



Body mass index: Implications on disease severity and postoperative complications in patients with Crohn's disease undergoing abdominal surgery

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ABSTRACT

Background: Obesity is increasing in prevalence among patients with Crohn's disease, but how body mass index affects disease severity and postoperative outcomes remains unknown.

Methods: A retrospective review of ileocolic resections for Crohn's disease performed at a single institution between January 2007 and December 2017 was conducted. On the day of surgery, patients were grouped by body mass index into underweight, normal weight, overweight, and obese categories. Intergroup comparisons and trend tests were performed on disease characteristics and postoperative outcomes. A multivariable model for superficial surgical site infection was constructed.

Results: A total of 758 patients were identified; 80 (11%) patients were underweight, 372 (49%) were normal weight, 178 (23%) were overweight, and 128 (17%) were obese. Both fistulizing Crohn's phenotype and preoperative immunosuppression occurred less frequently in obese patients compared with other body mass index groups (both $P < 0.01$). Conversion to open surgery and superficial surgical site infection were increased in obese patients, and obesity was an independent risk factor for superficial surgical site infection on multivariable analysis (odds ratio 3.0, 95% confidence interval: 1.6–5.6).

Conclusion: Although obese patients had less severe Crohn's disease at the time of surgery, they experienced increased postoperative infectious complications. Preoperative weight loss and consideration of alternative wound closure methods may reduce these complications.

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Introduction

An increasing proportion of patients presenting for colorectal surgery are obese, and obesity is clearly linked to increased rates of both open surgery and infectious postoperative complications.^{1,2} Although Crohn's disease (CD) is thought of as a disease of wasting and malnutrition, obesity rates in patients with CD are now similar to the general population, and there is a corresponding

increase in the number of obese patients with CD requiring surgery.^{1,3}

However, how obesity relates to disease behavior at surgery and how it affects postoperative outcomes remains unclear. The medical literature suggests that overweight and obese patients with CD may have a less severe disease phenotype,⁴ whereas the surgical literature is conflicted on whether obesity contributes to increased postoperative morbidity.^{1,5,6} No study, however, has examined the complex interplay between disease phenotype, body mass index (BMI), and postoperative outcomes.

Therefore, this study aimed to determine the following: (1) the association between BMI and CD characteristics at the time of surgery and (2) the effect of BMI on perioperative characteristics

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and postoperative outcomes in a large cohort of patients with CD undergoing ileocolic resection.

Methods

Patients

Institutional review board approval was obtained. A centralized diagnostic index was then queried for adult patients (≥ 18 years of age) undergoing ileocolic resection for CD between January 1, 2007, and December 31, 2017, at the Mayo Clinic (Rochester, MN) within the Division of Colon and Rectal Surgery. For patients who underwent multiple ileocolic resections at our institution within the study period, only their most recent operation was included. Patients were grouped according to their BMI on the day of surgery using the World Health Organization BMI classification, where underweight is BMI < 18.5 kg/m², normal weight is BMI 18.5 to 24.9 kg/m², overweight is BMI 25.0 to 29.9 kg/m², and obese is BMI ≥ 30 kg/m².^{2,7}

Data collection

A retrospective chart review was conducted to collect preoperative patient demographics and CD characteristics, intraoperative data, and postoperative complications data. Preoperative data abstracted included patient age, sex, BMI, American Society of Anesthesiologist class, diagnosis of diabetes mellitus, active tobacco use, and serum laboratories. Hemoglobin, white blood cell count, and C-reactive protein were recorded if they were drawn within 2 weeks of surgery, and albumin was recorded if it was drawn within 4 weeks of surgery. CD characteristics included the Montreal classification⁸ age at diagnosis (A1: < 17 years, A2: 17–40 years, and A3: > 40 years) and disease phenotype (B1: non-stricturing and nonpenetrating, B2: stricturing, and B3: penetrating); any prior intestinal resection for CD, as reported by the patient, including any operations performed at outside institutions; and the patient's current immunosuppressant regimen. Patients were considered to be taking corticosteroids and immunomodulators (azathioprine, methotrexate, 6-mercaptopurine, tacrolimus, and mycophenolate) if the last dose was within 4 weeks of surgery; they were considered to be exposed to biologics (anti-tumor necrosis factor agents: infliximab, adalimumab, and certolizumab; other biologics: vedolizumab, ustekinumab, and natalizumab) if the last dose was within 12 weeks of surgery.

