

A Peer-Reviewed Publication

BARIATRIC TIMES

Clinical Developments and Metabolic Insights in Total Bariatric Patient Care

Volume 7, Number 1

January 2010

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REVIEW

Treatment Considerations for Osteoarthritic Knee Pain in Patients with Obesity

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INTRODUCTION

Knee pain is among the most common of health concerns in the population, and the subset of bariatric patients is no exception.^{1,2} Independently, in the United States, obesity has prevalence in excess of 33 percent, and a 2006 Centers for Disease Control and Prevention (CDC) survey of adults reported an 18-percent incidence of knee pain within the past 30 days.^{3,4} Bariatric patients have a well-established positive association with knee osteoarthritis, and it has been previously noted that body mass index (BMI) in young adulthood, a time when many patients are now choosing to pursue bariatric

surgical options, may be a good predictor of subsequent osteoarthritis in later years.⁵⁻⁷

While the etiology of knee pain and treatment modalities can be wide ranging, this article will focus on existing medical knowledge of knee pain secondary to osteoarthritis in the bariatric population, considerations of the treatment options available for those afflicted with that diagnosis, and a discussion of the “best questions to address” in terms of future collaboration between and treatment options available to primary care physicians, orthopedic surgeons, and bariatric physicians and surgeons. **Continued on Page XX**

REVIEW



MARGINAL ULCERS AFTER ROUX-EN-Y GASTRIC BYPASS: PAIN FOR THE PATIENT...PAIN FOR THE SURGEON

by CAMELLIA RACU, MD, MPH;
AMIR MEHRAN, MD, FACS, FASMBS

EPIDEMIOLOGY: WHAT DO WE KNOW ABOUT MARGINAL ULCERS?

Marginal ulcers represent one of the most problematic postoperative complications following Roux-en-Y gastric bypass (RYGB). A marginal ulcer, or stomal ulceration, refers to the development of mucosal erosion at the gastrojejunal anastomosis, typically on the jejunal side. Marginal ulcers develop most often after gastric bypass procedures where the gastric remnant or distal stomach is stapled but not divided. The documented incidence of marginal ulcers is quite variable, ranging from 0.6 to 16 percent.^{1,2} The true incidence is very likely much higher than reported, since documented ulcers represent only those that are identified on endoscopy and many may be treated medically based on symptoms without ever undergoing an endoscopic evaluation. Csendes et al³ published a prospective study of routine postoperative endoscopic evaluation, which revealed that of the identified marginal ulcers, 28 percent were asymptomatic.

REVIEW, CE ACCREDITED

NUTRITION IN THE MANAGEMENT OF NONALCOHOLIC FATTY LIVER

by JACQUELINE JACQUES, ND

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD), which includes non-alcoholic steatohepatitis (NASH), is common in patients qualifying for weight loss surgery (WLS). Risk factors for NAFLD include obesity,

diabetes, and insulin resistance. Of these, obesity is considered to be the greatest single risk factor. Incidence of NAFLD in patients with obesity or type 2 diabetes can be as high as 90 percent.¹ It is estimated that between 50 and 60 percent of preoperative

bariatric surgery patients meet the diagnostic criteria for NASH.²

The enlargement of the liver due to fatty infiltration and, in the case of NASH, inflammation, can significantly interfere with the surgical field in WLS procedures. Obscuring of the surgical

