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ORIGINAL CONTRIBUTIONS

Correlation Between Symptomatic Gastro-Esophageal Reflux Disease (GERD) and Erosive Esophagitis (EE) Post-vertical Sleeve Gastrectomy (VSG)

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Abstract

Background Laparoscopic sleeve gastrectomy (LSG) has become the preferred bariatric procedure in many countries. However, there is one shortcoming of LSG in the long-term follow-up and this is the onset of GERD and erosive esophagitis (EE). Current evidence of the effect of SG on GERD did not consolidate to a consensus. In this study, we objectively evaluate the incidence of EE 1 year post-LSG with upper endoscopy (EGD) and try to identify the significant variables and possible underlying mechanisms of the EE post-LSG.

Methods Over a period of 5 years (2011–2016) at Singapore General Hospital, we retrospectively reviewed a prospectively collected database of a cohort of patients whom had LSG by a single surgeon who routinely performed EGD pre-operative and 1 year post-operative to assess EE and hiatal hernia. Patient's endoscopic findings and demographic and anthropometric data were analyzed.

Results We identified a total of 97 obese patients who underwent LSG at our hospital by studied surgeon. Sixty-three patients (64.9% of original sample) were finally evaluated in the present study, 40 (59.7%) of whom were female. The mean (range) age of patients was 38.2 (18–66) years, and mean BMI was 36.3 ± 4.1 kg/m^2. Median time to follow-up EGD was 13 months (range, 12–15). Following LSG, there was a significant decrease in both BMI (42.1 ± 1.2 vs. 29.9 ± 1.0 kg/m^2) and percentage excess weight loss of 56.6 ± 3.6%. The prevalence of EE on endoscopy increased from 9 (14.3%) to 28 (44.4%) patients. Of which 15 (23.8%) were grade A, 11 (17.5%) were grade B, and 2 (3.2%) were grade C. There was no correlation between GERD symptoms with EE; however, our study found a trend suggesting higher prevalence of EE with a sleeve diameter measuring > 2 cm wide ($p = 0.069$).

Conclusion Although LSG is effective in treating obesity and its metabolic syndromes, the prevalence of EE increased significantly 1 year after the surgery. Since we do not fully understand the long-term impact of chronic esophagitis in post-sleeve population, we recommend follow-up EGD assessment post-operatively and treat the esophagitis if present.

Keywords Gastro-esophageal reflux disease · Erosive esophagitis · Vertical sleeve gastrectomy · Sleeve diameter · Upper endoscopy

Introduction

Obesity is a worldwide epidemic. According to 2014 data from the World Health Organization (WHO), it is estimated that > 1.9 billion adults aged 18 years and older are overweight (body mass index, BMI ≥ 25 kg/m^2), with > 600 million of these adults in the obese range (BMI ≥ 30 kg/m^2) [1]. The impact of obesity on overall health is significant, with an associated 50 to 100% increased risk of premature death when compared to individuals of a healthy weight [2]. An estimated 300,000 deaths annually are attributed to obesity, with

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obesity-related comorbid medical conditions contributing substantially to preventable morbidity and mortality [3]. Bariatric surgery, in conjunction with intensive lifestyle interventions and medical treatments, has been shown to produce marked weight loss and improvement in many obesity-related comorbidities [4].

Originally, laparoscopic Roux-en-Y gastric bypass has traditionally been the most widely performed bariatric surgery operation. In recent years, there has been a paradigm shift favoring LSG as the commonest bariatric surgical operation [5]. In 2014, the International Federation for the Surgery of Obesity and Metabolic Disorder (IFSO) reported 265,898 (45.9%) sleeve gastrectomy cases compared to 229,455 (39.6%) of Roux-en-Y gastric bypass.

