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Original article

Prospective clinical cohort study: low incidence of Barrett esophagus but high rate of reflux disease at 5-year follow-up after sleeve gastrectomy versus Roux-en-Y gastric bypass

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Abstract

Background: Gastroesophageal reflux disease seems more frequent after laparoscopic sleeve gastrectomy (LSG) than Roux-en-Y gastric bypass (LRYGB). Retrospective case series have raised concerns about a high incidence of Barrett esophagus (BE) after LSG.

Objective: This prospective clinical cohort study compared the incidence of BE ≥5 years after LSG and LRYGB.

Setting: St. Clara Hospital, Basel, and University Hospital, Zürich, Switzerland.

Methods: Patients were recruited from 2 bariatric centers where preoperative gastroscopy is standard practice and LRYGB is preferred for patients with preexisting gastroesophageal reflux disease. At follow-up ≥5 years after surgery, patients underwent gastroscopy with quadrantic biopsies from the squamocolumnar junction and metaplastic segment. Symptoms were assessed using validated questionnaires. Wireless pH measurement assessed esophageal acid exposure.

Results: A total of 169 patients were included, with a median 7.0 ± 1.5 years after surgery. In the LSG group (n = 83), 3 patients had endoscopically and histologically confirmed de novo BE; in the LRYGB group (n = 86), there were 2 patients with BE, 1 de novo and 1 preexisting (de novo BE, 3.6% versus 1.2%; $P = .362$). At follow-up, reflux symptoms were reported more frequently by the LSG group than by the LRYGB group (51.9% versus 10.5%). Similarly, moderate-to-severe reflux esophagitis (Los Angeles grade B–D) was more common (27.7% versus 5.8%) despite greater

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use of proton pump inhibitors (49.4% versus 19.7%), and pathologic acid exposure was more frequent in patients who underwent LSG than in patients who underwent LRYGB.

Conclusions: After at least 5 years of follow-up, a higher incidence of reflux symptoms, reflux esophagitis, and pathologic esophageal acid exposure was found in patients who underwent LSG compared with patients who underwent LRYGB. However, the incidence of BE after LSG was low and not significantly different between the 2 groups. (Surg Obes Relat Dis 2023;■:1–9.)

Keywords: Obesity; Bariatric surgery; Sleeve gastrectomy; Roux-en-Y gastric bypass; Barrett; esophagus; Gastroesophageal reflux disease

The most performed bariatric surgical procedures are laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) [1]. This surgery is not without risks, but the risks are generally outweighed by the benefits of sustainable weight loss in patients with morbid obesity. Nevertheless, the potential long-term adverse effects of any operation must be considered. A randomized clinical trial from our institutions (the Swiss Multicenter Bypass or Sleeve Study [SM-BOSS]) reported that 31.8% of patients had new or worsened reflux symptoms 5 years after LSG compared with only 6.3% of patients after LRYGB [2]. Reports from retrospective studies have raised concerns about the incidence of Barrett esophagus (BE) after LSG [3–5]. Although the baseline risk of BE at preoperative assessment before bariatric surgery is not high [6], a pooled analysis of 10 observational studies reported a prevalence of BE of 10%–19% after LSG, with the risk of this condition increasing with the duration of follow-up [7]. This is important because BE is a premalignant condition [8,9], and cases of esophageal carcinoma after LSG have been reported [10]. By contrast, the incidence of BE after LRYGB has not been reported, but it is assumed to be low because acid reflux is rare after this form of surgery.

In community-based studies, reflux symptoms are reported by up 20% of the population, and upper gastrointestinal endoscopy reveals reflux esophagitis in up to 20% of patients with BE in 1%–2% in the general population [11–13]. Longitudinal studies show that chronic reflux symptoms and erosive reflux esophagitis are risk factors for developing de novo BE, and the risk for developing esophageal adenocarcinoma in patients with long-segment BE (>3 cm) is approximately .5% per year [14,15]. Within this group, the risk of progression to BE and esophageal adenocarcinoma is estimated to be twice as high for individuals with obesity than for population control individuals [16]. The aim of bariatric surgery is to reduce body weight, and this could reduce the risk not only of adverse metabolic and cardiac outcomes but also of metaplastic and neoplastic change in the esophagus; however, the beneficial effects of weight loss could be more than offset by increased risk from pathologic acid reflux after LSG. The relative importance of these 2 factors is unknown, and the long-term risk of developing BE after LSG and LRYGB has not been compared in well-designed studies.

