ORIGINAL ARTICLE

Anastomotic Stricture Formation after Roux-En-Y Gastric Bypass Surgery: A Single Center Retrospective Cohort Study

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ABSTRACT

AIM: Roux-en-Y gastric bypass is used for treating medically-complicated obesity. Gastrojejunal anastomotic stricture is a common complication reported in 3% to 27% of these patients. The pathogenesis of postoperative strictures is not well understood, but ischemia has been hypothesized as a major cause. The aim of this study was to evaluate potential factors that could increase the risk of a post-operative anastomotic stricture.

METHODS: The records of 165 patients who had gastric bypass from June 2006 to March 2011 were reviewed. Demographics, co-morbidities, smoking status, surgical approach, medication use, and H. pylori status were noted, as well as a diagnosis of gastrojejunal stricture and/or marginal ulceration.

RESULTS: Thirty-four symptomatic patients (21%) developed gastrojejunal stricture, while 26 patients (16%) developed marginal ulceration. The majority were women (89%) with a mean age of 43 years and mean body mass index of 51 kg/m². Caucasians were at a higher risk for developing a stricture. Proton pump inhibitor use and marginal ulceration were significantly associated with risk of stricture, and there was a strong trend in patients with obstructive sleep apnea. Post-operative strictures were successfully treated with an average of two dilation sessions using an endoscopic through-the-scope balloon dilator.

CONCLUSION: After gastric bypass, proton pump inhibitor use and marginal ulceration were associated with anastomotic stricture formation. Strictures were more common in Caucasians. A trend towards an increased risk of strictures in patients with sleep apnea was observed, supporting the role of ischemia. Endoscopic balloon dilation relieved symptoms in all patients.

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Key words: Obesity; Bariatric surgery; Gastric bypass surgery; Gastrojejunostomy; Anastomotic stricture; Endoscopy

INTRODUCTION

Obesity has become a global health epidemic leading to a tremendous social and economic burden on healthcare. The prevalence of obesity in the United States had risen by 2009-2010 to include 35.5% of adult men and 35.8% of adult women[1]. Unfortunately, the medical management of obesity by weight loss programs has not achieved sustainable goals for the treatment of medically-complicated obesity[2].

Bariatric surgery has rapidly become a viable therapy for the management of obesity and its medical complications[3]. An estimated 220,000 bariatric surgical procedures are performed yearly in the US and Canada[4]. Among the bariatric surgical procedures, Roux-en-Y gastric bypass (RYGB) is the most common worldwide bariatric procedure, comprising 46.6% of all bariatric surgical procedures[5]. Both open and laparoscopic RYGB are performed for surgical management of medically-complicated obesity. The benefit of using a surgical approach to weight reduction in patients with medically complicated obesity is supported by data from a 7-year prospective study in which there was a 40% decrease in long-term mortality in patients who underwent RYGB compared with a control group.

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group who received non operative medical therapy

Despite proven benefits in the management of obesity, RYGB is associated with multiple symptoms, complications, nutritional deficiencies and medical disorders post-operatively[3]. The most commonly reported complications that occur in patients after RYGB include marginal ulceration, gastrojejunal (GJ) anastomotic stricture and anastomotic leak.

The incidence of GJ stricture following RYGB has been reported to range from 3 to 27%[10]. Intraoperative factors such as surgeon experience, surgical technique, tension at the anastomosis, foreign body reaction have been suggested to predispose to stricture formation[11-13]. Preoperative factors that have been suggested to predispose to stricture formation include age, sleep apnea, hypertension and gastroesophageal reflux (GERD)[8,14]. The surgical literature has focused on surgical factors that may result in anastomotic stricture formation. These surgical technique issues may be more important for early stricture formation, but are less likely to help in understanding the pathophysiology of many later post-operative anastomotic strictures.