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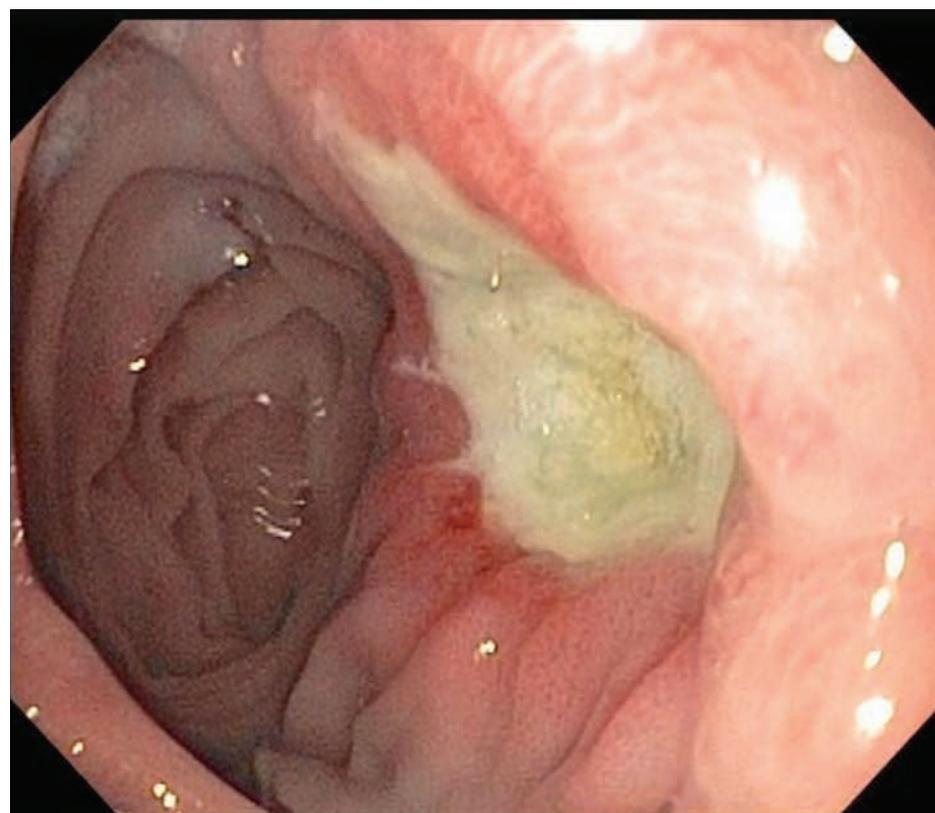
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Marginal Ulcers after Roux-en-Y Gastric Bypass: Pain for the Patient...Pain for the Surgeon

by CAMELLIA RACU, MD, MPH; AMIR MEHRAN, MD, FACS, FASMBS

Bariatric Times. 2010;7(1):XX-XX



ABSTRACT

With the rising number of Roux en-Y gastric bypasses performed around the world, general surgeons should expect to face an equally rising number of early- and late-term complications. Marginal or anastomotic ulcers constitute the majority of these cases, representing as many as 52 percent of postoperative complications.¹³

Marginal ulceration is a challenging problem, which can cause significant morbidity in the postoperative bariatric patient. Its etiology remains elusive and perhaps multifactorial, including both exogenous and intrinsic or technical factors. In addition, while prevention is key, it is often difficult to achieve.

While most of these types of ulcers do respond to medical therapy, there is a select group of patients that continues to suffer from symptomatic, nonhealing ulcers, despite appropriate medical treatment, and requires surgical intervention. The current body of literature does not contain a great deal on the subject of optimal surgical management for marginal ulcers intractable to medical therapy, perhaps a reflection of marginal ulcers' unclear etiology.

This review aims to summarize the current knowledge on marginal ulcers, starting with the diagnosis and medical management, and focusing on current approaches to surgical management, including innovative techniques. The goal is to recognize risk factors, promote patient adherence with treatment, and to become well versed with surgical options and preventive measures.

KEY WORDS

marginal ulcers, stomal ulceration, anastomotic ulcer, gastric bypass surgery, Roux-en-Y gastric bypass, bariatric surgery

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The prospective nature of marginal ulcers revealed an interesting distribution of incidence over time: a high incidence of marginal ulcer at one month after surgery, and a low incidence at 1 or 2 years after gastric bypass surgery.³ In one study by Patel et al,⁴ five percent of their patients developed marginal ulcers, and approximately one-third of those patients required revisional surgery. Upon investigation, 72 percent of these patients were found to have gastro-gastric fistulas.

A number of risk factors have been identified to contribute to marginal ulcer formation. Smoking and use of nonsteroidal anti-inflammatory agents (NSAIDs) are among the top offenders. In addition, patients with large gastric pouches or those with breakdown of the staple line are also at high risk for marginal

ulceration.⁵ A partial anastomotic stricture has also been found to be associated with marginal ulceration.³ A study by Gumbs et al¹⁰ identified that a gastro-gastric fistula is present in 19 percent of patients who developed a marginal ulcer. While the pathogenesis is not clearly elucidated, one proposed mechanism responsible for ulcer formation involves high acid production or another agent that erodes the integrity of the mucosal barrier. MacLean et al⁶ described 'stitch ulcers,' implicating permanent suture in mucosal erosion. The change from permanent to absorbable suture was found to significantly decrease the incidence of postoperative marginal ulcers.⁷ Other factors, such as alcohol use, steroids, *Helicobacter pylori*, nonadherence, and chronic anticoagulation, can lead to postoperative marginal ulceration. The exact link between *H. pylori* and the development of marginal ulcers is

unclear; however, researchers have identified this bacteria to be a risk factor.^{8,9}