This prospective clinical cohort study provides a systematic assessment of the incidence of reflux symptoms and mucosal disease after bariatric surgery, with particular attention to the de novo development of BE after LSG. A similar number of patients who underwent LRYGB were included as an active comparison group with similar preoperative characteristics. Additionally, insight into the causes of symptoms and disease was provided by physiologic measurement performed in a subset of patients.

Methods

Study design

The study protocol was approved by the local ethics committee, and the study was conducted following the principles of the Declaration of Helsinki and registered (NCT03410849). To summarize, this prospective clinical cohort study compared the incidence of reflux symptoms and mucosal disease, including BE (primary outcome), in patients who underwent LSG and those who underwent LRYGB.

Patients and study outcomes

The primary endpoint was the cumulative incidence of BE ≥5 years after primary LSG or LRYGB. Secondary endpoints included prevalence and severity of reflux esophagitis (endoscopy), reflux symptoms (questionnaires), use of proton pump inhibitors (PPIs), severity of acid reflux (pH measurement), weight loss, and remission of co-morbidities.

This study was performed at 2 centers in Switzerland where preoperative gastroscopy is standard practice before bariatric operations and LRYGB is the preferred procedure in patients with evidence of severe gastroesophageal reflux disease (GERD) or a large hiatal hernia. Randomization was not considered to be appropriate because it is known that LSG increases the risk of reflux symptoms and disease.

Consecutive patients who had undergone surgery at least 5 years previously were contacted, going backward in time (i.e., operation date) until sufficient patients consented to participate. Individuals who consented to complete questionnaires and repeat gastroscopy with biopsies were recruited (cost covered by a research grant). In a subgroup, wireless pH measurement (Bravo Reflux Testing System, Medtronic) and high-resolution manometry (HRM; Mano-Scan 360, Medtronic) was performed. Patients stopped PPI medication 1 week prior to investigation. The pH sensor was placed 6 cm above the squamocolumnar junction (position checked by endoscopy). Patients were instructed to log symptoms, meals, and changes in position on the data receiver. After 48 hours, data documenting percentage acid exposure time (pH <4) and the number of acid reflux events were uploaded, anonymized, and transferred to a workstation (note that non–acid reflux events are not detected by the Bravo system). Results were analyzed by investigators blinded to patient allocation (A.J. and M.F.) using proprietary software and classified by the Lyon classification [17].

Definition of Barrett mucosa and reflux esophagitis

BE is identified during endoscopic examination by the presence of "salmon pink" mucosa in the distal esophagus that extends above the proximal extent of the gastric folds [18,19]. The Prague classification system measures the circumferential (C) and maximal (M) extents for BE lengths [20]. Endoscopic biopsies are required to confirm the change from squamous to columnar epithelium with intestinal metaplasia (containing goblet cells) [21,22]. Histologic investigation was performed on anonymized samples at a separate institution (MV).

The Los Angeles (LA) classification system describes the severity of reflux esophagitis using a 5-point severity scale where zero means no esophagitis; grade A, ≥1 mucosal breaks of <5 mm confined to the mucosal folds; grade B, ≥1 mucosal breaks of >5 mm; grade C, mucosal breaks that are continuous between the tops of ≥2 mucosal folds but involving <75% of the esophageal circumference; and grade D, mucosal breaks that involve ≥75% of the esophageal circumference. Clinically relevant reflux esophagitis (i.e., rarely seen in health, associated with pathologic acid exposure) was defined as LA grades B–D [23].

Questionnaires

Esophageal Dysphagia Questionnaire (EDQ) documented swallowing problems. Reflux and dyspeptic symptoms were assessed by the Gastro-Esophageal Reflux Disease Questionnaire (GERD-Q) [24] and the Leuven Postprandial Distress Scale (LPDS) [25]. The Hospital Anxiety and Depression Scale (HADS) and the Visceral Sensitivity Index (VSI) were used to assess psychological state and somatization, respectively [26].

