



Bariatric surgery and gastroesophageal reflux disease

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Abstract: With the rapidly increasing prevalence of obesity globally, the practice of bariatric surgery is being adopted routinely to prevent the development of chronic conditions as well as some forms of cancers associated with obesity. Gastroesophageal reflux disease (GERD) is one of those chronic conditions. Furthermore, there is accumulating data that obesity is associated with complications related to longstanding GERD such as erosive esophagitis (EE), Barrett's esophagus (BE), and esophageal adenocarcinoma (EAC). Central obesity, rather than body mass index (BMI), appears to be more closely associated with these complications. It should be expected, therefore, that weight loss procedures should result in improvement in GERD symptoms and its associated complications. However, in reality the different bariatric surgical procedures have unpredictable effects on an established GERD and may even produce GERD symptoms for the very first time (*de novo*). In this review, we explore the literature studying the effects of bariatric surgical operations on GERD. Roux-en-Y gastric bypass appears to have the most beneficial effect on GERD. On the other hand, laparoscopic sleeve gastrectomy and laparoscopic adjustable gastric banding (LAGB) are linked with long-term increased prevalence of GERD. We argue that GERD is an extremely important preoperative consideration for any patient undergoing bariatric surgery and therefore should be thoroughly investigated objectively (with 24-hour pH study and high-resolution manometry) to select the most suitable bariatric procedure for patients for their long-term success.

Keywords: Bariatric surgery; gastroesophageal reflux disease (GERD); laparoscopic adjustable gastric banding (LAGB); laparoscopic Roux-en-Y gastric bypass (LRYGB); laparoscopic sleeve gastrectomy

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Background

Obesity is a global epidemic with increasing prevalence. The latest Centers for Disease Control and Prevention data shows that the prevalence in the United States has risen to 40% of adults and 18.5% in the young (1). Globally, an estimated 200 million men and 500 million women are

obese, representing 10% of the world's population (2).

Obesity is a well-documented risk factor for many health conditions including cardiovascular disease, type-2 diabetes mellitus, osteoarthritis and some cancers (3). Furthermore, obesity is an important and independent risk factor for gastroesophageal reflux disease (GERD) and weight loss seems to be associated with significant improvement in

symptoms of GERD (3).

The pathophysiology of GERD in adults is not fully understood but it is considered to be multifactorial (4). It is due to a mixture of hereditary and functional factors that result in abnormal relaxation of the lower esophageal sphincter (LES) or increased pressure from the stomach [e.g., from a hiatus hernia (HH) or increased intra-abdominal pressure] (5). The diagnosis of GERD is made clinically, with typical symptoms of heartburn, acid or water brash, regurgitation, dysphagia and odynophagia (6). However, atypical symptoms or extra-esophageal symptoms such as cough, sinusitis and pharyngitis can predominate and confuse the issue (6). The severity can only be assessed objectively by 24 or 48 hours ambulatory pH study or by a wireless pH Bravo monitoring device which can be utilized for up to 96 hours (7). Untreated GERD can result in reflux erosive esophagitis (EE), necrosis, ulceration, strictures and Barrett's esophagus (BE) (8). Ten percent of cases of BE can progress to esophageal adenocarcinoma (EAC) (6).

What is the relationship between obesity and GERD? Abdominal obesity has been postulated to promote GERD by elevating intra-abdominal pressure, which promotes reflux and the development of HH (9). Studies comparing computerized tomography-measured abdominal fat composition showed that patients with EE, BE and EAC had greater intra-abdominal visceral adiposity than controls (10). The metabolically active visceral abdominal fat may also predispose to BE and EAC by GERD-independent mechanisms that promote the progression from inflammation to metaplasia and neoplasia; these include alterations in the levels of adipokines, cytokines and chemokines, as well as the insulin/insulin growth factor pathways (11). Hampel *et al.* conducted a meta-analysis exploring the link between obesity and GERD (12). Nine studies were included and six found a statistically significant association with obesity and GERD. Increasing body mass index (BMI) was also associated with progressive risk of GERD, EE and EAC, likely driven by increased intra-abdominal pressure and the gastroesophageal pressure gradient.

