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Marginal ulcer disease after bariatric gastric bypass surgery. Can chronic proton pump inhibitor therapy reduce it?

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Abstract

Background : Marginal ulcer disease after gastric bypass surgery for obesity is a common postoperative complication in the long-term. Postoperative prophylactic proton pump inhibitors (PPIs) are recommended for its prevention. However, there is no consensus on the ideal PPI, the daily dosage and the duration for this purpose. Aims : To analyse the incidence of marginal ulcer disease in patients undergoing gastric bypass surgery followed by chronic PPI therapy, and risk factors related to it. Material and methods : Observational, single-centre, retrospective study of patients who underwent bariatric gastric bypass surgery from 2017 to 2019, and with at least a 2-year follow-up. Univariate analysis was performed to identify possible risk factors for its development. Results : The marginal ulcer rate was 4.7% in a total sample of 85 patients. No risk factors were identified in the univariate analysis, although male gender showed a trend toward significance (p 0.063). Intensive PPI treatment was enough for ulcer healing in all cases. Conclusions : The marginal ulcer rate was low in patients following a chronic PPI therapy after gastric bypass. Moreover, all cases were of mild severity and intensification of PPI therapy was sufficient treatment for the healing of the ulcers

Keywords:

- Anastomotic ulcer disease
- Marginal ulcer disease
- Bariatric gastric bypass
- PPI therapy

Introduction

Obesity is an epidemic, multifactorial entity. Its incidence is increasing in developed countries, with a prevalence of 16% in 2020 in Spain (1). Although its treatment is multimodal, surgical treatment has shown the best results in the long-term, both in weight loss and in the improvement of conditions associated to metabolic syndrome. Roux-en-Y gastric bypass (RYGB) is still considered the gold standard technique (2). Marginal ulcer formation in the gastrojejunal anastomosis after gastric by-pass surgery involves a large part of the long-term morbidity associated to this technique, which can led to severe major complications such as acute gastrointestinal bleeding, anastomotic stenosis, intestinal perforation or leakage, requiring surgery for its treatment in some cases (3). Its incidence is around 1-16% (2). Some of the described factors associated to its formation include smoking, corticosteroid therapy, non-steroidal anti-inflammatory drugs (NSAIDs) intake and helicobacter pylori (HP) infection (2). On the contrary, prolonged therapy with PPIs after surgery has been described as a possible protective factor (2). In the absence of a worldwide consensus,In the literature, the time of postoperative PPI administration differs between 30 days to 2 years, some authors argue for lifelong usage (2). However, some studies have shown a decrease in the incidence of postoperative marginal ulcer disease by extending this treatment to 6 or even 12 months (2). Historically in our centre, following local protocols, patients who undergo bariatric gastric bypass surgery are chronically treated with PPIs (Omeprazol 20 mg per day). The main objective of this study is to analyse the incidence of ulcer disease in our cohort The secondary objectives are to analyse the possible risk factors for its development and to describe the treatment applied to patients diagnosed with marginal ulcer.

Materials and methods

This is a retrospective, observational and single-centre cohort study including patients above 18 years of age who underwent bariatric gastric bypass surgery between 2017 and 2019. Patients in whom revision surgery was performed and those who underwent restrictive techniques were excluded. Clinical, demographic and surgical variables were collected, in addition to short (three months after surgery)- and long-term (above 3 months) results with a minimum follow-up period of 2 years. Results are reported descriptively. Continuous data are presented as mean and standard deviation (SD) or median and interquartile range (IQR) according to the distribution of the variable. Categorical data are presented as frequency count (n) and/or percentage (%). For the univariate analysis of possible risk factors, non-parametric tests such as Fisher's and chi square tests were used when appropriate. Differences were considered significant at $p< 0.05$. A multivariate analysis was planned including the statistically significant risk factors identified in the univariate analysis. All the analysis was carried out using SPSS v.26 statistical software (IBM Corp., Armonk, NY, USA).

Results

In total, 85 patients underwent bariatric gastric bypass during the period of the study. Their baseline demographic and clinical characteristics are shown in Table 1. 71.8% of patients were women, with a median BMI of 44.08 (41.81-47.18) prior to bariatric surgery. Regarding analysed comorbidities, it is important to note that 47.1% of patients showed high blood pressure (HTA), 36.5% diabetes mellitus (DM), 45.9% obstructive sleep apnea syndrome (OSAS) and 58.8% nonalcoholic fatty liver disease (NAFLD) diagnosed by abdominal ultrasonography. In addition, 63.5% of patients was consdered of high anesthetic risk (ASA III) according to the American Society of Anesthesiologists (ASA) classification.

