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GERD after Roux-en-Y Gastric Bypass: Prevalence and Risk Factors Analysis

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Abstract: *Background and Objectives.* Prevalence of GERD is increased among individuals with obesity and RYGB is considered as the most effective procedure to control GERD and obesity. However, some patients continue to have GERD after RYGB. The aim of the study was to investigate the prevalence and the risk factors of GERD after RYGB. *Material and Methods*. This prospective study included 180 patients operated with RYGB and followed for on average of 12.2 (0.6) years. 126 (70%) patients agreed to participate in online consultations and provided data on weight, GERD symptoms, filled GERD-HRQL, TFEQ-18 and GSRS questionnaires. *Results.* The average age before surgery was 42.7 (10.5) years and BMI was 45.2 (6.4) kg/m^2. 128 (71.1%) were females and preoperative GERD was diagnosed in 74 (41.1%) patients. At 12 years follow-up the mean %EBMIL and %TWL were 60.37 and 25.73, respectively. The median %WR was 18.0 (39.0). The GERD was present in 30 (23.8%) patients, of whom 12 (40%) continued to have GERD symptoms and 18 (60%) developed de novo GERD. The GERD-HRQL score significantly decreased from 3.0 (8.0) at baseline to 2.0 (5.0) (p=0.028) at 12 years. GSRS Diarrhea and Indigestion median scores increased significantly, from 1.33 (0.67) to 1.5 (2.42) (p<0.001) and from 1.88 (1.5) to 2.25 (1.25) (p<0.001), respectively. No change in emotional eating and cognitive restraint scores was observed, uncontrolled eating score decreased from median of 51.85 (25.9) to 37.0 (33.3) (p<0.001). In multivariate analysis %WR > 11 (OR = 3.22, p=0.029) and GSRS Diarrhea score (OR = 3.21, p=0.027) were significant predictors of GERD 12-years after RYGB. *Conclusions.* RYGB is an effective procedure to control GERD, however 23.8% had persistent or de novo GERD after 12 years. The independent risk factors associated with GERD after RYGB were WR > 11% and GSRS Diarrhea score > 3.2.

Keywords: bariatric surgery; Roux-en-Y gastric bypass; GERD; prevalence; risk factors

1. Introduction

The prevalence of obesity has steadily increased during the last five decades [1]. Obesity is a risk factor for cardiovascular, metabolic, musculoskeletal diseases and some types of cancer. There is also a well established relation between obesity and gastroesophageal reflux disease (GERD). Hampel H. et al. [2] have perfomed meta-analysis and found that BMI greater than 30 kg/m2 increased the risk of GERD symptoms and esophageal adenocarcinoma, pooled adjusted odds ratio (OR) 1.94 (CI 95%, 1.468 to 2.566) and 2.78 (CI 95%, 1.850 to 4.164), respectively. The main mechanism for higher prevalence of GERD among individuals with obesity could be an increased intraabdominal pressure together with decreased lower esophageal sphincter pressure which result in pathological esophageal

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acid exposure [3]. Furthermore, hiatal hernias increase the risk of GERD symptoms also and higher prevalence of hiatal hernias is observed among the individuals with obesity [4,5].

Currently, bariatric surgery is the most effective long-term treatment for obesity. The prevalence of GERD symptoms among the patients considered for bariatric surgery is in a range from 40.8% to 62.4% [6–8]. Given high prevalence rate, bariatric surgeons must take into consideration GERD symptoms when choosing relevant surgical procedure. Sleeve gastrectomy is the most common primary surgical procedure for obesity in the world, but majority of the surgeons would choose Roux-en-Y gastric bypass (RYGB) for the patient with obesity and severe GERD. However, there is still controversy about which bariatric surgical procedure should be offered for the patients with mild reflux.