Bariatric surgery has demonstrated significant and durable weight loss. It has significantly evolved over the last decade. The current bariatric surgery procedures offered include restrictive procedures such as the laparoscopic vertical sleeve gastrectomy (LVSG) and laparoscopic adjustable gastric banding (LAGB) or malabsorptive procedures such as laparoscopic Roux-en-Y gastric bypass (LRYGB) (3). The case-volumes in the United States have shifted with most recent data showing LVSG accounting for 60%

of bariatric surgery while 18% are LRYGB and 3% are LAGB (13). In theory, bariatric surgery should result in reduced GERD through facilitating sustainable weight loss. However, studies have demonstrated varying responses of GERD to bariatric surgery, depending on which surgery is performed. Therefore, the preoperative evaluation of all such patients is important in preparation for bariatric surgery as no one operation is appropriate for all patients. In 2008, the American Society for Gastrointestinal Endoscopy recommended a preoperative upper gastrointestinal endoscopy for all bariatric surgery patients due to the high number of incidental clinically significant findings which include HH, esophagitis, gastritis, BE, peptic ulcer disease or upper gastrointestinal tumors (14). Barium swallow studies can be an important adjunct to identify HH, however, they are notoriously underestimate the presence of HH if static images are obtained and therefore dynamic fluoroscopic study should always be performed. In more recent guidelines, the recommendations are more lenient with the decision to perform preoperative upper gastrointestinal endoscopy to be individualized and tailored to the surgeon, the patient and the type of bariatric surgery (15). The potential benefits of undertaking these preoperative assessments remains valid.

The aim of the present review article was to assess the impact of various bariatric surgical procedures, not on weight loss, but GERD.

LVSG and GERD

LVSG is popular due to its relative simplicity compared to other bariatric operations and success in providing sustained weight loss. However, studies describing its effects on GERD have demonstrated conflicting outcomes, and there is growing evidence that it may have negative impact on GERD.

Stenard and Iannelli conducted the largest systematic review of LVSG and GERD which included 25 studies (16). The findings were mixed. Thirteen studies found worsening of GERD post-LVSG across 5,953 patients with a mean BMI of 42 ± 4 kg/m² (range, 37–55.5 kg/m²) and mean follow up of 29 ± 22 months (range, 3–72 months) (16). Only one study was prospective whereas the rest were retrospective. The evaluation of GERD was heterogenous, and although all studies had preoperative endoscopy data, postoperative evaluation varied (16). These included esophageal manometry, contrast studies and 24-hour ambulatory pH studies, with the majority including subjective clinical evaluation by means of symptoms of validated questions (e.g., Montreal's criteria) (16). Twelve studies found clinical

improvement on GERD across 1,863 patients, with a mean BMI of 51 ± 13 kg/m² (range, 36.5–65 kg/m²) and mean follow-up 20 ± 15 months (range, 6–60 months) (16). A majority of the studies were based on clinical evaluation, again with only a few utilizing endoscopy, 24-hour ambulatory pH studies, esophageal manometry or contrast studies (16). With the aforementioned findings, the authors proposed caution with performing LVSG due to the unquantified potential for worsening rates of GERD (16).

Chiu *et al.* conducted a systemic review of 15 studies analyzing the effects of LVSG on GERD (17). Again, there was discordance with four studies showing an increase in GERD after LVSG while seven studies showing an improvement (17). Three studies only included the postoperative prevalence of GERD and one did not include any data on both pre- and postoperative prevalence (17). For the studies where overall prevalence of GERD following LVSG reduced, it was noted that patients with pre-existing GERD had shown improvement, however, new GERD developed in a proportion of patients (17). However, Chiu *et al.* did not quantify the number or proportion of new cases of GERD and therefore it is difficult to make any firm conclusions based on retrospective nature of this review and subjective provision of the data (17).

Oor *et al.* conducted the first meta-analysis on this topic and like the authors above, they were unable to provide uniformed consensus conclusions due to the high heterogeneity of available studies (18). They included 33 studies with 8,092 patients undergoing LVSG (18). The majority of the studies ($k=30$) reported clinical evaluation of GERD symptoms postoperatively, while four included use of anti-acid medications and eight studies utilized functional tests (18). Interestingly, the studies utilizing validated questionnaires had a risk difference of 4.3% postoperatively, while the eight studies with functional tests had paradoxical results (18). The pooled incidence of *de novo* GERD was 20%. Given this, the authors made no definite conclusions, stating only that there appears to be an increased prevalence of GERD symptoms post LVSG (18).

