CHAPTER 3
Symptomatic marginal ulcer disease after Roux-en-Y gastric bypass; incidence, risk factors and management

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Abstract

Background: One of the long-term complications of laparoscopic Roux-and-Y gastric bypass (LRYGB) is the development of marginal ulcers (MU). The aim of the present study is to assess the incidence, risk factors, symptomatology and management of patients with symptomatic MU after LRYGB surgery.

Methods and patient selection: A consecutive series of patients who underwent a LRYGB from 2006 until 2011 were evaluated in this study. Signs of abdominal pain, pyrosis, nausea or other symptoms of ulcer disease were analysed. Acute symptoms of (perforated) MU such as severe abdominal pain, vomiting, melena and hematemesis were also collected. Patient baseline characteristics, medication and intoxications were recorded. Statistical analysis was performed to identify risk factors associated with MU.

Results: A total of 350 patients underwent a LRYGB. Minimal follow up was 24 months. Twenty-three patients (6.6%) developed a symptomatic MU of which four (1.1%) presented with perforation. Smoking, the use of corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) were significantly associated with the development of MU. Five out of 23 patients (22%) underwent surgery. All other patients could be treated conservatively.

Conclusion: Marginal ulcers occurred in 6.6% of the patients after a LRYGBP. Smoking, the use of corticosteroids and the use of NSAIDs were associated with an increased risk of MU. Most patients were managed conservatively.
Introduction

Morbid obesity is a major health problem in the Western World (1). Bariatric surgery offers the only long-lasting treatment with excellent effects on co-morbidity and weight loss (2). Laparoscopic Roux and Y gastric bypass (LRYGB) is currently the ‘gold standard’ weight reducing procedure because of its superior results in sustained weight loss and the reduction of diabetes and other co-morbidities. Nowadays, around 49% of bariatric procedures consist of LRYGB. This procedure has become relatively safe with acceptable short-term morbidity of 10% and a mortality around the 0.2% (2,3).

Several long-term complications can occur, even years after surgery. One of these complications is the development of an ulcer at the gastrojejunal anastomosis. These ulcers have been described as a marginal ulcer, ischemic ulcer or anastomotic ulcer. In the present study, it is referred to as marginal ulcer(s) (MU). In literature, the incidence of MU ranges between 0.6 and 16 percent, depending on the definition and screening method (in some centres patients undergo standard postoperative gastroscopy, in others only symptomatic patients are screened) (4-6).

The pathogenesis of MU remains unclear. The position and size of the gastric pouch (larger pouch, more acid production), the use of foreign suture material (non-absorbable suture material, staples) and tension at the anastomosis are all thought to contribute to development of MU (8-10). Other factors that seem to be associated with MU are diabetes, smoking, the use of anticoagulants and/or non-steroidal anti-inflammatory drugs (NSAID’s). Marginal ulcer tends to occur late after surgery. The influence of Helicobacter Pylori (H. Pylori) on MU is still unclear (5,11-14).

The usual symptoms of peptic ulcer disease are chronic abdominal pain, pyrosis, reflux and nausea. A considerable amount of the patients with MU present with these symptoms after LRYGB, however 28-61% have no symptoms at all (15-16). Sometimes massive bleeding or perforation develops without any preceding signs. Therefore, MU is a potentially life-threatening complication making early identification important (17-20).

The aim of the present study is to assess the incidence, symptoms and management of MU in a consecutive series of patients who underwent LRYGB surgery.
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Methods

An electronic database of consecutive patients undergoing bariatric surgery at the department of surgery, Sint Lucas Andreas Hospital, Amsterdam, the Netherlands was retrospectively reviewed. From January 2007 until August 2011, 350 patients underwent a LRYGB. Fifty-seven patients (16.3%) underwent a revisional operation. Fifty-five patients (96.5%) had an Adjustable Gastric Band (AGB) converted into a LRYGB and two patients (3.5%) a laparoscopic sleeve gastrectomy (LSG) into a LRYGB. Patients between 18-65 years of age with morbid obesity according to the IFSO criteria were included \(^{(2)}\). Minimal follow up was 24 months.