Intraoperative data collected included whether the surgery was a laparoscopic or open-operative approach; there was a conversion to open surgery (defined by surgical dictation of conversion); additional stricturoplasty, small-bowel resection, or colon resection beyond ileocolic resection were performed; an anastomosis was performed; and a diverting loop ileostomy was constructed.

Postoperative data collected included the duration of stay during the index hospitalization and whether there were infectious complications, ileus/partial small-bowel obstruction, and unplanned reoperation within 30 days of surgery and unplanned hospital readmission within 30 days of discharge. Infectious complications included superficial surgical site infection (sSSI), intra-abdominal septic complications (intra-abdominal abscess or anastomotic leak), urinary tract infection, pneumonia, bacteremia or fungemia, infected ascites, infected intra-abdominal hematoma, bowel perforation, and *clostridium difficile*. Ileus or partial small-bowel obstruction was defined as the need for unplanned nasogastric decompression or total parenteral nutrition and resolution without operative intervention. A variable called prolonged length of stay was created by finding the 75th percentile for length of stay (7 days) and defining a stay longer than 7 days as prolonged.

Statistics

Categorical variables were expressed as number (percent), and continuous variables were expressed as median (interquartile range). Demographics, disease characteristics, operative characteristics, and postoperative outcomes were compared between the four BMI categories by χ^2 analysis or Fisher exact test for categorical variables and by Kruskal-Wallis test for continuous variables. Missing data were excluded from univariate analyses. Cochran-Armitage trend tests were performed to assess the relationship between BMI category and CD phenotype, preoperative immunosuppression, and sSSI. Univariate comparisons using χ^2 analysis and Fisher exact test for categorical variables and Wilcoxon rank sum test for continuous variables on the outcome of sSSI were also performed. Variables with $P < 0.10$ on univariate analysis along with disease phenotype were then entered into a multivariable model for sSSI. Significance was set at $P < 0.05$, and all analysis was performed using JMP, version 14.1.0 PRO (SAS Institute Inc., Cary, NC).

Results

A total of 758 patients underwent ileocolic resection for CD during the study period. According to BMI, 80 (11%) patients were

Table 1
Demographics and laboratory findings

Variable	Underweight (n = 80)	Normal weight (n = 372)	Overweight (n = 178)	Obese (n = 128)	P value
Age (years)*	28 (23–35)	34 (25–48)	42 (33–59)	42 (32–54)	<.01
Sex (female)	47 (59)	203 (55)	81 (46)	76 (59)	.06
BMI (kg/m ²)*	17.4 (16.3–18.1)	21.8 (20.2–23.2)	27.1 (26.0–28.2)	33.0 (31.1–35.7)	<.01
ASA class					
I	7 (9)	30 (8)	9 (5)	1 (1)	<.01
II	64 (80)	309 (84)	140 (80)	100 (78)	
III/IV	9 (11)	31 (8)	26 (15)	27 (21)	
Tobacco use	16 (20)	78 (21)	33 (19)	22 (17)	.79
Diabetes mellitus	0 (0)	3 (1)	7 (4)	11 (9)	<.01
Hemoglobin (g/dL)*	11.6 (10.8–12.8)	12.3 (10.8–13.5)	13.3 (12.1–14.5)	12.8 (11.5–13.8)	<.01
Leukocyte count ($\times 10^9/L$)*	8.25 (6.7–10.1)	7.6 (5.9–9.8)	7.6 (6.0–10.7)	8.2 (6.4–12.0)	.23
CRP (mg/L)*	24.3 (4.3–48.2)	10.9 (3.6–37.9)	4.7 (3.0–12.8)	9.6 (3.0–27.4)	.04
Albumin, (g/dL)*	3.8 (3.4–4.1)	4.0 (3.5–4.3)	4.1 (3.8–4.3)	4.2 (3.9–4.3)	<.01

Data are n (%), unless otherwise indicated. Laboratory values were not drawn within the preoperative window in 40% to 60% of patients depending on the specific test.