Doug Hess performed the first open sleeve gastrectomy operation as part of a two-stage duodenal switch operation for the super morbidly obese almost 29 years ago [6, 7], although Picard Marceau published the modified sleeve gastrectomy in conjunction with biliopancreatic diversion around the same period [8]. In the late 1990s, it was recognized that there was significant excess weight loss and improvement in obesity-related comorbid conditions even before completion of the second stage of the operation, with outcomes comparable to the two-stage duodenal switch procedure. It was as a result of these findings that the stand-alone sleeve gastrectomy operation was born, and in 2000, Dr. Michel Gagner performed the first LSG as part of a duodenal switch operation, giving rise to the operation performed today [9].

As LSG has become more popular, we are also seeing increased incidence of de novo gastro-esophageal reflux disease (GERD) and worsening of pre-existing GERD. The criteria for diagnosis of GERD are not always clear and the use of preoperative endoscopy and other diagnostic tools varies among studies. Published data on the incidence of GERD after sleeve gastrectomy are contradictory and comparisons between studies are difficult due to study heterogeneity [10].

Chiu et al. published a systematic review of the effect of laparoscopic sleeve gastrectomy on GERD symptoms. They demonstrated an increase in GERD symptoms in four studies; while seven studies showed a decrease in symptomology after sleeve gastrectomy. No consensus was reached by Chiu et al. instead, they concluded that dedicated studies which objectively evaluate GERD symptomology after sleeve gastrectomy are needed to more clearly define the correlation between sleeve gastrectomy and GERD [11]. Despite the non-consensus, we are currently seeing many surgeons routinely excluding patients with GERD as candidates for laparoscopic sleeve gastrectomy [9]. Therefore, it is imperative that we examine the relationship of sleeve gastrectomy with GERD as many patients may have been unnecessarily excluded. In our study, we objectively evaluate the presence of erosive esophagitis as surrogate marker for the onset of GERD, 1 year post-sleeve gastrectomy.

Patients and Methods

Patients with a body mass index (BMI) > 37.5 kg/m^2 or a BMI > 32.5 kg/m^2 with obesity-related comorbidities were evaluated by a multidisciplinary team consisting of dietitians, endocrinologists, physiotherapists, psychologists, and surgeons at the Singapore General Hospital weight management program. Those who failed medical weight management, e.g., control of caloric intake, behavioral modification, and/or pharmacological therapy after 6 months were subsequently considered for bariatric surgery. The patients' anthropometrics, age, sex, and race, were recorded before surgery. Patients completed detailed questionnaires pre-operatively. These included comprehensive documentation of reflux symptomology, details of proton pump inhibitor medication use, smoking, and alcohol history. We also take into account the GERD symptoms before or after meals. Esophago-gastroduodenoscopic (EGD) examination of the esophagus and stomach prior to surgery and at 12 months post-operatively were also carried out and images documented. All data including images of EGD examination were captured in our database—REDCap (Research Electronic Data Capture). The ethical committee of Singapore General Hospital approved this study.

Preoperative Evaluation of the Esophagus

All patients pre-operatively underwent endoscopy evaluation of the esophagus. The esophagus, stomach, and duodenal bulb mucosa was carefully inspected and findings recorded in EndoPRO iQ software (Pentax Medical, Tokyo, Japan). Esophagitis, if present, in our patients were graded according to the Los Angeles (LA) classification [12]. Details of the classification system are shown on Fig. 1.

A hiatal hernia diagnosis is made based on the presence of a diaphragmatic indentation of at least 2 cm distal to the squamocolumnar junction or Z line and the proximal margins of the gastric mucosal folds on endoscopic examination (Fig. 2).

Laparoscopic Sleeve Gastrectomy

All operations were performed in a single center. LSG was performed using five ports placed in the upper abdomen through the anterior abdominal wall (Fig. 3). The abdominal cavity was insufflated with CO_2 and abdominal pressure maintained at 15 mmHg. Dissection was commenced at approximately 3 cm proximal to the pylorus; the omentum separated from the greater curvature by dividing the branches of the gastro-epiploic vessels and the short gastric vessels using a Harmonic scalpel (Ethicon Endosurgery, Cincinnati, OH). Special attention was paid in completely exposing the left crus