As an additional potential non-surgical factor, gastric pouch acid secretion has been proposed in older literature as a mechanism for ulceration and potentially stricture formation at the GJ anastomosis after RYGB[16-19]. However, subsequent studies reported that the acid suppressive therapy had no significant effect on stomal stenosis or ulceration[6,20-22]. By contrast, other studies have suggested that proton pump inhibitor (PPI) therapy following gastric bypass surgery may either prevent or treat marginal ulcers[23-25]. Hence, it has become a common practice to use PPIs prophylactically after RYGB to reduce the risk of marginal ulcer formation. However, based on the above contradictory studies[6,20-22,23-25], the role of PPIs and gastric acid in stricture formation after RYGB remains controversial.

With the increasing number of patients undergoing bariatric surgery for treatment of medically-complicated obesity, gastroenterologists are increasing being asked to see bariatric patients to prevent and treat post-operative complications. There is inconclusive evidence concerning the risk factors that are important for post-operative development of gastrojejunal strictures in RYGB patients. Based on the above prior studies, we hypothesized that ischemia would be a major cause of post-operative gastrojejunal stricture formation. Therefore, the primary aim of this study was to evaluate the association between endoscopically diagnosed GJ strictures and potential predictive factors. The secondary aim of this present study was to examine the outcomes of endoscopic management of GJ strictures.

METHODS

This is a retrospective cohort study of 165 patients who underwent RYGB from June 2006 to March 2011 at a large, urban teaching hospital. This study was performed after obtaining Internal Review Board (IRB) approval on February 27, 2012 from Authors’ Institution. All RYGB surgeries were performed at Authors’ Institution. Patients who underwent open RYGB, laparoscopic RYGB, and revision of RYGB were included in this study.

Authors’ institution has a joint medical-surgical clinic staffed both by a dedicated gastroenterologist as well as by bariatric surgeons. Patients were seen by bariatric gastroenterology for a group of post-operative symptoms that included abdominal pain, nausea, vomiting, heartburn, early satiety, dysphagia and dyspepsia. Conventional upper endoscopy was performed in all symptomatic patients by a single gastroenterologist using a standard Olympus GIF-1803 Adult Gastroscope. Marginal ulceration was defined as a mucosal disruption of any depth occurring distal to the gastrojejunal anastomosis in the common channel. Anastomotic stricture was defined as an inability to pass or significant resistance to the passage of the Olympus Adult Gastroscope through the gastrojejunal anastomosis, and this complication was diagnosed only by upper endoscopy. Gastrojejunal strictures were treated with endoscopic pneumatic dilation using a through-the-scope Olympus CRE single use esophageal balloon dilator with balloon inflation of 10 to 18 mm for 1 minute. One patient required 9 dilations for recurrent symptoms and recurrent GJ stricture; triamcinolone was injected submucosally (10 mg in each of four quadrants), using a published protocol[26], with subsequent symptomatic improvement.

A chart review was conducted to determine the endoscopic findings including the presence of or absence of an anastomotic stricture and marginal ulceration, and to record potential predictive factors. We also recorded the outcomes of endoscopic management of GJ anastomotic strictures. Exposure to a non-steroidal anti-inflammatory drug (NSAID) or to a PPI was considered to be present if the medication was being used both at the time of surgery and at the time of upper endoscopy. The presence or absence of gastroesophageal reflux (GERD) was also recorded. All patients had been instructed to quit smoking and smoking cessation was confirmed prior to RYGB surgery; smoking (≥1 cigarette/day) was therefore considered to be present only if it was noted at the time of the upper endoscopy. Additionally, patient demographics (age, gender, ethnicity, and body mass index or BMI) and information with regards to co-morbidities were also recorded.

Statistical analysis was performed using standardized STATA software (Stata Corp, Texas). Univariate analysis was performed using Chi-square test with Yates correction or Fisher’s exact test for discrete variables and student’s T test as appropriate. A potential association between BMI and GJ stricture was assessed using Wilcoxon rank-sum test. When multiple factors were significantly associated with a dichotomous outcome, stepwise multiple logistic regressions were used to develop a multivariate model. The confounding factor was also corrected for the variables in logistic regression. The results were reported as adjusted odds ratios (AOR) and 95% confidence intervals (CI). A P value of less than 0.05 was considered to be statistically significant.