ASA, American Society of Anesthesiologists.

* Median (interquartile range).

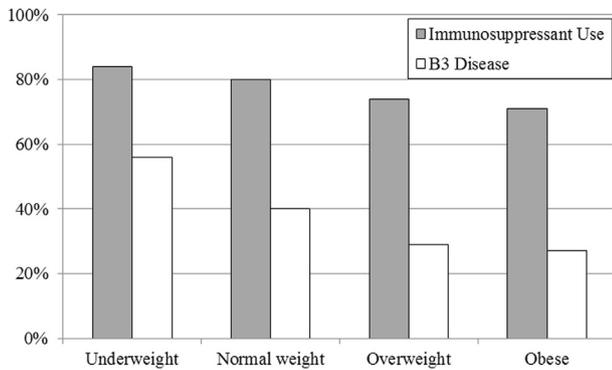


Fig 1. Trends for the use of preoperative immunosuppression and Montreal class B3 disease by BMI classification; $P < 0.01$ for both trends.

underweight, 372 (49%) were normal weight, 178 (23%) were overweight, and 128 (17%) were obese. Fifty-four percent of the patients were female, with a median age of 37 years (interquartile range, 28–52). Underweight patients were younger and more often American Society of Anesthesiologist class I or II compared with obese patients. Obese patients had a higher median hemoglobin and albumin than underweight patients and a lower median C-reactive protein (Table I).

With respect to CD characteristics, over one-half of the underweight patients had intra-abdominal fistulizing disease at surgery, with a significant negative trend observed between Montreal class B3 disease and increasing BMI class ($P < 0.01$; Fig 1). Similarly, a negative trend also existed between the use of preoperative immunosuppression and increasing BMI class ($P < 0.01$; Fig 1). Underweight patients were also diagnosed with CD at a younger age compared with obese patients. Neither history of a prior intestinal resection for CD nor the number of prior intestinal resections differed between BMI groups (Table II).

Over 90% of the operations were elective, which did not differ by BMI category. One-half of the operations overall were completed laparoscopically, and this proportion was similar across the different BMI categories. Conversion to open surgery occurred in 18% of cases overall, and this was highest in the obese group at 29%. The requirements for additional stricturoplasty, small-bowel resection, and colon resection were similar across BMI categories. BMI class also did not appear to influence the use of a diverting loop ileostomy (Table III).

The rate of sSSI was significantly different across BMI categories, with a significant positive trend for the occurrence of sSSI across increasing BMI categories (Fig 2). Other infectious complications, including intra-abdominal sepsis, unplanned readmission, and unplanned reoperation, did not differ between the BMI categories. Likewise, overall length of stay and the rate of prolonged length of stay was similar across the four BMI categories (Table IV). After adjusting for disease phenotype and operative approach, obesity remained a risk factor for sSSI (odds ratio 2.96; 95% confidence interval: 1.57–5.58) (Table V).

Discussion

A substantial proportion of patients with CD who undergo ileocolic resection are obese. Although their CD appears less severe, according to both disease phenotype and preoperative medication requirements, they require conversion from laparoscopic to open surgery more frequently and suffer an increased rate of post-operative infectious complications, particularly sSSI. An increased emphasis on the importance of maintaining a healthy BMI during annual medical exams in patients with CD may allow an increased proportion of operations to be completed laparoscopically, and the consideration of alternative skin closure methods may reduce sSSI when patients do require surgical intervention.

A striking difference existed in the rate of fistulizing CD at surgery across the BMI categories, with an underweight BMI having the highest rate. This is in line with prior work demonstrating that a fistulizing phenotype is an independent risk factor for malnutrition among hospitalized patients with CD nationally,⁹ and increased disease activity results in increased protein demands.¹⁰ Inability to maintain adequate caloric intake with these increased metabolic demands would result in the higher prevalence of underweight BMI among patients with fistulizing disease. Interestingly, prior single-institution studies of the impact of BMI on patients being treated medically for CD have not demonstrated a significant difference in the proportion of fistulizing disease by BMI category. These studies, however, are limited because their focus is primarily on the impact of obesity on CD and, subsequently, the combination of underweight and normal-weight BMI categories.^{4,11} The studies on the impact of BMI on patients presenting for surgical management of CD are even more limited in this respect, as they have either not commented on disease phenotype^{1,5,6} or excluded underweight patients altogether.⁶

