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Original article

Acid-related complications after laparoscopic Roux-en-Y gastric bypass: risk factors and impact of proton pump inhibitors

Jeff Wennerlund, M.D.^{a,*}, Ulf Gunnarsson, M.D., Ph.D.^a, Karin Strigård, M.D., Ph.D.^a, Magnus Sundbom, M.D., Ph.D.^b

^aDepartment of Surgical and Perioperative Sciences, Surgery, Umeå University, Umeå, Sweden

^bDepartment of Surgical Sciences, Uppsala University, Uppsala, Sweden

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Abstract

Background: Laparoscopic Roux-en-Y (LRYGB) gastric bypass is an effective treatment for morbid obesity. Acid-related complications after LRYGB could be prevented by prophylactic proton pump inhibition (PPI).

Objective: To identify the effect of PPI prophylaxis on short-term, acid-related complications in a large cohort.

Setting: National Registry, Sweden.

Methods: A total of 37,301 patients who underwent LRYGB in Sweden from 2009 to 2014 were identified in the Scandinavian Obesity Surgery Registry. Patient-specific factors were cross matched with socioeconomic variables and information on PPI dispensation. A logistic regression model was used to analyze acid-related complications (e.g., marginal ulcer, stricture, and perforation) within 30 days and at 1 year postoperatively.

Results: PPI prophylaxis did not reduce the rate of acid-related complications. Instead, prolonged operation time (odds ratio [OR] 2.19 [1.53–3.13]) and immigrant background (OR 1.72 [1.17–2.53]) increased the risk of marginal ulcer within 30 days. At 1 year, medical treatment for diabetes (OR 1.75 [1.14–2.67]) and dyspepsia (OR 1.71 [1.06–2.75]), larger gastric pouch (OR 2.19 [1.528–3.248]), longer operation time (OR 1.67 [1.11–2.51]), smoking (OR 2.59 [1.77–3.78]), and immigrant background (OR 1.60 [1.08–2.36]) increased the risk for marginal ulcer, while older age (OR 2.20 [1.05–4.63]) predisposed for stricture. Inferior weight loss was associated with marginal ulcer at 1 year (OR 1.50 [1.04–2.15]).

Conclusion: PPI prophylaxis did not reduce the risk for marginal ulcer and stricture. The risk for these complications was increased by several co-morbidities, smoking, immigrant background, and surgical factors. Routine use of PPI prophylaxis cannot be recommended, but smoking cessation and optimal surgery could be important. (Surg Obes Relat Dis 2020;16:620–625.) © 2020 American Society for Bariatric Surgery. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Key words: Gastric bypass; Proton pump inhibition; Marginal ulcer; Stricture

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*Correspondence: Jeff Wennerlund, Department of Surgery, Lycksele Hospital, 92182 Lycksele, Sweden.

E-mail address: Jeff.Wennerlund@regionvasterbotten.se (J. Wennerlund).

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Obesity is a growing healthcare issue worldwide [1] and, in parallel, bariatric surgery has vastly increased since the turn of the millennium [2]. Laparoscopic Roux-en-Y gastric bypass (LRYGB) is an effective treatment for morbid obesity and diabetes [3–5]. LRYGB has been performed in increasing numbers in Sweden, and has a low mortality rate of <.02% [6]. Although LRYGB is a relatively safe surgical procedure, known complications can have a major impact on the individual patient.

The Scandinavian Obesity Surgery Registry (SOReg) is a national quality registry. Registry data reveal an overall complication rate of approximately 8% [6], and acid-related complications include marginal ulcer, stenosis, and perforation at the gastrojejunal anastomosis. Proton pump inhibitors (PPI) are widely used as treatment for ulcers and other acid-related conditions because of its acid-suppressing mechanism. PPI is also used as prophylaxis in various situations (e.g., long-term treatment with acetylsalicylic acid and major thoracic and abdominal surgery). Although many bariatric centers use PPI prophylaxis after LRYGB, there is no consensus or recommendation on dose or duration [7–9]. In a previous systematic review of 7 publications including 2114 patients, PPI prophylaxis reduced the risk for marginal ulcer by 50% [10], but others report contradicting results [9,11–15]. One circumstance where PPI prophylaxis could be of particular value is in the case of previous *Helicobacter pylori* infection [11].

This study aimed to determine if PPI prophylaxis is effective in reducing acid-related complications after LRYGB in a multiregistry epidemiologic study.

