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Marginal ulceration after laparoscopic gastric bypass: an analysis of predisposing factors in 260 patients

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Abstract
Background: Marginal ulceration after Roux-en-Y gastric bypass (RYGB) is diagnosed in 1% to 16% of patients. The factors predisposing patients to marginal ulceration are still unclear.
Methods: A total of 260 patients who underwent laparoscopic RYGB were retrospectively reviewed. Data regarding demographics, comorbidities, body mass index (BMI), *Helicobacter pylori* infection, gastrojejunal (GJ) anastomotic leaks, postoperative bleeding, operative time, type of suture material, and marginal ulcer formation were collected. Fisher's exact test was used for statistical analysis of discrete variables, and Student's *t*-test was used for continuous variables. Statistical significance was set at an alpha of 0.05.
Results: The overall marginal ulceration rate was 7%. Demographic data (age, gender distribution, BMI) did not differ significantly between patients who experienced marginal ulceration and those who did not ($p > 0.05$). Similarly, technical factors (choice of permanent or absorbable suture for the GJ anastomosis, attending as primary surgeon, robotic GJ, operative time, postoperative hematocrit drop) were not statistically different between the two groups ($p > 0.05$). Finally, the prevalence of comorbidities (diabetes, hypertension, obstructive sleep apnea, musculoskeletal complaints, dyslipidemia, gastroesophageal reflux disease [GERD] and peptic ulcer disease [PUD]) did not differ significantly between the two groups ($p > 0.05$). However, preoperative *H. pylori* infection, although adequately treated, was twice as common among the patients who had marginal ulceration (32%) as among those who did not (12%) ($p = 0.02$). All the patients who experienced marginal ulcers had complete resolution of symptoms with proton pump inhibitors and sucralfate. No reoperations were required for marginal ulceration.
Conclusion: Helicobacter pylori may potentiate marginal ulcer formation. The authors hypothesize that *H. pylori* damages the mucosal barrier in a way that persists postoperatively, which may precipitate marginal ulceration even when the organism has been medically eradicated.

Key words: Anastomotic ulcer — Bariatric — Gastric bypass — *Helicobacter pylori* — Laparoscopy — Marginal ulcer — Obesity

Obesity is an epidemic on the rise in the United States and the world [28, 38, 39]. Currently, the most effective means of weight loss and long-term weight loss maintenance is bariatric surgery [19, 25, 37]. In the United States, Roux-en-Y gastric bypass (RYGB) is the most commonly performed bariatric operation [1, 11, 32]. Whether open or laparoscopic, RYGB has been associated with excellent surgical outcomes and low complication rates [1].

Marginal ulceration remains a morbid complication of RYGB, occurring in 1% to 16% of patients [9, 17, 30, 31]. Although the mechanisms underlying the development of marginal ulceration have not been completely elucidated, the etiology of this complication is likely to be multifactorial. We set out to identify patient or technique-specific factors that may predispose to marginal ulcer formation after laparoscopic RYGB.

Materials and methods

Between January 2004 and July 2005, 260 patients underwent laparoscopic RYGB at the University of California, Davis Medical Center. These patients had surgery consecutively, and no patient was excluded from the analysis.

Our technique for laparoscopic RYGB includes a side-to-side GIA-stapled jejunojejunostomy with a retrocolic, retrogastric alimentary

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Table 1. Multivariable comparison of the two experimental groups

	Non-MU	MU	*p* Value
Demographics			
Mean age (years)	42	40	NS
Male (%)	10	11	NS
Mean BMI (kg/m^2)	44	45	NS
Comorbidities (%)			
Diabetes	23	16	0.6
Hypertension	49	37	0.4
Obstructive sleep apnea	50	37	0.3
Musculoskeletal disorder	79	74	0.6
Dyslipidemia	42	37	0.8
GERD	49	53	0.8
GERD requiring medication	53	30	0.1
PUD	3	0	1.0
Technical			
Permanent suture (%)	53	47	0.8
Absorbable suture (%)	47	53	0.8
Attending as primary surgeon (%)	22	11	0.4
Robotic GJ (5)	22	5	0.1
Mean OR time (min)	178	172	0.5
Positive leak test (%)	9	16	0.4
Hct drop (%)	7	5	1.0
H. pylori (%)	12	32	0.02

MU, marginal ulceration; NS, not significant; BMI, body mass index; GERD, gastroesophageal reflux disease; PUD, peptic ulcer disease; GJ, gastrojejunostomy; OR, operating room; Hct, hematocrit

limb and closure of all mesenteric defects. The gastrojejunostomy (GJ) is a two-layer anastomosis. The inner layer consists of a GIA-stapled side-to-side posterior row with a running sewn gastroenterotomy closure, whereas the outer layer is hand-sewn circumferentially. The GJ is routinely tested for leak with endoscopic insufflation.