Table II
Crohn's disease characteristics

Variable	Underweight (n = 80)	Normal weight (n = 372)	Overweight (n = 178)	Obese (n = 128)	P value
Montreal classification age					
A1	21 (26)	72 (19)	14 (8)	7 (6)	<.01
A2	54 (68)	254 (68)	124 (70)	86 (68)	
A3	5 (6)	45 (12)	39 (22)	33 (26)	
Montreal classification behavior					
B1	3 (4)	38 (10)	27 (15)	9 (7)	<.01
B2	32 (40)	186 (50)	100 (56)	85 (66)	
B3	45 (56)	148 (40)	51 (29)	34 (27)	
History of prior CD intestinal resection	22 (28)	129 (35)	72 (40)	45 (35)	.23
Number of prior CD intestinal resections*	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	.20
Corticosteroids	30 (38)	103 (28)	61 (34)	31 (24)	.08
Immunomodulators	24 (30)	156 (42)	75 (42)	41 (32)	.06
Biologic	49 (61)	213 (57)	94 (53)	71 (55)	.60†
Anti-TNF	45	194	84	63	
Other biologic	4	19	10	8	

Data are n (%), unless otherwise indicated.

* Median (interquartile range).

† Comparison is for any biologic across the four BMI categories.

Table III
Perioperative and intraoperative characteristics

Variable	Underweight	Normal weight	Overweight	Obese	P value
Urgent/emergency case status	10 (13)	39 (10)	11 (6)	10 (8)	.26
Completed laparoscopically	46 (58)	178 (48)	95 (53)	58 (45)	.22
Converted to open surgery*	7 (13)	32 (15)	19 (17)	24 (29)	.03
Additional stricturoplasty	5 (6)	28 (8)	10 (6)	3 (2)	.21
Additional small-bowel resection	8 (10)	29 (8)	11 (6)	7 (5)	.58
Additional colon resection	8 (10)	27 (7)	14 (8)	5 (4)	.37
Diverting loop ileostomy utilization†	7 (9)	33 (9)	14 (8)	10 (8)	.96

Data are n (%).

* Of 459 cases attempted laparoscopically to start.

† Of 733 patients with a primary ileocolic anastomosis.

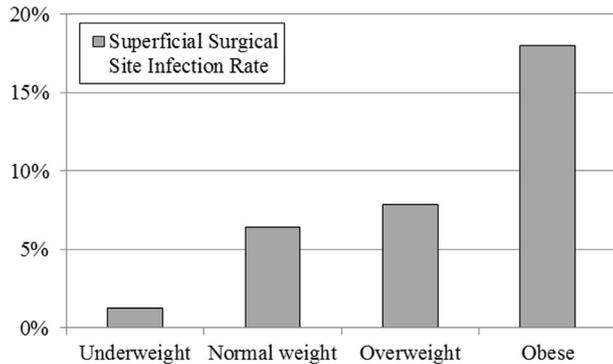


Fig 2. Trend in superficial surgical site infection by BMI classification; $P < 0.01$ for trend.

The finding of potentially less severe CD with increasing BMI is also supported by the decreased rate of preoperative immunosuppression use in obese patients. This has been previously demonstrated in a medical cohort of patients with CD, where the obese patients were less likely to have been treated with either steroids or anti-tumor necrosis factor agents.⁴ In the surgical literature, increased rates of preoperative steroid use have been shown in both underweight patients⁵ and in nonobese patients compared with obese patients.¹ This could be a reflection of increased disease severity in underweight patients necessitating a greater use of rescue therapy with steroids. The idea of increased disease flares and more active disease in underweight patients is further supported by a prior cohort study of patients with CD, where an increased rate of hospitalizations and operations was

observed in underweight and normal-weight patients compared with overweight and obese patients.⁴

