



Original Article

# Bariatric Surgery in Patients with Inflammatory Bowel Disease: An Accessible Path? Report of a Case Series and Review of the Literature

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## Abstract

**Background and aims:** Morbid obesity is an emerging problem in the inflammatory bowel disease [IBD] population. Bariatric and IBD surgeries share technical difficulties and elevated morbidity. However, nothing is known about the possibility of performing bariatric surgery in patients with a definite diagnosis of IBD. The aim of this study was to evaluate safety and efficacy of restrictive bariatric surgical procedures in IBD patients.

**Methods:** Six patients with morbid obesity and IBD were operated on with restrictive bariatric surgery and concomitant or deferred IBD surgery. We compared BMI, excess weight loss, and perioperative complications of restrictive bariatric surgery in IBD with a control group of 95 bariatric patients. We also evaluated clinical, biochemical, pharmacological, and endoscopic characteristics before and after surgery in IBD patients.

**Results:** Perioperative results, in terms of BMI, excess weight loss, and complications after restrictive bariatric surgery, were comparable between obese IBD and control patients. IBD patients experienced a significant postoperative reduction in BMI, CRP levels, WCC, and systolic blood pressure and a significant increment in hemoglobin levels. None of the patients reported signs of malabsorption. All the patients except one were able to discontinue steroids, were in endoscopic remission at 1 year, and were in clinical remission at the latest follow-up visit. Two patients halved azathioprine dosage. One patient had a postoperative clinical recurrence treated with adalimumab.

**Conclusions:** Bariatric surgery seems to be safe and effective in IBD patients. Concomitant ileocolic resection does not increase perioperative complications. Relationship between IBD and obesity remains unclear, but weight loss could be useful in the pharmacological control of IBD.

**Keywords:** Crohn's disease; ulcerative colitis; surgery; bariatric surgery; morbid obesity; complications

## 1. Introduction

Morbid obesity and inflammatory bowel diseases [IBD] are growing social and medical problems worldwide. Obesity is associated to immune system dysregulation, resulting in low-grade chronic inflammation mediated by a number of cytokines, such as interleukin-6 and tumor necrosis factor-alpha [TNF $\alpha$ ], which play a central role also in IBD.<sup>1</sup> Pharmacological treatment of obese patients is challenging,

due to the large volume of distribution.<sup>2,3</sup> Recent reports suggest a prevalence of morbid obesity in IBD patients of 15–20%, especially in those with Crohn's disease [CD].<sup>4</sup> A body mass index [BMI] over 35, with related comorbidities, is a definite indication for bariatric surgery in order to avoid long-term complications. The two main surgical approaches are restrictive [reduction of gastric volume] or malabsorptive [bypass], depending on BMI and comorbidities.

Bariatric and IBD surgeries share technical difficulties and elevated morbidity. However, nothing is known about the possibility of performing a bariatric operation in patients with a definite diagnosis of IBD, or combining bariatric and IBD surgery.

The aim of the present study was to evaluate safety and efficacy of bariatric surgery in obese IBD patients.

## 2. Materials and Methods

Between January 2007 and December 2012, 161 morbid obese patients and 418 IBD patients [310 with Crohn's disease, 108 with ulcerative colitis [UC]] underwent surgery at the Department of Surgery, 'Luigi Sacco' University Hospital in Milan, Italy. Six patients [5 CD and 1 UC] presented with both morbid obesity and IBD, and received a bariatric operation with concomitant or deferred IBD surgical treatment. In all patients, clinical, hematologic, radiologic, endoscopic and surgical data were prospectively collected in the 'Luigi Sacco' IBD computerized database, approved by the Ethical Committee. In particular, IBD patients were screened for gastric and jejuno-ileal CD locations through a recent gastroduodenoscopy and magnetic resonance imaging [MRI] of the small bowel. The patients were classified for IBD using the Montreal Classification.<sup>5</sup> All the patients had a long history of obesity with many attempts at weight reduction with diet and improvement of physical activity. The decision to operate was taken after the evaluation of the patient during a regular IBD multidisciplinary meeting [MDM], on the basis of clinical, radiologic and endoscopic findings, in the presence of the senior bariatric surgeon [DF]. Postoperative scheduled follow-up was performed at 3, 6, and 12 months for the first year and every 6 months for the next 4 years. Endoscopic remission of CD was evaluated at 12 months. The latest follow-up up dating was June 2014. Postoperative complications were reported as intra-abdominal septic complications [IASC] related to the surgical procedure. Clinical recurrence was defined as the presence of CD-related symptoms associated with radiologic, endoscopic, and laboratory findings requiring treatment with high doses of steroids or an induction regimen with anti-TNF $\alpha$  agents. Ileocaecal resections were performed as minimal resections with macroscopic, but not microscopic, disease-free margins as previously reported.<sup>6-10</sup> Bariatric procedures were performed using restrictive, and not malabsorptive, techniques [Figure 1].

