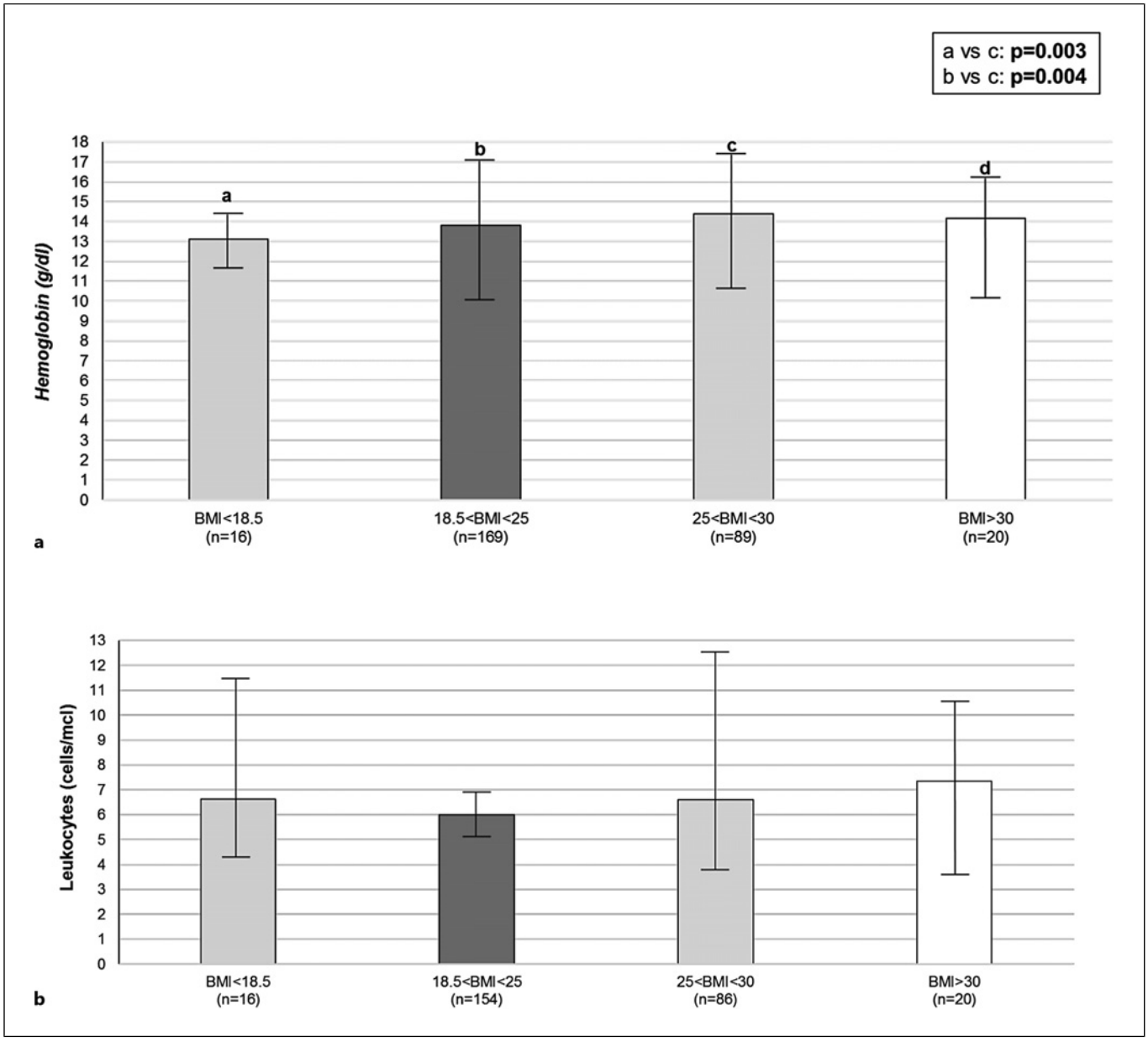
Table 2. Biochemical characteristics of IBD patients subgrouped according to BMI

	BMI			
	underweight (<18.5) (*n* = 16)	normal weight (18.5–25) (*n* = 170)	overweight (25–30) (*n* = 92)	obese (>30) (*n* = 22)
Erythrocytes, million/μg, median [range]	4.56 [3.89–7.72][a] (*n* = 16)	4.7 [3.2–6.94][b] (*n* = 167)	4.9 [3.69–7.76][c] (*n* = 89)	4.88 [3.48–5.74][d] (*n* = 20)
Hemoglobin, g/dL, median [range]	13.1 [11.7–14.5][a] (*n* = 16)	13.8 [10–17.2][b] (*n* = 169)	14.4 [10.5–17.5][c] (*n* = 89)	14.15 [10.2–16.2][d] (*n* = 20)
Leucocytes, cell/μg, median [range]	6.63 [4.1–11.6][a] (*n* = 16)	6.0 [5–6.9][b] (*n* = 154)	6.6 [3.7–12.6][c] (*n* = 86)	7.35 [3.6–10.7][d] (*n* = 20)
Platelets, cells/μg, median [range]	348 [140–413][a] (*n* = 15)	254 [59–612][b] (*n* = 155)	256 [98–488][c] (*n* = 81)	251 [116–414][d] (*n* = 19)
Iron, μg/dL, median [range]	67 [27–110][a] (*n* = 15)	71 [12–241][b] (*n* = 158)	79 [17–181][c] (*n* = 77)	79 [31–172][d] (*n* = 19)
Ferritin, ng/mL, median [range]	23 [4–139][a] (*n* = 12)	60 [5–369][b] (*n* = 153)	65 [8–321][c] (*n* = 79)	94 [30–231][d] (*n* = 18)
Albumin, g/dL, median [range]	3.7 [3.3–4.5][a] (*n* = 7)	4.2 [2.75–5.8][b] (*n* = 131)	4.1 [3.2–5.4][c] (*n* = 54)	4.3 [3.6–5.1][d] (*n* = 16)
Total cholesterol, mg/dL, median [range]	158 [149–192][a] (*n* = 6)	161 [47–269][b] (*n* = 126)	179 [78–283][c] (*n* = 61)	189 [135–273][d] (*n* = 19)
Triglycerides, mg/dL, median [range]	62 [43–284][a] (*n* = 7)	85 [37–251][b] (*n* = 123)	119.5 [52–371][c] (*n* = 50)	113 [70–390][d] (*n* = 20)
Cobalamin, pg/mL, median [range]	348 [227–1,129][a] (*n* = 13)	319 [127–989][b] (*n* = 149)	330 [120–832][c] (*n* = 61)	356 [218–764][d] (*n* = 20)
Folate, ng/mL, median [range]	4.6 [1.55–13.2][a] (*n* = 11)	6.4 [1.5–21][b] (*n* = 151)	6.6 [1.2–19.5][c] (*n* = 66)	7.5 [3.5–20][d] (*n* = 18)
Systemic CS therapy 3 months before enrollment, *n* (%)	(*n* = 1, 6.25%)[a]	(*n* = 15, 8.8%)[b]	(*n* = 8, 8.8%)[c]	(*n* = 2, 10.5%)[d]
Low absorbable CS therapy 3 months before enrollment, *n* (%)	(*n* = 3, 18.7%)[a]	(*n* = 47, 27.6%)[b]	(*n* = 10, 10.9%)[c]	(*n* = 4, 21%)[d]