Statistical analysis

Prospective power calculations were based on observational case series [3,4]. Assuming BE incidences of 15% after LSG and 1% after RYGB in patients ≥5 years after surgery, mathematical modeling indicated that sample sizes of 165 LSG and 75 RYGB patients would be required for >80% study power with a significance level of .05. Study recruitment was halted in March 2020 at the onset of the SARS-CoV-2 pandemic. Interim analysis revealed a lower BE incidence in the LSG group than expected. The study was stopped because there was no prospect of reaching significance without increasing patient numbers well above original estimates (~600 patients). On this basis it would not have been feasible or ethical to continue the study after the lockdown was lifted.

Statistical analysis was performed with R (R Foundation). For continuous variables, the within-subject differences of follow-up against baseline were tested with Wilcoxon tests between treatments. For Barrett-related and unpaired categorical data, Fisher's exact test was used for between-treatment comparison. For de novo and remissions data, odds ratio and significances were computed with function glm. For paired binary categorical variables, the odds ratio was computed from the interaction in a generalized mixed model with function glmer in package lme4 [27,28]. Multivariate analysis was applied to identify demographic and clinical variables that were independently associated with GERD. Bayesian statistics were applied to measure the prediction accuracy by the area under the curve (AUC). The out-of-sample predictive fit was estimated with cross-validation using package propred [29].

Results

Of 1063 patients who underwent LRYGB ≥5 years prior to study commencement, 169 did not meet the inclusion criteria, were lost to follow-up, or had died. Of the remaining 894 patients, 236 were contacted, and 86 were willing to participate. Of 347 patients with LSG, 113 did not meet the inclusion criteria, were lost to follow-up, or had died. Of the remaining 234 patients, 154 were contacted, and 83 were willing to participate. Eleven patients (4 LSG, 7 LRYGB) had had a gastroscopy due to upper gastrointestinal symptoms in the 12 months before the study began and were excluded (none had BE). Twenty-two LSG-patients had been converted to LRYGB due to therapy-refractory reflux disease. In all these patients, preoperative endoscopy had shown reflux esophagitis, but BE was not identified in any case.

In the final analysis, 169 patients were included (83 LSG, 86 LRYGB) with a median 7.0 years (range, 5–13.5 yr) after surgery. Baseline characteristics are described in Table 1. Preoperatively, there were no differences between the 2 intervention groups concerning sex, age, weight, and prevalence of co-morbidities. As expected from the clinical

Table 1
Demographic, anthropometric, and key clinical data from patients who completed the prospective study

Factor	Before surgery		At follow-up (>5 yr after surgery)		
	Sleeve gastrectomy	Gastric bypass	Sleeve gastrectomy	Gastric bypass	*P* value,* LSG versus LRYGB
Number	83	86	83	86	—
Female sex, n (%)	55 (66.3)	62 (72.1)	—	—	—
Age (yr), median [IQR]	45.00 [36.00, 54.00]	45.00 [37.25, 55.00]	53.00 [42.00, 60.50]	52.00 [44.00, 62.00]	—
BMI (kg/m^2), median [IQR]	44.73 [41.19, 48.74]	42.93 [39.62, 46.68]	32.95 [29.76, 37.22]	30.42 [27.36, 34.11]	—
Years after surgery, mean ± SD	—	—	7.3 ± 1.6	6.7 ± 1.3	—
%EBMIL after 5 yr, median [IQR]	—	—	53.62 [36.81, 74.07]	71.81 [53.10, 88.51]	.002
%EBMIL at follow-up, median [IQR]	—	—	57.60 [39.18, 74.78]	67.39 [53.71, 86.79]	.001
Change in BMI (kg/m^2) after 5 yr, median [IQR]	—	—	10.24 [7.97, 13.36]	10.94 [8.93, 14.53]	.073
Change in BMI (kg/m^2) at follow-up, median [IQR]	—	—	10.33 [7.96, 14.16]	11.63 [9.42, 14.63]	.051
Diabetes, n (%)	20/83 (24.1)	27/86 (31.4)	12/83 (14.5)	13/86 (15.1)	—
OSAS, n (%)	23/83 (27.7)	23/86 (26.7)	7/83 (8.4)	8/86 (9.3)	—
NSAR use, n (%)	12/83 (14.5)	9/86 (10.5)	19/83 (22.9)	10/86 (11.6)	—
Current smoker	—	—	19/82 (23.2)	19/85 (22.4)	—

LSG = laparoscopic sleeve gastrectomy; LRYGB = laparoscopic Roux-en-Y gastric bypass; IQR = interquartile range; BMI = body mass index; SD = standard deviation; %EBMIL = percent excessive BMI loss; OSAS = obstructive sleep apnea; NSAR = xxx.

