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Reflux following bariatric surgery

Fabrizio Rebecchi, Elettra Ugliono, Mario Morino

Department of Surgical Sciences, University of Torino, Torino 10126, Italy.

Correspondence to: Dr. Elettra Ugliono, Department of Surgical Sciences, University of Torino, Corso A.M. Dogliotti 14, Torino 10126, Italy. E-mail: elettra.ugliono@unito.it

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Abstract

Bariatric surgery is the most effective treatment for morbidly obese patients. Studies investigating the relationship between bariatric surgery and gastroesophageal reflux disease (GERD) are discordant. Depending on the type of intervention, pre-existing GERD can improve, worsen, or develop "*de novo*" in previously unaffected patients. Therefore, a review of the literature is performed to evaluate the effects of different bariatric surgical procedures on GERD. Currently, the bariatric surgical procedures more frequently performed are laparoscopic sleeve gastrectomy (LSG) and gastric bypass. The majority of studies examining the relationship between GERD and bariatric surgery are low quality, small, and non-randomized. Furthermore, GERD has been investigated through clinical symptoms scales or questionnaires, which often do not correlate with objective endoscopic or functional findings. Therefore, the interpretation of the results of these studies is challenging. Roux-en-Y gastric bypass is considered the preferred surgical operation for bariatric patients with GERD. Despite contradictory results reported among the studies, GERD seems to be a major issue after LSG. Preliminary results on mini-gastric bypass/one anastomosis gastric bypass seem to indicate that biliary reflux might be overrated, but more long-term results are mandatory before drawing conclusions. Further studies are needed to clarify the role of extensive preoperative examinations prior to bariatric surgery, even in asymptomatic patients, and provide clear guidance regarding the indications for the bariatric surgery technique of choice according to the patient's characteristics.

Keywords: Bariatric surgery, sleeve gastrectomy, Roux-en-Y gastric bypass, one anastomosis gastric bypass, mini-gastric bypass, gastroesophageal reflux disease (GERD)

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common clinical condition caused by the reflux of gastric contents into the esophagus, causing troublesome symptoms or complications[1].

The close relationship between GERD and obesity is well-established. Previous research showed that increasing body mass index (BMI) is associated with a higher risk of developing GERD symptoms and complications, such as erosive esophagitis and Barrett's esophagus, the incidences of which in the bariatric population are reported to be 13%-26% and 0.1%-6%, respectively[2-3]. Moreover, weight reduction leads to improvement in GERD symptoms and reduction in esophageal acid exposure time[4].

The primary pathogenetic mechanism of GERD in obese patients is the increased intra-abdominal pressure caused by abdominal adiposity, which promotes the gastric contents to ascend into the esophagus and contributes to hiatal hernia formation[5,6]. In fact, the prevalence of hiatal hernia is higher than in the general population and is reported in up to 40% of morbidly obese patients[7].

Furthermore, obesity is linked to an increased frequency of transient lower esophageal sphincter relaxations, probably caused by the postprandial mechanical distension of the proximal stomach[8].

Bariatric surgery is the most effective long-term treatment for obesity[9]. Currently, there are two principal bariatric operations performed worldwide: laparoscopic sleeve gastrectomy (LSG) and gastric bypass[10].

There is controversy surrounding which bariatric procedure should be offered to obese patients with GERD. While both procedures were demonstrated to be equally effective in promoting weight reduction and resolution of comorbidities, there is debate regarding other aspects, such as long-term maintenance of weight control and GERD[11].

Depending on the type of operation, preoperative GERD symptoms can worsen postoperatively, while "*de novo*" GERD can occur after bariatric surgery in previously unaffected patients.

This article reviews the current literature on GERD after bariatric surgery.

SLEEVE GASTRECTOMY

LSG consists of creating a stapled tubular stomach tailored on a bougie; therefore, weight loss is induced by the reduced gastric reservoir function, leading to early satiety, and by the reduction in ghrelin levels due to the removal of the gastric fundus. LSG overcomes the disadvantages of other bariatric procedures, avoiding gastrointestinal anastomoses, the use of foreign materials, and determines fewer postoperative nutritional deficiencies compared to pure malabsorptive procedures[12,13].

Data in the literature concerning GERD after LSG are confusing, with some authors reporting an improvement while others a worsening of GERD symptoms[14].