Pre-operative screening:

All patients underwent pre-operative screening, including physical examination (co morbidity, use of medication, body mass index (BMI) and abdominal circumference), psychological examination, screening for obstructive sleep apnoea and preoperative upper endoscopic evaluation. Patients were advised to quit smoking before surgery and if necessary NSAIDs were replaced by non-ulcerogenic analgetics (e.g. Tramadol or Paracetamol).

Surgical procedure:

A standardized LRYGB was performed by three experienced bariatric surgeons or under their direct supervision. In all but one patient the gastric bypass was laparoscopically completed. The one (0.3%) conversion to open procedure was because of adhesions that impaired sight. In case of a revisional operation, the procedure began with removal of the band followed by a direct revision into LRYGB. Pneumoperitoneum was obtained with a Veress needle inserted at Palmer’s point or with direct introduction with optical guidance. A total of five trocars were used. In all patients, the proximal jejunal limb was identified and the future site of the gastrojejunostomy (GJ) was “dry fitted” to assess if a tension free anastomosis was technically feasible. The pouch was created in the lesser curvature using 1 horizontal and 2-3 vertical firings of a 45 mm linear Endo-GIA Universal\(^{\text{TM}}\) stapler (Johnson and Johnson, Sommerville, NY, USA), resulting in a pouch size around the 30 ml. The Roux limb anastomosed in an antecolic, antegastric position. The GJ was stapled with 30 mm of the same 45 mm linear stapler. The anterior aspect of the GJ was closed using interrupted VICRYL 2.0 (Ethicon inc. a Johnson and Johnson Company, Sommerville, NY, USA) or V-loc\(^{\text{TM}}\) (Covidien, Dublin, Ireland). Subsequently 120-150 cm small bowel was measured after which the side

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to side jejuno-jejunostomy (JJ) was created with 45 mm of the same linear stapler (the anterior side was closed with absorbable suture material, as previously described). Finally, the connecting omega limb was divided with the stapler, completing the Roux-en-Y limb. Pneumatic testing of the GJ was used to verify the integrity of the anastomosis. The port a cath was removed in the case of a revisional procedure before the skin was closed. The operation time was documented and pouch size was estimated based on number of staplers used to create the pouch.

**Pouch size**
Pouch size was measured in retrospect counting the number of vertical firings of the endoscopic stapler. The number of horizontal firings was always one.

**Diagnosis of MU**
Upper endoscopy was used very liberate. All patients with upper abdominal pain, pyrosis, nausea and/or other gastric complaints were submitted to upper gastro-intestinal endoscopy.
All MU were diagnosed at endoscopy. Healing was checked with repeated endoscopy.

**Statistical Analysis**
All data were analysed using SPSS 18.0 for Windows (SPSS Inc. Chicago Illinois, USA). Age, gender, co-morbidities, intoxications, medication use and initial BMI were scored as possible predictors for MU as well as size of the pouch (number of staples used) and duration of operation. The Independent Students T- and Mann-Whitney U test were used to assess any statistical significance for continuous variables and the Chi-square/ Fishers exact test for the dichotomous variables. Logistic regression analysis was performed to determine any association between the significant risk factors. 2-sided P-values of less than 0.05 were considered significant.
Results

A total of 350 patients were included. The majority of patients were female, 276 (78.9%). The mean age at surgery was 44 years (range 18-66 years) and mean BMI was 45.6 kg/m² (range 31.9-68.7). There were no significant differences in baseline or operative characteristics between patients with and without marginal ulceration Table 1.

The mean follow-up for the total group was 41 months ranging from 24-71. The mean follow-up for the control group was 40 and for the MU group 44 (p = 0.2).

