



Alimentary Tract

Prevalence of gastroesophageal reflux and risk factors for erosive esophagitis in obese patients considered for bariatric surgery



Ala I. Sharara^{a,*}, Luma Basma O. Rustom^a, Halim Bou Daher^a, Hussein H. Rimmani^a, Rani H. Shayto^a, Mohamad Minhem^b, Yervant Ichkhanian^a, Hanaa Aridi^b, Amr Al-Abbas^b, Yasser Shaib^a, Ramzi Alami^b, Bassem Safadi^b

^a Division of Gastroenterology, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon

^b Division of General Surgery, Department of Surgery, American University of Beirut Medical Center, Beirut, Lebanon

ARTICLE INFO

Article history:

Received 3 December 2018

Accepted 10 April 2019

Available online 7 May 2019

Keywords:

Acid

Endoscopy

Gastric bypass

Proton pump inhibitor

Sleeve gastrectomy

ABSTRACT

Background: Gastroesophageal reflux disease (GERD) is common in obese individuals. Prospective studies investigating validated GERD questionnaires and clinical parameters at identifying erosive esophagitis (EE) in this population are limited.

Objective: To prospectively evaluate the prevalence of GERD in obese patients considered for bariatric surgery and identify risk and predictive factors for EE.

Methods: Eligible patients completed two validated questionnaires: GERDQ and Nocturnal Symptom Severity Impact (N-GSSIQ) before routine esophagogastroduodenoscopy.

Results: 242 consecutive patients were enrolled (130 females; mean age 37.8 ± 11.8 years; mean BMI 40.4 ± 5.3 kg/m²). The overall prevalence of gastroesophageal reflux (GERDQ ≥ 8 , EE and/or PPI use) was 62.4%. EE was identified in 82 patients (33.9%) including 13/62 (21.0%) receiving PPIs at baseline. Multivariate logistic regression identified GERDQ ≥ 8 (OR = 6.3, 95%CI 3.0–13.1), hiatal hernia (OR = 4.2, 95%CI 1.6–10.7), abnormal Hill grade (OR = 2.7, 95%CI 1.4–5.4), and tobacco use (OR = 2.5, 95%CI 1.2–4.9) as independent risk factors for EE. A pre-endoscopic composite assessment including GERDQ ≥ 8 and presence of severe nocturnal reflux symptoms had 90% specificity and 20.7% sensitivity in identifying EE (NPV 68.9% and PPV 51.5%).

Conclusion: GERD is highly prevalent in obese patients. Anthropometric data and GERD questionnaires have limited accuracy at predicting erosive disease. Pre-operative endoscopic assessment in this population appears warranted.

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1. Introduction

Ranking as the most frequent gastrointestinal diagnosis observed in outpatient clinics in the United States [1] gastroesophageal reflux disease (GERD) is an exceedingly common disorder with an estimated prevalence of 18.1%–27.8% [2]. Epidemiological data have demonstrated that obesity is an important risk factor for the development of GERD and is associated with esophageal complications such as erosive esophagitis, Barrett's esophagus, and esophageal adenocarcinoma [3,4]. The association of GERD with obesity is particularly important given that obesity rates have nearly tripled worldwide since 1975 resulting in a

global health problem of epidemic proportion. In 2016 and according to the World Health Organization, 650 million adults (13% of all adults) and over 340 million children and adolescents aged 5–19 were overweight or obese. The pathophysiological disturbances in obesity predisposing to GERD are complex and include increased intra-abdominal pressure [5], impaired gastric emptying [6], decreased lower esophageal sphincter (LES) pressure, and increased frequency of transient LES relaxation [7,8]. In addition, obese individuals may have an increased prevalence of hiatal hernia [9]. Central obesity, rather than BMI, appears to be more closely associated with GERD [3,10] and high-resolution manometry suggests that both intragastric pressure and gastroesophageal pressure gradient are primarily correlated with waist circumference.

Erosive esophagitis (EE) is characterized by presence of mucosal breaks on endoscopy at or above the gastroesophageal junction that result when acid exposure overcomes local esophageal mucosal defense mechanisms. Compared to non-erosive reflux disease

* Corresponding author at: Division of Gastroenterology, American University of Beirut Medical Center, P.O. Box 11-0236/16-B, Beirut, Lebanon.

E-mail addresses: ala.sharara@aub.edu.lb, as08@aub.edu.lb (A.I. Sharara).