Methods

SOReg started in 2007 and now encompasses all 44 clinics that perform bariatric surgery in Sweden. Most centers in Norway have been affiliated in recent years [6]. From 2009 through 2014, 37,301 primary LRYGB procedures were identified in SOReg Sweden. Information from 2 other national registries provided socioeconomic data and information on dispensation of PPI from pharmacies. Statistics Sweden, a government agency that provides official statistics in many fields [16], matched socioeconomic data with information on PPI prescriptions from the Pharmaceutical Registry, kept by the National Board of Health and Welfare. This registry collects information on all prescriptions and sales to monitor amounts and trends in prescription drugs. All pharmacies that dispense prescription medication are, by law, obliged to report to the registry [17].

Baseline information was collected from SOReg, including sex, age, body mass index (BMI; kg/m²), presence of co-morbidity (type 2 diabetes, hypertension, dyspepsia, and sleep apnea), and smoking habit, the latter being a non-obligatory variable. The registry defines the presence of co-morbidity as a diagnosed medical condition that is under treatment. Surgical information included operative time

and total stapling length of the gastric pouch, as a surrogate for gastric pouch size. Postoperatively, information was collected at a 6-week follow-up (for 0–30 d) and at 1-year follow-up (31–365 d). This information included any complications, such as marginal ulcer, stricture, and perforation. Weight loss was reported in percentage of excess weight loss, as an indicator of quality and general compliance.

Statistics Sweden provided information on income, level of education, marital status, permanent mail address, and whether patients had domestic or immigrant background [16]. Urban addresses were selected from metropolitan areas with >100,000 inhabitants, or communities with a major hospital and at least 87,000 inhabitants [16]. The Pharmaceutical Registry provided details of PPI prescription and dispensation. To determine which patients had access to PPI postoperatively, operation date and pharmacy dispensation of PPI were cross-matched. The definition of having access to PPI for the purpose of prophylaxis was if the dispensation date was within 7 days before or 3 days after surgery. This was chosen to eliminate patients who suffered an early postoperative complication in hospital, and who were subsequently prescribed PPI as treatment for a specific complication, or those who were on treatment with PPI before surgery, defined as dyspepsia in SOReg. Extraction of data from SOReg was performed in September 2016 and the results were cross-matched and de-identified with an anonymous key identifier by Statistics Sweden.

The study was approved by the Regional Ethics Review Board in Umeå 1/12/2016, Dnr 2015/367-31. The study was registered at BioMed Central September 20, 2016 with reference number ISRCTN12963684.

Statistical methods

Data from the 3 sources were compiled into a Microsoft Access database (Redmond, WA, USA) using the anonymous key identifier. Logistic regression models were created with complication as dependent variable, and patient characteristics, follow-up variables, and PPI dispensation as independent variables. For early and later analyses, only those patients with complete smoking status were included. Analyses for univariate logistic regression were performed for each complication, and in cases of statistical significance ($P < .05$), multivariate analyses were also performed. All variables included in the multivariate analyses are presented in Tables 1 and 2. Statistical computations were performed in Statistica version 13 (StatSoft, Tulsa, OK, USA).

Results

Basic characteristics

The median age of the 37,301 cases was 41 years, median BMI was 41.4, and 75.8% were women. Patients lost to follow-up were 1.5% at 6 weeks, and 8.3% at 1 year. Smoking habit was not registered for 24.3% at baseline and 55.6% at

Table 1
Logistic regression analysis of variables that predispose for complications 0 to 30 days post LRYGB

	Odds ratio	95% confidence interval	P value
Marginal ulcer			
Hypertension	1.433	.974–2.108	.068
Diabetes	1.243	.795–1.945	.341
Operation time >63 min	2.189	1.534–3.126	<.000
Lower income	.991	.890–1.103	.870
No college education	.949	.883–1.021	.162
Immigrant background	1.721	1.170–2.531	.006
Stricture			
BMI	1.696	1.033–2.784	.038

LRYGB = laparoscopic Roux-en-Y gastric bypass; BMI = body mass index.

Multivariate analysis of significant univariate variables.

1 year. Table 3 summarizes the baseline variables, including co-morbidities, socioeconomic factors, and surgical data.