While the exact etiology of marginal ulcers remains obscure, some mechanisms have been postulated. NSAIDs lead to mucosal damage, smoking causes mucosal ischemia, and foreign bodies (suture or staples) can lead to mucosal breakdown and ulceration. A high acid milieu can arise from a dilated gastric reservoir or, in the setting of a gastro-gastric fistula, the acid produced in the gastric remnant can reflux into the gastric pouch via the fistula and break down the mucosal integrity. The jejunum just distal to the gastrojejunal anastomosis is bathed in this acid and, given that it does not have the acid buffering capability of the duodenum, it becomes vulnerable to ulcer formation.¹⁰

Csendes et al³ proposed several explanations about marginal ulcers that develop in the early postoperative period. In the immediate 3 to 4 weeks after surgery, it is unlikely that the few parietal cells of the small gastric pouch would produce excess acid to cause an ulcer. A significantly higher incidence of ulcers was found in the gastric bypass procedures that retained the gastric remnant and less marginal ulcers when the gastric remnant was removed. This technical difference was suggested to have a critical role in the pathogenesis of marginal ulcers after gastric bypass. Other explanations include the use of electrocautery, an element of ischemia, an inflammatory reaction to the surgical suture even if absorbable, and some association with partial anastomotic stricture also in response to an inflammatory reaction.

Late anastomotic ulcers, typically occurring at one year or later following gastric bypass surgery, are

the often described as marginal ulcers in the majority of literature. This entity is usually caused by a high production of gastric acid, likely due to a large gastric pouch, either made at the time of construction or dilation of the pouch over time, which results in increased parietal cell mass.³ These late anastomotic ulcers tend to have aggressive behavior and can result in acute perforation or severe bleeding, mandating emergent surgical intervention.^{3,11,12}

DIAGNOSIS: HOW TO RECOGNIZE MARGINAL ULCERS?

Post-gastric bypass patients often present with a constellation of upper gastrointestinal symptoms that can be difficult to interpret and differentiate. Patients with marginal ulcers typically present with abdominal pain, nausea, and vomiting, as well as in more extreme cases, hematemesis, stomal obstruction, or even perforation. In 2008, Patel et al⁴ reported abdominal pain, at 66.6 percent, the most common presentation of intractability leading to surgical revision. As such, when these patients present with vague abdominal symptoms, they require a focused and thorough investigation.

Endoscopy is the diagnostic study of choice. Lee et al¹³ demonstrated that endoscopy is accurate in the evaluation of postoperative upper gastrointestinal symptoms; likewise, it was found to be safe and effective for the management of post gastric bypass complications. At endoscopy, biopsies should be performed to evaluate for *H. pylori*. Evaluation for gastro-gastric fistula should also be conducted, both at endoscopy as well as with an upper gastrointestinal series, which should include left lateral decubitus views. Lee et al⁷ also found that patients who present with upper gastrointestinal symptoms early in the postoperative period, less than

three months, are more likely to have abnormal findings on upper endoscopy.¹³ Marginal ulcers were identified in 15.8 percent of the patients evaluated with endoscopy for upper gastrointestinal symptoms. Of all symptomatic patients who underwent upper endoscopy, 70 percent were found to have an abnormality associated with their gastric bypass surgery. However, only 4.7 percent of patients who underwent endoscopy in the first three months developed marginal ulcers, while 26 percent were identified beyond the first three months.¹³

MEDICAL MANAGEMENT: WHAT MEDICAL THERAPIES ARE AVAILABLE AND HOW EFFECTIVE ARE THEY?