BMI, body mass index; CS, corticosteroids. *Statistical analysis: erythrocytes (million/μg)*: a vs. b, $p = 0.88$; a vs. c, $p = 0.23$; a vs. d, $p = 0.75$; b vs. c, $\mathbf{p = 0.011}$; b vs. d, $p = 0.66$; c vs. d, $p = 0.35$; *hemoglobin (g/dL)*: a vs. b, $p = 0.06$; a vs. c, $\mathbf{p = 0.003}$; a vs. d, $p = 0.09$; b vs. c, $\mathbf{p = 0.004}$; b vs. d, $p = 0.81$; c vs. d, $p = 0.21$; *leucocytes (cell/μg)* a vs. b, $p = 0.16$; a vs. c, $p = 0.20$; a vs. d, $p = 0.24$; b vs. c, $p = 0.58$; b vs. d, $p = 0.91$; c vs. d, $p = 0.65$; *platelets (cells/μg)*: a vs. b, $p = 0.61$; a vs. c, $p = 0.08$; a vs. d, $p = 0.13$; b vs. c, $p = 0.76$; b vs. d, $p = 0.61$; c vs. d, $p = 0.75$; *iron (μg/dL)*: a vs. b, $p = 0.83$; a vs. c, $p = 0.23$; a vs. d, $p = 0.6$; b vs. c, $p = 0.06$; b vs. d, $p = 0.69$; c vs. d, $p = 0.47$; *ferritin (ng/mL)*: a vs. b, $\mathbf{p = 0.03}$; a vs. c, $\mathbf{p = 0.02}$; a vs. d, $\mathbf{p = 0.0009}$; b vs. c, $p = 0.66$; b vs. d, $p = 0.13$; c vs. d, $p = 0.21$; *albumin (g/dL)*: a vs. b, $p = 0.05$; a vs. c, $\mathbf{p = 0.04}$; a vs. d, $\mathbf{p = 0.04}$; b vs. c, $p = 0.88$; b vs. d, $p = 0.56$; c vs. d, $p = 0.63$; *total cholesterol (mg/dL)*: a vs. b, $p = 0.88$; a vs. c, $p = 0.58$; a vs. d, $p = 0.06$; b vs. c, $p = 0.06$; b vs. d, $\mathbf{p = 0.003}$; c vs. d, $p = 0.09$; *triglycerides (mg/dL)*: a vs. b, $p = 0.75$; a vs. c, $p = 0.17$; a vs. d, $p = 0.16$; b vs. c, $\mathbf{p < 0.0001}$; b vs. d, $\mathbf{p = 0.0001}$; c vs. d, $p = 0.53$; *cobalamin (pg/mL)*: a vs. b, $p = 0.11$; a vs. c, $p = 0.27$; a vs. d, $p = 0.67$; b vs. c, $p = 0.59$; b vs. d, $p = 0.18$; c vs. d, $p = 0.41$; folate (ng/mL): a vs. b, $p = 0.48$; a vs. c, $p = 0.4$; a vs. d, $p = 0.28$; b vs. c, $p = 0.78$; b vs. d, $p = 0.48$; c vs. d, $p = 0.6$; systemic corticosteroids therapy 3 months before enrollment: a vs. b, $p = 0.72$ a vs. c, $p = 0.74$; a vs. d, $p = 0.74$; b vs. c, $p = 0.97$; b vs. d, $p = 0.96$; c vs. d, $p = 0.95$; low absorbable corticosteroids therapy 3 months before enrollment: a vs. b, $p = 0.44$ a vs. c, $p = 0.37$; a vs. d, $p = 0.96$; b vs. c, $\mathbf{p = 0.001}$; b vs. d, $p = 0.34$; c vs. d, $p = 0.34$.