Data were collected under approval from the institutional review board. For each patient, we collected data regarding demographics (age, gender, preoperative body mass index [BMI]), the presence of medical comorbidities (diabetes mellitus, hypertension, obstructive sleep apnea, musculoskeletal complaints, dyslipidemia, gastroesophageal reflux disease [GERD], peptic ulcer disease [PUD]), technical factors (choice of permanent or absorbable suture for the inner layer of the GJ, attending as primary surgeon, robotic GJ, operative time, postoperative hematocrit drop), and preoperative *Helicobacter pylori* infection.

Helicobacter pylori was diagnosed by a commercial enzyme-linked immunoassay (ELISA) serum assay (Diamedix Inc, Miami, FL, USA) with a sensitivity of 98% and a specificity of 94%. Marginal ulcers were diagnosed by upper endoscopy (EGD). Postoperative EGD was performed for all patients with epigastric pain, persistent nausea and vomiting, or gastrointestinal hemorrhage. At the time of the study, all the patients were postoperatively prescribed 3 months of H_2-blocker therapy.

Fisher's exact test was used for statistical analysis of discrete variables, and Student's *t*-test was used for continuous variables. Statistical significance was set at an alpha of 0.05 for all analyses.

Results

Among the 260 patients, the average age was 42 years and the average BMI was 44 kg/m^2. The patients were predominantly female (90%). There were no significant differences in demographics between the two study groups (marginal ulceration vs no marginal ulceration) (Table 1).

The overall mean follow-up period was 10.2 months. The mean follow-up period was 10 months for the no marginal ulceration group and 12 months for the marginal ulceration group ($p = 0.2$, nonsignificant difference). Overall, marginal ulcers developed in 19 (7%) of the 260 patients. The mean time to onset of marginal ulceration symptoms after surgery was 4.3 months (range, 1–12 months) (Fig. 1). Epigastric pain was the most common presenting symptom, occurring in 89% of the patients and as the only symptom in 47% of these patients. Nausea, with or without vomiting, developed in 42% of patients, whereas only 21% experienced bleeding from their ulcers.

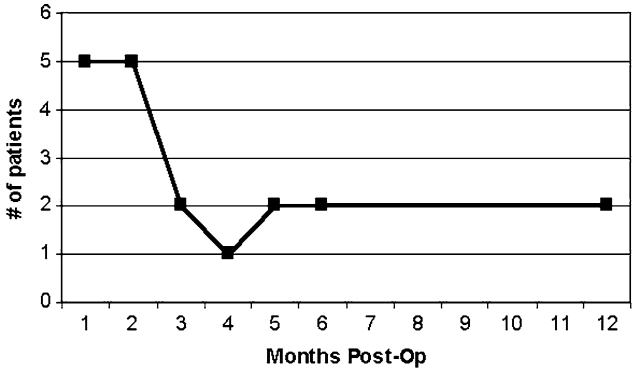

Fig. 1. Incidence of marginal ulcers over time.

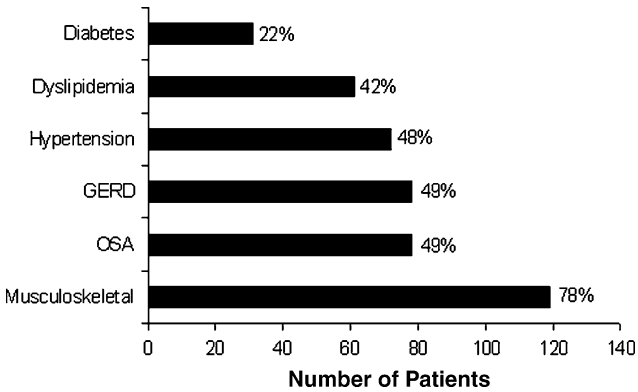

Fig. 2. Comorbidity profile of patient population. GERD, gastroesophageal reflux disease; OSA, obstructive sleep apnea

The comorbidity profile of our population is summarized in Fig 2. There were no statistical differences in the prevalence of any comorbidity between the two groups (Table 1). Notably, there was no difference in the prevalence of GERD ($p = 0.8$), GERD requiring medical treatment ($p = 0.1$), or history of PUD ($p = 1.0$).