(NERD), EE is associated with higher distal acid exposure time (percentage time with pH <4) and higher percentage of reflux episodes reaching the proximal esophagus [11]. Risk factors associated with EE are male gender, overweight and obesity (especially abdominal visceral obesity), a history of GERD symptoms of >1 year, alcohol and tobacco use [12,13] and the presence of a hiatal hernia [13,14].

Laparoscopic sleeve gastrectomy (LSG) is the fastest growing and most common bariatric procedure in the United States and worldwide [15,16] accounting for over 50% of bariatric surgeries. Several studies have evaluated the effects of LSG on pre-existing and new onset gastroesophageal reflux showing controversial results with some reporting amelioration of reflux [17], while others showed de novo GER or worsening of preoperative GER [18]. The problem of GER post-LSG and the need for long term PPI use, particularly with concerns regarding long-term safety of PPIs, is an area of active debate. Current guidelines recommend the performance of an upper endoscopy prior to bariatric surgery to assess for the presence of mucosal changes and/or hiatal hernia [19]. Some authors have suggested that sleeve gastrectomy should probably be avoided in patients with symptomatic gastroesophageal reflux disease and endoscopic evidence of hiatus hernia or reflux esophagitis [20].

In the absence of well-designed prospective studies that use validated GERD questionnaires and investigate clinical risk factors for GERD and erosive esophagitis, as well as the post-operative GER outcomes, the optimal management of this patient population remains unclear. The aim of this study is to evaluate the prevalence of GERD and predictive factors for EE in obese patients considered for bariatric surgery. This analysis is part of an ongoing 5-year prospective study designed to identify the incidence and prevalence of GERD post-LSG as well as identify risk factors for PPI dependence post-operatively.

2. Methods

2.1. Study design

This is a cross-sectional prospective cohort study conducted on obese patients scheduled for elective bariatric surgery at a tertiary care center in Beirut, Lebanon. Adult patients considered for bariatric surgery were enrolled after informed consent. Exclusion criteria were age less than 18 years, prior esophageal or gastric surgery, or failure to provide an informed consent. The Institutional Review Board approved the study on 5 October 2015 (IRB ID# IM.AS1.45). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

2.2. Patient population and recruitment methodology

Consecutive patients undergoing routine EGD prior to bariatric surgery were enrolled. All patients received prior evaluation by a specialist bariatric surgeon and were referred to EGD after initial metabolic evaluation. Patients were interviewed prior to endoscopy. General demographic data including gender, age, height, weight, BMI, waist circumference (WC), and the use of PPI or H₂ antagonists were collected. Waist circumference was measured using a stretch-resistant tape from the midpoint between the lower margin of the least palpable rib and the top of the iliac crests. The frequency and severity of GERD symptoms in patients was assessed by two validated questionnaires, the GERDQ and the Nocturnal GERD Symptom Severity and Impact Questionnaire (N-GSSIQ). The endoscopist -blinded to the above baseline information- completed the endoscopic data immediately following examination. These included presence or absence of EE (with photodocumentation),

Table 1
Baseline demographics and endoscopic data of the study subjects.

Characteristics	Patients (N = 242)
	Mean ± SD
Age (years)	37.8 ± 11.8
BMI (kg/M ²)	40.4 ± 5.3
Waist circumference (cm)	125.3 ± 14.3
	N (%)
Males	112 (46.3)
PPI-dependent	62 (25.7)
Tobacco use	95 (39.3)
Alcohol use	15 (6.2)
Erosive esophagitis	82 (33.9)
• LA Class 1	61 (25.2)
• LA Class 2	21 (8.7)
Hiatal hernia	38 (15.7)
• Small (1–3 cm)	30 (12.4)
• Moderate (>3 cm)	8 (3.3)
Metabolic syndrome	122 (50.4)
Nocturnal reflux	47 (19.4)
GERDQ score ≥ 8	98 (40.7)
Abnormal hill grade	123 (50.8)

grade of EE using the LA classification, presence and size of hiatal hernia, and gastroesophageal flap valve endoscopic grading (Hill grade).

2.3. Statistical analysis

Analysis was performed using Statistical Package for the Social Sciences (SPSS) version 24.0. Patient characteristics are presented using mean ± SD for the continuous variables and frequency percentages (%) for categorical variables. Continuous variables were compared using the independent sample t-test whereas the Chi-square test of independence or the Fisher's exact test were used for comparing different categories. All tests were two-tailed with a confidence level of 95%. p Values less than 0.05 were considered statistically significant. Covariates with significant p-values on univariate analysis were entered into the multivariate logistic regression model. A Backward:LR method was used.