Categorical variables: before and ≥5 years after surgery by treatment group. Continuous variables: before and after surgery by treatment group.

* *P* values are computed with Wilcoxon tests.

policy of our bariatric centers, reflux symptoms and reflux esophagitis were *less prevalent* in the group that subsequently underwent LSG.

Primary endpoint: incidence of BE

Before surgery, BE was documented in 1 LRYGB patient (Prague classification: C1, M3). At follow-up, 3 of 83 patients who underwent LSG (3.6%) had endoscopically and histologically confirmed de novo BE. In the LRYGB group, there was 1 de novo case of 86 patients (1.6%; LSG versus LRYGB; $P = .362$). In the LSG group, there were 2 short- (C0, M1) and 1 long-segment BE (C3, M5). In the LRYGB group, there was 1 de novo short-segment BE (C0, M1).

Secondary endpoints

Prevalence and severity of GERD. Clinical diagnosis of GERD based on all available information was noted in preoperative assessment in 12 of 83 patients who underwent LSG (14.5%) and 27 of 86 patients who underwent LRYGB (31.4%) (Table 2, Fig. 1; also see Supplementary Table 1). At follow-up, GERD was more common in the LSG group than in the LRYGB group (44 of 83 patients [53.0%] versus 23 of 86 patients [26.7%], respectively). Patients with GERD present before surgery reported remission in 4 of 12 patients who underwent LSG (33.3%) and in 15 of 27 patients who underwent LRYGB (55.6%). De novo development of GERD was more common in patients who underwent LSG (36 of 71; 50.7%) than in patients who underwent LRYGB (11 of 59; 18.6%).

Use of PPIs. Preoperatively, 7 of 83 patients who underwent LSG (8.4%) and 11 of 86 patients who underwent LRYGB (12.8%) used PPIs. At follow-up, PPI use was more common in the LSG group than in the LRYGB group (42 of 83 [50.6%] versus 17 of 86 [19.8%]). Fewer patients who underwent LSG than patients who underwent LRYGB stopped PPI treatment after surgery (3 of 7 LSG patients [42.9%] versus 7 of 11 LRYGB patients [63.6%]). Patients who underwent LSG who had not taken PPIs before surgery were more likely than patients who underwent LRYGB to use PPIs after surgery (38 of 76 LSG patients [50.0%] versus 13 of 75 LRYGB patients [17.3%]).

Hiatal hernia was described in preoperative endoscopy in 17 of 83 patients who underwent LSG (20.5%) and 23 of 86 patients who underwent LRYGB (26.7%). At follow-up, hiatal hernia was found in more patients who underwent LSG than patients who underwent LRYGB (33 of 83 LSG patients [40.2%] versus 16 of 86 LRYGB patients [18.6%]). Six of 17 patients who underwent LSG (35.3%) with hiatal hernia before surgery had no hernia at follow-up versus 16 of 23 patients who underwent LRYGB (69.6%). De novo development of hiatal hernia was more common in patients who underwent LSG than in patients who underwent LRYGB (19 of 53 [35.8%] versus 9 of 63 [14.3%], respectively).

Reflux esophagitis was present in the preoperative endoscopy in 19 of 83 patients who underwent LSG (23.0%) and 24 of 86 patients who underwent LRYGB (27.9%). At follow-up, the presence of esophagitis was more common in patients who underwent LSG than in patients who underwent LRYGB (48 of 83 [57.8%] versus 23 of 86 [26.7%], respectively), with clinically relevant erosive disease (LA grades B–D) documented in 23 of 83 patients who underwent LSG (27.7%) versus 5 of 86 patients who underwent

Table 2
Prevalence of gastroesophageal reflux disease and incidence of Barrett esophagus