Several possible pathogenetic mechanisms have been proposed to justify the effects of LSG on GERD. On the one hand, the theoretical mechanisms of GERD worsening after LSG could be the surgical disruption of the angle of His, the reduced tone of the lower esophageal sphincter due to sling fibers resection during the creation of the gastric sleeve, and the increased intragastric pressure of the sleeve due to gastric volume and accommodation reductions. On the other hand, a reduction in GERD after LSG could be explained by the

decreased number of acid-producing parietal cells, the accelerated gastric emptying due to the resection of the gastric fundus, and the weight loss itself induced by LSG[15].

The majority of studies investigating GERD after LSG rely on clinical evaluation of symptoms or endoscopic findings. For instance, Oor *et al.*[16] performed in 2016 a systematic review and meta-analysis including 33 articles for a total of 8092 obese patients submitted to LSG. They pooled the results of the 11 studies reporting pre- and postoperative GERD clinical assessment with validated questionnaires and estimated a slightly increased risk (4.3%) of postoperative GERD prevalence after LSG. The incidence of "*de novo*" GERD after LSG ranged from 0%-34.9%, with a pooled incidence of 20%, while "*de novo*" erosive esophagitis ranged from 6.3%-63.3%. In a more recent systematic review and meta-analysis, Yeung *et al.*[17] included 46 retrospective and cohort studies for a total of 10,718 patients who underwent LSG. They found that, in patients with reflux complaints before LSG, GERD symptoms increased by 19%, whereas "*de novo*" reflux occurred in 23% of patients after LSG. However, these data need to be interpreted with caution since the simple evaluation of symptoms is not sufficient for GERD diagnosis, as it cannot allow identifying silent reflux or differentiating GERD from other GERD-like pathologies (such as visceral hypersensitivity)[18]. Conversely, endoscopy can only diagnose the presence of hiatal hernia and GERD complications but cannot identify non-erosive disease. In fact, the correct diagnosis of GERD is made only with functional instrumental evaluation by means of esophageal manometry and ambulatory 24 h pH(-impedance) monitoring.

Recently, Balla *et al.*[19] performed a systematic review of 12 studies objectively evaluating pre- and postoperative GERD by means of esophageal manometry and/or pH-metry. Despite a wide heterogeneity of data that did not allow performing a meta-analysis due to the different diagnostic techniques (conventional *vs.* high-resolution manometry) and parameters considered, LSG appeared to negatively impact GERD when objectively evaluated. Of the 12 studies included in the systematic review, seven reported a reduction in lower esophageal sphincter tone, while nine reported a worsening of DeMeester's score and esophageal acid exposure time compared to baseline. However, the substantial heterogeneity between the studies might limit the reliability of the results.

Despite a standardized surgical technique, sleeve shapes can differ, and there is increasing evidence that the configuration of the gastric tube could play a role in the pathogenesis of GERD after LSG.

Technical failures during gastric transection might result in gastric stenosis, which manifests with symptoms such as dysphagia, regurgitation, food intolerance, and GERD. The reported incidence of gastric stenosis after LSG in the literature ranges from 0.1% to 3.9%[20]. Gastric stenosis can occur in the case of a sharp angulation of the laparoscopic stapler, a twisting of the gastric wall during gastric transection, or the construction of a too narrow sleeve (calibration on a small bougie size or oversewing of the staple line)[21].

This uncommon but serious complication is diagnosed through upper gastrointestinal series with contrast medium and could require endoscopic dilatations or surgical reintervention.

Some authors have radiologically evaluated the anatomy of the gastric remnant after LSG and examined how these findings affect postoperative clinical outcomes[22].

For instance, Toro *et al.*[23] classified the sleeve configurations depicted in radiological contrast studies into four patterns: tubular (37%), which is the desired sleeve shape; upper pouch (8%), which is due to an incomplete fundus resection; lower pouch (22%), which is caused by excessive antral preservation; and

dumbbell (33%), which is defined as the presence of a combined upper and lower pouch[23]. They demonstrated that the upper pouch shape was associated with higher severity of GERD and lower satiety control.

Therefore, it is of paramount importance to pay meticulous attention to technical details while performing LSG to minimize the risk of postoperative GERD.

To reduce the negative impact of LSG on GERD, some authors have advocated the routinary repair of all intraoperatively detected hiatal hernias regardless of size[24].