Clinical Characteristics of Overweight/Obese versus Normal Weight CD Patients

When assessing the 141 CD patients considered in this analysis, 89 (63.1%) were normal weight and 52 (36.9%) overweight or obese patients. Among the clinical characteristics considered, in CD group the frequency of perianal disease was significantly higher in the subgroup of overweight/obese patients than in normal weight patients (12 [23%] vs. 9 [10.1%], $p = 0.03$) (Table 4). Differently, CD localization and



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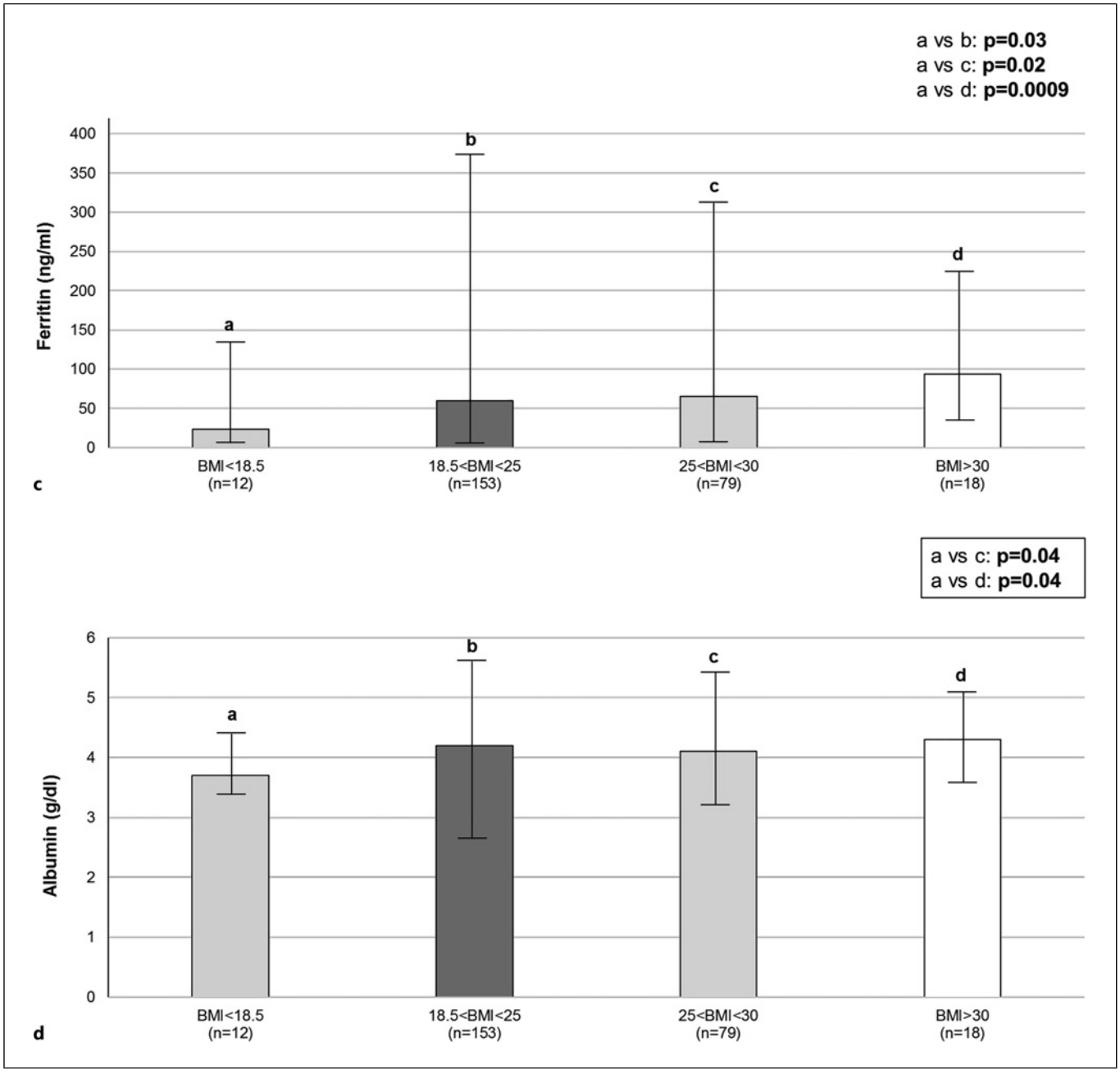
behavior were comparable between normal weight and overweight or obese patients (Table 3). History of ISS or biologics use was also comparable between groups (p = 0.38). In the tested CD population, biologics failure was more frequently observed in overweight/obese versus normal weight patients (0 [0%] vs. 4 [23.4%], p = 0.01) (Table 4). Differently, loss of response and adverse events were comparable between groups (Table 4).

Clinical Characteristics of Overweight/Obese versus Normal Weight UC Patients

Among the 143 UC patients considered in this analysis, there were 81 (56.6%) normal weight patients and 62 (63.4%) overweight or obese patients. Among the clinical characteristics considered in UC group, the median age, the age at diagnosis of UC, UC duration, and the proportion of males were significantly higher in the subgroup of overweight/obese than in normal weight patients (60



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[27–83] vs. 47 [20–87], $p = 0.0001$; 41 [13–67] vs. 28 [8–72], $p = 0.02$; 16 [1–42] vs. 10 [1–42], $p = 0.01$; 40 (64.5%) vs. 38 (46.7%), $p = 0.03$), respectively (Table 5). Proctitis and extensive UC were more frequent in overweight or obese patients (E1: 18 [29%] vs. 11 [13.6%], $p = 0.02$; E3: 35 [56.4%] vs. 31 [38.3%], $p = 0.03$). Differently, left-sided UC was more frequent in normal weight then in overweight or obese patients (E2: 39 [48.1%] vs. 19 [30.6%], $p = 0.03$). History of ISS use was comparable between groups (14 [17.3%] vs. 7 [11.3%], $p = 0.31$), while prior biologics use was more frequent in normal weight then in overweight or obese UC patients (15 [18.5%] vs. 4 [6.4%], $p = 0.03$) (Table 4). Lack of response, loss of response, and adverse events were comparable between normal weight and overweight/obese UC patients (Table 5).