Treatment for a marginal ulcer is dependent on its etiology. For smokers, smoking cessation is imperative. The use of proton pump inhibitors in the immediate postoperative period, for the first 3 to 4 months, is critical from a prophylactic perspective. The length of therapy is not universal and mostly dependent on the program, but varies anywhere from the initial postoperative hospitalization through the first few months until oral intake normalizes.⁵ For a documented marginal ulcer either by symptoms or endoscopy, initial treatment involves starting a proton pump inhibitor and sucralfate suspension (1g oral liquid q6hr) for a period of 3 to 6 months. For comprehensive therapy, a breath or serology test should be performed for *H. pylori*; medical eradication treatment includes two antibiotics and a proton pump inhibitor.¹⁴

In 2009, Lee et al¹³ found that 12 of 1,079 patients who had documented marginal ulcers by endoscopy all responded to medical treatment in the form of oral sucralfate suspension and proton pump inhibitor therapy. Complete healing of these ulcers was demonstrated on upper endoscopy performed at 2 to 8 weeks after medical therapy.¹³ Once ulcers form, the large majority of patients do respond to medical therapy. Alternatively, if a marginal ulcer is left untreated or persists despite appropriate medical treatment, it can lead to stricture formation and ultimately gastric outlet obstruction, which requires numerous endoscopic dilatations.⁹ Thus, it is imperative to assess whether the ulcer is responding to medical therapy and has evidence of healing on repeat endoscopy. Failure to heal requires surgical intervention.

SURGICAL INTERVENTION: WHEN IS IT TIME TO OPERATE?

Although marginal ulcers have traditionally been thought of as relatively rare complications following

RYGB and those requiring revision even more uncommon, recent data reveal that the reoperation rate is greater than initially believed.⁴ In addition to medical intractability, surgical indications include patients with gastro-gastric fistula and a marginal ulcer, patients with chronic anemia secondary to slow blood loss from the gastrointestinal tract, and patients with massive bleeding from the marginal ulcer. Those with a gastro-gastric fistula require surgical division of the pouch from the gastric remnant, or a remnant gastrectomy.¹⁵ An alternative approach is the use of upper endoscopy with fibrin applied to seal the fistula.¹⁰ In addition, endoscopy is also useful for removal of foreign bodies, such as sutures or staples, that keep the ulcers from healing. For medical intractability, the standard surgical treatment involves resection of the entire ulcer bed at the gastrojejunostomy and reconstructing the anatomy with a new gastrojejunostomy.¹⁴ The presence of a marginal ulcer and a nonhealing gastro-gastric fistula typically mandates immediate surgical management. For a simple marginal ulcer, surgery is indicated when ulcer symptoms persist despite maximum proton pump inhibitor therapy and sucralfate for three months without healing, risk factors such as smoking and NSAIDs have been eliminated, and the patient's nutritional status has been optimized.

SURGICAL MANAGEMENT OPTIONS

Revision of a gastric bypass for marginal ulcer management can be performed either through an open or laparoscopic approach; this largely depends on the surgeon's experience with bariatric surgery revisions and advanced laparoscopy, as well as the approach of the patient's initial operation. Nguyen et al¹¹ described revisional surgery for marginal ulcers to involve resection of the gastrojejunostomy containing the ulcer and reconstruction. The laparoscopic approach is favored, if technically possible, for its benefits of decreased postoperative pain, faster recovery, and less wound complications.¹⁴ The technique involves placement of five trocars, taking adhesions down between the stomach and liver, retracting the liver, dissecting the gastric pouch out from the gastric remnant, completely mobilizing the Roux limb and, if in the retrocolic position, dividing it 3 to 5cm distal to the gastrojejunostomy to place it in the antecolic position. Next, the gastric pouch is mobilized, divided, and transected 1cm above the gastrojejunostomy to excise the ulcerated portion, followed by reanastomosis with the use of a linear or circular stapler. If the circular stapler is used, a 25mm anvil is introduced via the transoral route

into the gastric pouch. The circular stapler is introduced trans-abdominally and placed through the opening in the Roux limb. The gastrojejunostomy is constructed by approximating the anvil in the pouch to the circular stapler in the Roux limb. The enterotomy left in the jejunum is closed with a linear stapler. An intraoperative endoscopy is performed with the gastrojejunostomy submerged under water to test the anastomosis for air leak. On Postoperative Day 1 (POD 1), the patient undergoes an upper gastrointestinal gastrografen study to delineate the reconstructed anatomy and rule out leak or obstruction. The patient is started on a bariatric clear liquid diet if the study is normal and is discharged on POD 2 with a proton pump inhibitor for the immediate 6 to 8 weeks postoperatively.¹⁴