A specific informed consent was obtained from all the patients. In order to assess safety and efficacy of bariatric surgery in IBD patients, we used as a control group all the morbid obese patients submitted to restrictive surgery in the same period. We compared weight, BMI, excess weight loss, and perioperative complications [IASC] in the two groups. In the IBD group, we evaluated C-reactive protein [CRP] and white cell count [WCC] as a mean ( $\pm$  standard deviation [SD]) of three repeated measures 1 year before surgery and at the scheduled follow-up at 3, 6 and 12 months after surgery. Hemoglobin, blood glucose, blood pressure, vitamin B<sub>12</sub>, vitamin D, folic acid, BMI, stools per day, blood in stool, and medications were reported pre- and postoperatively. Endoscopic findings before bariatric operation were reported in terms of Rutgeerts' score for patients with previous IBD surgery,<sup>11</sup> the Mayo endoscopic subscore<sup>12</sup> for the patient with UC, and a simplified endoscopic score for the patient with colonic CD [SES-CD].<sup>13</sup> Postoperative Rutgeerts' score was obtained 1 year after bariatric or combined surgery. Statistical analysis was performed using Statistica software [Stat Soft, Statistica 8.0]. Student's t test, single or paired, was used for continuous variables where appropriate. Differences in proportions were compared with chi-squared tests.

## 3. Results

Among 161 morbid obese patients with BMI between 35 and 50, 101 [62%] received a restrictive bariatric operation. Six [5.9%] had a concomitant diagnosis of IBD, and 95 [94.1%] were used as a control group.

Preoperative patients characteristics are reported in Table 1. The number of preoperative clinical relapses is reported with all the pharmacological shifts adopted. Surgical procedures, pre- and postoperative clinical, biochemical, and endoscopic assessments are listed in Table 2. In particular, the indication for surgery in cases 5 and 6 was fibrostenotic disease of the terminal ileum. These patients were treated by minimal ileocecal resection with side-to-side anastomosis [European Crohn's and Colitis Organization Guidelines 2006 and 2010].<sup>14,15</sup> Case 2 presented with proctitis [SES-CD 9] and complex, unmanageable perianal fistulas, and received a terminal colostomy with rectal closure. Preoperative medications during the past 3 months before surgery and postoperative adjuvant treatment, with

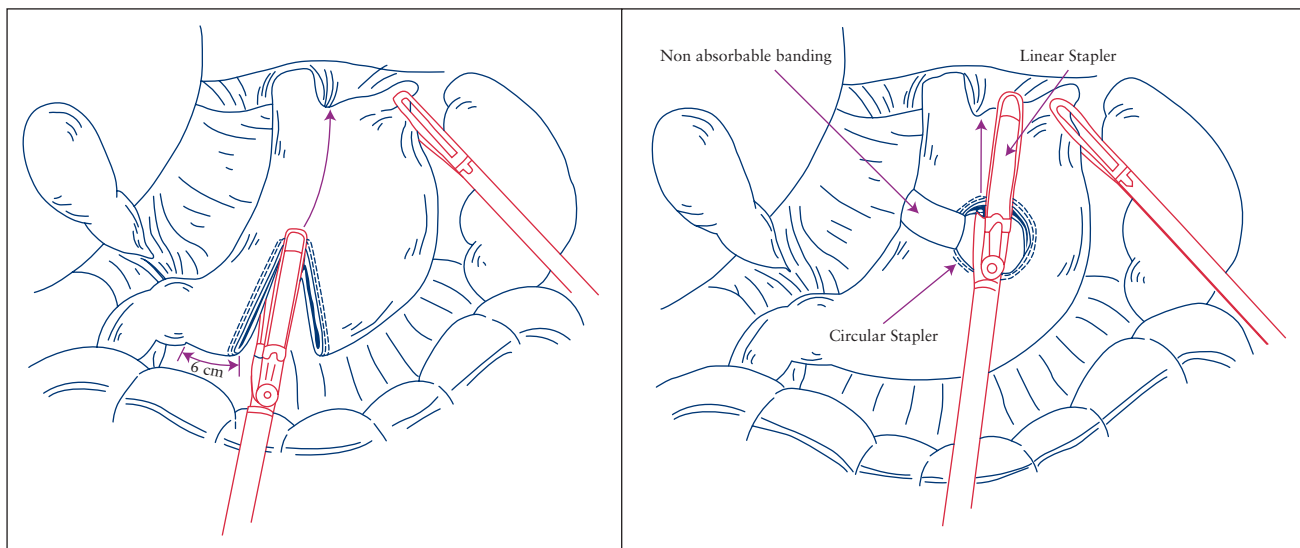


Figure 1. Schematic diagrams of sleeve gastrectomy [left panel] and Maclean gastroplasty [right panel].