Early complications and risk factors

Marginal ulcer occurred in .5% (n = 175) within 30 days. Stenosis or stricture at the gastrojejunal anastomosis, sometimes associated with a marginal ulcer, was reported in .2% (n = 83). Nine of the cases with stricture also had a marginal ulcer. In the multivariate analyses, the risk of marginal ulcer increased with immigrant background (odds ratio [OR] 1.72 [1.17–2.53]) and long operation time (OR 2.19 [1.53–3.13]), while stricture was more common with higher baseline BMI (OR 1.70 [1.03–2.78]). The presence of PPI prophylaxis did not influence these early complications (Table 1).

Complications and risk factors at 1 year

At the 1-year follow-up (31–365 d), 340 marginal ulcers (.9%), 78 perforations (.2%), and 70 strictures (.2%) had occurred. Among the strictures, 22 had a

simultaneous marginal ulcer. In the multivariate analyses, the risk of marginal ulcer during the first postoperative year increased with diabetes (OR 1.75 [1.14–2.67]), dyspepsia (OR 1.71 [1.06–2.75]), smoking (OR 2.59 [1.77–3.78]), longer stapling length on the gastric pouch (OR 2.19 [1.53–3.25]), longer operation time (OR 1.67 [1.11–2.51]), and immigrant background (OR 1.60 [1.08–2.36]). Older age (OR 2.20 [1.05–4.63]) increased the risk for stricture. Poor weight loss (excess weight loss <81%) was also associated with marginal ulcer (OR 1.50 [1.04–2.15]) (Table 2).

Discussion

In this large national cohort, PPI prophylaxis did not protect against acid-related complications in contrast to previous studies [10]. The risk for these complications were instead increased by several co-morbidities, as well as demographic and surgical factors. Marginal ulcer at 1 year was also associated with poor weight loss.

Table 2
Logistic regression analysis of variables that predispose for complications 31 to 365 days after LRYGP

	Odds ratio	95% confidence interval	P value
Marginal ulcer			
Age >41 yr	1.352	.923–1.980	.122
Diabetes	1.746	1.143–2.668	.010
Dyspepsia	1.706	1.058–2.751	.028
Stapling length >150 mm	2.185	1.528–3.248	<.000
Operation time >63 min	1.667	1.108–2.510	.014
Smoking	2.586	1.768–3.782	<.000
Inferior weight loss, EWL* <81%	1.496	1.040–2.152	.030
Immigrant background	1.600	1.085–2.361	.018
Perforation			
Lower education	.895	.572–1.399	.626
Unmarried	1.216	.717–2.061	.469
Urban resident	.770	.443–1.338	.354
Stricture			
Age >41 yr	2.204	1.048–4.633	.037

LRYGP = laparoscopic Roux-en-Y gastric bypass; EWL = estimated weight loss.

Multivariate analysis of significant univariate variables.

* Percentage of excess weight exceeding BMI 25 kg/m² that was lost after surgery.

Table 3
Baseline demographic characteristics of primary laparoscopic Roux-en-Y gastric bypass (LRYGB) in Sweden 2009 to 2014

	Primary LRYGB (n = 37,301)	
Patient characteristics		
Sex	76% female (n = 28,278)	24% male (n = 9023)
Age, yr	41 (15–75)	
BMI, kg/m ²	41 (28–86)	
Co-morbidities		
Diabetes	14.2% (n = 5302)	
Hypertension	25.3% (n = 9458)	
Sleep apnea	9.9% (n = 3711)	
Dyspepsia (on PPI treatment)	9.7% (n = 3632)	
Socioeconomic factors		
Ethnic background	80% Swedish (n = 29,975)	20% immigrant (n = 7324)
College education	15.8% (study population)	25.7% (general population)
Marital status	32.3% married (n = 12,074)	
Urban/rural address	40.5% larger city (n = 15,117)	58.6% small town (n = 21,873)
Average yearly income 2011	\$21,119 (study population)	\$35,762 (general population)
Smoking	11.2% active (n = 4173)	12.6% previously (n = 4717)
Operative data		
Operation time, min	63, interquartile range 26–100	
Stapling length of gastric pouch, mm	150 (45–360)	
PPI retrieval within –7/+3 d of surgery	38.5% (n = 14,365)	
Excess weight loss*	36% at 6 wk	81% at 1 yr

BMI = body mass index; PPI = proton pump inhibitor.

Data presented as median (range) and percentage, respectively.

* Percentage of excess weight exceeding BMI 25 kg/m² that was lost after surgery.