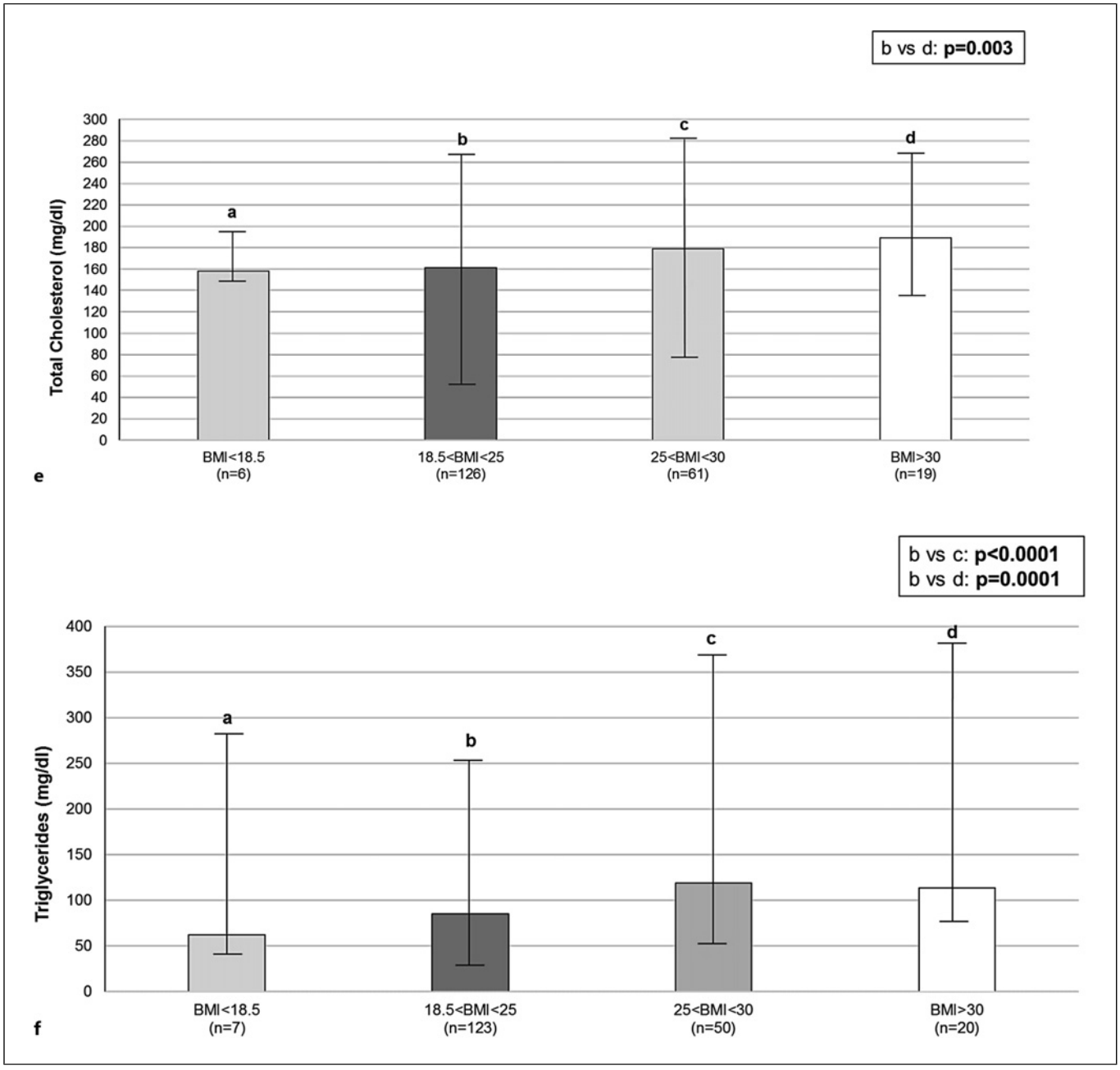

Fig. 1. a–f Histograms showing comparisons among IBD patients subgrouped according to BMI categories (underweight, BMI <18.5; normal weight, BMI 18.5–25; overweight, BMI 25–30; obese, BMI >30) in terms of levels of: hemoglobin (**a**), leukocytes (**b**), ferritin (**c**), albumin (**d**), cholesterol (**e**), triglycerides (**f**). Only significant differences have been reported. As shown, significant differences between BMI subgroups included: lower Hb levels (gr/dL) in underweight versus overweight patients (p = 0.003) and normal weight versus overweight (p = 0.004) (**a**); lower ferritin levels (mg/dL) between underweight and, separately, normal weight, overweight, and obese patients (p = 0.03; p = 0.02; p = 0.0009, respectively) (**c**); lower albumin levels (gr/dL) in underweight vs overweight and, separately, versus obese patients (p = 0.04 for both) (**d**); lower cholesterol levels (mg/dL) between normal weight and obese patients (p = 0.003) (**e**); lower triglycerides levels (mg/dL) between normal weight and, separately, overweight and obese patients (p < 0.0001 and p = 0.0001, respectively) (**f**). No other significant differences were observed between subgroups.

Table 3. Demographic and clinical characteristics of normal weight and overweight and obese patients with IBD