Even though RYGB has a better control of GERD symptoms about one third of the patients still need to take anti-reflux medications 10 years after surgery [9]. The reason for this is unknown. The possible risk factors for postoperative GERD after RYGB could be insufficient weight loss or weight regain with increased intraabdominal pressure, hiatal hernia, larger pouch or anastomotic stricture/ulcer, eating behavior or functional gastrointestinal disorders such as irritable bowel syndrome. The goal of this prospective study was to investigate the prevalence of GERD more than 10 years after RYGB and explore the influence of weight loss, BMI, weight regain, eating and gastrointestinal functional disorders on persistence or occurrence of GERD.

2. Materials and Methods

This is a continuation of prospective study, which included 180 patients operated with RYGB from September, 2010 to January, 2013 at Surgery department, Lithuanian University of Health Sciences hospital. The detailed protocol and one year results have been published previously [10]. In summary, patients were eligible for the study if they fulfilled standard criteria for bariatric surgery approved by Lithuanian Sickness Fund (age between 18 and 65 years, and BMI ≥ 40 kg/m^2 or BMI ≥ 35 kg/m^2 with at least one co-morbidity, such as hypertension, type 2 diabetes mellitus, arthrosis, sleep apnea or infertility for woman) and signed informed consent. The Ethical committee of Lithuanian University of Health Sciences approved the study (protocol Nr. BE-2-59).

The proportion of males and females was 28.9% and 71.1%, respectively. Average age was 42.7 (10.5) years and BMI was 45.2 (6.4) kg/m^2. Laparoscopic RYGB was performed in all cases with 20-30 ml pouch, 50 cm biliopancreatic limb and 150 cm Roux limb. In the current study the patients were interviewed online on average 12.2 (0.6) years after primary surgery. Information about patients' weight changes, gastrointestinal symptoms and eating behaviour were collected.

GERD symptoms were evaluated at baseline and 12 years after RYGB using The Gastroesophageal Reflux Disease-Health Related Quality of Life (GERD-HRQL) questionnaire [11]. GERD-HRQL was developed to estimate typical symptoms of GERD and assess response to the medical or surgical treatment. It consists of a total of 11 items, 10 of which are measured from 0 to 5 and are used to calculate the total GERD-HRQL score by adding the individual item scores. Item 11 evaluates patient's satisfaction with the present situation, by asking if they are satisfied, neutral or dissatisfied (10). The GERD was diagnosed preoperatively if the patients had erosive esophagitis on gastroscopy or were on continuous PPI treatment, or GERD-HRQL score ≥ 8. Postoperative GERD diagnosis was based on continuous PPI treatment or GERD-HRQL score ≥ 8.

The Gastrointestinal Symptom Rating Scale (GSRS) questionnaire has 15 items evaluated on a 7-point Likert scale [12]. The mean values for diarrhea, indigestion, constipation, abdominal pain, and reflux were calculated. The higher is the score, the more severe are the symptoms.

Three different aspects of eating behavior - cognitive restraint (CR), uncontrolled eating (UE) and emotional eating (EE) were evaluated by TFEQ-R18. CR is a restriction of food intake to maintain body weight, UE is a loss of control of eating provoked by hunger feeling and EE is caused by emotional stimulus. There are 18 items, and each is scored between 1 to 4 [13]. The item scores were summated into CR, UE, and EE scale scores. The raw scale scores were transformed to a 0–100 scale [100 – (((raw score − lowest possible raw score)/possible raw score range) × 100)]. The higher values on the respective scales are indicating more of the behavior.

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Percent Excess BMI loss (%EBMIL) at 12 years follow-up was estimated by the formula: [pre-operative BMI kg/m² – BMI kg/m² at 12-year follow-up] / [pre-operative BMI kg/m² - 25 kg/m²] x 100. Percent weight regain (%WR) was estimated as [Total body weight in kg at 12-year follow-up – Total body weight in kg at nadir] / [Total body weight in kg at baseline - Total body weight in kg at nadir] x 100. Percent of total weight loss (%TWL) was calculated as [Total body weight in kg at baseline – Total body weight in kg at 12-year follow-up] / Total body weight in kg at baseline x 100.

