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Gastro Esophageal Reflux Disease after Sleeve Gastrectomy: A Real Issue and Future Perspectives

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Abstract

Bariatric surgery, fueled by an obesity epidemic, increased rapidly worldwide. According to the report from International Federation for the Study of Obesity and Metabolic Disorders (IFSO) survey, 579,517 bariatric procedures were performed worldwide in 2014. Among various bariatric procedures, Laparoscopic Sleeve Gastrectomy (LSG) was the most commonly performed procedure although it was the newest bariatric procedure. Since it was firstly proposed as a primary bariatric surgery, LSG is growing rapidly across the world because of its relative simple technique and efficacy, despite the paucity of long-term results. However, the main long-term drawback of L is the development of *de novo* Gastro Esophageal Reflux Disease (GERD). The present article examines and discusses the development and management of this new and important issue and covers four major fields: (1) GERD in obesity; (2) GERD after LSG; (3) Management of GERD after LSG; and (4) Future perspective.

Keywords: Laparoscopic sleeve gastrectomy; GERD; Revision surgery; RYGB

Introduction

Obesity and its related metabolic disorders are increasing to epidemic proportions at an alarming rate worldwide [1]. It is estimated that more than 300 million adults worldwide are obese (Body Mass Index [BMI] >30 kg/m^2) and 20% of them are morbidly obese (BMI >35 kg/m^2). In Taiwan, the incidence of morbidly obese patients (BMI >35 kg/m^2) has doubled the incidence in the past decade and consisted 1.5% of the population in a recent survey [2]. Bariatric surgery had been proven to produce sustainable effect in morbid obesity with weight reduction and remission of co-morbidities [3,4]. However, the type of bariatric procedures evolved in the past 5 decades. Laparoscopic Sleeve Gastrectomy (LSG), a procedure with vertical resection of 75% of the greater curvature side of the stomach, has been gaining popularity as a stand-alone bariatric surgery worldwide since the proposal as a primary bariatric procedure [5,6]. According to the latest International Federation for the Study of Obesity and Metabolic Disorders (IFSO) survey, among 579,517 bariatric procedures performed worldwide in 2014, LSG was the most commonly performed procedure that reached 45.9% [7]. LSG has the advantages of relative technical simplicity, fewer impacts on the gut physiology and few potential serious postoperative complications, but Gastro-Esophageal Reflux Disease (GERD) is a major side-effect after LSG faced by surgeons [8-10]. Although pre-operative existed GERD might be improved after LSG but many patients developed *de novo* GERD. It is estimated that more than half of the patients required Proton Pump Inhibitor (PPI) after LSG and some might develop Barrette's esophagus at long-term follow-up [11-17]. How to control and treat this chronic and debilitating condition is currently a very new health issue. Unfortunately, long-term data of LSG was inadequate and current medical treatment has been relatively unsatisfactory in the treatment of this situation. The present review summarizes the recent data in GERD after LSG, and discusses the possible management of this problem.

Gastro Esophageal Reflux Disease (GERD) and Obesity

GERD was defined as when reflux of stomach contents in the esophagus cause troublesome symptoms, including heartburn, regurgitation, laryngitis, dysphagia and chronic cough [18]. Prolonged acid or bile exposure of the esophagus may produce Barrett's esophagus, a pre-cancer lesion of lower esophagus [17]. The diagnosis of GERD can be established by typical symptoms [19]. Other investigating modalities included endoscopy, barium swallowing, 24-hour esophageal pH monitoring, esophageal manometry and symptom reporting, but there is no gold standard [19].

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Obesity, especially central or abdominal visceral obesity, was known to be the most important risk factor of GERD [20-23]. Obese patients usually show increased numbers of reflux symptoms and increased esophageal acid exposure on conventional pH studies and an increased risk of erosive esophagi is detected during Esophagogastro duodenoscopy. The main reason is that obesity will increase the intra-abdominal pressure which then will increase the intragastric pressure and gastroesophageal pressure gradient, and incidence of a hiatal hernia [23]. In one study, the increase of Body Mass Index (BMI) was found to result in the impairment of gastroesophageal ant reflux function [20]. Also, obesity seems to impair esophageal motor function, such as esophageal dysmotility, including impaired complete bolus transit at impedance, defective Lower Esophageal Sphincter (LES), non specific motility disorder, nutcracker esophagus, distal spasm, and even achalasia [23]. The presence of hiatal hernia increases the distance between LES and diaphragmatic crus which may defect the anti-reflux mechanism and the development of GERD [23]. About half of the morbid obese patients had co-existed hiatal hernia at the time of bariatric surgery [24]. On the other hand, about 50% of the morbidly obese patients had associated GERD and required medication before bariatric surgery [25-27]. According to the Bariatric Outcomes Longitudinal Database data, 46% of the bariatric patients had medication for GERD before surgery [25]. Bariatric surgery significantly reduced the GERD score and medication 1-y after surgery but the reduction is more prominent after RYGB than after LSG [25-27]. In addition, at 1-y after surgery, LSG patients had a significantly higher rate of new acid reduction medication when compared to gastric bypass patients (35 *vs* 7.3%, $p < 0.01$) [27]. Because GERD in morbidly obese patients is more associated with the presence of hiatal henia rather than BMI itself, hiatal hernia repair thus, is becoming important in bariatric surgery, especially in LSG [28-30]. However, contrary data existed [31].