Table 1. Demographic and clinical characteristics of total sample (n= 85).

Gender **Male** **Female**	 24 (28.2%) 61 (71.8%)
Age (years)	47 (39.50-56)
Weight (kg)	120 (109-133.50)
BMI	44.08 (41.81-47.18)
HTA	40 (47.1%)
DM	31 (36.5%)
COPD	4 (4.7%)
OSAS	39 (45.9%)
Cardiovascular comorbidity	10 (11.8%)
NAFLD	50 (58.8%)
Previous abdominal surgery	26 (30.6%)
Smoker	11 (12.9%)
OH intake	26 (30.6%)
NSAIDs intake	13 (1 (5.3%)
Corticoid treatment	8 (9.4%)
OA intake	2 (2.4%)
PPI intake	31 (36.5%)
HP infection	22 (25.9%)
ASA classification risk **II** **III**	 31 (36.5%) 54 (63.5%)

SD: standard desviation; Kgr : kilograms; BMI : body mass index; AH HTA: arterial hypertension; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; OSAS: obstructive sleep apnea syndrome; NAFLD : nonalcoholic fatty liver disease; OH: alcohol (any intake); NSAIDs : non-steroidal anti-inflammatory drugs; OA : oral anticonceptives; PPI: protomp pump inhibitor; HP: helicobacter pylori; ASA : American Society of Anesthesiologists.

Surgical details and postoperative short-term results are shown in Table 2. Only one patient underwent one anastomosis gastric bypass (OAGB), while the rest of the patients underwent laparoscopic RYGB. Mechanical 25mm circular stapled gastrojejunal anastomosis (OrVil™ device, Medtronic, Minneapolis, MN, USA) was performed in 91.8% of cases, and in 83.50% of patients an alimentary limb of 150 cm or less was performed. In 90.60% of pacient a biliary limb of 60 cm was performed.

Table 2. Surgical details and postoperative short term complications (n= 85).

Type of surgery	
RYGB	84 (98.82 %)
OAGB	1 (1.17 %)
Type of anastomosis	
Gastrojejunal	
Circular stapled anastomosis	78 (91.8 %)
Handed end to side anastomosis	1 (1.17 %)
Stapled end to side anastomosis	5 (5.90 %)
Jejuno-jejunal	83 (100 %)
Stapled side-to-side anastomosis	
Alimentary limb lenght	
≤ 150 cm	71 (83.50 %)
>150 cm	14 (16.50 %)
Biliary limb lenght	
60 cm	90.60%
70 cm	1.2%
80 cm	1.2%
100cm	2.4%
150 cm	1.2%
Clavien-Dindo	
I	67 (78.80 %)
II	8 (9.4 %)
III	9 (10.6 %)
IV	1 (1.20 %)
V	0 (0%)
Postoperative bleeding	11 (12.94%)
Medical treatment	9 (10.6 %)
Endoscopic treatment	1 (1.2 %)
Urgent surgery	1 (1.2 %)
Anastomotic leak	3 (3.52%)
Non surgical approach	2 (2.4 %)
Surgical approach	1 (1.2 %)

RYGB: Roux en y gastric bypass; OAGB: one anastomosis gastric bypass.

Among the postoperative short-term complications, acute bleeding was the most common (12.94%), but only one patient (1.2%) required surgical treatment. The postoperative leak rate was 3.52%.

In regard of long-term complications (above 3 months after surgery) (Table 3), marginal ulcer rate was 4.70% being all of them diagnosed by gastroscopy. All of them were circular gastrointestinal and side-to-side jejuno-jejunal anastomosis performed. Regarding the related symptoms, while half of the patients described epigastralgia, the other half were diagnosed after an acute lower gastrointestinal bleeding. All of them were mild on severity and were successfully treated with an intensive course of PPIs during the acute episode (Omeprazol 80 mgr initial intravenous bolus followed by 40 mgr every 12 hours), not requiring surgery in any case. All cases experimented symptoms relief after the medical treatment, and the healing of the ulcer was confirmed by endoscopy in 50% of cases. Univariate analysis of different factors that could be related to anastomotic gastrojejunal ulcer formation was performed (Table 4), and none of the analysed factors showed a significant association with the marginal ulcer disease. However, male gender showed a trend toward significance (p 0.063). Given the absence of statistically significant risk factors in the univariate analysis, the multivariate analysis was not performed.