Recently, Chen *et al.*[25] performed a systematic review and meta-analysis comparing the outcomes of LSG with or without additional cruroplasty. Considering the four studies directly comparing the two techniques, they found that GERD symptoms remission was higher in the hiatal hernia repair group (OR: 2.97, 95%CI: 1.78-4.95, $P < 0.0001$). At the same time, no significant differences were observed concerning the incidence of "*de novo*" GERD symptoms.

These results are in contrast with those reported by Małczak *et al.*[26] in a systematic review and meta-analysis including five studies comparing LSG with concomitant hiatal hernia *vs.* LSG alone. The authors concluded that the addition of a cruroplasty did not provide advantages in terms of GERD symptoms resolution and "*de novo*" GERD occurrence, while reporting a longer operative time for the cruroplasty group.

Therefore, we can conclude that the role of aggressive hiatal hernia repair during LSG is not yet defined.

Some authors have proposed the addition of fundoplication after LSG. Several techniques have been described, involving the creation of a Collis-Nissen, Nissen-Rossetti, Dor, or Toupet antireflux valve[27]. Preliminary reports show the safety and feasibility of these procedures, with acceptable rates of postoperative complications and improvement of GERD symptoms and reduced rate of esophagitis at short-term follow-up[28,29]. However, no comparative studies with LSG alone are available, and data regarding long-term follow-up and objective functional evaluation of GERD are awaited before evaluating the introduction of this procedure in clinical practice.

Definitively, there is an increasingly recognized incidence of GERD symptoms and esophageal mucosal injury after LSG, although the higher risks of Barrett's esophagus and dysplasia after LSG are not yet well established since the data in the literature are controversial.

Therefore, even in the absence of strong evidence, the major bariatric surgical scientific societies provided position statements recommending strict endoscopic surveillance after LSG to enable early detection of early esophagogastric malignancies[30,31].

ROUX-EN-Y GASTRIC BYPASS

Roux-en-Y gastric bypass (RYGB) is considered the procedure of choice for obese patients with GERD because it combines the control of GERD symptoms with the benefits of weight loss and resolution of obesity-related comorbidities[32].

The mechanisms proposed to explain the effects of RYGB on GERD include the reduced acid production of the gastric pouch, which contains a lower number of acid-producing parietal cells; the faster emptying of the gastric pouch, which prevents regurgitation of gastric content; and the diversion of bile from the Roux limb[14].

Several studies have attempted to elucidate the relationship between RYGB and GERD, mainly through the analysis of symptoms, demonstrating a substantial improvement in GERD symptoms after RYGB[33,34]. For instance, the long-term results of the Swiss Multicenter Bypass or Sleeve Study (SM-BOSS), a randomized clinical trial comparing LSG (n = 107) and RYGB (n = 110), reported a considerable rate of remission of GERD symptoms after RYGB at five-year follow-up, significantly higher than after LSG (60.4% *vs.* 25%, $P < 0.002$)[35]. In addition, during the study period, 9 out of 16 LSG reoperations were conversions to RYGB due to GERD.

Furthermore, RYGB is associated with erosive esophagitis and Barrett's esophagus regression[36,37]. In a meta-analysis performed by the International Federation for the Surgery of Obesity and Metabolic disorders (IFSO) Barrett's Oesophagus task force, RYGB seems to induce Barrett's esophagus remission in 62.9% of patients (95%CI: 53.4%-71.6%), while no studies reporting Barrett's esophagus remission after LSG are available in the literature[38]. Therefore, the authors encouraged performing RYGB in the case of a preoperative finding of Barrett's esophagus.

However, data on an objective functional examination that could fully elucidate the relationship between GERD and RYGB are scarce in the literature.