GERD after Sleeve Gastrectomy

LSG was proven to be an effective weight loss surgery with significant weight loss and decrease of abdominal visceral fat [8-10]. The accompanied decrease of intra-abdominal pressure may contribute to the improvement of GERD symptoms and reduce the medication of GERD after LSG [25-27,31]. Althuwaini et al. [15] recently reported that although the majority of the patients did not develop new-onset symptoms or even had improved symptoms of GERD after LSG, there remained a significant proportion that developed new-onset symptoms or had worsening of symptoms of GERD after SG (ranging from as high as 35.7% for symptoms of regurgitation to as low as 16.0% for heartburn causing sleep disruption) [15]. They concluded that some regurgitation was non-acid food regurgitation and hypothesized that regurgitation of gastric contents could have a major role in patient symptoms and might not be assessed completely by the questionnaire. Mandeville et al. [12] also reported a significant increase in GERD and PPI dependency after LSG in spite a satisfactory long-term effect on weight loss was achieved. Data from the Bariatric Outcomes Longitudinal Database, bariatric surgery can significantly reduce the GERD score and medication 1-y after surgery [25]. However the reduction of medication was higher in RYGB (56.2%) than LSG (37.3%). LSG is a significant negative predictor for GERD relief after bariatric surgery [25]. The main reason for this negative predictor is the *de novo*, new onset, GERD after LSG [27]. Although the data was controversial at the beginning, more and more studies reported the development of *de novo* GERD in many patients without any symptoms before surgery but developed GERD after SG [10-17]. With long-term follow-up, the incidence of GERD can be high up to half of the patients (Table 1). Most worrisome was that some patients developed Barrett's esophagus, a pre-cancer lesion of esophageal cancer. Genco et al. [17] noticed the postoperative presence of 76% of esophagitis and/or GERD symptoms and, alarmed, a 17% of newly diagnosed Barrett's Esophagus [17]. Therefore, GERD becomes the most important long-term complication of LSG and should be closely monitored in the future. Some of the important points related to the development of GERD after LSG are introduced as follows:

Pathophysiological change of LSG and GERD

Several anatomic and pathophysiologic changes of the Lower Esophageal Sphincter (LES) function secondary to the creation of the gastric sleeve that might cause GERD after LSG have been hypothesized. The most important mechanism for the development of GERD after LSG is probably related to the intragastric high pressure after resection of the fundus. Some Authors demonstrated by means of High Resolution Mometry (HRM) and combined 24-h pH and Multichannel Intra-Luminal Impedance (MII-pH) how the increased intra-gastric pressure caused by the tubulization of stomach can provoke increased post prandial reflux [32-34]. The persistent high pressure in LSG may also contribute to the defect of LES, hiatal hernia and intra thoracic migration of the LSG tube. The second mechanism is related to the destruction of LES by LSG. It is possible that LSG may severe the sling fiber around Esophao-Cardiac (EC) junction and impair the LES. Klaus and Weiss first said that esophageal function, as in particular LES function, appears to be affected by LSG [35]. In their observational study, patients with normal LES function and lack of GERD symptoms developed *de novo* GERD after LSG, and patients with preoperative GERD and hypo-tensive LES developed worse GERD following LSG. Therefore, it is recommended to leave 1 cm to 2 cm from EC junction at the last cut of LSG, in order to avoid the leakage as well as to preserve the sling fiber of LES.

Intra-thoracic gastric tube migration was recently proposed to be an important pathology for GERD after LSG [36]. Intra-thoracic migration of gastric tube might further impair the LES and aggravate the GERD symptoms. The possible reasons for intra thoracic migration were the pressure gradient between thorax and abdomen, development of hiatal hernia and the high intragastric pressure after LSG.