Technical factors also were similar between the two groups. The mean operative time and postoperative hematocrit drop were not significantly different. Similarly, there were no significant differences when the GJ was constructed with the surgical robot or when the attending was the primary surgeon. The prevalence of intraoperative GJ leaks, all subjected to repair, was not significantly different between the groups. During the study period, the suture material used for the inner layer of the GJ anastomosis was changed from permanent to absorbable suture. For the first 136 cases, permanent suture was used, and for the subsequent 124 cases,

absorbable suture was used. The marginal ulceration rate was 7% (9/136) in the permanent suture group and 8% (10/124) in the absorbable suture group ($p = 0.8$, nonsignificant difference).

Of the 19 patients with marginal ulceration, 6 (32%) were seropositive for *H. pylori* antibody preoperatively. In contrast, only 12% of the patients without marginal ulceration were found to have preoperative *H. pylori* infection (88% of the patients without marginal ulceration were tested for *H. pylori* preoperatively). The higher rate of preoperative *H. pylori* infection among patients who experienced marginal ulcers was statistically significant ($p = 0.02$). All the patients found to have *H. pylori* infections were treated preoperatively with a standard 2-week course of antibiotics and proton pump inhibitors.

Overall, 68% of the patients in whom marginal ulceration developed were checked postoperatively for *H. pylori*, and none had positive test results. Specifically, 50% of the patients who were seropositive for *H. pylori* preoperatively and had marginal ulceration were rechecked for the organism postoperatively by EGD, and none showed positive test results. Suture remnants were visible in 32% of the ulcer beds on EGD (44% of the cases with permanent suture and 20% of the cases with absorbable suture used for the GJ; $p = 0.3$, nonsignificant difference).

Preoperative EGD was selectively performed for 36% of the patients for various clinical indications. Among the patients who did not experience ulcers, 38% had gastritis, 8% had healed ulcers from previous PUD, and 4% had Barrett's esophagus. Of the patients in whom marginal ulceration developed, 26% underwent a preoperative EGD. This test showed gastritis in 80% of these patients. No patient who experienced marginal ulceration had preoperative PUD or Barrett's esophagus. All the patients with gastritis diagnosed by EGD were treated with proton pump inhibitors preoperatively. The rate of gastritis shown on preoperative EGD was not significantly different between the two groups ($p = 0.15$).

We were able to define the nonsteroidal antiinflammatory drug (NSAID) usage among the patients who experienced marginal ulceration. Only one patient took NSAIDs postoperatively, despite a directive to avoid such medications. Another patient required NSAIDs up to the time of surgery, but did not need them postoperatively. Thus, only 2 (11%) of the 19 patients in whom marginal ulcers developed had documented NSAID use.

All the patients who experienced marginal ulceration had complete resolution of their symptoms with proton pump inhibitors and sucralfate. No reoperations were required for marginal ulcers.

Discussion

Marginal ulceration is a significant complication of Roux-en-Y gastric bypass. This phenomenon has been recognized and studied since the advent of the procedure. Several factors, including gastric acid, foreign body reaction, exogenous substances, and *H. pylori* infection, have been implicated as potential etiologies of this complication.

Gastric acid

It is hypothesized that peptic digestion of the unprotected jejunal mucosa leads to marginal ulceration and that this process is augmented by the secretion of gastric acid from parietal cells within the gastric pouch. Initially, large pouch size (> 50 ml) was thought to predispose patients to marginal ulceration [24]. The larger parietal cell mass in the pouch was thought to create a higher volume of gastric acid, with less of this acid passed into the antrum and duodenum. Thus, it was proposed that the decrease in inhibitory feedback to antral G-cells upregulated gastrin and, thereby, gastric acid secretion [23, 24]. Indeed, reducing the size of the gastric pouch has been shown to decrease the incidence of marginal ulcers [27].

The orientation of the gastric pouch also has been hypothesized to play a role in acid secretion and the formation of marginal ulceration. The lesser curvature, with its high concentration of parietal cells, may lead to marginal ulceration if too much of the magenstrasse is included in the pouch [4, 14, 18]. Sapala et al. [31] found that creating a pouch limited to the cardia resulted in a 0.01% marginal ulceration rate at 1 year among 173 patients.

Staple line disruption, with resultant gastrogastric fistula, is yet another phenomenon that ultimately results in increased acid in the gastric pouch. Staple line dehiscence is seen primarily when the pouch is created by an undivided staple line through the proximal stomach [4, 5, 8]. Clearly, once a connection between the gastric remnant and the pouch is established, the jejunal mucosa is exposed to a greater volume of low-pH fluid. Several studies have now demonstrated that by separating the remnant stomach from the gastric pouch, as commonly performed in current bariatric surgery, the incidence of marginal ulceration can be lowered [4, 12, 21].