Factor	Before surgery		At follow-up (>5 yr after surgery)	
	Sleeve gastrectomy	Gastric bypass	Sleeve gastrectomy	Gastric bypass
Number	83	86	83	86
Clinical diagnosis of GERD	12/83 (14.5)	27/86 (31.4)	44/86 (53.0)	23/86 (26.7)
PPI use	7/83 (8.4)	11/86 (12.8)	42/83 (50.6)	17/86 (19.8)
On daily basis	7/83 (8.4)	10/86 (11.6)	26/83 (31.3)	10/86 (11.6)
If needed	0/83	1/86 (1.2)	15/83 (18.1)	7/86 (8.1)
Endoscopy findings				
Hiatal hernia	17/83 (20.5)	23/86 (26.7)	33/83 (39.8)	16/86 (18.6)
Reflux esophagitis	19/83 (22.9)	24/86 (27.9)	48/83 (57.8)	23/86 (26.7)
LA grade A	13/19 (68.4)	14/24 (58.3)	25/48 (52.1)	18/23 (78.3)
LA grade B	6/19 (31.6)	10/24 (41.7)	15/48 (31.3)	4/23 (17.4)
LA grade C	0/17	0/24	7/48 (14.6)	1/23 (4.3)
LA grade D	0/17	0/24	1/48 (2.1)	0/23
Barrett esophagus	0/83	1/86 (1.2)	3/83 (3.6)	2/86 (2.3)
Stenosis of stomach			2/83 (2.4)	2/86 (2.3)
Ulceration foot, point anastomosis			0/83	2/86 (2.3)
Histopathology				
Intestinal metaplasia (Barrett)	0/83	1/86 (1.2)	3/83 (3.6)	2/86 (2.3)
Dysplasia/carcinoma	0/83	0/86	0/83	0/86

GERD = gastroesophageal reflux disease; PPI = proton pump inhibitor; LA = Los Angeles classification of reflux esophagitis.
Values are given as counts (%). Categorical variables: before and ≥5 years after surgery by treatment group.

LRYGB (5.8%). One of 17 patients who underwent LSG (5.9%) and 14 of 24 patients who underwent LRYGB (58.3%) with esophagitis before surgery experienced remission. De novo development of esophagitis was more common in patients who underwent LSG (27 of 50; 54.0%) than in patients who underwent LRYGB (13 of 62; 21.0%), and there was a shift in the distribution toward more severe disease (Fig. 2).

Symptoms of reflux and dysphagia at 5-year follow-up

Clinically relevant GERD-Q scores (>8 points) were more frequent in patients who underwent LSG than in patients who underwent LRYGB (41 of 79 [51.9%] versus 9 of 86 [10.5%], respectively; Table 3), and moderate-to-severe dyspeptic symptoms also were more frequent in the LSG group than in the LRYGB group (24 of 79 [30.4%] versus 8 of 86 [9.3%], respectively). Swallowing problems were not common and psychometric assessments were similar in both groups (data not shown).

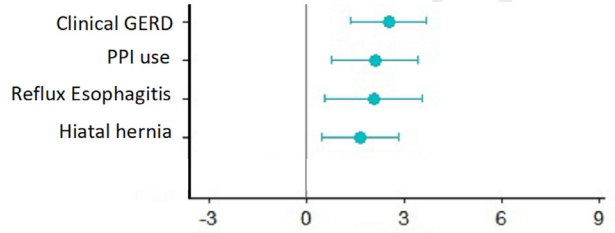

Fig. 1. Relative effects of laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass on gastroesophageal reflux disease. Results for Barrett esophagus are not shown because the incidence was low and the confidence intervals wide. Log-odds ratios for all transitions as estimated from a logistic mixed model, ordered by log-odds. A value of zero indicates no change. An odds ratio >1 indicates that the condition is more frequent following laparoscopic sleeve gastrectomy. This considers the distribution of all other values and the within-subject correlation.

Physiologic investigations

HRM and wireless pH measurements were performed in a subset of 45 patients who underwent LSG and 60 patients who underwent LRYGB. Clinically relevant motility disorders as defined by the Chicago Classification version 4.0 were infrequent, with no differences between the groups (details will be reported separately [30]). The results showed higher median (interquartile range [IQR]) acid exposure (10.30 [5.10, 16.30] versus .45 [.10, 1.33] times per pH <4) with more acid reflux events per day (71.00 [29.00, 89.00] versus 9.00 [4.00, 18.50]) in patients who underwent LSG compared with patients who underwent LRYGB. The proportion of symptoms associated with reflux (symptom index) was a median 33% (.00, 66.00) in the LSG group with very few symptoms in the LYRGB group triggered by reflux events. In the LSG group, there was an association between symptom severity (GERD-Q), acid exposure (r^2 = .38), and reflux esophagitis (r^2 = .32).