Statistical Analysis

The SPSS program, version 29.0 (SPSS Inc., Chicago, IL), was used for the statistical analyses. Normality of variables was estimated with Kolmogorov–Smirnov test. Continuous variables with normal distribution are presented as means and standard deviation (SD), abnormally distributed as median with interquartile range. Categorical variables are presented in numbers and percentage. The GERD-HRQL score, TFEQ-R18 factors scores and GSRS dimensions scores were abnormally distributed at baseline, 1 and 12-year follow-ups. The means of these paired samples' scores were compared using Wilcoxon Signed Ranks test. Cut-point values of continues variables for univariate and multivariate logistic regression was identified by ROC Analysis. Multivariate logistic regression was used to identify significant predictors of GERD at 12 years follow-up. A p value < 0.05 was considered statistically significant.

3. Results

The preoperative patients' characteristics are presented in the **Table 1**. During preoperative gastroscopy hiatal hernia was diagnosed in 37 (20.6%) cases. Forty-nine (27.2%) patients had erosive esophagitis and 37 (20.6%) were on continuous PPI treatment. Finally, 74 (41.1%) patients had erosive esophagitis, or daily PPI treatment or GERD-HRQL score ≥ 8 and were diagnosed with GERD. 12 years after RYGB 30 (23.8%) patients had GERD. Among those who had no GERD at baseline fifty-four (75%) continued to have no GERD symptoms at 12-year follow-up and 18 (25%) developed de novo GERD. Among patients who had GERD, 42 (77.8%) reported that GERD resolved and 12 (22.2%) continued to have GERD symptoms.

Table 1. Preoperative patients' characteristics.

Characteristics	Patients (n=180)
Age, y mean (SD)	42.7 (10.5)
Sex, M/F	52/128
BMI, kg/m2 mean (SD)	45.2 (6.4)
Waist circumference, cm mean (SD)	127.1 (15.6)
Smoking n (%)	59 (32.7)
Erosive esophagitis n (%)	49 (27.2)
Hiatal hernia n (%)	37 (20.6)
GERD-HRQL score, median (min-max)	3.0 (8.0)
PPI use n (%)	37 (20.6)
GERD n (%)	74 (41.1)
Hypertension n (%)	108 (60)
Diabetes mellitus n (%)	14 (7.8)
Dyslipidemia n (%)	131 (72.8)

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At 12 years follow-up the data were available for 126 (70%) patients, 38 (30.2%) males and 88 (69.8%) females. The average BMI was 33.0 (5.9), %EBMIL and %TWL was 60.37 and 25.73%, respectively. The median %WR was 18.0 (39.0) and 71 patient (59.7%) experienced > 10 %WR.

The GERD-HRQL score median at baseline was 3.0 (8.0) and decreased to 0 (1.0) ($p<0.001$) and 2.0 (5.0) ($p=0.028$), 1 and 12 years after surgery, respectively. Significant increase ($p<0.001$) in GERD-HRQL score was observed between 1 and 12 years. The median GSRS Diarrhea score at baseline was 1.33 (0.67), 1.0 (0.75) after 1 year and 1.5 (2.42) after 12 years. The change between baseline and 1-year scores was insignificant, however, 12 years after RYGB GSRS Diarrhea score increased significantly as compared to baseline ($p<0.001$) and 1-year ($p=0.002$) scores. GSRS Indigestion score was 1.88 (1.5) at baseline. One year after RYGB it decreased to 1.25 (0.75) ($p<0.001$), however 12 years after surgery it increased to 2.25 (1.25) ($p<0.001$). There were no significant changes in GSRS Constipation score at baseline, 1 year and 12 years after RYGB, which was 1.33 (1.0), 1.0 (1.0) and 1.0 (1.0), respectively.

The median UE score at baseline was 51.85 (25.9) and decreased after 1 and 12 years to 25.9 (6.5) ($p<0.001$) and 37.0 (33.3) ($p<0.001$), respectively. Statistically significant ($p<0.001$) increase of UE score from 1 to 12-year follow-up was observed. The baseline median value of CR was 55.5 (11.1) and did not change 1 and 12 years after surgery. The EE median score at baseline was 33.3 (44.4) and decreased to 11.1 (13.9) 1 year after surgery ($p<0.001$). Twelve years after surgery median EE score returned to baseline level and was 33.3 (22.2).