RESULTS

A total of 165 individuals underwent RYGB: 80 laparoscopic (49%), 64 open (39%) and 13 revisional (7.8%). The mean age of these patients was 43.4 years (SD=9.8), while the mean body mass index was 51 kg/m² (SD=10.7). Among these 165 subjects, 89% of the patients were women and the majority of the subjects were African-American (71.5%) followed by non-Hispanic Caucasians (24.2%) (Table 1).

Thirty four symptomatic patients (20.6%) developed GJ strictures. This patient group included 28 women and 6 men with a mean age of 37.5 to 81.5 kg/m² (range 46.5 years (range 27 to 62 years) and a mean BMI of 50 kg/m² (range 37.5 to 81.5 kg/m²).

As shown in table 2, Black Americans developed fewer strictures compared to Caucasians (12.7% vs. 37.5%, AOR 0.28, 95% CI 0.11-0.72). Older individuals were more likely to develop a GJ stricture (AOR 1.04, 95% CI 1.01-1.08). There was no significant difference with respect to gender or BMI. Additionally, there was no association between obesity-related co-morbidities and the rates of GJ stricture when examining diabetes mellitus, hypertension, coronary artery disease and gastroesophageal reflux (Table 2). NSAIDs use (with or without aspirin) and a history of gastric Helicobacter pylori infection were also not associated with GJ stricture (Table 2).
The frequency of strictures was significantly higher in patients who also developed marginal ulceration post-operatively compared to those who did not develop marginal ulceration (42% vs. 16.6%, OR 3.6, 95% CI 1.4-8.9). PPI use was also found to be an independent predictor for GJ stricture after adjusting for other significant variables in stepwise logistic regression (AOR 3.5, 95% CI 1.5-8.3) (Table 3). Patients with osteoarthritis showed an increasing trend toward stricture formation in multivariate model ($p=0.065$, AOR 2.2, 95% CI 0.95-5.22) (Table 3). The incidence of marginal ulceration in this present study was 15.75% (26/165). About 11 of 34 strictures had an associated ulcer identified at endoscopy. The occurrence of marginal ulceration, Caucasian race, sleep apnea, and older patient age as risk factors for the development of GJ strictures after RYGB surgery. It is difficult from the present results to be certain whether pre-operative factors that are important in GJ stricture formation after RYGB include: patient age, sleep apnea, hypertension, and gastroesophageal reflux. The results of our present study support the importance of PPI use, marginal ulceration, Caucasian race, sleep apnea, and older patient age as risk factors for the development of GJ strictures after RYGB surgery. It is difficult from the present results to be certain whether pre-operative eradication therapy for gastric Helicobacter pylori reduced the risk of post-operative GJ stricture formation.

DISCUSSION

Gastrojejunal anastomotic stricture formation is a relatively frequent post-operative complication after RYGB surgery\[10\]. In this present study, the rate of GJ stricture formation (21%) was comparable to previously published results\[11\].

Previous studies suggested\[9,14\] that pre-operative factors that are important in GJ stricture formation after RYGB include: patient age, sleep apnea, hypertension, and gastroesophageal reflux. The results of our present study support the importance of PPI use, marginal ulceration, Caucasian race, sleep apnea, and older patient age as risk factors for the development of GJ strictures after RYGB surgery. It is difficult from the present results to be certain whether pre-operative eradication therapy for gastric Helicobacter pylori reduced the risk of post-operative GJ stricture formation.