Anatomical factor related to LSG technique which might induce *de novo* GERD

There is increasing evidence supporting that some technique points might be important on the incidence of postoperative GERD. The shape of the gastric sleeve plays a major role in leading to GERD. In particular, the main surgical technical issues are a relative narrowing of the mid portion of the sleeve, a redundant upper part of the sleeve. Keidar et al. [37] reviewed the UGI Gastrografin series in patients who developed postoperative GERD after LSG and found that a combination of dilated upper portion of the sleeve and a relative narrowing of the mid-stomach was present in all the patients. This anatomical situation may be secondary to a too narrow construction of the sleeve in association with retention of part of the gastric fundus by stapling far away from the left pillar of the crus, in order to minimize the risk of postoperative upper gastric fistulas. It has been speculated that the relative mid-gastric narrowing impairs the emptying of the upper part of the sleeve, causes food stasis and fermentation, while the retained fundus keeps producing acid, thus

Table 1: Long term results of SG in literature.

	Case No	F/U y	Bougie size, F	BMI (Kg/m2)	%TWL	%EWL	Revision rate %	GERD %	PPI use %	Barrett's %
Pork [9]	61	7	36	37.3	27.8	72.6	16.9%	17	50%	NA
Felsereich [10]	49	10	40.4	35.5	26.3	53	36%	45%	NA	NA
Arman [11]	65	11	34	11	21	62.5	25.4%	21.4%	NA	NA
Mandeville [12]	100	10	34	40.6	NA	60.8	29.5%	50%	50%	NA
Kowalewski [13]	127	10	36	51.6	23.5	51.1	NA	60%	47%	NA
Cadiot [14]	272	8	NA	44.8	22.9	53.9	NA	7%	NA	NA
Althuwaini [15]	213	8	32	47.8	38	84.1	NA	47%	21%	NA
Boza [16]	121	5	60	34.9	NA	62.9	NA	26.7%	NA	NA
Geno [17]	110	3	48	45.8	NA	74.1	NA	73.6%	NA	17.2%

BMI: Body Mass Index; F/U: follow-up; %TWL: Percentage Total Weight Loss; %EWL: Percentage Excess Weight Loss; GERD: Gastroesophageal Reflux Disease; PPI: Proton Pump Inhibitor.

favoring the onset of reflux of acid gastric contents into the esophagus. Similar findings were recently reported by Toro et al. [38]. They reviewed 76 patients with routine upper gastrointestinal series after LSG and classified the LSG as upper pouch, lower pouch, tubular or dumbbell. They found that patients with the upper pouch shape had the highest severity of GERD symptoms. The lower pouch shape was on the contrary associated with fewer GERD symptoms, suggesting an effective gastric emptying when the antrum is preserved. In the other hand, Himpens et al. [8] reported a two peaks type of GERD symptoms in their patients of follow up for 6 years. They detected a decrease of the incidence of GERD symptoms at 3 years after LSG, maybe secondary to the increase in gastric compliance, and a late reappearance of GERD incidence at 6 years that might be explained by weight regain with associated increased intra-abdominal pressure. Their finding emphasized the importance of long-term follow-up for LSG. They also noticed dilatation of the proximal sleeve leading to the formation of a "neofundus", which should be a technical error.

Gastric tube stenosis, either true stenosis or functional stenosis, is another important reason for the development of GERD after LSG [39]. The functional stenosis included gastric tube twisting or torsion or kinking. Usually is the result of technical error in un-symmetric resection of the anterior and posterior wall. Therefore, special attention should be given in leaving a wide angle and symmetrically cutting the anterior and when performing wall, gradually narrowing the gastric tube proximally.

Another point is the presence of a concomitant hiatal hernia. As previous mentioned, hiatal hernia is commonly present in morbid obesity patients. The presence of hiatal hernia may defect the LES and induce intra thoracic migration of the gastric tube. Therefore, repair of concomitant hiatal hernia is recommended for LSG [29,31]. Although controversial results existed, a recent systematic review by Mahawar et al [30] found that adding a crura repair to a SG can be a safe technique in obese with preoperative hiatal hernia, with acceptable post-operative GERD rates.

The last issue is the size of bougie. Several randomized trial had demonstrated that using a larger bougie size didn't reduce the weight loss comparing to using a smaller bougie [40,41]. However, using a small bougie size will increase the postoperative incidence of GERD. Therefore, using a bougie size less than 32 Fr size should be avoided [42].