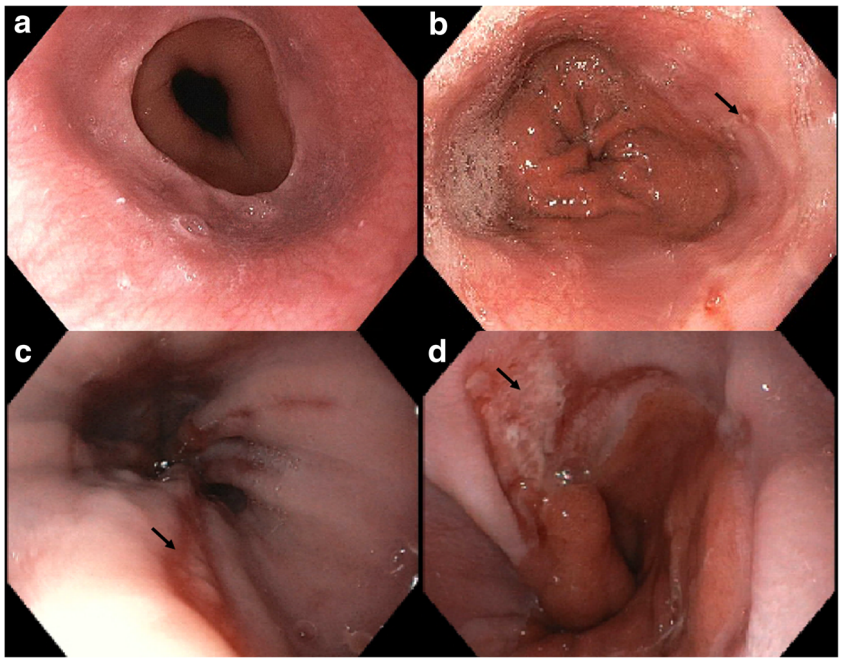

Fig. 1 Los Angeles (LA) classification of erosive esophagitis. A Hiatal hernia, B grade A esophagitis, C grade B esophagitis, and D grade C esophagitis

of the diaphragm and ensuring complete clearance of the posterior aspect of the fundus. Prior to the formation of the gastric tube, a 36-Fr calibration tube was inserted orally and the stomach tubularized with the applications of an endoscopic stapler (Echelon-Flex green, gold, and blue cartridges, Ethicon Endosurgery, Cincinnati, OH). After this was completed, the calibration tube was then removed and the staple line inspected for tissue continuation and the absence of bleeding. No drains were used in our procedure. The disconnected stomach was removed in an endoscopic bag (Endo Catch 15 mm, Medtronic, Minnesota, United States) via the 15-mm opening at the umbilicus. All fascial closure was carried out with 2-0 Ethibond suture (Johnson & Johnson Medical N.V., Belgium).

In the first post-operative day, all patients were commenced on our post-bariatric surgery protocol, which included small quantities of clear liquids, progressing to a full liquid diet by the afternoon. Discharge of the patient usually occurs at post-operative days 1–2 once discharge criteria are achieved and reviewed by our multidisciplinary team at 2 weeks post-operatively followed by review at 1 month, 3 months, 6 months, and subsequently annually. Discharged criteria included (1) able to drink 1.5 l of fluid per day and tolerating prescribed liquid diet, (2) pain adequately controlled with oral analgesia, (3) able to ambulate without assistance, and (4) understand and accept the written information sheets provided.