Table 3. Long term complications (N= 85).

Anastomotic ulcer	4 (4.70 %)
Time period between surgery and ulcer diagnosis (months)	24 (8.6-39.4) 4 (100 %)
Internal hernia	8 (9.41%)

Table 4. Risk factors associated with ulcer development in the gastrojejunal anastomosis (n= 85).

Risk factor	Anastomotic ulcer (N=4)	No anastomotic ulcer (N= 79)	P value
Gender Male	3 (75 %)	20 (25.31 %)	0.063
HTA	3 (75 %)	37 (46.8 %)	0.348
DM	3 (75 %)	27 (34.1 %)	0.132
COPD	1 (25 %)	3 (3.80 %)	0.182
OSAS	1 (25 %)	38 (48.1 %)	0.619
Cardiovascular comorbidity	1 (25 %)	9 (11.40 %)	0.408
NAFLD	2 (50 %)	47 (59.5 %)	0.612
Smoker	0 (0 %)	11 (13.9 %)	1
OH intake	2 (50 %)	23 (29.10 %)	0.587
NSAIDs	0 (0 %)	12 (15.2 %)	1
Corticoid treatment	1 (25 %)	7 (8.90 %)	0.339
OA intake	0 (0 %)	2 (2.5 %)	1
PPI before surgery	1 (25 %)	29 (36.7 %)	1
PPI after surgery	2 (50 %)	60 (75.90 %)	0.233
HP infection	0 (0 %)	22 (27.80 %)	1
ASA risk III	4 (100 %)	49 (62.0 %)	0.123

HTA: arterial hypertension; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; OSAS: obstructive sleep apnea syndrome; NAFLD: nonalcoholic fatty liver disease; OH: alcohol; NSAIDs : non-steroidal anti-inflammatory drugs; OA : oral anticonceptives; PPI: protomp pump inhibitor; HP : helicobacter pylori; ASA: American Society of Anesthesiologists.

Discussion

Gastric acidity is known as the cause of marginal ulcer formation after RYGB (2). A large gastric pouch including part of the antrum contains more parietal cells than a small one, which has been associated with an increase of marginal ulcer disease rate (1). Moreover, acidity in the gastric pouch is not buffered by the duodenum. Medical treatment based on acid suppression (PPIs) has led to its use as a prophylactic treatment (5), although the best type, dosage and duration of it is not well established. Kang et al (6) observed that increasing the duration of prophylaxis from 30 to 90 days after surgery showed a reduction of symptomatic marginal ulceration from 12.4% to 6.5%. Moreover, Baksi et al (7) proposed increasing the duration of prophylaxis from 6 to 12 months in their OAGB cohort. In our sample, compared to the incidence described on the literature (1-16%), the rate of anastomotic ulcer was low (4.7%) following a chronic postoperative PPI treatment, which may account for the low incidence rate. In the univariate analysis, no significant risk factors for ulcer formation were identified; the analysis could be underpowered due to the relatively small sample size (n=85) and the low rate of the analysed outcome (ulcer rate). However, it is worth of noting that, as the overall sample was mainly female (71.8%), 3 of the 4 patients who presented with ulcer were male, and it showed a trend towards significant association in the univariate analysis. Furthermore, none of the patients who developed ulcer disease required endoscopic or surgical treatment, and so the clinical severity of the disease in all cases was mild.

This study has several limitations. Firstly, it is a retrospective single-centre observational study, without a control group treated with different prophylactic strategy to compare. Secondly, the small overall sample and the small amount

of patients with the target variable underpowered the statistical analysis, and so risk factors associated to its development could not be identified. In addition, we do not perform regular endoscopy during the follow-up in our centre, and patients with asymptomatic ulcer disease could be undiagnosed. However, this study shows a low rate ulcer disease in patients treated with chronic PPI treatment after a follow up of at least two years. Further prospective and controlled studies are needed with larger samples and comparison groups to clarify if chronic PPI treatment could be the indicated prophylactic therapy for, at least, those patients at higher risk of ulcer disease development after bariatric gastric bypass surgery.

Conclusions

The rate of marginal ulcer in our sample was low (4.7%) and all cases were mild, successfully treated only with intensified PPI treatment. PPI therapy followed chronically after surgery could be related to it. Further studies are needed to identify patients at higher risk, and in whom chronic postoperative PPI therapy could be recommended.

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