Three variables, which were significant in univariate analysis, were entered into multivariate logistic regression model (**Table 2).** %WR > 11 (odd ratio (OR) = 3.22 [95% confidence interval (CI) 1.13, 9.22], $p=0.029$) and GSRS Diarrhea score (OR = 3.21, 95%CI 1.14, 9.06, $p=0.027$) were significant predictors of GERD 12-years after RYGB. Model accounted for the 22.2% of total variance and correct prediction rate was 76.7%.

Table 2. Factors associated with GERD 12 years after RYGB.

Factor		**Univariate Models**		**Mutivariable Model**	
	N	Beta (95% CI)	P value	Beta (95% CI)	P value
Sex (Ref=male)	126	1.25 (0.50, 3.13)	0.633		
Age, years (Ref ≤55.6)	126	1.28 (0.56, 2.92)	0.559		
BMI kg/m² (Ref ≤31.7)	120	1.88 (0.78, 4.51)	0.157		
%EBMIL (Ref >39.9)	120	0.79 (0.24, 2.60)	0.700		
%TWL (Ref >18.7)	120	0.78 (0.26, 2.32)	0.658		
%Weight regain (Ref≤11.0)	120	3.22 (1.19, 8.67)	0.021	3.22 (1.13, 9.22)	0.029
Uncontrolled eating (Ref ≤47.0)	126	2.00 (0.87, 4.60)	0.103		
Cognitive restraint (Ref ≤41.7)	126	1.50 (0.47, 4.84)	0.497		
Emotional eating (Ref ≤38.9)	126	0.82 (0.31, 2.14)	0.684		
GSRS Diarrhea score (Ref ≤3.20)	126	5.31 (2.19, 12.91)	<0.001	3.21 (1.14, 9.06)	0.027
GSRS Indigestion score (Ref≤2.15)	126	4.73 (1.77, 12.60)	0.002	2.45 (0.81, 7.42)	0.113
GSRS Constipation score (Ref≤1.5)	126	0.86 (0.35, 2.01)	0.734		

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Preoperative GERD (Ref=no)	126	1.17 (0.51, 2.69)	0.717
Hiatal hernia, (Ref=no)	106	0.62 (0.16, 2.34)	0.475

4. Discussion

This study was an extension of our previously published prospective study [10] and provided 12 year follow-up data on weight loss, GERD, gastrointestinal symptoms and eating behavior of the patients operated with RYGB. More than half of our patient population experienced more than 10 %WR and weight regain was found to be a significant predictor of GERD 12 years after surgery. Another factor that increased the risk of GERD was GSRS Diarrhea score more than 3.2. These findings allow us to get some insight why GERD continues or appears *de novo* after RYGB.

Previous studies have demonstrated increased prevalence of GERD in bariatric surgery candidates, which was in a range from 40.8% to 62.4% [6–8]. Similarly, 41.1% of bariatric surgery patients presenting in our center had GERD preoperatively. RYGB is considered one the most effective procedures in the treatment of obesity and GERD. The possible mechanisms of GERD improvement after RYGB could be decreased intragastric pressure, exclusion of fundus and creation of low-pressure gastric pouch [14]. However, even after RYGB some patients experience persistent or de novo GERD. In the present study 12 years after RYGB GERD resolution was observed in 77.8% of cases and 25% reported de novo GERD. Similarly, Santanicola A. et al. [7] investigated 45 patients on average 99.9 months after RYGB and found GERD resolution rate of 69.6% and new onset of GERD in 18.2% of cases. However, the possible mechanisms of GERD persistence or the new onset after RYGB are poorly understood. Petrucciani N., et al. [8] have found that preoperative GERD (OR=2.65, p<0.0001), glycemic imbalances defined as post-prandial symptoms, which has impact on quality of life and occurs at least more than 2 times per month (OR=0.32, p=0.006), anastomotic ulcer (OR=0.35, p<0.0001) and %TWL at 10 years ≥25 (OR=0.524, p= 0.021) were significant risk factors related to GERD 10 years after RYGB [8]. We were unable to confirm the finding that preoperative GERD has influence on the GERD 12 years after surgery because more patients in our study had de novo GERD as compared to those who had persistent GERD. We asked our patients about current diseases, and no one have mentioned anastomotic ulcer. However, the question has not directly addressed the history of peptic ulcer, thus we were unable to include this possible risk factor into our analysis.