Technique point of SG for the prevention of *de Novo* GERD

To summarize the current consensus of technique point of LSG in order to avoid *de novo* GERD, the operation is started from devascularization of the greater curvature side, all the way to left esophago-cardiac junction with full exposure of the left crus. Any coexisted hiatal hernia should be carefully checked and repaired. The resection of greater curvature side should be started from 4cm above the pyloric ring and leaving a very wide portion at the angle area. Then, continually resect the gastric tube toward EC junction. The resection should be symmetric at anterior and posterior wall without any tube twisting or torsion. The tube should be gradually narrowed toward EC junction, but end at 1 cm to 2 cm lateral to the EC junction to spare the EC junction. A continuous suture to invaginate all the stapler line with a bougie size up to 36 or more is recommended. The tube may then be fixed to retroperitoneum tissue to avoid the intra thoracic migration [43].

New technique proposed for preventing GERD

Actually, there are some studies suggesting combinations of ant reflux surgery with LSG to avoid the *de novo* GERD or to drastically reduce it. Actually, some authors have started adding a real fundoplication to avoid any kind of postoperative GERD. Haswalli et al. [44] recommended LSG with the addition of posterior hiatoplasty and anterior fundoplication to treat morbid obese patients with reflux. Le Page et al. [45] presented the effects of a sleeve gastrectomy associated with fundoplication in 4 patients with symptoms of reflux and delayed gastric emptying who also had hiatal hernia. A fundoplication in 120º associated with the LSG was performed. All patients improved in scores of symptoms in a GERD questionnaire. Another study from Nocca et al. [46] performed a Nissen-Sleeve on 25 obese patients with pre-existing GERD; at 12 months follow up, only 12% of them still experienced GERD symptoms or were taking PPIs [46]. Lee et al. [47] also presented a similar technique of Nissen fundoplication with gastric placation to have a similar result but without resection of stomach. Recently, Olmi et al. [48] fashioned a Rossetti-Sleeve technique (total fundoplication resembling the Rossetti modification of classical Nissen wrap). Using this technique, they reported that 95% of the patients did not complain any GERD symptoms at 1-y follow-up. However, objective data regarding reflux exposure are lacking in this case series. In conclusion, further studies are needed to evaluate the effective usefulness of a combination between LSG and anti-reflux surgery in obese patients due to the paucity of these data.

Treatment of GERD after SG

De novo GERD is increasing with increasing numbers of LSG performed. Medical treatment may be required in half of the patients

with LSG and significant portion of these patients may require revision surgery in the long-term [10-17,25-27].

Medical treatment

Medication including anta-acid drugs, H2 blocker, Proptom Pump Inhibitor (PPI) and mucosa protecting drugs are usually effective in controlling GERD symptoms. In severe GERD patients, the symptoms usually required daily PPI to control. However, prolong PPI usage may increase the risk of pneumonia and bone fracture [49]. Therefore, intervention treatment may be considered in patients with intractable GERD.

Conversion to RY gastric bypass

In patients with intractable GERD refractory to medical treatment, limited surgical options are available. Traditionally, RYGB has been the recommended as a highly effective anti-reflux bariatric procedure for patients with pre-operatively co-existed GERD and resolved GERD symptoms in up to 90% of patients [50-52]. Because of RYGB appears to be the safest treatment in severe obese patients in terms of avoiding GERD symptoms, there was the need to convert from LSG into RYGB, when LSG lead to unresponsive to medical management GERD. To date, conversion of LSG to LRYGB is also the procedure of choice in patients with objectively documented postoperative GERD. Several studies have reported excellent results in terms of improvement or resolution of reflux symptoms [53-56]. These patients were studied by Parmar et al. [53] whose study demonstrated that the conversion was very effective for GERD with 100% patients reporting improvement in symptoms, and 80% patients were able to stop their anti-acid medications [53]. More importantly, a recent study reported that RYGB may reverse the Barrett's esophagus, both endoscopic and histologic regression to normal mucosa [57]. Also, LSG can be converted into another kind of bypass, Single Anastomosis Gastric Bypass (SAGB). Safety and long-term effects of SAGB are proven [58] and SAGB gives the opportunity to convert the high-pressure system into a low-pressure system, improving GERD and additionally including the option on further weight loss, which is not always achieved by RYGB [59-61].