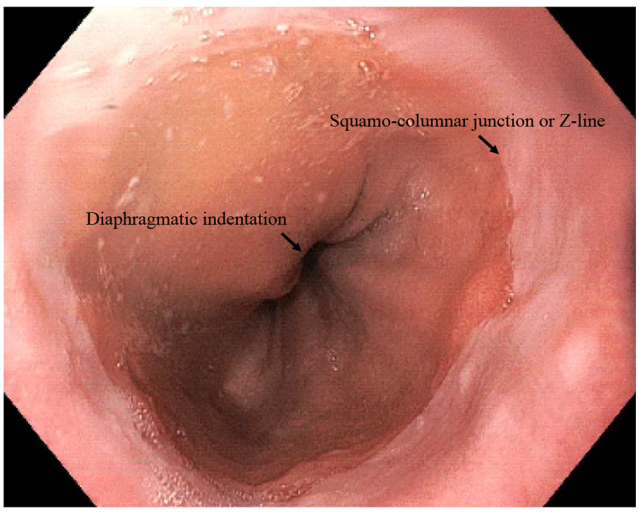

Fig. 2 Hiatal hernia diagnosis is made based on the presence of a diaphragmatic indentation of at least 2 cm distal to the squamo-columnar junction or Z line

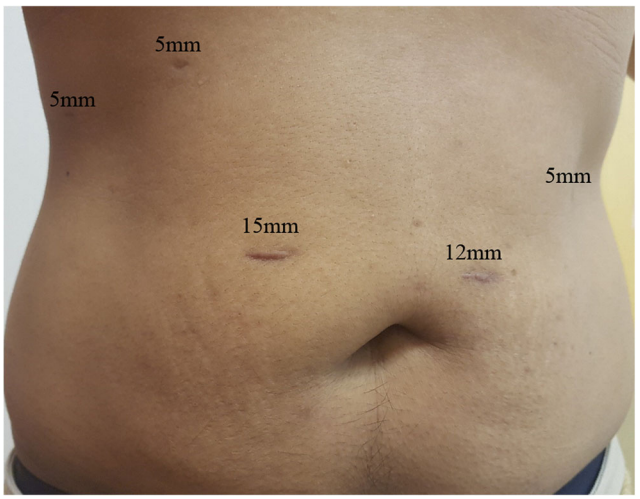

Fig. 3 Laparoscopic sleeve gastrectomy was performed using five ports placed in upper abdomen through the anterior abdominal wall

Post-operative Evaluation of the Esophagus

Post-operative evaluation of the esophagus was carried out 1 year post-operative. Similar to pre-operative examination, the mucosae of the esophagus, stomach and duodenal bulb were evaluated in addition to the new-stapled line. Due to the tubular shape of the modified stomach, a 9.9-mm diameter endoscope (GIF-HQ190, Olympus, Tokyo, Japan) was utilized to safely retroflex in the gastric antrum in order to properly evaluate the distal esophageal and proximal stomach mucosa. Endoscopic measurement of sleeve diameter is mainly performed visually, a visual estimation using the endoscope as guide in retroflex view (Fig. 4). All images and description of the findings were recorded in EndoPRO iQ software (Pentax Medical, Tokyo, Japan).

Similar to the pre-operative stage, the patients will complete a comprehensive questionnaire. This questionnaire is repeated at a 6-month interval.

Statistical Analysis

Descriptive results regarding categorical variables were given as percentages (%) of subjects affected. Normally distributed continuous variables were presented as the mean ± standard deviation (SD). Following LSG, patients were divided into two groups according to the presence or absence of EE. Characteristics of these two groups were compared by using Student's *t* test or chi-square test. $P < 0.05$ was taken to indicate statistical significance. All analyses were performed using GraphPad Prism version 7 software (GraphPad Software, Inc., La Jolla, CA).

Results

Between October 2011 and August 2016, we carried out a retrospective review of all of the records for patients who underwent bariatric surgery at Singapore General Hospital. Ninety seven (97) patients with body mass index (BMI) of over 32.5 kg/m^2 underwent laparoscopic sleeve gastrectomy at our hospital by a single surgeon who routinely performed upper endoscopy 12 months post-sleeve gastrectomy. Thirty-four (35.1%) patients were excluded either due to loss of follow-up or incomplete/absence of endoscopic examination at 1 year.

Sixty-three patients (64.9%) were included in our study. Demographics of this population included a mean age of 38.2 years (range, 18–66) with mean BMI of 42.1 ± 1.2 kg/m^2. There were 40 (63.5%) females in our study and 23 (36.5%) males.