However, a central role for gastric acid in the development of marginal ulceration has been challenged by several studies that have found a virtual absence of acid secretion within the gastric pouch after gastric bypass [2, 21, 24, 35]. Yet, this significant decrease in acid secretion after gastric bypass may not be universal. Mason et al. [24] found that although gastric acid secretion is nearly absent in most patients after gastric bypass, 43% of their patients had a low pH within the pouch. Additionally, serum gastrin levels were found to be universally low after gastric bypass [24]. Thus, it was postulated that gastric acid secretion is primarily driven by gastrin in most obese patients, but that in patients who continue to have low gastric pH after surgery, vagal innervation may dominate acid secretion. Such patients were found to be at higher risk for marginal ulcers. Further investigations supported the findings of increased acid production [18] and prolonged duration of low gastric pH (< 4) [16] after gastric bypass among patients who experienced marginal ulceration.

Thus, gastric acid seems to predispose patients to the development of marginal ulcers. This is further supported by evidence that acid suppression alone is effective in healing marginal ulcers [6, 10, 15, 16, 18, 26].

Foreign body

The foreign body (staples or suture material) used to construct the GJ has been hypothesized to cause an inflammatory reaction and lead to ulcer formation. Capella et al. [5, 6] decreased the marginal ulcer rate from 5.1% to 1.5% by switching from a stapled to a hand-sewn GJ, with absorbable suture used for the inner layer and permanent suture for the outer layer. The marginal ulceration rate further decreased to 0.4% when absorbable suture was used for both layers [6]. In a study of 3,285 patients, the marginal ulceration rate was significantly higher when the inner row of the GJ was constructed with permanent suture (2.6%) rather than absorbable suture (1.3%) [29]. We did not find a change in marginal ulceration rate when the type of suture used for the GJ was changed.

Exogenous substances

In the general population, NSAIDs have clearly been shown to cause gastric ulcers. In the context of marginal ulceration after gastric bypass, NSAIDs are believed to predispose patients to this complication [17], but a direct correlation has not been conclusively defined, especially among symptomatic patients [3]. Only 11% of our patients in whom marginal ulcers developed reported NSAID use. Smoking also may predispose patients to the development of marginal ulceration [3, 34]. Only one of our patients with marginal ulceration admitted to smoking. This patient also used NSAIDs.

Helicobacter pylori

Helicobacter pylori has been implicated as a possible causative agent in the formation of marginal ulcers after gastric bypass [7]. Findings have shown marginal ulceration to be less common among patients preoperatively screened and treated for *H. pylori* than among patients who were not screened, and thus not treated [33].

In our series, we found that marginal ulceration was significantly more common among patients infected with *H. pylori* preoperatively, even when adequately treated before gastric bypass. Furthermore, none of the patients who experienced marginal ulceration and were tested for *H. pylori* postoperatively had evidence of ongoing infection. Other investigators also have reported this lack of correlation between postoperative *H. pylori* infection and marginal ulceration [22, 34].

The actual mechanisms of *H. pylori* pathogenesis still are under active investigation. However, it seems clear that *H. pylori* incites a cytokine-mediated inflammatory response, which leads to gastritis, intestinal metaplasia, and ultimately ulcer formation [36]. Chronic gastritis and intestinal metaplasia slowly regress after *H. pylori* eradication, often taking more than a year to resolve [13, 20].

Our data suggest that a history of *H. pylori* infection may predispose to marginal ulcer formation after gastric bypass. Our mean follow-up period of 10 months is certainly sufficient to have identified the vast majority of the ulcers, which tend to occur within the first 2 to 3 months after gastric bypass and are rare (0.5%) after 6 months from surgery [16, 26, 30]. Certainly, the ideal method for screening patients to detect marginal ulceration would be routine EGD for all postoperative patients. Because this approach is impractical, we use EGD selectively on the basis of patient symptoms. This limitation, shared by other investigators who have studied marginal ulceration, may underestimate the true incidence of this postoperative complication.

Two pieces of data emerge from our study. First, we present evidence of an association between preoperative *H. pylori* infection and marginal ulceration. Second, there is a well-documented absence of *H. pylori* postoperatively among marginal ulceration patients. We thus postulate that anastomotic ulcer formation after gastric bypass may be potentiated by preoperative injury to the gastric mucosa induced by *H. pylori* infection, even in the absence of ongoing infection by the organism postoperatively.

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