In our study BMI, %EBMIL and %TWL at 12-year follow-up had no impact on persistence or occurrence of new GERD. However, WR more than 11% was significant risk factor (OR=3.22, p=0.029) associated with postoperative GERD. It could be related to increased intraabdominal pressure, but even the diet or eating behavior may have an impact on persistence or occurrence of the GERD. The Nurses' Health Study II included 42 955 women and during 392 215 person-years identified 9291 cases with GERD symptoms. Higher prudent dietary score and ≤ 2 cups daily of coffee, tea or soda drinks reduced the risk of GERD symptoms, hazard ratio 0.87 (0.84-0.91) and 0.92 (0.88-0.97), respectively [15]. Recent study in Chinese student population found that emotional eating was related to laryngopharyngeal reflux (OR=6.8, p<0.001) [16]. However, no significant correlation between emotional eating, uncontrolled eating, or cognitive restraint and GERD-HRQL score was found in our patient cohort at baseline and 1 year after RYGB [10], and after 12 years there was no evident relation between eating behavior and postoperative GERD.

In the present study hiatal hernia was diagnosed in 20.6% of cases and was comparable to the prevalence of 15.7% - 47.8% in the recently published studies [6,7]. There is still controversy regarding the role of small hiatal hernias on persistence of GERD after RYGB. Khouri A., et al. [17] compared GERD-HRQL scores 1 year after RYGB between patients who had small hiatal hernias without repair and patients without hiatal hernias. In both groups GERD-HRQL score decreased significantly from baseline to 1 year without significant difference between the groups [17]. No one of our patients underwent hiatal hernia repair during primary procedure and 12 years after surgery presence of hiatal hernia did not increase the risk of persistent or de novo GERD.

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We have also explored relation of gastrointestinal symptoms to GERD 12 years after surgery using GSRS questionnaire. Only GSRS Diarrhea score more than 3.2 was significantly related to postoperative GERD (OR=3.21, p=0.027). Systematic literature review has shown significant overlap between irritable bowel syndrome (IBS) and GERD, where prevalence of GERD among the patients diagnosed with IBS was 39.3% and IBS prevalence among patients with GERD reached 48.8% [18]. One explanation could be that the relation between GERD and IBS symptoms maybe caused due to similar underlying gastrointestinal dysfunction [19]. Also, more esophageal dysmotility have been found after RYGB as compared to non-operated individuals with obesity [20] and high-resolution manometry study have shown abnormal peristalsis in the Roux limb in the majority of patients after total gastrectomy [21]. So future studies should additionally explore the impact of functional gastrointestinal disorders on persistence or occurrence of GERD symptoms after RYGB.

There are several limitations of the study. First, we used self-reported weight to estimate long-term weight loss and weight regain. It is known that patients with obesity tend to underreport their actual weight. However, this should not have had and impact on the results of the current study, because even a relatively small %WR was significantly related to postoperative GERD. Second, the rate of hiatal hernias in our population could be underestimated because preoperative gastroscopy was done in different centers without uniform protocol and was not supplemented by upper GI study, which is more sensitive in diagnosing hiatal hernias [22]. Finally, postoperative gastroscopy was not routinely performed and some cases of silent GERD could have been missed.

5. Conclusions

RYGB is an effective procedure to control GERD, however 23.8% had persistent or de novo GERD after 12 years. The independent risk factors associated with GERD after RYGB were WR > 11% and GSRS Diarrhea score > 3.2. Future research are needed to better understand the mechanisms that lead to persistence or occurrence of GERD after RYGB.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.
Conflicts of Interest: The authors declare no conflicts of interest.

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