Predictors of outcome

Multivariate analysis with cross-validation included the operative group, preoperative GERD diagnosis, demographic variables, and body mass index (BMI) at follow-up as predictors of GERD after surgery (Supplementary Table 2). The LSG operation was the most relevant predictor

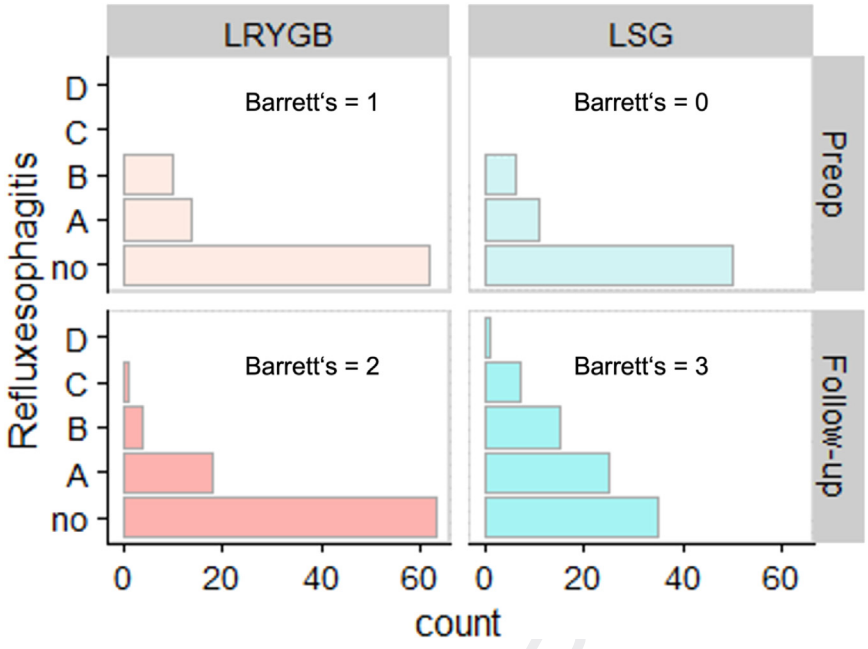

Fig. 2. Grade of reflux esophagitis (Los Angeles classification) before and after bariatric surgery. Following laparoscopic sleeve gastrectomy, there is an increase in the frequency and severity of mucosal inflammation, whereas the opposite is the case after laparoscopic Roux-en-Y gastric bypass.

of a postoperative diagnosis of GERD, with an AUC of .62 (95% CI, .52–.71). Adding preoperative GERD as a second predictor increased the AUC to .64 (95% CI, .55–.74). Adding sex, age, and BMI did not alter the results.

Weight loss and resolution of diabetes

Reduction in body weight expressed as percent excess BMI loss at 5 years was 53.6% in the LSG group and 71.8% in the LRYGB group ($P = .002$). At follow-up (median of 7.0 ± 1.5 yr), percent excess BMI loss was 57.6% in the LSG group and 67.4% in the LRYGB group ($P = .001$).

Preoperatively, 20 of 83 patients who underwent LSG (24.1%) and 27 of 86 patients who underwent LRYGB (31.4%) had type 2 diabetes. At follow-up, the remission rate was 11 of 20 (55.0%) in patients who underwent LSG and 14 of 27 (51.9%) in patients who underwent LRYGB. De novo diabetes was seen in 3 of 63 patients who