Median time to follow-up endoscopic examination was 13 months (range, 12–15). At 1 year post-operative, patients had a 29.3% decrease in BMI and 57% decrease in excess weight loss (Table 1). Pre-operatively, nine patients with a diagnosis of erosive esophagitis were classified as LA grade A in eight patients, and LA grade B in one patient.

Following laparoscopic sleeve gastrectomy, the prevalence of GERD symptoms increased from 20 (31.7%) to 30 patients (47.6%). Twenty (31.7%) patients experienced new GERD symptoms and 10 (15.9%) patients experienced an increase in pre-existing GERD symptoms compared to 10 (15.9%) patients who experienced resolution of symptoms. At the endoscopic examination 1 year after sleeve gastrectomy, the prevalence of erosive esophagitis (EE) increased from 9 (14.3%) to 28 patients (44.4%). Of which 15 patients were classified as LA grade A esophagitis, 11 patients were classified as LA grade B esophagitis, and 2 patients were classified as LA grade C esophagitis. None of the patients has grade D erosive esophagitis.

Interestingly, there was no correlation between GERD symptomology with endoscopic evidence of erosive esophagitis. Nine patients with erosive esophagitis had no symptoms at all (Table 2). When we compared the clinical characteristics and endoscopic findings of patients with or without endoscopic evidence of erosive esophagitis; smoking, alcohol consumption, percentage of excess weight loss (%EWL), and presence of hiatal hernia (Table 1) on endoscopy had no significant impact. There appears to be an association of sleeve diameter > 2 cm with erosive esophagitis after surgery (Fig. 5). Although this difference did not reach statistical significance in our study ($p = 0.069$), we suspect that this is due

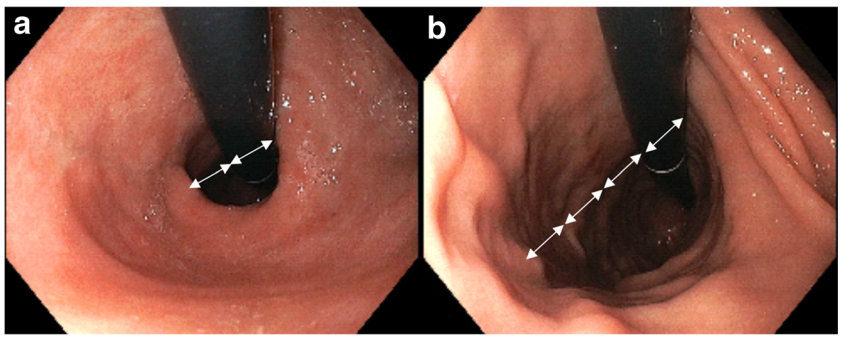

Fig. 4 Endoscopic measurement of sleeve diameter is mainly performed visually, a visual estimation using the 9.9-mm endoscope as guide in retroflex view

Table 1 Baseline characteristics and endoscopic data of study population

	Normal esophagus $n = 35$	Erosive esophagitis $n = 28$	p
Mean age (range)	40.29 (20–58)	37.24 (18–66)	0.2
Gender			
Male, *n* (%)	9 (25.7)	14 (50)	0.9
Female, *n* (%)	26 (74.3)	14 (50)	
Race			
Chinese, *n* (%)	14 (40)	18 (64.3)	0.114
Malay, *n* (%)	15 (42.9)	7 (25)	
Indian, *n* (%)	6 (17.1)	2 (7.1)	
Other, *n* (%)	0 (0)	1 (3.6)	
Height (cm) ± SD	164.8 ± 2.04	165.9 ± 1.70	0.694
Pre-operative weight (kg) ± SD	113.7 ± 3.72	118.4 ± 5.34	0.465
Post-operative weight (kg) ± SD	80.9 ± 3.37	82.6 ± 2.74	0.699
Pre-operative BMI (kg/m^2) ± SD	41.8 ± 1.02	42.7 ± 1.50	0.612
Post-operative BMI (kg/m^2) ± SD	30.2 ± 1.18	29.5 ± 0.83	0.639
Actual weight loss (kg)	32.0 ± 2.36	36.9 ± 2.95	0.199
% excess weight loss (%)	53.7 ± 3.53	60.3 ± 3.77	0.212
Post-operative PPI, *n* (%)	17 (48.6)	14 (50)	0.912
Smoking, *n* (%)	5 (14.3)	6 (21.4)	0.466
Alcohol consumption, *n* (%)	4 (11.4)	2 (7.1)	0.572
EGD findings			
Hiatus hernia, *n* (%)	6 (17.1)	6 (21.4)	0.646
Sleeve diameter, *n* (%)			
≤ 2 cm	15 (42.9)	7 (25)	0.069
> 2 cm	20 (57.1)	21 (75)	