After RYGB surgery for medically-complicated obesity in

Table 1 Baseline characteristics of the study population.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of subjects (% of 165 total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Caucasians</td>
<td>48 (24%)</td>
</tr>
<tr>
<td>Black Americans</td>
<td>118 (71%)</td>
</tr>
<tr>
<td>Proton Pump Inhibitor Use</td>
<td>18 (11%)</td>
</tr>
<tr>
<td>Marginal Ulceration</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Black Americans vs. Caucasians</td>
<td>15 (9) vs. 33 (20)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (6%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>23 (14%)</td>
</tr>
<tr>
<td>Gastroesophageal Reflux</td>
<td>10 (6%)</td>
</tr>
<tr>
<td>NSAID Use</td>
<td>11 (7%)</td>
</tr>
<tr>
<td>History of Helicobacter pylori</td>
<td>15 (9%)</td>
</tr>
</tbody>
</table>

Table 2 Independent predictive factors for gastrojejunal stricture formation in univariate analysis.

<table>
<thead>
<tr>
<th>Predictive factor</th>
<th>Stricture</th>
<th>No stricture</th>
<th>$p$ value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>Caucasians</td>
<td>15 (25)</td>
<td>0.001</td>
<td>0.24 (0.10-0.56)</td>
</tr>
<tr>
<td>Female</td>
<td>28 (19)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>7 (16)</td>
<td></td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>NSAID Use</td>
<td>2 (12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of H. pylori</td>
<td>2 (12)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Independent predictive factors for gastrojejunal stricture formation in multivariate logistic regression.

<table>
<thead>
<tr>
<th>Predictive factor</th>
<th>Adjusted odds ratio</th>
<th>$p$ value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>0.28</td>
<td>0.009</td>
<td>0.009</td>
</tr>
<tr>
<td>Proton Pump Inhibitor Use</td>
<td>3.48</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td>Marginal Ulceration</td>
<td>2.23</td>
<td>0.065</td>
<td>0.065</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Gender</td>
<td>1.7</td>
<td>0.87</td>
<td>0.87</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>1.0</td>
<td>0.87</td>
<td>0.87</td>
</tr>
</tbody>
</table>

our present study, marginal ulceration and PPI use significantly increased the risk of GJ stricture formation. These are interesting findings that partially contradict previously published studies describing the etiology of post-surgical stricture and ulceration following RYGB surgery. Multiple prior studies have suggested that mechanisms involved in post-operative stricture formation include the inflammatory response, ulceration caused by acid produced by parietal cells remaining in the neo-gastric pouch, ulceration due to ischemia, and other potential causes of ulceration, including NSAID therapy, smoking and alcohol consumption.[12,18,19,20,22]

The role of acid suppression has been widely studied for prevention of marginal ulceration and healing.[22-25] But the mechanism by which acid production increases the risk of stricture formation has been debated. The amount of acid production correlates with the size of the post-operative gastric pouch. Mason has demonstrated experimentally that a larger gastric pouch leads to a higher incidence of ulcer/stricture.[26] Sapala also reported higher rates of stenosis with increased gastric pouch acidity.[19]

By contrast, smaller gastric pouch sizes, even down to 15 mL or less, have produced rates of ulcer/stricture that parallel Mason’s original results with a 70 mL pouch[27-29]. In a study by Pope and associates, the two study groups were equally on acid suppressive therapy and ulcer/stricture after RYGB does not appear to be explained by acid injury.[29]. Similarly, Wilson et al.[22] reported that the risk of GJ stricture was not affected by PPI use. In our present study, 53% of individuals who were using PPIs developed GJ stricture compared to only 26% in the no stricture group (p=0.003). Since the association between GERD and PPI was significant, a correction factor was included in the multivariate analysis. Despite this, the overall risk of PPI use in stricture formation remained unchanged (p=0.014). This novel finding in our present study not only strengthens the existing evidence that post-operative stricture formation is independent of gastric pouch size and acid production, but also suggests that a non-acid mechanism, such as antioxidant production,[29] should be considered in evaluation of the pathogenesis of post-operative strictures.