	All IBD patients (n = 284)	Normal weight (n = 170)	Overweight/obese (n = 114)	p value
Age, median [range]	53 [20–87]	50 [20–87]	56 [25–83]	0.001
Age at IBD, median [range]	33 [8–74]	31 [8–74]	36 [13–69]	0.11
Gender (male), n (%)	157 (55.3)	86 (50.6)	71 (62.3)	0.05
IBD duration, median [range]	13.5 [1–57]	12 [1–57]	16 [1–45]	0.01
BMI, median [range], n (%)	24.4 [18.5–39.4]	22.6 [18.5–24.9]	27.1 [25–39.4]	<0.0001
18.5–24.9	170 (59.8)	170 (100)	/	
25–29.9	92 (32.4)	/	92 (80.7)	
>30	22 (7.8)	/	22 (19.3)	
>24.9	114 (40.1)	/	114 (100)	
UC, n (%)	143 (50.4)	81 (47.6)	62 (54.4)	0.26
E1	29 (10.2)	11 (6.5)	18 (15.8)	0.01
E2	58 (20.4)	39 (23)	19 (16.7)	0.12
E3	56 (19.8)	31 (18.2)	25 (22)	0.44
CD, n (%)	141 (49.6)	89 (52.4)	52 (45.6)	0.26
L1	97 (34.1)	62 (36.5)	35 (30.7)	0.31
L2	12 (4.2)	8 (4.7)	4 (3.5)	0.62
L3	32 (11.3)	19 (11.8)	13 (11.4)	0.95
L4	9 (3.2)	7 (4.1)	2 (1.7)	0.26
B1	37 (13)	24 (14.1)	13 (11.4)	0.5
B2	76 (26.8)	44 (25.9)	32 (28)	0.68
B3	28 (9.9)	21 (12.3)	7 (6.1)	0.08
Perianal disease, n (%)	21 (7.4)	9 (5.3)	12 (10.5)	0.09
IBD-related surgery, n (%)	85 (30)	56 (33)	29 (25.4)	0.17
1	47 (55.3)	32 (57.1)	15 (51.7)	0.2
2	23 (27.1)	17 (30.3)	6 (20.7)	0.15
>2	15 (17.6)	7 (12.5)	8 (27.6)	0.28
Surgical complications, n (%)	13 (4.6)	8 (4.7)	5 (4.4)	0.71
Smoking habits, n (%)				
Yes	29 (10.2)	17 (10)	12 (10.5)	0.88
No/Ex	255 (89.8)	153 (90)	102 (89.5)	
Comorbidities, n (%)	31 (10.9)	18 (10.6)	13 (11.4)	0.82
EIMs, n (%)	52 (18.3)	35 (20.6)	17 (15)	0.22
ISS, n (%)	73 (25.7)	47 (27.6)	26 (22.8)	0.36
Thiopurines	64 (87.7)	42 (89.4)	22 (84.6)	0.55
Methotrexate	10 (13.7)	4 (8.5)	6 (23.1)	0.08
Lack of response, n (%)	4 (5.5)	2 (4.2)	2 (7.7)	0.53
Loss of response, n (%)	14 (19.2)	7 (14.9)	7 (26.9)	0.21
Adverse events, n (%)	38 (52)	25 (53.2)	13 (50)	0.79
Biologics, n (%)	59 (20.8)	38 (22.3)	21 (18.4)	0.4
IFX	50 (84.7)	32 (84.2)	18 (85.7)	0.87
ADA	22 (37.3)	16 (42.1)	6 (28.6)	0.3
GOL	1 (1.7)	1 (2.6)	0 (0)	0.45
VDZ	5 (8.5)	3 (7.9)	2 (9.5)	0.82
UST	2 (3.4)	1 (2.6)	1 (4.8)	0.66
Biologics, n (%)				
Lack of response	11 (18.6)	6 (15.8)	5 (23.8)	0.44
Loss of response	22 (37.3)	16 (42.1)	6 (28.6)	0.3
Adverse events	27 (45.8)	19 (50)	8 (38.1)	0.37

Table 3 (continued)

	All IBD patients (n = 284)	Normal weight (n = 170)	Overweight/obese (n = 114)	p value
IFX, *n* (%)				
Lack of response	5 (10)	3 (9.4)	2 (11.1)	0.84
Loss of response	15 (30)	12 (37.5)	3 (16.7)	0.12
Adverse events	24 (48)	17 (53.1)	7 (38.9)	0.33
ADA, *n* (%)				
Lack of response	7 (31.8)	6 (37.5)	1 (16.7)	0.35
Loss of response	9 (40.9)	7 (43.75)	2 (33.3)	0.65
Adverse events	6 (27.3)	4 (25)	2 (33.3)	0.69
VDZ, *n* (%)				
Lack of response	4 (80)	2 (66.7)	2 (100)	0.36
Loss of response	1 (20)	1 (33.4)	0 (0)	0.36
Adverse events	0 (0)	0 (0)	0 (0)	N/A
UST, *n* (%)				
Lack of response	0 (0)	0 (0)	0 (0)	N/A
Loss of response	2 (100)	1 (100)	1 (100)	N/A
Adverse events	0 (0)	0 (0)	0 (0)	N/A
GOL, *n* (%)				
Lack of response	0 (0)	0 (0)	0 (0)	N/A
Loss of response	0 (0)	0 (0)	0 (0)	N/A
Adverse events	1 (100)	1 (100)	0 (0)	N/A

IBD, inflammatory bowel disease; BMI, body mass index; CD, Crohn's disease; UC, ulcerative colitis; EIMs, extraintestinal manifestations; L1, ileum; L2, colon; L3, ileum-colon; L4, upper gastrointestinal tract; B1, non-stricturing-non-penetrating; B2, structuring; B3, penetrating; E1, proctitis; E2, left-sided colitis; E3, pancolitis; PD, perianal disease; ISS, immunosuppressors; IFX, infliximab; ADA, adalimumab; GOL, golimumab; VDZ, vedolizumab; UST, ustekinumab, N/A, not applicable.

Discussion

The prevalence of both obesity and IBD is increasing, particularly in westernized countries. As observed in the general population, an increased frequency of overweight and obesity has been suggested in IBD, associated with restrictive forms of malnutrition [12]. The rapid evolution of IBD treatment strategies, allowing a deeper control of inflammation, may also contribute to the reduced risk of malabsorption and of malnutrition in IBD. Nevertheless, different types of malnutrition as sarcopenic obesity have been described in several diseases including IBD. Current evidence hypothesizes the concomitant role and interplay between gut dysbiosis, chronic inflammation, and malnutrition in the pathogenesis of sarcopenic obesity in several conditions, including IBD [24–26]. A dysregulated gut immune response leads to several events at this level. Among these, higher levels of several mediators (including IFN-γ, IL-12, IL-18, IL-23, TNF-α) able to perpetuate the inflammatory process of unknown etiology and to induce tissue damage in IBD have been described [27]. Higher levels of some of these cytokines, including TNF-α and IL-6, have also been associated with skeletal muscle wasting and reduced muscle mass [28, 29]. Recent limited evidences reported that chronic inflammation related to obesity in IBD patients determines higher levels of pro-inflammatory cytokines in the mesenterial adipose tissue, thus further increasing the inflammatory burden at this level [30]. Steroid treatments, a reduced physical activity due to fatigue and poor general condition, may also be involved in subgroups of patients.