Himpens *et al.* conducted a randomized study with one and three year follow-up comparing LAGB and LVSG (19). Eighty patients were randomized equally into each arm. GERD was determined by the usage and change of usage of proton pump inhibitors (PPIs) (19). They found that 75% of patients who underwent LVSG with pre-existing GERD had resolution, however, 21.8% new cases developed at the first year (19). By three years, only 3.1% reported GERD (19).

The anatomical and physiological effects on GERD

post LVSG have multi-factorial explanations. In cases of *de novo* GERD, it is thought to be due to decreased gastric emptying, reduced LES pressure, blunting of the angle of His, decreased compliance and reduced volume of the stomach and increased intra-gastric pressure secondary to the narrow gastric pouch and herniation of part of the sleeve into the mediastinum (17,20). Indeed, several investigators such as Braghetto *et al.* have shown patients with LVSG to have reduced LES pressure via esophageal manometry (21). Himpens *et al.* postulated that a lack of gastric compliance, emptying and blunting of angle of His was responsible for GERD at one year, and that this compliance improved by three years accounting for the reduced *de novo* GERD (19).

The shape of the sleeve itself can be a significant cause of GERD. Keidar *et al.* studied 716 patients who underwent a LVSG and suffered GERD postoperatively (22). Using barium swallow studies, they identified that all 716 patients had a dilated upper sleeve with a relative narrowing of the mid-stomach (22).

Genco *et al.* evaluated the incidence of GERD in patients undergoing LVSG with pre- and postoperative endoscopic and histologic examinations (23). Of 110 patients, they found a significant increase in GERD symptoms and PPI intake (23). They also found a significant increase in the incidence of EE, as well as new diagnosis of BE in 17.2% of patients. GERD is, therefore, an important long-term complication to consider and evaluate post-LVSG (23). Genco *et al.* advocated for endoscopic surveillance after LVSG, irrespective of the presence of GERD symptoms (23).

In view of these results, the improvement in GERD post-LVSG can be postulated to be anatomical (e.g., resection of acid-producing gastric fundus, accelerated gastric emptying and reduced gastric volume) or systemic (reduced intra-abdominal pressure due to weight loss).

The role of HH repair in bariatric surgery is an important consideration for patients with GERD. Concurrent LVSG with HH repair has been explored with more contemporary studies showing supportive evidence of improvement in GERD. Soricelli *et al.* studied 378 bariatric patients undergoing LVSG (24). Sixty patients had pre-operative GERD and 42 patients had a pre-operative diagnosis of HH (24). Intra-operatively, a further 55 patients were found to have HH (24). Ninety-seven patients underwent concurrent LVSG with HH repair (24). They found significantly higher rates of *de novo* GERD symptoms in patients who did not undergo a concurrent HH repair with their LVSG (22.9% vs. 0%, $P=0.01$) (24). Daes *et al.* also found resolution of GERD in 94% of their patients (25). In their study cohort of

134 patients, 34 were found to have HH (25). Twenty-nine of these patients had preoperative GERD (25). All 34 underwent LVSG with HH repair and at 6 to 12 months follow up only 2 of 134 patients had symptoms of GERD (25). Both patients had preoperative large HH with a persistent small HH diagnosed on post-operative endoscopy (25).

LVSG should be carefully considered for patients with significant preoperative GERD. They may be suitable for alternative bariatric operations. Similarly, there should be an awareness for the potential development or worsening of GERD.

LAGB and GERD

LAGB has had mixed results with GERD. de Jong *et al.* conducted a systemic review to explore this (26). There were 20 studies with 3,307 patients (26). There was a significant reduction in GERD symptoms reported from 33.7% preoperatively to 7.7% postoperatively, and PPI usage reduced from 27.5% to 9.5% (26). A subset of patients developed *de novo* GERD (15%) and new onset of reflux esophagitis (29.4%) (26).