Longer operation time was 1 of 2 significant risk factors for both early and later marginal ulcers. Prolonged operation time is probably indicative of less surgical experience and/or mishaps during surgery [6]. This points to suboptimal surgery as a risk factor for marginal ulcer [18,19], especially considering that longer stapling length more than doubled the risk for marginal ulcer at 1 year. This concurs with a recent paper on 14,168 primary LRYGB, where we demonstrated that the relative risk for marginal ulcer increased with the size of the gastric pouch (14% for each additional centimeter of stapling used for the gastric pouch [20]). These surgical factors represent important steps that the surgeon can take to reduce future complications.

The other significant factor for both early and later marginal ulcers was immigrant background, which poses an interesting challenge. As there is no obvious physiologic explanation, speculation could be made over a number of features that could be indicative of immigrants in Sweden. These could include higher *H. pylori* incidence, different cultural and eating habits, poor postoperative compliance, and patient delay. Smoking was a strong factor for developing marginal ulcer at 1 year in agreement with previous findings [21]. The discrepancy in risk factors for early and later marginal ulcers could be indicative of the slow development and late presentation of ulcers, when taking into account the relatively high odds ratios for smoking and long stapling length at 1 year. The risk factors for the relatively few occurring strictures was higher baseline BMI at 30 days, and older age at 1 year, with the latter showing a

significant odds ratio. This suggests that older patients have inferior or prolonged healing ability, which is especially important at the gastrojejunal anastomosis.

Marginal ulcers are associated with poor weight loss at 1 year but not at the early follow-up. Clinically, this could be a result of poor eating habits because of epigastric pain in conjunction with meals, and an increased intake of fast calories in fluids that are easier to ingest. It is therefore important to reduce this complication because it yields an inferior surgical result.

SOReg data

SOReg data generally reveal fewer complications than many studies from other countries. In the case of marginal ulcer, the annual rate varies between approximately 2% in SOReg [6] and up to 25% in other reports, depending on definition and method of diagnosis [19,22,23]. The SOReg definition stipulates a symptomatic and endoscopically verified ulcer near the gastrojejunal anastomosis [6], while others include epigastric pain, nausea, and other acid-related symptoms [23]. Gastroscopy is not routinely performed postoperatively in Sweden unless mild-to-moderate symptoms do not respond to initial PPI treatment, which is often prescribed generously. The low stricture rate in SOReg does hint at the small scope of the problem with marginal ulcers. Furthermore, the standard operative procedure in Sweden with a generally small pouch minimizes exposure of anastomosed small bowel to gastric acid. In

other words, the low complication rate reported in SOReg could be evidence of high-quality Swedish bariatric surgery.

Strengths and limitations

Important strengths in this study include the large cohort derived from a validated quality registry, with the ability to cross-match data with other high-quality registries, alongside a uniform operative procedure performed nationwide. Specific information from the Pharmaceutical Registry on whether or not patients were dispensed PPI in close conjunction to surgery made this unique analysis possible on whether or not prophylactic PPI helps reduce postoperative acid-related complications.

Limitations in this study include absence of information in SOReg on the presence of *H. pylori* and nonsteroidal anti-inflammatory drugs consumption, as well as the reduced availability of data on smoking, as it is a nonobligatory variable in the registry. However, including patients with unknown smoking habit in the analysis only resulted in small differences. Hypertension for marginal ulcer and older age instead of BMI for stricture were statistically significant within 30 days. At 1 year, smoking and immigrant background lost statistical significance for marginal ulcer, while long operation time and lack of PPI prophylaxis were significant for perforation, as well as poor weight loss for stricture. Furthermore, although only sold in very small packages (14 tablets), consumption of over-the-counter PPI could not be ruled out. However, all patients are questioned concerning dyspepsia, including gastroesophageal reflux and PPI consumption preoperatively in conjunction with SOReg registration. Also, we have not reported on the type and amount of PPI, although it could be extracted for a later study, but our experience is standard doses of omeprazole or esomeprazole are most commonly used when prescribing prophylaxis.

Conclusion

PPI prophylaxis did not reduce the risk for marginal ulcer and stricture in this nationwide study. The risk for these complications, however, was mainly increased by smoking, diabetes, dyspepsia, immigrant background, and surgical factors. Based on the present results, we cannot recommend routine use of PPI prophylaxis, but would like to stress the importance of smoking cessation and optimal surgery.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

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