Currently, a frequency of 15–40% of obese and 20–40% overweight patients has been reported in IBD [13, 14]. These findings are in agreement with present observations from our prospective study, reporting a high frequency (40.2%) of obese and overweight IBD patients. Our tested IBD population includes residents in a country (Italy) characterized by a relatively low prevalence of obesity in the general non-IBD population [31]. This observation may add relevance to present findings showing, in the tested IBD population, a high frequency of overweight/

Table 4. Demographic and clinical characteristics of normal weight and overweight and obese patients with CD

	All CD patients (n = 141)	Normal weight (n = 89)	Overweight/obese (n = 52)	p value
Age, median [range]	53 [22–86]	53 [22–86]	52 [25–74]	0.94
Age at IBD, median [range]	31 [11–74]	32 [11–74]	29.5 [15–69]	0.31
Gender (male), n (%)	79 (56)	48 (54)	31 (59.6)	0.51
IBD duration, median [range]	15 [1–57]	13 [1–57]	16 [1–45]	0.22
BMI, median [range], n (%)	23.9 [18.5–34]	22.7 [18.5–24.9]	26.6 [25–34]	<0.0001
18.5–24.9	89 (63.1)	89 (100)	N/A	
25–29.9	43 (30.5)	N/A	43 (82.7)	
>30	9 (6.4)	N/A	9 (17.3)	
>24.9	52 (36.9)	N/A	52 (100)	
CD, n (%)	141 (100)	89 (100)	52 (100)	
L1	97 (68.8)	62 (70)	35 (67.3)	0.77
L2	12 (8.5)	8 (9)	4 (7.7)	0.79
L3	32 (22.7)	19 (21)	13 (25)	0.61
L4	9 (6.4)	7 (7.9)	2 (3.8)	0.34
B1	37 (26.2)	24 (27)	13 (25)	0.79
B2	76 (53.9)	44 (49.4)	32 (61.5)	0.16
B3	28 (19.9)	21 (23.6)	7 (13.5)	0.14
Perianal disease, n (%)	21 (14.9)	9 (10.1)	12 (23)	0.03
IBD-related surgery, n (%)	76 (53.9)	49 (55)	27 (51.9)	0.71
1	39 (51.3)	25 (51)	14 (51.8)	0.94
2	23 (30.7)	17 (34.7)	6 (22.2)	0.25
>2	14 (18.4)	7 (14.3)	7 (25.9)	0.21
Surgical complications, n (%)	13 (17.1)	8 (16.3)	5 (18.5)	0.8
Smoking habits, n (%)				
Yes	19 (13.5)	11 (12.4)	8 (15.4)	0.61
No/Ex	122 (86.5)	78 (87.6)	44 (84.6)	
Comorbidities, n (%)	15 (10.6)	10 (11.2)	5 (9.6)	0.76
EIMs, n (%)	24 (17)	16 (18)	8 (15.4)	0.69
ISS, n (%)	52 (36.9)	33 (37)	19 (36.5)	0.94
Thiopurines	44 (84.6)	29 (87.9)	15 (78.9)	0.39
Methotrexate	9 (17.3)	3 (9.1)	6 (31.6)	0.03
Lack of response, n (%)	3 (5.8)	2 (6.1)	1 (5.3)	0.9
Loss of response, n (%)	12 (23.1)	6 (18.2)	6 (31.6)	0.26
Adverse events, n (%)	29 (55.8)	18 (54.5)	11 (57.9)	0.81
Biologics, n (%)	40 (28.4)	23 (25.8)	17 (32.7)	0.38
IFX	36 (90)	21 (91.3)	15 (88.2)	0.74
ADA	13 (32.5)	8 (34.8)	5 (29.4)	0.72
GOL	1 (2.5)	1 (4.3)	0 (0)	0.38
VDZ	2 (5)	0 (0)	2 (11.8)	0.09
UST	2 (5)	1 (4.3)	1 (5.9)	0.82
Biologics, n (%)				
Lack of response	4 (10)	0 (0)	4 (23.5)	0.01
Loss of response	16 (40)	11 (47.8)	5 (29.4)	0.23
Adverse events	21 (52.5)	13 (56.5)	8 (47.1)	0.55
IFX, n (%)				
Lack of response	1 (2.8)	0 (0)	1 (6.7)	0.23
Loss of response	11 (30.6)	8 (38.1)	3 (20)	0.24
Adverse events	19 (52.8)	12 (57.1)	7 (46.7)	0.53

Table 4 (continued)

	All CD patients (n = 141)	Normal weight (n = 89)	Overweight/obese (n = 52)	p value
ADA, *n* (%)				
Lack of response	2 (15.4)	1 (12.5)	1 (20)	0.71
Loss of response	7 (53.8)	6 (75)	1 (20)	0.05
Adverse events	5 (38.5)	3 (37.5)	2 (40)	0.9
VDZ, *n* (%)				
Lack of response	2 (100)	0 (0)	2 (100)	N/A
Loss of response	0 (0)	0 (0)	0 (0)	N/A
Adverse events	0 (0)	0 (0)	0 (0)	N/A
UST, *n* (%)				
Lack of response	0 (0)	0 (0)	0 (0)	N/A
Loss of response	2 (100)	1 (100)	1 (100)	N/A
Adverse events	0 (0)	0 (0)	0 (0)	N/A
GOL, *n* (%)				
Lack of response	0 (0)	0 (0)	0 (0)	N/A
Loss of response	0 (0)	0 (0)	0 (0)	N/A
Adverse events	1 (100)	1 (100)	0 (0)	N/A