Although obesity may be associated with a less severe CD phenotype, it is associated with increased operative complexity, as shown here by the increased rate of conversion to open surgery in obese patients. Although it is difficult to contextualize the conversion rate, because the definition of conversion to open surgery differs from study to study, the 29% rate we observed in obese patients seems to be higher than the conversion rates reported in various studies on colectomy and proctectomy for cancer.¹² Because both an operative indication of CD and obesity are independently linked to increased rates of conversion to open surgery, the presence of both risk factors increases the odds of conversion compared with the presence of only one.¹³ Earlier studies on surgery in patients with inflammatory bowel disease have also shown increased operative times and increased blood loss in obese patients.¹⁶ Recognition of the increased operative complexity in obese patients is important because increased operative time, conversion from laparoscopic to open surgery, and open surgery are all associated with increased postoperative complications after colorectal surgery.^{14,15} Owing to the unremitting nature of CD, up to 50% of patients will require CD-related surgery within 10 years of diagnosis.¹⁶ It is therefore critical that providers both recognize the growing prevalence of obesity in patients with CD and emphasize the importance of a healthy weight in these patients. If weight loss is successful, more patients may be able to undergo laparoscopic resection and realize the benefits of laparoscopic surgery.

Weight loss before a patient's CD becomes medically refractory and surgery is required may also reduce the risk of postoperative morbidity, particularly sSSI. Obesity increases sSSI risk in a multifactorial manner, with impaired tissue oxygenation¹⁷ and reduced tissue concentration of prophylactic antibiotics both likely

Table IV
Complications and length of stay

Outcome	Underweight (n = 80)	Normal weight (n = 372)	Overweight (n = 178)	Obese (n = 128)	P value
Any infectious complication	12 (15)	72 (19)	39 (22)	32 (25)	0.31
sSSI	1 (1)	24 (6)	14 (8)	23 (18)	<.01
IASC	7 (9)	33 (9)	22 (12)	6 (5)	.15
UTI	4 (5)	12 (3)	5 (3)	8 (6)	.34
Bacteremia	0 (0)	2 (1)	1 (1)	1 (1)	.0
Pneumonia	4 (5)	5 (1)	2 (1)	2 (2)	.17
Clostridium difficile infection	0 (0)	4 (1)	4 (2)	2 (2)	.51
Ileus/partial small-bowel obstruction	8 (10)	53 (14)	25 (14)	21 (16)	.64
Venous thromboembolism	1 (1)	2 (0.5)	2 (1)	1 (1)	.67
Readmission	10 (13)	49 (13)	30 (17)	20 (16)	.64
Unplanned reoperation	6 (8)	18 (5)	11 (6)	8 (6)	.77
Length of stay*	5 (4–7)	5 (4–7)	5 (4–7)	5 (4–6)	.60
Prolonged length of stay	15 (19)	76 (20)	38 (21)	22 (17)	.81

Data are n (%), unless otherwise indicated.

IASC, intra-abdominal septic complication; UTI, urinary tract infection.

* Median (interquartile range).

Table V
Univariate and multivariable analysis of superficial surgical site infection

Variable	Univariate P value	Multivariable odds ratio (95% confidence interval)
Age	.11	—
Sex	.32	—
BMI category	<.01	Normal: Reference Underweight: 0.20 (0.03–1.49) Overweight: 1.26 (0.63–2.53) Obese: 2.96 (1.57–5.58)
Diabetes mellitus	.07	No: Reference Yes: 1.60 (0.49–5.21)
Tobacco use	.55	—
Montreal class age	.94	—
Montreal class phenotype	.69	B1: Reference B2: 1.26 (0.47–3.37) B3: 1.11 (0.39–3.13)
Corticosteroids	.86	—
Immunomodulators	.25	—
Biologic	.29	—
Hemoglobin	.61	—
White blood cell count	.71	—
Albumin	.15	—
CRP	.58	—
ASA class	.60	—
Case status	.74	—
Surgical approach	<.01	Laparoscopic: Reference Open: 1.99 (1.12–3.50)
Additional small-bowel resection	.80	—
Additional stricturoplasty	.67	—
Additional colon resection	.76	—