3. Results

A total of 242 consecutive patients were enrolled and 53.7% (130) were females. Mean age was 37.8 ± 11.8 years; mean BMI was 40.4 ± 5.3 kg/M² (nearly equally divided between ≤40 vs. >40), and mean waist circumference was 125.3 ± 14.3 cm. Daily PPI use at baseline was documented in 62 patients (25.7%). A high probability GERDQ score (≥8) was present in 99 patients (40.9%) while 47 patients (19.1%) described nocturnal reflux symptoms. On endoscopic evaluation, Hiatal hernia (HH) was present in 15.7% of patients. EE was identified in a total of 82 patients (33.9%) including 69 of 180 not taking PPIs (38.3%) and 13 of 62 on PPIs (21.0%). An abnormal LES flap valve (Hill grade >1) was noted in 123 patients (50.8%).

The overall prevalence of gastroesophageal reflux, defined as high-probability GERDQ score ≥8 or presence of EE or daily use of PPIs was 62.4%. In addition, 31 patients (12.8%) had silent or inconspicuous, yet important, GERD defined as presence of EE with low probability symptom score (GERDQ <8) and no or infrequent PPI use. Table 1 summarizes the baseline clinical and endoscopic characteristics of the study subjects.

Forty-nine patients on PPI therapy were excluded from the EE analysis because of absence of erosive disease. EE was more common in patients with GERDQ ≥ 8 vs. <8 (70.6% vs. 27.2%, p < 0.001), in patients with HH vs. those without (69.7% vs. 36.9% p < 0.001), and in subjects with severe nocturnal GER symptoms compared

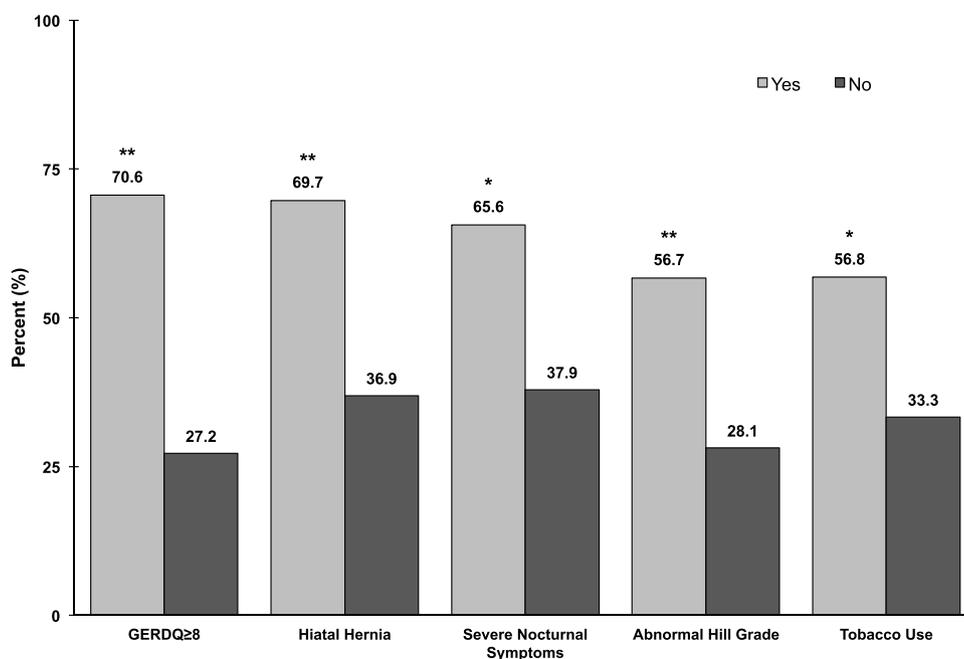


Fig. 1. Factors associated with erosive esophagitis on univariate analysis (* $p < 0.05$; ** $p < 0.001$).

to those with no or minor symptoms (65.6% vs. 37.9%, $p = 0.004$) [Insert Fig. 1].