Chen *et al.* explored this further (27). They performed high-resolution esophageal manometry and 24-hour ambulatory esophageal pH study on three groups: asymptomatic LAGB (n=14), symptomatic LAGB (n=20) and preoperative reflux patients (n=20) (27). They found that symptomatic patients had a significantly larger gastric pouch with higher esophageal acid exposure (P<0.001) (27). The symptomatic group also had significantly LES resting tone and impaired contractility of the lower esophageal segment (27).

Himpens *et al.* found that although GERD was only present in 8.8% of patients at one year, by three years 20.5% of LAGB patients had developed *de novo* GERD, following the opposite trend to LVSG (19). It appears that LAGB provides short-term improvement of GERD symptoms (19). The subset of patients who develop new onset disease, it is difficult to tell whether this is from pathologic GERD or complications of LAGB (19). It is postulated that the band placement may create a high-pressure system promoting GERD (19). The authors did not explore or discuss the effects of volume of filling within the band for LAGB patients or whether emptying the band improved symptoms (19).

In summary, there is evidence to support the short-term improvement with GERD after LAGB. However, there appears to be a proportion of patients who develop *de novo* GERD or following gastric band complication such as slippage of band in the long-term.

LRYGB and GERD

LRYGB is considered most effective bariatric procedure for GERD (3,28). Indeed, it has been recommended as the procedure of choice for patients with intractable GERD following standard anti-reflux surgery, although, this notion is increasingly being challenged in recent literature.

In patients with severe GERD symptoms post LVSG, with resistance to maximal medical therapy, revisional surgery has been advocated: LRYGB is the procedure of choice in these patients. Cheung *et al.* conducted a systematic review of studies examining patients undergoing revisional bariatric surgery for failed weight loss (29). GERD was assessed in three studies, and found that all patients (n=15) had complete resolution of GERD symptoms with repeat LRYGB (29). Parmar *et al.* converted 22 LVSG to LRYGB and found that 100% of patients reported improvement in GERD symptoms, and 80% were able to cease medications (30).

Many studies have shown significant improvement in GERD with LRYGB. Frezza *et al.* studied 152 patients with pre-existing GERD who underwent LRYGB (31). There was a significant decrease in all GERD-related symptoms including heartburn, water brash, wheezing, laryngitis and aspiration (P<0.01). The use of medications dropped significantly for both PPI and H₂ blockers (P<0.01) (31). Perry *et al.* performed LRYGB on 57 patients with persistent GERD. At a mean follow-up of 18 months, all patients experienced a clinical improvement or no symptoms of GERD (32).

Madalosso *et al.* studied 53 patients and evaluated them for GERD preoperatively, at six months and at 39 months post-surgery (33). There was a statistically significant reduction in GERD as assessed by the Montreal Consensus as well as an esophageal acid exposure assessment (33). They found the reduced incidence of GERD and reflux esophagitis was statistically significantly between preoperative, six and 39 months (33).

Mendes-Filho *et al.* conducted a systematic review exploring conversion of previous anti-reflux surgeries to LRYGB for refractory GERD (34). They found six studies where gastric bypass was used, with a total of 121 patients (34). Ninety-nine of the patients underwent LRYGB while 22 underwent open RYGB (34). One hundred and six patients had total remission of symptoms, while 12 showed partial improvement (34). In the studies which included use of PPI, 29 out of 35 patients ceased their use (34).

Recently, Holmberg *et al.* has contested this long-standing

notion and postulated that the effect has been overstated (35). They studied all adult patients who underwent RYGB in Sweden which included 2,454 patients (35). The median follow-up was 4.6 years (IQR 3.1–6.3). They defined postoperative reflux as residual or recurring symptoms of GERD with use of acid suppression medications for beyond six months postoperatively (35). Interestingly, they found GERD persisted in 48.8% of patients within two years of RYGB and persisted for up to 10 years after surgery (35). The strongest risk factor for postoperative GERD was high-dose preoperative acid suppression (35). In comparison, less than 10% of patients have persisting GERD after the traditional anti-reflux surgery of fundoplication (35). Despite these findings, the authors concede that RYGB remains the most effect bariatric procedure in reducing GERD for the aforementioned reasons (35).