contributing.¹⁸ Diagnostic indication also contributes to sSSI rate, with CD having been shown to have a higher relative impact compared with benign neoplasm and colon cancer.¹⁹ This likely accounts for the increased rate of sSSI in obese patients we observed in our study compared with the 14.5% rate Wick et al observed in their study of colectomies for a variety of colorectal pathologies.² Incision size and operative approach also play a role in the development of sSSI, with an open approach significant on multivariable analysis. Because laparoscopic operations also require enlargement of a port site for specimen extraction, the need for an enlarged laparoscopic extraction site in obese patients could contribute to the increased sSSI rate. Duraes et al have previously demonstrated that as BMI increased, extraction site size also increased after laparoscopic surgery for CD, and that increased extraction size was associated with an increased rate of sSSIs.²⁰ This is consistent with our personal experience of requiring a larger extraction site in obese patients. Because sSSIs are a costly complication and associated with an increased rate of unplanned hospital readmission,² strategies are needed to reduce rates of sSSIs. These could include increased utilization of combined mechanical and antibiotic bowel preparation;²¹ an emphasis on preoperative weight loss, when possible; and consideration of wound healing by secondary intention,²² particularly in patients who undergo open operations or who have an enlarged extraction site.

Although we did not observe an increased rate of intra-abdominal septic complications in either the underweight or obese BMI groups compared with normal-weight patients, prior studies have shown increased rates of intra-abdominal septic complications in patients with preoperative weight loss.²³ Therefore, in order to optimize surgical outcomes, the multiple ways malnutrition can manifest should be considered when evaluating a patient with CD preoperatively. These manifestations should include awareness of BMI < 18.5 kg/m², weight loss of greater than 5% to 10% over the prior 3 to 6 months, or a combination of low BMI (<20 or 22 kg/m² depending on age) and recent weight loss.²⁴ Patients who meet any of these criteria for malnutrition should

be considered for preoperative exclusive enteral nutrition, which has been shown to reduce infectious morbidity after surgery for CD.²⁵ The surgeon should also be aware that underweight BMI is associated with an increased risk of penetrating disease and potentially a more technically difficult operation.

Because the present study is a retrospective cohort study, there are inherent limitations. First, we cannot assess extraction site size and how this may differ based on BMI because the specific incision length is not routinely dictated in the operative note. Second, we cannot assess other potential markers of malnutrition, such as preoperative weight loss, because this is not commonly recorded in the medical record. Third, it is possible that obese patients are less frequently on immunosuppressive medications preoperatively owing to early medication cessation secondary to lack of response from inadequate drug dosages, as has been shown previously.³ Fourth, we cannot directly determine how many patients did not have a return of bowel function by postoperative day 7 but did not require a nasogastric tube or total parenteral nutrition, but we did account for this by creating a prolonged-length-of-stay variable. Fifth, the study is not designed to answer the causal question of whether obesity precedes the development of fistulizing disease and is protective against its development or the alternative where patients who do not have a fistulizing disease phenotype are better able to maintain and gain weight. Sixth, we did not use volumetric computed tomography scans to measure mesenteric obesity, so we had to use BMI to categorize a patient as underweight, normal weight, or obese. Last, because this is a retrospective cohort study limited by the time frame of data collected, we cannot assess how BMI affects long-term CD recurrence and whether BMI affects the need for future CD-related intestinal resection. In spite of these limitations, our study presents data on the relationship between BMI, disease severity, and postoperative outcomes in a large number of patients with CD undergoing the same operation, as compared with prior studies that combined all patients with inflammatory bowel disease and a variety of operations.

In conclusion, although underweight patients with CD may have a more severe disease phenotype at the time of surgery, they experienced decreased postoperative infectious complications compared with obese patients with CD. As obesity continues to increase among patients with CD, it will become increasingly important to counsel patients about maintaining a normal BMI. This may reduce the proportion of patients who are obese with CD presenting for surgery and allow for an increased utilization of laparoscopic surgery. In addition, increased awareness of incision size and consideration of wound healing by secondary intention may reduce postoperative sSSI rates in this complex patient population.

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Conflict of interest/Disclosure

Nicholas McKenna, Elizabeth Habermann, Martin Zielinski, and Kellie Mathis—none; Amy Lightner is a consultant for Takeda.

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