Some authors have reported a reduced esophageal acid exposure after RYGB. For instance, Madalosso *et al.*[33] performed clinical assessment, endoscopic evaluation, esophageal manometry, and ambulatory pH monitoring in 86 patients before surgery and at three-year follow-up, showing a significant reduction in GERD symptoms prevalence (64% *vs.* 33%, $P < 0.001$). Furthermore, normalization of pathologic acid exposure occurred in 45% of the patients with preoperative abnormal findings at pH monitoring. Similar results were reported by Mejia-Rivas *et al.*[34] who performed 24 h pH monitoring before and six months after RYGB on 20 patients. The percentage of esophageal acid exposure time dropped from 10.7% ± 6.7% to 1.6% ± 1.2% ($P < 0.001$) and DeMeester's score fell from 48.3 ± 8.5 to 7.7 ± 1.4 after RYGB. Rebecchi *et al.*[39] divided 86 patients submitted to RYGB into two groups depending on the presence of preoperative GERD at 24 h pH-impedance esophageal monitoring. In the 32 patients with preoperative pathologic reflux, acid reflux normalized, while there was an increase in postoperative esophageal exposure to weakly acidic reflux 60 months after RYGB. Thus, they concluded that weakly acidic reflux, which could be due to dysmotility of the Roux limb, could be responsible for the small percentage of patients still experiencing GERD after RYGB.

Several authors have suggested RYGB is also the preferred strategy for GERD patients with BMI > 35 kg/m^2. Laparoscopic fundoplication is considered the most effective surgical treatment for GERD[40]. However, concerns have been raised regarding the magnitude and durability of the effects of this procedure in the bariatric population, given the pathophysiology of GERD in obese patients[41,42]. Abdelrahman *et al.*[43] performed a systematic review and meta-analysis of 13 observational studies comparing the outcomes of laparoscopic fundoplication in obese (n = 1753) and non-obese (n = 6246) patients. The results of the study show that, while the perioperative outcomes were similar between the two groups, an increased rate of GERD recurrence in obese patients (11.4% *vs.* 3.4%) was observed at follow-up. Therefore, RYGB should be considered the procedure of choice for controlling GERD symptoms in patients with BMI > 35 kg/m^2 who

fulfill the 1991 National Institute of Health consensus criteria, given the durability of its effects over time and the additional benefits of weight loss and resolution of obesity-related comorbidities[44-46].

RYGB has also been proposed as a revisional procedure after failed fundoplication. Laparoscopic antireflux failure requiring reoperation is reported to occur in 3%-7% of patients[47]. According to a systematic review performed by Furnée *et al.*[48], including 81 studies for a total of 4584 reoperations considered, the main indications for reoperation after laparoscopic antireflux surgery were recurrent GERD (41.7%) and dysphagia (16.6%). The most frequent reason for fundoplication failure was intrathoracic wrap migration, which occurred in 27.9% of patients, and redo fundoplication was the most frequently adopted approach.

More recently, several authors have compared the outcomes of redo fundoplication *vs.* conversion to RYGB after primary antireflux surgery. For instance, in an observational study by Shao *et al.*[49], 101 patients undergoing revisional RYGB and 79 patients undergoing redo fundoplication were analyzed. The two procedures were equally effective in controlling GERD, with an 85.5% success rate at long-term follow-up. Similar results were reported by Yamamoto *et al.*[50], who performed a retrospective review of patients who underwent redo fundoplication (n = 119) and revisional RYGB (n = 64). The overall satisfaction rate was 87% and did not differ between the two groups. Furthermore, in a subset analysis, they found that morbidly obese patients who underwent revisional RYGB had improved clinical outcomes compared to those who underwent redo fundoplication. Therefore, RYGB should be considered a valuable reoperative strategy, especially in morbidly obese patients, after primary failed antireflux surgery.

Finally, RYGB has been proposed as a revisional procedure after LSG. In a recent systematic review and meta-analysis including 17 articles for a total of 556 patients who underwent conversion from LSG to RYGB, Matar *et al.*[51] showed that the most frequent indications for revision were insufficient weight loss/weight regain (52%) and severe GERD (30.4%). They reported that conversion to RYGB resulted in effective weight loss, with a percentage of excess weight loss of 40% at 12-month follow-up, and a complete resolution of GERD symptoms occurred in 79.9% of patients at one year and 91.3% at two years after revisional RYGB.

MINI-GASTRIC BYPASS/ ONE ANASTOMOSIS GASTRIC BYPASS

Mini-gastric bypass/one anastomosis gastric bypass (MGB/OAGB) has been proposed in recent years as a potential alternative to RYGB. Some authors consider this modification of Mason's loop gastric bypass attractive due to the advantages of a shorter operative time and a lower rate of complications, reducing possible anastomotic leakage sites[52,53].