On univariate analysis, severe nocturnal symptoms, GERDQ score ≥ 8 , presence of HH, abnormal LES flap valve (Hill grade), and use of tobacco were significantly associated with EE ($p = 0.004$, $p < 0.001$, $p < 0.001$, $p < 0.001$ and $p = 0.001$ respectively). Gender, BMI (≤ 40 vs. > 40) and WC were not associated with the presence of EE. Multivariate logistic regression analysis showed that GERDQ ≥ 8 (OR = 6.3, 95%CI 3.0–13.1), presence of HH (OR = 4.2, 95%CI 1.6–10.7), abnormal Hill grade (OR = 2.7, 95%CI 1.4–5.4), as well as use of tobacco (OR = 2.5, 95%CI 1.2–4.9) were the only independent risk factors for EE. A pre-endoscopic composite risk assessment including GERDQ ≥ 8 and the presence of severe nocturnal reflux symptoms had 90% specificity, and 20.7% sensitivity in identifying EE (NPV 68.9% and PPV 51.5%).

4. Discussion

Dedicated prospective screening endoscopy studies evaluating GERD in the obese populations are limited and are primarily restricted to pre-bariatric surgery populations [5,21,22]. Mora et al. examined 224 pre-surgical morbidly obese patients using clinical history and objective tests consisting of endoscopy, esophageal manometry, and 24-h esophageal pH monitoring. Heartburn and regurgitation were highly prevalent (50% and 23% respectively), and an abnormal esophageal pH-metry and erosive esophagitis were identified in 54.2% and 17.3% of patients respectively. Risk factors for EE were not investigated but the study could not identify a correlation between the degree of obesity and severity of symptoms or objective tests for esophageal abnormalities. A cross-sectional study from China examined the risk of EE in 260 obese patients referred for bariatric surgery [5]. Baseline endoscopic examination as well as demographic variables, anthropometric measurements, and metabolic factors were collected. The prevalence of erosive esophagitis in this population was 32.3% mirroring that of our study. Increased waist circumference (OR = 1.03; 95% CI 1.01–1.04), insulin resistance (OR = 1.57; 95% CI 1.06–2.31), and presence of reflux symptoms (OR = 2.40; 95% CI = 1.22–4.74) were independent risk factors associated with EE. Our study was also

designed to systematically examine the prevalence of gastroesophageal reflux using validated questionnaires (namely GERDQ and N-GSSIQ) and investigate the risk factors for erosive esophagitis in an unselected obese population considered for bariatric surgery. In this well characterized study cohort of 242 consecutive individuals, we show that nearly two-thirds suffer from gastroesophageal reflux and one quarter is already dependent on PPIs to control symptoms. Importantly, by performing routine perioperative endoscopic examination independent of symptoms, we documented evidence of erosive reflux disease in one third of all patients, including in a good percentage (21.0%) of daily PPI recipients. Moreover, clinically silent or inconspicuous erosive GERD was unmasked in 12.9% of patients.

The above information is significant and is particularly serious when one considers the scale of the problem worldwide. With gastroesophageal reflux disease ranking as one of the top five most costly gastrointestinal disorders (accounting for an estimated \$9.8 billion in expenditures annually due to direct costs alone), the associated economic burden is substantial. Additional indirect costs are underappreciated but include lower quality of life, diminished work productivity and absenteeism. A cost-of-disease analysis in patients with gastroesophageal reflux disease enrolled in the ProGERD study showed that GERD health resource utilization was associated with significant mean direct and indirect costs, with higher costs for patients with erosive reflux disease compared to those with non-erosive reflux disease [23].

Although the frequency of acid reflux appears to correlate more with erosive esophagitis than non-erosive reflux disease (NERD), some studies have failed to show a significant difference between NERD and mild to moderate erosive disease in terms of acid exposure time and esophageal motor abnormalities [22]. Compared with NERD, erosive disease is associated with worse quality of life, higher complications including bleeding, stricture and possibly Barrett's metaplasia, as well as the need for long-term acid-suppressive therapy. Few prospective studies have examined the risk factors for erosive disease [12,14]. The ProGERD study examined a large number of patients with symptomatic heartburn and identified male gender, overweight, regular use of alcohol, long standing symptoms for greater than one year, and smoking as independent risk

factors for erosive disease [12]. In addition, El-Serag et al. showed that obesity and the duration and severity of symptoms were associated with worse grades of esophagitis [14]. In contrast to BMI or waist circumference, abdominal visceral adipose tissue volume is associated with an increased risk of erosive esophagitis in males and females [24]. The World Health Organization characterizes the global obesity epidemic as a leading public health problem affecting both developed and developing countries. According to the American Society for Metabolic and Bariatric Surgery, nearly 216,000 individuals underwent bariatric surgery in the United States in 2016 with an increase of 36.7% over a five-year period from 2011 to 2016 [15]. Laparoscopic sleeve gastrectomy (LSG) accounts for more than 50%–60% of bariatric surgeries worldwide [16]. Enthusiasm for this relatively simple procedure has however been increasingly tempered by emerging concerns of persistent gastroesophageal reflux affecting as many as 50% of patients [25] as a result of either persistent or de novo reflux after surgery.