Non-RY bypass revision surgery

Because patients who chose to have LSG usually object to the proposal RYGB before surgery, converting to a RYGB to resolve their GERD are usually unacceptable. Therefore, other endoscopic or surgical treatments are also been developed. Laparoscopic anterior fundoplication with posterior crural approximation had been reported, however this procedure is reserved for those who had proximal gastric pouch dilatation [62]. Dilated upper sleeve was found to be an important risk for GERD after LSG [37]. However, without a sizable dilated pouch, anterior wrap is not possible to be performed. Desart et al. [63] reported successful treatment of *de novo* GERD after LSG using LINX® magnetic sphincter augmentation system (Torax Medical Inc, Shoreview, MN, United States) in 7 consecutive patients without a hiatal hernia or tube kinking. All patients reported a significant improvement in GERD symptoms at 2 weeks to 4 weeks after surgery. Recently, Ramiro et al. [64] described a technique using ligamentum teres to perform cardiopexy together with crural repair. Their technique stressed on the importance of the hiatal repair and the lower esophageal sphincter function but not addressing the issue with gastric tube kinking that happen in this series of patients. Another possible technique, Hill gastropexy was proposed by Sanchez-Pernaute A et al. [65]. This technique corroborated with the finding of Saber A et al. [36] who stressed the importance of reducing the intra-thoracic sleeve migration. While these results are promising, the few patients evaluated and the lack of long-term follow-up do not let draw any conclusion. In a recent report, Macedo reported the experience of hiatal repair in 9 patients with GERD after LSG [66]. They concluded that although the procedure was safe, most of the patients had improvement of their symptoms partially but still required medication for their symptoms. Therefore, longer follow up and monitoring will help to determine the long-term efficacy of these techniques.

At the moment, we don't recommend this technique in some conditions. In those with Barrett's esophagus, choosing this procedure may need further consideration. Barrett's esophagus carries potential malignant transformation in the long term [67]. Therefore, this procedure is not recommended as this procedure had not been proven in its long term efficacy. In another group of patient with true stenosis of the gastric tube, this procedure is not suitable. Patient with these conditions may be beneficial from RYGB.

New endoscopy treatment

Endoscopic approaches to GERD treatment had been developed as a bridge between medical treatment and surgical treatment. Some endoscopic techniques, such as intra-luminal plication or mucosal injection had been tried but failed. The Stretta procedure (Mederi Therapeutics Inc, Greenwich, CT, USA) which applies radiofrequency ablation to the LES remains an available technique for the treatment of GERD [68]. There is data examining the long-term durability of Stretta, with the data up to 8 years [69,70].

Future Perspective

In a decade, LSG has become the most popular bariatric/metabolic surgical procedure. Tens thousands cases of LSG are performed in many countries worldwide. Although weight loss and patients' satisfaction are both high, surgeons start to face many patients requiring PPI for their persistent GERD. Some technique errors causing anatomy defects prone to GERD development were identified and consensus for LSG technique was achieved. However, *de novo* GERD after LSG may not be avoided because LSG creates an intra-gastric high pressure system which is prone for GERD development. Thus, the true incidence of *de novo* GERD after LSG and accompanied Barette's esophagus remained to be decided.

At present, patients should not be deprived LSG as a primary bariatric procedure which is a relative safe and effective treatment for morbid obesity. However, the patients should be notified for the risk of GERD. At present, LSG should be avoided in patients with concomitant significant GERD before surgery. Surgeons should be aware the risk of GERD after LSG, and be familiar with the management and follow-up of GERD after LSG.

Conclusion

The success of bariatric surgery in obese individuals (BMI >35 kg/m^2) has led to a paradigm shift of metabolic surgery for the treatment of T2DM, including patients with a BMI <35 kg/m^2. A rapidly increasing demand for bariatric/metabolic surgery occurred worldwide with a huge number of bariatric/metabolic surgeries being performed worldwide yearly. Among various procedures, LSG is the leading procedure now because of the relative technically easier and efficacy. Although significant weight loss may alleviate GERD symptoms in morbid obese patients, LSG can exacerbate GERD in some patients and cause *de novo* reflux in others. The development

of GERD after LSG is related to some anatomic situation caused by surgical technique but also due to the intra-gastric high pressure after LSG. Care should be taken to perform a correctively fashioned sleeve and avoid a dilated upper pouch when performing LSG and simultaneous LSG and repair of hiatal hernia is recommended. Conversion to RYGB is necessary in patients with intractable GERD after LSG although some non-RYGB options are available. The anatomic and physiologic cause of *de novo* GERD after LSG should be continually investigated. Further studies and long-term follow-up of GERD after LSG are needed to clarify these issues in the future.

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