Despite the favorable safety and efficacy outcomes of this procedure, controversies regarding possible long-term complications have limited its widespread adoption[54]. The most concerning issue related to MGB/OAGB is GERD, which can occur in up to 0%-30% of patients after MGB/OAGB[55]. The main theoretical pathogenetic mechanism of GERD after MGB/OAGB seems to be biliary reflux, which is responsible for the onset of alkaline gastritis and increases the risk of gastroesophageal malignancies in the long term.

MGB/OAGB opponents justify their reticence by quoting previous studies reporting reflux-inducing characteristics of Mason's gastric bypass, which led to abandoning this procedure[56,57].

The evidence from the current literature suggests that the risk of biliary reflux seems to be lower than previously expected, affecting < 2% of patients, with no increased rate of esophagogastric malignancies[58]. However, according to a recent systematic review, almost 20% of reoperations following MGB/OAGB, which are reported to be 1.34%, were conversions to RYGB due to bile reflux. The authors concluded that, even if bile reflux seems not to be a major issue after MGB/OAGB, regular endoscopic follow-up is advisable[59].

These results need to be interpreted with caution since the majority of the studies reporting the outcomes of MGB/OAGB come from a few selected experienced groups, with a short-term follow-up. Long-term results and objective evaluations are warranted before drawing conclusions on MGB/OAGB.

ADDITIONAL BARIATRIC PROCEDURES

Additional bariatric procedures less commonly performed are biliopancreatic diversion with duodenal switch (BPD/DS) and single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S).

In the BPD/DS technique, a sleeve gastrectomy is associated with a duodenal transection, and the reconstruction of the intestinal continuity is performed on a Roux-en-Y configuration through duodeno-ileal and ileo-ileal anastomoses. It was first described by Gagner in 2000 in a series of 40 consecutive patients, demonstrating the feasibility of the procedure despite its complexity[60]. BPD/DS has been proposed as a primary bariatric procedure in super-obese patients since it provides the highest rates of weight loss and diabetes resolution compared to other bariatric procedures[61,62]. However, the widespread use of BPD/DS has been limited by the technical difficulty and associated increased perioperative morbidity, mortality, and long-term complications[63,64].

There are limited data in the literature concerning the effects of BPD/DS on GERD, reporting worrisome rates of GERD symptoms after surgery. For instance, Bolckmans *et al.*[65] reviewed 153 BPD/DS patients and observed a 43.8% rate of "*de novo*" GERD occurrence at a mean follow-up of 130 months. In another study including 76 consecutive patients undergoing primary BPD/DS at the Mayo Clinic, Badaoui *et al.*[66] found that, even though the resolution of GERD symptoms occurred in 44.7% of patients, "no effect" and "*de novo* " GERD were reported by 36.8% and 18.4% of patients, respectively. To date, BPD/DS is rarely performed as a primary operation but is gaining increasing interest as a revisional bariatric procedure, especially after LSG[67]. However, a recent expert consensus panel recommended avoiding revisional BPD/DS in patients requiring conversion of a primary bariatric procedure due to GERD[68].

SADI-S is a simplified version of BPD/DS, introduced in 2007 by Sànchez-Pernaute[69]. After the creation of the sleeve gastrectomy, the duodenum is transected, and the intestinal continuity is restored through a single duodeno-ileal anastomosis, similar to a Billroth II operation. The reduced complexity of this procedure, requiring only one anastomosis, made this technique attractive as a primary and revisional bariatric procedure after LSG failure. However, currently, there are only case series with limited follow-ups published in the literature, and no information regarding the effects of SADI-S on GERD is still available[70].

CONCLUSIONS

The heterogeneity of the studies investigating the effects of LSG on GERD makes it difficult to draw conclusions. However, the overall impression is that LSG negatively impacts pre-existing GERD and is associated with a non-negligible rate of postoperative *de novo* GERD. Therefore, LSG should be considered carefully in bariatric patients with preoperative GERD symptoms or complications. RYGB is considered the preferred surgical procedure for obese patients with GERD, with excellent results in terms of symptoms

control and weight loss outcomes, as both a primary and a revisional bariatric procedure. Conflicting data on biliary reflux control and a lack of long-term clinical data make it difficult to provide recommendations regarding the adoption of MGB/OAGB.

Further research aiming to elucidate the pathogenesis of the effects of bariatric procedures on GERD is warranted to allow more precise patient selection criteria before surgery.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Rebecchi F, Ugliono E

Performed data acquisition, as well as provided administrative, technical, and material support: Morino M

Availability of data and materials

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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