Table 3
Questionnaire results: somatic and psychological symptoms

Result	Sleeve gastrectomy	Gastric bypass
EDQ (swallowing function)		
Sum score, median [IQR]	0 [0, 0]	0 [0, 0]
GERD-Q (reflux symptoms)		
Sum score, median [IQR]	8.00 [6.00, 10.00]	6.00 [6.00, 6.00]
Patients reaching cutoff ≥8 points, n (%)	44/79 (55.7)	9/86 (10.5)
LPDS (dyspeptic symptoms)		
Sum score, median [IQR]	5.00 [2.00, 10.50]	2.00 [0, 4.00]
Patients with a score of 0–4 points (normal), n (%)	38/79 (48.1)	67/86 (77.9)
Patients with a score of 5–8 points (mild), n (%)	17/79 (21.5)	11/86 (12.8)
Patients with a score of 9–16 points (moderate), n (%)	17/79 (21.5)	4/86 (4.6)
Patients with a score of 17–32 points (severe), n (%)	7/79 (8.9)	4/86 (4.6)
HADS (anxiety and depression)		
Sum score, median [IQR]	6.00 [2.00, 11.50]	4.00 [2.00, 8.00]
Anxiety scale = HADS-D/A; cutoff ≥11 points, n (%)	9/79 (11.4)	5/86 (5.8)
Depression scale = HADS-D/D; cutoff ≥9 points, n (%)	7/79 (8.9)	6/86 (7.0)
VSI (visceral sensitivity/somatization)		
Sum score, median [IQR]	25.00 [16.00, 34.00]	19.50 [15.25, 32.75]

EDQ = Esophageal Dysphagia Questionnaire; IQR = interquartile range; GERD-Q = Gastro-Esophageal Reflux Disease Questionnaire; LPDS = Leuven Postprandial Distress Scale; HADS = Hospital Anxiety and Depression Scale; D/A = xxx; D/D = xxx; VSI = Visceral Sensitivity Index. Q10

underwent LSG (4.8%) and in none of the patients who underwent LYRGB.

Discussion

This prospective cohort study reports the incidence of BE ≥5 years after LSG and LRYGB. In addition, clinical, endoscopic, and physiologic measurements provide insights into the prevalence and causes of GERD after bariatric surgery.

The findings confirm that the risk of reflux symptoms and disease is greater after LSG than after LRYGB, but the de novo development of BE (primary endpoint) was rare and was not significantly more common ≥5 years after LSG (3.6%) than after LRYGB (1.2%). This is not higher than could be expected after the same time period in a general population of patients with reflux esophagitis on endoscopy [31,32]. These results contrast with those from the majority of retrospective case series [3–5], although 2 recent studies performed to check these alarming findings did not show such a high de novo BE incidence [33,34]. A meta-analysis of 10 studies that included 680 patients who had undergone endoscopy 6 months to 10 years after LSG showed a pooled prevalence of 11.6% for BE (95% CI, 8.1%–16.4%) after 5 years, with the risk of developing metaplasia increasing over time [7]. If this prospective study had confirmed these findings, then LSG would have been established as an important risk factor for this premalignant condition; instead, a relatively low incidence of BE was observed. Previous studies have major limitations that likely explain the discrepant findings. First, preoperative endoscopy was not routinely performed, and therefore, it is not known whether BE was present at baseline or developed de novo during follow-up. This is relevant because, in addition to GERD, the prevalence of BE increases with obesity and the presence of metabolic syndrome, with or without type 2 diabetes (i.e., key indications for bariatric surgery) [16,35,36]. Second, the indication for gastroscopy after LSG was not defined. If investigations were performed to investigate reflux symptoms, then this selection bias would increase the apparent prevalence of BE. Third, the endoscopic finding was not always confirmed by histology, and it is known that this leads to overdiagnosis of BE [20]. Our study addressed this issue by recruiting unselected patients who had completed ≥5 years of follow-up after bariatric surgery and met entry criteria at our institutions. The nonrandomized study design is representative of "real life" clinical practice in which LRYGB is preferred in patients with preexisting GERD and large hiatal hernias. Indeed, as noted in the Methods section, the high prevalence of GERD after LSG makes a randomized controlled trial comparing these 2 procedures ethically difficult to justify. Although it is possible that patients with upper gastrointestinal symptoms are over-represented in patients who consented to participate, approximately half the patients enrolled after LSG did not have clinically relevant reflux symptoms (GERDQ <8). As well as recruiting a more representative population of patients who underwent LSG, we also studied patients who underwent LRYGB to exclude the possibility that demographic or clinical factors present at baseline drove the de novo development of BE (active comparator group). Preoperatively, the 2 groups were well matched (Table 1) except for GERD, which was *less prevalent* in the group that subsequently underwent LSG because patients with obesity and this condition were preferentially referred for LRYGB—a strategy most bariatric centers follow [37]. A limitation of this research is that the study was stopped early due to the SARS-Cov2 pandemic (see Statistical Analysis section). Interim analysis revealed a lower BE incidence in the LSG group than expected. On this basis, the decision was made to stop the study because there was no prospect of reaching significance without increasing patient numbers well above original estimates. Nevertheless, although the absolute risk is low, an increase in the relative risk of developing BE after LSG compared with LRYGB cannot be excluded. Indeed, the risk of BE after LSG may be higher in centers that routinely perform LSG in patients with clinically relevant GERD. Conversely, LRYGB has even been shown to be associated with regression of BE and dysplasia in some patients [38].