**Table 1.** Patients' characteristics.

	Case 1 Crohn's	Case 2 Crohn's	Case 3 ulcerative colitis	Case 4 Crohn's	Case 5 Crohn's	Case 6 Crohn's
Preoperative CDAl and MAYO scores	210	254	9	201	114	281
Gender	F	M	F	M	F	F
Age [years]	54	43	48	54	30	54
Diagnosis	Obesity, Crohn's disease	Obesity, Crohn's disease	Obesity, UC	Obesity, Crohn's disease	Obesity, Crohn's disease	Obesity, Crohn's disease
Comorbidities	Psoriasis, polyarthritis	Hiatus hernia, esophagitis	Diabetes, hypertension, polyfibromyalgia	Hiatus hernia, sleep apnea, left surrenectomy	Hypertension, hepatic steatosis	Diabetes, asthma, gastritis
IBD localization	Ileocecal	Rectum and perianal disease	Pancolitis	Ileocecal	Ileocecal	Ileocecal
Montreal classification	A2 L2B2 p	A2 L2B1 p	E3	A2 L1B2	A2 L1B2	A3 L1B2
Previous IBD surgery	Ileocecal resection		/	/	/	/
Age at diagnosis [years]	29	33	22	40	23	49
IBD disease duration [years]	24	4	21	13	6	1
Number preoperative relapses	7	1	1	4	3	1
Therapy shifts*	5 steroids, 1 adalimumab, 1 infliximab	1 steroids, 1 infliximab	1 steroids	2 steroids, 1 adalimumab, 1 infliximab	1 steroids, 1 adalimumab, 1 infliximab	1 steroids

\*Number of trial drug.

related dosages, have been reported. All the patients discontinued steroids, and two patients halved the azathioprine dosage. A statistically significant difference was found in CRP and WCC reduction, and hemoglobin increase. Even if no statistical difference was present in the blood glucose values, two patients experienced a normalization of diabetes. A statistically significant reduction was observed in systolic blood pressure. No differences were present in vitamin B<sub>12</sub>, vitamin D and folic acid as markers of intestinal absorption.

In four out of five CD patients the disease was in endoscopic remission at 1 year [Rutgeerts score i0i1], whereas in one patient it was moderately active [Rutgeerts score i2]. Postoperative follow-up was 57.8 [± 29.8 SD] months. During follow-up, Case 1 developed a long-term complication of the Maclean gastrectomy 5 years after surgery [Figure 1]. She presented with recurrent vomiting and dysphagia. The stomach had a clepsydra shape and it was technically impossible to perform a sleeve gastrectomy. She underwent to a gastrectomy with short limbs, Roux-en-Y, gastric bypass in order to minimize malabsorption. Case 2 experienced a complete healing of the rectum and perianal fistulas; he had his colostomy closed in 2009; and he was asymptomatic with deep disease remission at latest follow-up visit. Case 3, 2 years after bariatric surgery, underwent to a total abdominal colectomy for a colorectal cancer in the sigmoid colon [pT3N0M0G2] discovered during regular endoscopic screening. She received adjuvant chemotherapy, and in 2012 she underwent proctectomy and ileo-pouch-anal anastomosis with a 'J' pouch.

Comparisons between IBD and non-IBD obese patients in terms of BMI, excess weight loss, and perioperative complications are reported in Table 3. There were eight perioperative complications in the non IBD group [three gastric bleeding, four fistula, one gastric stenosis] that required three reoperations. There was one gastric suture bleeding in the IBD group and no reoperations. No statistical significance was found between the two groups.

#### 4. Discussion

Obesity is a public health problem that has reached epidemic proportions worldwide, involving both rich and poor countries, with an estimated 500 millions obese adults and 1.5 billion overweight or obese people.<sup>1,16-18</sup>

In recent years, obesity has been associated with chronic systemic inflammation due to the innate immune system activation in adipose tissue that promotes an increase in the production and release of pro-inflammatory cytokines.<sup>1,2,3,18</sup> Recent reports seem to show an emerging trend toward overweight in mild or quiescent CD, reflecting adequate control of inflammation, older age, and sedentary lifestyle. The prevalence of obese patients in IBD population, especially in CD, has been reported at 15–20%.<sup>16,19</sup> However, the relationship between obesity and IBD has been poorly investigated.