Patient characteristics

MU was diagnosed in 23 patients (6.6%). Patients with symptomatic MU were not statistically different in age (44.2 vs. 45.7 years, p = 0.51), pre-operative BMI (45.7 vs. 44.7 kg/m² p = 0.50), and pre-operative weight (134 vs. 131 kg p = 0.57) compared to patients without MU. More patients with MU were male (34.8 vs 20.2%) but this was not statistically significant (p= 0.11).

Eight of the 23 patients (34.8%) with MU, suffered from Diabetes Mellitus type II of which 3 were insulin depended at time of surgery. In the non-MU group there were 119 (36.4%) patients with Diabetes Mellitus type II, not insulin depended (p= 1.0).

Operative characteristics

The pouch was completed with a mean of 3.3 staples in the MU group versus 3.4 in the control group. In 2 (8.7%) patients in the MU group the anterior side of the anastomosis was completed with the V-locTM compared to 55 (16.8%) in the non-MU group. In all the other patients the anterior side was sutured with uninterrupted Vicryl 2.0. This was not statistical significant (p=0.4)

The mean operative time was 122 minutes (with a mean of 118 minutes in primary surgery and 146 minutes in revisional surgery). Mean duration of surgery in the MU group was 139 minutes compared to 121 in the patients without MU and did not differ significantly. Five of the ulcers occurred in patients who had undergone revisional surgery (21.7%) compared to 18 in the primary surgery group. This was not statistical significant (p= 0.56).
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Table 1: Univariate analysis of potential risk factors associated with MU

<table>
<thead>
<tr>
<th></th>
<th>No MU</th>
<th>MU</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 327</td>
<td>N = 23</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (range)</td>
<td>44.2 (19-67)</td>
<td>45.7 (25-64)</td>
<td>0.51</td>
</tr>
<tr>
<td>Female/male</td>
<td>261/66</td>
<td>15/8</td>
<td>0.11</td>
</tr>
<tr>
<td>Mean BMI (kg/m$^2$) (range)</td>
<td>45.7 (31.1-68.7)</td>
<td>44.7 (33.4-55.0)</td>
<td>0.50</td>
</tr>
<tr>
<td>Mean Weight (kg) (range)</td>
<td>134 (85-235)</td>
<td>131 (90-182)</td>
<td>0.57</td>
</tr>
<tr>
<td><strong>Surgical aspects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary surgery (primary/revision)</td>
<td>275/52 (15.9%)</td>
<td>18/5 (21.7%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Time of surgery (minutes) (range)</td>
<td>121 (44-267)</td>
<td>139 (65-218)</td>
<td>0.11</td>
</tr>
<tr>
<td>Number of staples used</td>
<td>3.39</td>
<td>3.34</td>
<td>0.75</td>
</tr>
<tr>
<td>V-loc$^3$ (v-loc/vicryl)</td>
<td>55/272 (16.8%)</td>
<td>2/21 (8.7%)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>119 (36.4%)</td>
<td>8 (3.8%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>87 (26.6%)</td>
<td>6 (26.1%)</td>
<td>1.0</td>
</tr>
<tr>
<td>GERD$^2$</td>
<td>141 (43.1%)</td>
<td>12 (52.2%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>148 (45.3%)</td>
<td>11 (47.8%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Gastritis</td>
<td>73 (22.3%)</td>
<td>3 (13.0%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>57 (17.4%)</td>
<td>6 (26.1%)</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Intoxications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>90 (27.5)</td>
<td>6 (26.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Nicotine</td>
<td>63 (19.3)</td>
<td>9 (39.1)</td>
<td>0.019</td>
</tr>
<tr>
<td>Anti-coagulation</td>
<td>21 (6.4)</td>
<td>2 (8.7)</td>
<td>0.66</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>31 (9.5)</td>
<td>7 (30.4)</td>
<td>0.007</td>
</tr>
<tr>
<td>NSAIDs$^3$</td>
<td>20 (6.1)</td>
<td>5 (21.7)</td>
<td>0.017</td>
</tr>
</tbody>
</table>