IBD, inflammatory bowel disease; BMI, body mass index; CD, Crohn's disease; EIMs, extraintestinal manifestations; L1, ileum; L2, colon; L3, ileum-colon; L4, upper gastrointestinal tract; B1, non-stricturing-non-penetrating; B2, structuring; B3, penetrating; E1, proctitis; E2, left-sided colitis; E3, pancolitis; PD, perianal disease; ISS, immunosuppressors; IFX, infliximab; ADA, adalimumab; GOL, golimumab; VDZ, vedolizumab; UST, ustekinumab; N/A, not applicable.

obese IBD patients, and a very low proportion of underweight patients. All patients were enrolled in an outpatient setting and were in regular follow-up. Thus, a high compliance of patients and treatment optimization leading to a better disease control may have a role in our findings. Whether the same findings are also observed in the general IBD population cannot be answered by our study.

A higher median age at enrollment and a longer IBD duration was observed in overweight and obese patients. When subgrouping IBD patients according to IBD type, a higher median age at diagnosis was observed in overweight and obese patients with UC. This data is in agreement with a retrospective study from Blain et al. [15] including patients with CD [16]. An overall milder disease course in late-onset IBD patients may have a role in our finding.

The effect of obesity on natural history and outcome in UC and CD is undefined, while visceral adiposity seems to be associated to more complex CD phenotype [32]. In other inflammatory diseases such as psoriasis and rheumatoid arthritis, obesity has been associated with poor clinical outcomes [33, 34]. Moreover, in hospitalized IBD patients, obesity has been associated with a worse outcome [35]. In a cross-sectional study including CD patients, no difference in the prevalence of fistulae or strictures among obese versus normal weight patients was reported [17]. However, in the same year, an independent cross-sectional study reported less severe CD behavior between obese and normal weight patients [36]. A lower prevalence of penetrating disease but a comparable prevalence of stricturing disease need for surgery and perianal disease was indeed reported in obese patients [36]. In our study, we confirmed a comparable distribution of CD localization and behavior in CD patients subgrouped according to the BMI, thus further supporting no relationships between obesity and characteristics of the disease.

However, among the main findings of the present study, there is the observation, in the tested CD population, of a significantly higher frequency of PD in overweight and obese versus normal weight patients (p = 0.03). In CD, obesity has been proposed as a risk factor for PD, although with conflicting findings [16]. In the general population also a higher risk of perianal fistula, perianal abscesses, and recurrence has been reported in obese patients [37]. Whether systemic inflammation related to obesity may be involved in these findings cannot be answered by the present study. The reported differences in terms of intestinal microbiota in obese versus normal weight patients in the general population [38] and in CD patients with versus without PD [39], could play a role in the observed higher frequency of PD in obese CD patients.

Table 5. Demographic and clinical characteristics of normal weight and overweight and obese patients with UC

	All UC patients (n = 143)	Normal weight (n = 81)	Overweight/obese (n = 62)	p value
Age, median [range]	54 [20–87]	47 [20–87]	60 [27–83]	0.0001
Age at IBD, median [range]	35 [8–72]	28 [8–72]	41 [13–67]	0.02
Gender (male), *n* (%)	78 (54.5)	38 (46.7)	40 (64.5)	0.03
IBD duration, median [range]	13 [1–42]	10 [1–42]	16 [1–42]	0.01
BMI, median [range]	24.56 [18.5–39.4]	22.6 [18.5–24.9]	27.75 [25–39.4]	<0.0001
18.5–24.9	81 (56.6)	81 (100)	N/A	
25–29.9	49 (34.3)	N/A	49 (79)	
>30	13 (9.1)	N/A	13 (21)	
>24.9	62 (43.4)	N/A	62 (100)	
UC, *n* (%)	143 (100)	81 (100)	62 (100)	
E1	29 (20.3)	11 (13.6)	18 (29)	0.02
E2	58 (40.6)	39 (48.1)	19 (30.6)	0.03
E3	56 (39.1)	31 (38.3)	35 (56.4)	0.03
IBD-related surgery, *n* (%)	10 (7)	8 (9.8)	2 (3.2)	0.12
1	10 (100)	8 (100)	2 (100)	
2	0 (0)	0 (0)	0 (0)	
>2	0 (0)	0 (0)	0 (0)	
Surgical complications, *n* (%)	0 (0)	0 (0)	0 (0)	
Smoking habits, *n* (%)				
Yes	10 (7)	6 (7.4)	4 (6.4)	0.82
No/Ex	133 (93)	75 (92.6)	58 (93.6)	
Comorbidities, *n* (%)	16 (11.2)	11 (13.6)	5 (8)	0.29
EIMs, *n* (%)	28 (19.6)	19 (23.4)	9 (14.5)	0.18
ISS, *n* (%)	21 (14.7)	14 (17.3)	7 (11.3)	0.31
Thiopurines	20 (95.2)	13 (92.9)	7 (100)	0.46
Methotrexate	1 (4.8)	1 (7.1)	0 (0)	0.46
Lack of response, *n* (%)	1 (4.8)	0 (0)	1 (14.3)	0.14
Loss of response, *n* (%)	2 (9.5)	1 (7.1)	1 (14.3)	0.59
Adverse events, *n* (%)	9 (42.9)	7 (50)	2 (28.6)	0.34
Biologics, *n* (%)	19 (13.3)	15 (18.5)	4 (6.4)	0.03
IFX	14 (73.7)	11 (73.3)	3 (75)	0.94
ADA	9 (47.4)	8 (53.3)	1 (25)	0.31
GOL	0 (0)	0 (0)	0 (0)	
VDZ	3 (15.8)	3 (20)	0 (0)	0.32
UST	0 (0)	0 (0)	0 (0)	
Biologics, *n* (%)				
Lack of response	7 (36.8)	6 (40)	1 (25)	0.58
Loss of response	6 (31.6)	5 (33.3)	1 (25)	0.75
Adverse events	6 (31.6)	6 (40)	0 (0)	0.12
IFX, *n* (%)				
Lack of response	4 (28.6)	3 (27.3)	1 (33.3)	0.83
Loss of response	4 (28.6)	4 (36.4)	0 (0)	0.21
Adverse events	5 (35.7)	5 (45.4)	0 (0)	0.14
ADA, *n* (%)				
Lack of response	5 (55.5)	5 (6.2)	0 (0)	0.23
Loss of response	2 (22.2)	1 (1.2)	1 (100)	0.4
Adverse events	1 (11.1)	1 (1.2)	0 (0)	0.7