Blain et al.<sup>2</sup> compared obese with non-obese CD patients and found that obesity in Crohn's disease was associated with perianal complications and year-by-year disease activity, but not with the long-term disease course. The hypothesis was that increased friction and sweating between the skin folds of the perineum encouraged maceration and secondary bacterial infections, favouring abscess formation. They concluded that obesity is not a risk factor for Crohn's disease as for other chronic inflammatory disease [eg rheumatoid arthritis].

Hass et al.<sup>3</sup> evaluated CD overweight patients in terms of age at diagnosis, time to first surgery, total number of surgical procedures, and therapy escalation. They showed that CD patients with a

Table 2. Surgical procedures and outcomes.

Surgical procedure	Case 1 Crohn's	Case 2 Crohn's	Case 3 UC	Case 4 Crohn's	Case 5 Crohn's	Case 6 Crohn's	p-Value
BMI [kg/m <sup>2</sup> ]	Pre 35.7 Post 29.0	Sleeve gastrectomy, end colostomy [2007] 41.0 27.0	Sleeve gastrectomy [2008] 41.5 27.6	Sleeve gastrectomy [2012] 39.0 26.0	Sleeve gastrectomy, ileocecal resection [2012] 39.7 29.0	Sleeve gastrectomy, ileocecal resection [2012] 46.9 36.5	/ <0.001
Endoscopic IBD activity	Pre Rutgeerts' Endoscopic Score <sup>11</sup> i2	Proctitis + complex perianal disease [SES-CD 9] <sup>13</sup> Rutgeerts' Endoscopic Score <sup>11</sup> i0	Pancolitis Mayo Endoscopic Score <sup>12</sup> i2	Rutgeerts' Endoscopic Score <sup>11</sup> i2	Rutgeerts' Endoscopic Score <sup>11</sup> i0	Stricture terminal ileum	/
Stools/day	Pre 3-4 Post 1-2	Rutgeerts' Endoscopic Score <sup>11</sup> i0	Pancolitis Mayo Endoscopic Score <sup>12</sup> i1	Rutgeerts' Endoscopic Score <sup>11</sup> i2	Rutgeerts' Endoscopic Score <sup>11</sup> i0	Rutgeerts' Endoscopic Score <sup>11</sup> i0	/
Blood in stool	Pre no Post no	yes no	yes no	yes no	yes no	yes no	/
CRP	Pre 8.8 ± 8.7 Post 0.68 ± 1.08	7.75 ± 7.42 0.46 ± 0.72	7.45 ± 6.43 1.7 ± 0.707	53.4 ± 52 22.6 ± 20.3	14.7 ± 20.3 0.1 ± 4.4	11.56 ± 10.7 1.05 ± 1.06	<0.010
WCC	Pre 10816 ± 1284 Post 5990 ± 650	6180 ± 743 4083 ± 606	11740 ± 791 6145 ± 784	6640 ± 806 5870 ± 466	7130 ± 169 6550 ± 148	7965 ± 1279 7350 ± 636	<0.001
Hemoglobin [12-16g/dL]	Pre 10.3 Post 12.3	10.9 13.0	10.8 12.9	12.4 14.6	11.8 11.5	12.7 12.5	<0.040
Blood pressure	Pre 140/80 Post 130/80	140/80 130/85	150/80 120/80	130/80 120/75	150/100 130/70	140/80 120/80	<0.010
Blood glucose [65-110 mg/dL]	Pre 83.0 Post 78.0	94.0 81.0	207.0 81.0	92.0 85.0	102.0 96.0	153.0 91.0	N.S
Vit B <sub>12</sub> [130-700 ng/mL]	Pre 404.0 Post 205.0	363.0 456.0	566.0 422.0	102.0 144.0	191.0 275.0	368.0 319.0	N.S
Vit D [8-80 ng/mL]	Pre 28.7 Post 35.9	15.6 16.7	57.0 77.1	11.8 12.4	16.4 14.1	22.4 27.2	N.S
Folic acid [3-16 ng/mL]	Pre 4.0 Post 5.0	4.7 6.6	3.4 4.7	7.5 6.99	1.56 8.47	2.9 8.4	N.S
Medications	Pre Azathioprine 250 mg, infliximab, steroids	Aminosalicylates, steroids, infliximab	Aminosalicylates, azathioprine 250 mg, steroids	Steroids, azathioprine 250 mg, infliximab	Aminosalicylates, steroids	Aminosalicylates, steroids	/
	Post Azathioprine 12.5 mg	Azathioprine 12.5 mg	/	Adalimumab	Aminosalicylates	/	

UC, ulcerative colitis; N.S., not significant.