The following key points have been gleaned from the literature as key elements of laparoscopic revisional bariatric surgery for marginal ulcers. The use of intraoperative endoscopy is critical for revisional bariatric surgery as it helps to clarify the anatomy, including the gastric pouch, gastrojejunostomy, and the distal jejunum. Further, endoscopy facilitates dissection of the area of interest, serves as a guide for complete resection of the ulcerated region, and can be used to test the newly formed anastomosis for a leak.¹⁶ At University of California Los Angeles, we create the initial gastric pouch using the pars flaccida approach to the lesser sac. At the University of California Los Angeles, we create the initial gastric pouch using the pars flaccida approach to the lesser sac. The pars flaccida technique involves entering and dividing the often transparent lesser omentum that drapes over the caudate lobe of the liver. Vessels in the lesser omentum are divided with care to preserve the left hepatic artery. This window to the lesser sac allows retrogastric tunneling to the gastroesophageal junction, exposing the angle of His.^{17,18} For revisions, if the window to the lesser curve of the stomach is obliterated from previous dissection, the lesser sac can be approached from the greater curve using a retrograde tunneling maneuver with care not to injure the lesser curve vessels. If the gastric remnant has not been divided from the gastric pouch at the original operation, a linear endoscopic stapler is used to transect the stomach and a new pouch is created such that it is small in size and excludes the fundus. In addition to correcting staple line disruption, other elements to evaluate and address intraoperatively are pouch size and pouch orientation. If no other technical abnormalities or external risk factors are identified, St. Jean et al¹⁹ advocate performing a

truncal vagotomy to address the potential high parietal cell distribution in the gastric pouch. Most bariatric surgeons, however, do not advocate truncal vagotomy.

For perforated marginal ulcer, diagnostic laparoscopy with repair has been found to be safe and successful,²⁰ particularly in the first 24 hours of diagnosis and for patients without evidence of sepsis or hemodynamic instability. The first step is to perform a thorough investigation by mobilizing the remnant stomach, duodenum, and Roux limb to identify the source of perforation. Once identified, repair is performed by oversewing the perforation with a jejunal and omental patch.¹⁹ Others advocate primary closure with absorbable suture, reinforcement with a gastrosplenic ligament patch and fibrin sealant, and closed-suction drain placement.¹¹ If laparoscopic repair cannot be performed safely, the operative plan should be carried out in an open fashion. If primary closure is not possible, irrigation and drainage is the next appropriate approach.¹¹ If ischemia is suspected as the cause of the perforated marginal ulcer, then complete reconstruction of the gastrojejunostomy is indicated.¹⁶ In addition, if excess parietal cell mass is presumed to be the source of the ulcer, a truncal vagotomy with or without gastric pouch revision has been recommended.¹¹

At our institution, patients who demonstrate upper abdominal pain, nausea, emesis, hematemesis, or oral intolerance undergo an upper endoscopy and are started on proton pump inhibitor and sucralfate therapy followed by repeat endoscopy in eight weeks. Failure to have symptom resolution or healing of the marginal ulcer in three months is an indication for surgical intervention. Our practice's preoperative requirements for both initial and revisional bariatric surgery include mandatory cessation of smoking for at least three months and demonstration of being smoke-free by serology.

One of our patients failed maximal medical therapy at four months following laparoscopic RYGB (antecolic and antegastric approach), and required a gastrojejunostomy revision for marginal ulcer management. To manage this particular patient's marginal ulcer, we experimented with a new approach that we describe here. Intraoperatively, we found that the anterior gastrojejunal wall ulcer had perforated into the left lateral segment of the liver; we believe this was the reason that the ulcer did not heal with medical management. We revised her anastomosis by excising the anterior ulcerated wall, and primarily repaired the defect by approximating the gastric pouch to

the jejunal wall using absorbable suture in two layers. We were able to perform this limited revision because the rest of her anatomy appeared intact and the posterior staple line of the gastrojejunostomy was healthy and well vascularized. This innovative approach allowed us to address the nonhealing marginal ulcer while avoiding a major reconstruction that would potentially require an esophago-jejunal anastomosis and even a thoracotomy. The patient recovered well and remained asymptomatic in the immediate postoperative period. Nevertheless, the efficacy and longevity of this approach requires long-term follow up.