Stricture formation was significantly associated with marginal ulceration (p=0.005) in our present study. Marginal ulceration is a more common finding than stomal stenosis among RYGB patients that undergo endoscopy occurring approximately at 27-52% and 4-19% respectively.[22,25] Marginal ulcers typically occur within 1 year of post-operative period.[22,25,26]

In our present study, the majority (76%) of GJ strictures occurred within 12 months after RYGB surgery. When the location of ulceration is at the GJ anastomosis, healing of the ulceration resulting in scar tissue formation could lead to a stricture. Surprisingly, marginal ulcer formation was not affected by PPI use in this present study. Higher rates of marginal ulcers were reported in studies with increased gastric pouch acidity[22,25,26]. Marginal ulceration and healing of the ulceration resulting within 12 months after RYGB surgery. Multiple prior studies have suggested that mechanisms involved in post-operative stricture formation include the inflammatory response, ulceration caused by acid produced by parietal cells remaining in the neo-gastric pouch, ulceration due to ischemia, and other potential causes of ulceration, including NSAID therapy, smoking and alcohol consumption.[12,18,19,20,22]

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In agreement with our present study, Perugini et al identified sleep apnea as predictive of the complication of GJ stricture[26]. A risk of ischemia secondary to hypoxemia in patients with sleep apnea may explain stricture formation of the GJ anastomosis.

In our present study, GJ strictures were also more frequent in patients with osteoarthritis; however, after adjusting for BMI, this was not a significant association (p=0.065). The statistical power of our current study may be inadequate to identify a statistically significant association for this particular disorder.

Studies on ethnicity differences in patients with stricture formation are sparse. Generally Caucasians are the dominant ethnicity undergoing bariatric surgery.[22,24] Our bariatric center serves more Black Americans than Caucasians. Interestingly, in our present study Black Americans developed fewer strictures compared to Caucasians (12.7% vs. 37.5% respectively). Ethnicity differences in GJ stricture formation could not be explained using the results from our present study. There is a possible role for confounding factors in further understanding this important finding. In one previous study, post-operative strictures were more common in Caucasian[29], in agreement with the results from our present study.

There has been an ongoing transformation of RYGB surgery to the laparoscopic approach[26]. Post-operative strictures have been reported to be more common in laparoscopic than open RYGB procedures[32,34] and vice versa[27]. Unlike previous studies, the risk of GJ stricture in our present study was not affected by a laparoscopic (antecolic-antegastric) or open (retrocolic-retrogastric) approach in this analysis. Higher rates of post-operative stricture have been reported with tension at the anastomosis (antecolic-antegastric approach)[12,20,38] Stricture formation also appears to be more frequently when the gastrojejunostomy is fashioned with a smaller circular stapler (21 vs. 25 mm), and when using reinforcement sutures to attempt to limit stomal expansion[9,10,13,39]. Upon considering these findings, tension at the anastomosis may be less important than stomal size in the development of this complication.

Although there is a definite proven benefit for performing RYGB surgery in morbidly obese patients[8], the occurrence of post-operative stricture often leads to significant morbidity in the form of upper gastrointestinal symptoms. Post-operative stricture sometimes poses a post-surgical challenge in management to gastroenterologists and surgeons[40]. Studies have shown that upper endoscopic balloon dilation is a safe and effective method to relieve GJ stricture-related symptoms[15,37,40], and endoscopic management of GJ strictures has been proven to be quite successful[15,37]. In our present study, all patients who developed strictures achieved symptomatic improvement by endoscopic dilation without requiring revisional surgery, irrespective of early (within 90 days) or late (>90 days) occurrence of GJ strictures after RYGB. Nearly 40% of our patients required just one dilation, and overall an average of two dilations was performed with symptomatic improvement. Our findings are consistent with those previously reported by Peifer and associates[37].

The narrow confidence intervals and low p values support our belief that the sample size was adequate for our present study. However, a limitation of this present study is that it is a retrospective analysis. A prospective trial in which comorbidities were not controlled would not be ethical, although a prospective trial involving the use of PPIs would be of value. We were very strict while recording the patients’ use of PPIs in order to minimize the over estimation of risk association by considering only those patients using PPIs both at the time of RYGB surgery and at the time of upper endoscopy. Evaluation of the medication history documented by our endoscopy nurses in preoperative notes also minimized missing patients’ medication use.

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