Our findings confirm that the prevalence and severity of GERD were higher after LSG than after LRYGB whichever aspect of this multidimensional condition was considered: (1) reflux and dyspeptic symptoms *but not* dysphagia (rare in both groups); (2) reflux esophagitis, especially clinically relevant erosive disease; (3) pathologic acid exposure, reflux events, *and* reflux-associated symptoms; (4) use of PPIs (Table 2, Supplementary Table 1). Additionally, 22 patients who underwent LSG (∼13% of the total contacted) were excluded because they had been converted to LRYGB due to therapy-refractory reflux disease within the 5-year follow-up period. Importantly. none of this group had BE on endoscopy before reoperation. Only descriptive statistics are provided for these secondary endpoints because this was a nonrandomized trial; however, the results were consistent with those of the randomized SM-BOSS cohort comparing the outcomes of LSG and LRYGB [2]. Specifically, the proportion of patients suffering from GERD at 5 years after surgery was similar to that in this trial (around 50% in LSG patients and 25% in LRYGB patients) and reports from other nonrandomized cohort studies (50%–75% in LSG patients and 15%–30% in LRYGB patients) [39,40] as well as early 1-year follow-up from a randomized controlled trial [34].

Consistent with a previous analysis after 1-year follow-up [39], multivariate analysis showed that the operative group (LSG) and preoperative GERD diagnosis were independent predictors of a postoperative GERD diagnosis 5 years after bariatric surgery (Table 3). This is particularly striking because, as noted earlier, patients with bothersome symptoms or endoscopic evidence of reflux disease were referred

more often for LRYGB than for LSG. Sex and higher age and weight were not *independently* associated with a postoperative GERD diagnosis.

The 2 bariatric operations have very different effects on the structure and function of the upper gastrointestinal tract. Following LRYGB, most of the stomach is bypassed, and the potential for gastroesophageal reflux is greatly reduced. Indeed, consistent with previous reports [39,41], clinically relevant acid reflux was present in very few patients after LRYGB, and when it did occur, there was often evidence of obstruction at the gastrojejunal anastomosis or in the distal efferent loop. By contrast, although the incidence varies between centers, LSG has multiple effects on the esophagogastric junction and stomach that can cause de novo GERD or worsen existing GERD [39,40,42–47]. Detailed assessment by magnetic resonance imaging and high-resolution manometry have shown that a reduction in esophagogastric junction length and pressure, increased (more obtuse) esophagogastric insertion angle, and marked reduction (>80%) of gastric capacity are associated with the risk of GERD after this procedure [48]. It was noted that excess BMI loss was less in the LSG group than in the LRYGB group (56.9% versus 70.0%), but this factor did not appear to impact the risk of postoperative GERD.

Conclusion

This prospective, nonrandomized clinical cohort trial reports a low incidence of BE in 169 patients ≥5 years after bariatric surgery. The prevalences of reflux symptoms and esophagitis were higher in patients who underwent LSG than in patients who underwent LRYGB, but very few patients who underwent LSG (<4%) developed de novo BE during the follow-up period, and no dysplasia or neoplastic change was identified in any participant. This finding provides some reassurance for patients with obesity who have had LSG and also for doctors and surgeons caring for this cohort. Notwithstanding this finding, the high incidence of moderate-to-severe reflux esophagitis in LSG patients at follow-up supports the recommendations that (1) preoperative endoscopy should be performed to inform patient selection for bariatric procedures and (2) postoperative surveillance should be performed after LSG, even in the absence of GERD symptoms.

Disclosures

The Uniscientia Foundation supported this trial. The authors have no commercial associations that might be a conflict of interest in relation to this article. The sponsors had no role in study design, data accrual, data analysis, or manuscript preparation. All authors had full and independent access to all data and vouch for the integrity and accuracy of the analysis and its adherence to the protocol.

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