OUTCOMES: HOW SUCCESSFUL ARE OUR INTERVENTIONS?

Patel et al⁴ found that 87 percent of their 39 patients requiring revision for marginal ulceration remained symptom free following revisional surgery. Furthermore, for nonsmokers who have marginal ulcers, operative treatment is highly successful in providing definitive resolution of symptoms. In a comparison of open versus laparoscopic RYGB,⁴ the rate of patients requiring operative intervention for marginal ulcers is much higher for those who underwent an open RYGB, 2.1 percent versus 0.6 percent after laparoscopic RYGB ($p < .0025$).⁴

PREVENTION

The best therapy is to prevent ulcers from forming in the first place. Recommendations include smoking cessation and elimination of NSAIDs, steroids, and chronic anticoagulation prior to RYGB. Alternatively, for patients who are dependent on agents such as NSAIDs or steroids, a laparoscopic sleeve gastrectomy could be offered instead of the RYGB. Further, prophylactic measures can be taken by routinely treating all RYGB patients with proton pump inhibitors for three months postoperatively. Programs that have been able to completely treat marginal ulcers with high-dose proton pump inhibitors have also instituted a prophylactic regimen of PPI therapy postoperatively for all patients. Of those patients undergoing routine therapy, none subsequently developed marginal ulcers during the short-term follow-up of the study.¹⁰

Likewise, some programs require routine upper endoscopy as a precautionary measure. Preoperative esophagogastroduodenoscopy (EGD) with biopsies for *H. pylori* are performed, and positive patients are treated prior to bariatric surgery. An opposing view would argue that this places a significant financial burden on the healthcare system for relatively low yield, both in terms of identifying gastric malignant lesions as well as in terms of preventing

postoperative ulcer formation. At our institution, symptomatic patients or those with difficult-to-control gastroesophageal reflux disease selectively undergo preoperative EGD, and abnormalities such as ulcers and *H. pylori* require treatment prior to undergoing bariatric surgery.

A number of technical aspects can also be considered from a prevention standpoint. To minimize anastomotic ischemia, performing the gastrojejunostomy with proper surgical technique is critical; elements include approximating the tissue without tension, performing a meticulous dissection, and ensuring that the blood supply to the stomach and jejunum remain unaltered.¹⁶ With respect to the gastric pouch, its construction should exclude the fundus such that the remaining parietal cell mass and potential for acid production is minimized. Some also argue that a large fundus can expand, eliminating the restrictive feedback and leading to weight gain. In addition, repeated bariatric revisions may result in compromised blood flow to a new anastomosis, which places the patient at high risk for marginal ulceration.¹⁶

Avoiding absorbable suture has also been demonstrated to reduce marginal ulcer development.

In addition, nitinol anastomotic clips can serve as an alternative to suture or staples for creating the gastrojejunostomy. Eliminating such foreign bodies, which can serve as a nidus for marginal ulceration, is a key element to allowing an ulcer to heal. Nitinol, used in cardiac surgery, is also being applied in incisionless, or natural orifice, surgery for creation of intestinal anastomoses endoscopically with the goal of replicating the complex task of laparoscopic intracorporeal suturing. The claimed benefit of nitinol clips is that they are not ulcerogenic; thus, their use may eliminate marginal ulcers. Tucker et al²¹ published results of nitinol compression anastomosis clip for intestinal anastomoses in open RYGB in pigs. At two months, the anastomoses were found to be healed with a complete mucosal lining and no evidence of strictures. This solution would serve to revolutionize current anastomosing methods and perhaps change the RYGB complication profile by eliminating at least the technical component contributing to ulcers and associated strictures.

CONCLUSION

The number of RYGB procedures performed annually has increased dramatically over the last few years. As this number continues to rise both in the United States and worldwide, the ability to recognize and manage postoperative upper gastrointestinal symptoms, such as marginal ulcers, is imperative. This requires a close

partnership with our gastroenterology colleagues who must possess familiarity with the gastric bypass patient anatomy and the expertise to recognize and manage these patients' unique postoperative complications. Likewise, it requires a high index of suspicion and recognition of failed medical management such that patients suffering with intractable ulcers undergo appropriate surgical treatment without any unnecessary delays.

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FUNDING:

The authors have no financial disclosures relevant to the content of this article.

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