1 MU: Marginal ulcer
2 GERD: gastro-esophageal reflux disease
3 NSAIDs: non-steroidal inflammatory drugs

Presenting symptoms

Sixteen out of 23 patients (69.6%) presented with pyrosis and six patients (26.1%) with vomiting. Bleeding was the main symptom in two patients (8.7%). Four out of 23 (1.1%) patients had clinical signs (i.e. severe stomach pain, chills, fever, nausea, vomiting, tachycardia) of perforation. Five patients experienced two or more symptoms.
Medication history, substance abuse and smoking

Preoperatively six out of 23 patients (26.1%) with MU were regular alcohol consumers compared to 90 patients (27.5%) without MU ($p = 1.0$). Smoking was reported by nine (39%) patients with MU versus 63 (19.3%, $p = 0.019$) without MU. Anticoagulants were used by two (8.7%) vs 21 (6.4%, $p = 0.66$) patients. Seven (30.4%) patients used corticosteroids at the time of surgery compared to 31 (7.5%, $p = 0.007$) without MU and NSAID use prior to surgery was found in five (21.7%) patients versus 20 (6.1%, $p = 0.017$), respectively Table 1.

Table 2 shows the multivariate logistic regression analysis of the variables associated with MU. Smoking, the use of corticosteroids and NSAIDS at the time of surgery were independent statistical significant predictors for the development of postoperative marginal ulceration.

### Table 2: Logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
<th>Odd’s ratio</th>
<th>95% CI for Odd’s ratio</th>
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<tr>
<td>Corticosteroids</td>
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<td>4.46</td>
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<tr>
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<td>0.04</td>
<td>2.85</td>
<td>1.03 - 7.84</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>0.017</td>
<td>0.004</td>
<td>6.02</td>
<td>1.79 – 20.24</td>
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*NSAIDS: non-steroidal inflammatory drugs

*$OR$: odds ratio

*$includes all significant predictors

H. Pylori infection

The presence of *H. Pylori* infection when marginal ulcers were found was only tested in nine patients. All tested negative for *H. Pylori*. Two of the patients with MU had a history of *H. Pylori* infection prior to surgery and had undergone eradication therapy.

Ulcer characteristics

Nineteen patients had ulcers located exactly at the anastomosis. Four were situated near the gastrojejunostomy in the jejunum or the pouch. All ulcers were confirmed with upper gastrointestinal endoscopy. Four ulcers contained staples or suture material. The time between surgery and ulcer development ranged from one till 49 months. Eight (34.8%) patients developed ulcers within 3 months after surgery, two between 3 and 6 months and 12 after six months.

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Treatment

Conservative treatment was started in all patients who had MU with no signs of perforation or uncontrollable bleeding. Conservative treatment existed of PPI’s alone (26%) or combined with Sucralfate (Ulcogant®) (74%). Four patients who had a perforation underwent emergency laparoscopy. The perforations were oversewn with a vicryl 2.0 or V-loc, in one patient only a drain was placed. Abdominal drains were placed and/or an endoscopic feeding tube was placed in the alimentary limb in all patients. One patient who presented with massive bleeding underwent total revision of the anastomosis. A total of 5 (22%) patients underwent revisional surgery. Most ulcers healed within 3 months (74%). Healing was confirmed using upper gastrointestinal endoscopy after oversewing the perforation or after conservative therapy.

Discussion

The present study found that marginal ulcerations (MU) occurred in 6.6% of the patients after laparoscopic Roux en Y gastric bypass. The development of MU was associated with nicotine, NSAID and corticosteroid use. Approximately a quarter of all patients underwent surgery to manage the MU and the other patients could be managed conservatively.