Comparison studies

High quality trials have been challenging in bariatric surgery. There have been very few randomized controlled trials (RCT); most have been small feasibility studies for larger trials that did not progress to recruitment. Existing prospective studies have been very heterogenous in patient selection, operative approach, definition, diagnosis and evaluation of GERD. The following are current landmark prospective trials in this area.

The Swiss Multicenter Bypass or Sleeve Study (SM-BOSS) is an RCT comparing LRYGB and LVSG (36). Two hundred and seventeen patients were enrolled and randomly assigned to undergo LRYGB (n=110) or LVSG (n=107) (36). GERD remission was observed more frequently after LRYGB (60.4%) than after LVSG (25.0%) (36). GERD worsened (as defined by more symptoms or increase in acid suppressing therapy) more often after LVSG (31.8%) than after LRYGB (6.3%) (36). At five years, *de novo* GERD developed in 32% of LVSG patients compared to 11% of LRYGB patients (36). Nine percent of patients who underwent LVSG required a subsequent LRYGB to manage their refractory symptoms of GERD (36).

Similarly, but in a smaller RCT (n=100), Ignat *et al.* report two LVSG conversions to RYGB for severe GERD, with additional patients requiring medical management (37). However, the interpretation of these outcomes is confounded by the lack of description regarding the presence or absence of HH in patients receiving surgery. Similarly, concomitant HH repair within procedures and the preoperative use of physiological testing, such as 24-hour pH study and high-

resolution manometry, is not consistently reported.

The Sleeve *vs.* Bypass (SLEEVEPASS) study was another RCT comparing long-term outcomes between LVSG and LRYGB (38). This was a multicentered, multi-surgeon randomized control trial in Finland. Two hundred and forty patients were enrolled and randomized to undergo LVSG (n=121) or LRYGB (n=119) (38). GERD was not a primary or secondary outcome, and all those with severe GERD preoperatively or with large HH, were excluded from the study (38). This study also included five-year follow-up with 80.4% of patients reaching it (38). At five years, 6% of the LVSG patients required conversion from sleeve to LRYGB for severe reflux, while 9% required daily PPI. GERD was not reported in the LRYGB group (38).

Zhang *et al.* also conducted an RCT comparing long-term outcomes of LVSG and LRYGB. However, they did not explore GERD outcomes (39).

Biter *et al.* randomized 150 patients to LVSG or LRYGB, and compared their quality of life at preoperative, 2 and 12 months (40). They used the GerdQ (GERD Questionnaire) score only to assess reflux, with a higher score denoting more reflux (40). At 12 months there was an 85% completion rate (40). The GerdQ score increased significantly for patients undergoing LVSG at 2 and 12 months, while it decreased significantly for patients undergoing LRYGB (40).

BOLD (Bariatric Outcomes Longitudinal Database) is a prospective database of patients undergoing bariatric surgery. Using this database, Pallati *et al.* identified 36,938 patients who had preoperative evidence of GERD (41). After excluding patients with concomitant HH repair or fundoplication, there were 22,830 patients with six months follow up. Mean age was 47.6±11.1 years, with an 82% female population. Mean BMI was 46.3±8.0 kg/m² (41). Patients undergoing LRYGB, LAGB and LVSG all demonstrated significant reduction in their GERD symptom score (6-point scale). The GERD score improvement was maximal in LRYGB patients, followed by LAGB and then LVSG (41).

Conclusions

Obesity is an important risk factor for GERD. While bariatric surgery is the most effective and sustainable treatment for obesity, GERD must be considered for all patients undergoing such procedures. LRYGB has shown superiority over LVSG for alleviation and management of GERD symptoms from the available literature. It has

reported efficiency similar to Nissen fundoplication and is the options with refractory GERD post-fundoplication in obese patients. A patient's preoperative status should be evaluated to optimize their choice of bariatric surgery: patient selection is key. In appropriately worked-up patients who have GERD, LRYGB could be considered as the first option. In patients with HH, this should be evaluated, and treatment should be considered during their bariatric surgery. While LVSG continues to become more commonly performed, it is important to monitor these patients for the long-term risks of developing GERD and its sequelae. In case of troublesome GERD symptoms following LVSG and LAGB, revisional surgery with LRYGB seems to be the best option.

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