Table 5 (continued)

	All UC patients (n = 143)	Normal weight (n = 81)	Overweight/obese (n = 62)	p value
VDZ, *n* (%)				
Lack of response	2 (66.7)	2 (66.7)	0 (0)	N/A
Loss of response	1 (33.3)	1 (33.3)	0 (0)	N/A
Adverse events	0 (0)	0 (0)	0 (0)	N/A
UST, *n* (%)				
Lack of response	0 (0)	0 (0)	0 (0)	N/A
Loss of response	0 (0)	0 (0)	0 (0)	N/A
Adverse events	0 (0)	0 (0)	0 (0)	N/A
GOL, *n* (%)				
Lack of response	0 (0)	0 (0)	0 (0)	N/A
Loss of response	0 (0)	0 (0)	0 (0)	N/A
Adverse events	0 (0)	0 (0)	0 (0)	N/A

IBD, inflammatory bowel disease; BMI, body mass index; UC, ulcerative colitis; EIMs, extraintestinal manifestations; E1, proctitis; E2, left-sided colitis; E3, pancolitis; ISS, immunosuppressors; IFX, infliximab; ADA, adalimumab; GOL, golimumab; VDZ, vedolizumab; UST, ustekinumab; N/A, not applicable.

In our study population, UC extent significantly differed between obese or overweight versus normal weight patients. However, the distribution of UC extent in both groups did not show a defined pattern, thus suggesting that the observed differences may not assume clinical relevance. Current evidences also do not support a defined relationship between UC extent and nutritional status [36]. Nevertheless, higher rates of both IBD-related surgery and hospitalizations and longer hospital stay have been reported in obese versus normal weight UC patients [36].

Data regarding the possible relationships between BMI and efficacy of IBD treatments are not conclusive. A recent study in IBD patients reported lower rates of response to major treatments have been associated with higher levels of intra-abdominal visceral adipose tissue [30]. In the present study, no differences were observed between normal weight versus overweight and obese IBD patients in terms of need of ISS or biologics, primary or secondary failure to biologics or frequency of adverse events. However, when separately considering UC and CD patients, primary failure to biologics was more frequent in overweight/obese than in normal weight CD patients. Whether these findings are related to higher pro-inflammatory cytokines release and volume distribution in overweight/obese CD patients can only be hypothesized [39, 40]. In UC group, biologics were more frequently used in normal weight versus overweight/obese patients. A milder UC course in obese UC patients may be involved in this finding.

Obesity in IBD is currently a "hot topic," also taking into account its worldwide increase and burden in terms of morbidity in the general non-IBD population. Emerging evidences suggest a relevant impact of obesity also in terms of quality of life and obesity-related complications also in the IBD population [41, 42].

The main limitation of the present study includes the modality of assessment of overweight and obesity, assessed only according to the BMI. Indeed, although BMI still represents an easy and worldwide accepted diagnostic tool, the evaluation of body composition and especially the percentage of body fat percentage made with dual energy X-ray absorptiometry is a more accurate modality for defining the subgroups of normal weight obese or sarcopenic obese patients. Nevertheless, due to its objective, easy and reproducible assessment, BMI still represents a valuable marker of obesity in several clinical settings, including clinical trials [9, 10].

Among the strengths of the present study, there is the prospective design and the study population including consecutive patients referring to a tertiary IBD center. These characteristics of the study should provide a proper characterization and classification of IBD patients, treated according to current guidelines [19–21]. Clinical characteristics of the tested IBD patients are indeed comparable to the general IBD population, thus suggesting the reliability of the reported findings. Findings from the present prospective study assessing in a large IBD population the BMI distribution in relation to clinical characteristics and outcome may therefore provide new data regarding the possible relation between obesity and IBD, thus adding updated real-life findings useful for assessing the appropriate sample size for investigating obesity and sarcopenic obesity in IBD.

Conclusions

In conclusion, present data regarding IBD patients in regular follow-up, show a low proportion of underweight. In the same population, overweight and obese CD patients showed a higher frequency of perianal disease and refractoriness to biologics. Therefore, our results suggest that BMI may influence phenotype and responsiveness to biologics in CD. Overweight and obesity may represent a clinical challenge in the management of patients with IBD in the near future. A deeper understanding of the implications related to concomitant obesity in IBD represents a relevant issue deserving a multidisciplinary approach and further investigations.

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Statement of Ethics

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) and was approved by the Territorial Ethic Committee "Lazio Area 2" (protocol no. 5924). All patients gave a written informed consent to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

L.B. conceptualized the study. S.C.S., M.F., S.M., and C.M. managed data collection. B.N. and R.M. assisted with data analysis and interpretation, and prepared the manuscript. L.B. and B.N. conducted the data analysis and assisted with the preparation of the manuscript. All authors assisted with data interpretation and provided critical review of the manuscript.

Data Availability Statement

The data used in the present study is not open access or publicly available, due to their containing information that could compromise the privacy of research participants but are available upon reasonable request from the corresponding author (L.B.).

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