**Table 3.** Comparison between obese patients and IBD obese patients.

		Obese patients [n = 95]	IBD obese patients [n = 6]	p-Value
Weight [Kg]	Pre	113.4 ± 18.9 <sup>b</sup>	117.4 ± 16.4 <sup>c</sup>	N.S. <sup>a</sup>
	Post	79.7 ± 24.8 <sup>b</sup>	84.4 ± 19.2 <sup>c</sup>	N.S. <sup>a</sup>
BMI [kg/m <sup>2</sup> ]	Pre	43.7 ± 6.3	40.6 ± 1.7	N.S. <sup>a</sup>
	Post	29.4 ± 4.6	26.8 ± 1.1	N.S. <sup>a</sup>
Excess weight loss [%]		79.7 ± 24.8	74.5 ± 11.2	N.S. <sup>a</sup>
Perioperative complications		8 [8.5%]	1 [16%]	N.S. <sup>d</sup>

N.S., not significant.

<sup>a</sup>Student's t test.

<sup>b</sup>Weight pre vs weight post in obese patients,  $p < 0.001$ .

<sup>c</sup>Weight pre vs weight post in IBD obese patients,  $p < 0.001$ .

<sup>d</sup>Chi square test.

BMI  $\geq 25$  kg/m<sup>2</sup> were older at diagnosis, with a shorter time to first surgery. Their hypothesis was that overweight patients could have a more aggressive disease or they could be less responsive to immunomodulators due to the pharmacological volume of distribution.

The American College of Surgeons National Surgical Quality Improvement Program Database [2005–2008]<sup>18</sup> has shown longer operating times and higher overall postoperative morbidity in obese patients after major surgery for complicated Crohn's disease. Similarly, longer operating times and higher morbidity has been reported in UC patients submitted to restorative proctocolectomy, including a significantly increased risk of pelvic sepsis.<sup>14</sup>

In their review, Boutros and Maron<sup>16</sup> confirmed that both obesity and IBD heighten the complexity of surgery and postoperative care, and obesity alone enhances the technical difficulties and the risk of complications of IBD surgery.

There are some reports in the literature suggesting that bariatric surgery is a potential risk factor for the development of CD.<sup>21–23</sup> Ahn et al.<sup>23</sup> described three young adults, without family history of IBD or previous gastrointestinal disease, who developed CD 11 to 60 months after Roux-en-Y gastric bypass procedure. Some authors postulated that anatomic changes after malabsorptive bariatric surgery might promote a bacterial overgrowth that should trigger intestinal chronic inflammation. However, little is known about the interaction of bariatric and IBD surgery in patients with a definite diagnosis of IBD, or the impact of bariatric surgery on IBD course.<sup>24</sup> Lascano et al.<sup>25</sup> described a 39-year-old male affected by UC, hypertension, and morbid obesity, who after gastric bypass experienced clinical remission of UC and reduction in medications.

There are no reports to date on outcomes of ileoanal pouch procedure in patients with previous bariatric surgery. We described a UC patient who after a sleeve gastrectomy underwent a restorative proctocolectomy without complications and good functional results.

In our series we adopted a restrictive bariatric procedure, since nothing is known about the possible impact of a malabsorptive bypass in an IBD patient. Using this approach, we reached effective results in BMI reduction without significant perioperative complications or intestinal malabsorption. Furthermore, in those patients treated with concomitant IBD surgery we did not experience the possible mutual increase of complications. We registered a normalization of inflammatory markers, hemoglobin levels, and systolic blood pressure in patients with concomitant or deferred IBD surgery. The patient who experienced a postoperative clinical recurrence, treated with an anti-TNF $\alpha$  compound, might have a particularly aggressive CD. In fact, the patient had undergone two small bowel resections in the previous 5 years.

Since this is a small case series, it is impossible to know whether the positive trend in inflammation, in those patients who underwent

bariatric and IBD surgery, might have a benefit not only in weight loss but also in the removal of the active inflammatory bowel disease. However, most of the patients were non-responders to medical treatment with several therapeutic shifts prior to bariatric surgery. An intriguing hypothesis should be that on the one hand we have reduced systemic inflammation through the component due to obesity, on the other hand the fall of BMI has reduced the pharmacological volume of distribution to the normal therapeutic range.

In conclusion, further studies are needed to better understand the relationship between IBD and morbid obesity in terms of therapy and complications. Restrictive bariatric surgery in IBD patients should be considered in selected, highly motivated patients, non-responder to pharmacological treatment.

### Conflict of interest statement:

None declared.

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