The pathophysiology of MU is unknown and different mechanisms have been proposed. One hypothesis is that a larger pouch is associated with more gastrin producing cells and therefore the risk of the formation of marginal ulcers is higher. In the present group all pouches were created in the proximal part of the stomach as described by Capella et al (9). The authors also found that location and size of the pouch are of influence for the formation of marginal ulcers. Pouch size was about 20-30 ml. The present study found no significant difference in pouch size using the number of staples to quantify size of the pouch between patients with or without MU. However, the number of staples is an indication of the pouch size. Another hypothesis is that more complex operations are associated with a higher risk of MU formation. In the present study, operation time, and the number of revisional operations were not associated with the formation of MU.

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ischemia. Azagury et al. found a positive correlation between diabetes mellitus and MU. In the ulcer group, 72 percent suffered from DM and in the control group only 13 percent. However, D’Hondt et al. could not confirm this correlation (13, 14, 22). An association between DM and MU was not found in the present study.

In the present study, the incidence of symptomatic MU was around 6.6 percent. This is high compared to literature. However, the mean follow-up of 40.6 months is longer than in most studies. In the study of Garrido et al., patients underwent routine endoscopy after LRYGB and in 7.6% of the patients an ulcer was present (23).

In the present study, the use of corticosteroids was significantly associated with the development of MU. Most of the patients in bariatric surgery used corticosteroids as inhalation therapy for asthma or asthma-like symptoms (24). Although in general peptic ulcer disease corticosteroids are a rare cause of the ulcer, they do harm the gastric mucosa and cause different gastric conditions (25, 26).

Stopping smoking also reduced adverse events in the postoperative course attributable to smoking. In some centres patients are required to quit smoking prior to surgery (27). Nicotine is a significant risk factor for general peptic ulcers (28, 29).

The significant correlation between NSAID usage and MU found in this study has been previously reported (8, 11, 27). The actual amount of NSAIDs usage is hard to quantify because of possible over the counter usage. This also applies to the control group. All patients are advised not to use NSAIDs. If patients used NSAIDs preoperatively it was replaced with paracetamol and if necessary tramadol. In peptic ulcer disease, the association with NSAIDs is already proven (20– 23).

The prevalence of _H. Pylori_ infection in the preoperative workup is between 22.4 and 61.3 percent (24– 28). An infection with _H. Pylori_ was not routinely analysed in the patients with MU in the present study. In the patients tested, all tested negative. Most studies found no association between _H. Pylori_ and MU formation. More and more evidence suggest that a MU is formed by a different pathophysiology than a general peptic ulcer (14, 23, 27).

Almost 20% of the patients presented with suture material visible in the ulcer bed. Rasmussen et al. showed that in 32% of their patients, suture material was embedded that required endoscopic removal. If suture material was visible at endoscopy, it was removed.
The formation of MU decreased significantly when absorbable sutures were used (4;9;10). One study argued for standard postoperative upper endoscopy to remove suture material (38). Most of our patients presented with pyrosis as first symptom at the emergency room or outpatient clinic. Two studies, performing routine upper endoscopy showed that patients suffering from MU are often asymptomatic (16;39;40). Therefore, the real incidence of MU is hard to quantify when only symptomatic patients are examined.

Patients with MU are generally managed conservatively with PPI’s. Patients with more severe symptoms also receive sulcrafate® in addition to PPI’s. When bleeding is present, endoscopic treatment with clips or adrenaline injections can stop the bleeding. Retractable, perforated and uncontrollably bleeding ulcers require surgical management with revision of the anastomosis if endoscopic treatment has failed (18;30;41;42). The use of PPI’s as prophylactic therapy is not proven. Studies report varying results about the effectiveness of PPI prophylaxis but the incidence of MU in literature is of varies considerably, making analysis difficult. Overall there is a decrease of the incidence of MU in the group receiving PPI’s but follow up is limited (10;18;30;43-45).

Conclusion

Bariatric surgeons should be aware of the ulcerogenic potential of the LRYGB. Cessation of smoking and avoidance of NSAIDs is recommended. The use of corticosteroids should be minimized if possible.
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References