Understanding the burden of gastroesophageal reflux disease in the obese population takes on particular importance in view of the global obesity epidemic. The high incidence of GERD in such a large population (nearly 775 million obese people worldwide) constitutes an important health and economic burden. This includes, but is not limited to, higher use of PPIs [26] as well as the need for longer maintenance PPI therapy [27] leading to increased costs and risk of potential complications of chronic PPI use [28,29]. The magnitude of the problem is highlighted in our study where GERD symptoms, erosive esophagitis, and baseline dependence on PPIs were seen in 62.4%, 33.9%, and 25.7% of patients respectively. Of note, a retrospective study by Sheppard et al. found a comparable preoperative prevalence of PPI use of 30% in bariatric patients [30]. This percentage is much higher than the range (4–15%) reported in other studies conducted on the general population [31,32]. Another important consideration is the increasing number of obese individuals undergoing bariatric surgery worldwide and estimated at nearly 580,000 in 2014 [16]. LSG is associated with a high-rate of persistent post-operative gastroesophageal reflux and PPI dependence [18,30] and identification of factors predictive of persistent GER and PPI dependence post LSG is necessary. Retrospective studies have suggested that the presence of erosive esophagitis and baseline PPI dependence are factors to be considered when deciding on the need for pre-operative endoscopy [33] as well as on the preferred bariatric surgery [1,20]. And the 2015 joint statement by the ASMBS, SAGES and ASGE considered erosive esophagitis as a relative contraindication for LSG [34].

Our study has some strengths and few limitations. First, it is a prospective study conducted on a relatively large and well-characterized cohort of obese bariatric patients designed to investigate the prevalence of GERD (independent of symptoms) using validated GERD questionnaires and accurately categorized endoscopic findings including presence and grade of EE, presence or absence of hiatal hernia, and LES flap valve grade, a possible determinant of persistent or de novo GER following LSG [35]. Second, the 2 study endoscopists were blinded to the results of the GERD questionnaires administered prior to the procedure, thereby eliminating potential observer bias. There are, however, some limitations to our study. The absence of manometric and pH-impedance data as a gold standard for the diagnosis of GERD (and presence of hiatal hernia) is an important limitation. There is a possibility of selection bias since patients seeking bariatric surgery are generally younger and relatively healthier than obese patients in the general population. We also did not collect data on other factors that may be potentially associated with GERD and EE including patterns of obesity, specific food triggers (coffee, chocolate, etc.), binge eating, and/or use of non-acid suppressive medications with an effect on LES function. In our study, GERD was defined as GERDQ score ≥ 8 , presence of EE or daily PPI use; these criteria may overestimate

the prevalence of GERD and include patients with functional upper gastrointestinal symptoms.

In conclusion, gastroesophageal reflux, including erosive disease is highly prevalent in this cohort of obese patients considered for bariatric surgery. A high GERDQ score, presence of nocturnal GERD, hiatal hernia, or abnormal LES flap valve is associated with erosive esophagitis. A high GERDQ score was the only clinical risk factor associated with EE. A pre-endoscopic simple clinical composite assessment including GERDQ ≥ 8 and the presence of severe nocturnal reflux symptoms has good specificity but poor sensitivity in identifying EE. Given the existing controversy regarding the determinants of GER following laparoscopic sleeve gastrectomy, a pre-operative endoscopic assessment and careful discussion with the patient and the bariatric surgeon are recommended [19]. Avoiding LSG in patients with endoscopic evidence of erosive esophagitis may reduce post-operative reflux and PPI dependence as well as the incidence of revisional bypass surgery for refractory reflux [36,37]. Long-term follow-up of prospectively evaluated cohorts following LSG will help further clarify this important problem.

Conflict of interest

None declared.

Writing assistance

None.

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