to small sample size. Incidentally, all patients classified with grade C erosive esophagitis had sleeve diameters measuring more than 3 cm.

Discussion

In the investigations of GERD, a major disadvantage is the overreliance of subjective descriptions of patient's symptoms. As a result, many studies which use this indicator in their study are prone to subject bias. Studies which rely on objective measurement such as endoscopic evaluation with accepted classification system is probably the best method to make an official diagnosis of GERD as well as to objectively follow its progression during a course of treatment or treatments.

In this study, the prevalence of GERD based on our questionnaire increased from 31.7% pre-operatively to 47.6%, 1 year following sleeve gastrectomy. This is approximately, 15.9% more cases than previously reported in other series [13–17]. Objective evidence of GERD specifically erosive esophagitis as classified on endoscopy using the LA esophagitis classification system was identified in 14.3% of patients pre-operatively and after 1 year following sleeve gastrectomy, this increased to 44.4% of patients. This is approximately a third increase in number of patients. When we looked at other studies, Braghetto et al. reported a 15.5% increase in the development of de novo EE within 1–2 months after surgery [14]. Similarly, Tai et al. found a 66.7% increase in incidence of EE at 1 year after LSG [18]. Genco et al. reported a biliary-like esophageal reflux in 74.5% of patients post-sleeve

Table 2 Prevalence of GERD and erosive esophagitis 1 year after laparoscopic sleeve gastrectomy

Symptoms	EGD findings		
	Erosive esophagitis	Without esophagitis	Total
Gastro-esophageal reflux disease	11 (40.7%)	16 (59.3%)	27
Asymptomatic	9 (32.1%)	19 (67.9%)	28
Total	20	35	55

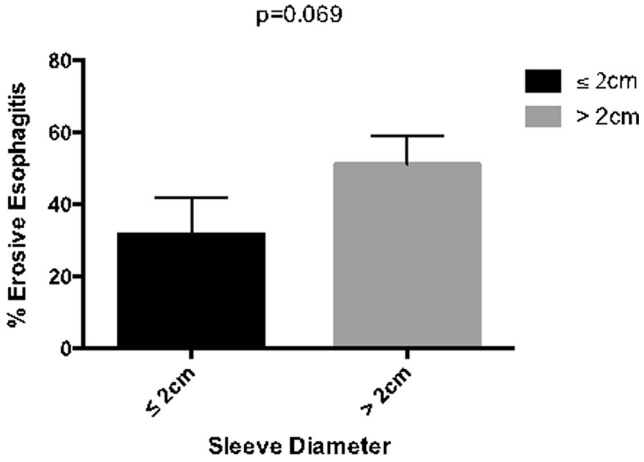

Fig. 5 Prevalence of erosive esophagitis (EE) with sleeve diameter of > 2 cm and ≤ 2 cm

gastrectomy and non-dysplastic Barrett's esophagus was diagnosed in 17.2% with mean follow-up of 58 months [19].

When we compared GERD symptoms reporting with endoscopic evidence, we found that the classical symptom of "heartburn or regurgitation" did not correlate with the presence or worsening of erosive esophagitis at upper GI endoscopy. This could be due to atypical acid-reflux-related symptoms like chest pain, globus pharyngeus, chronic cough, and asthma. Alternatively, it could be "silent GERD" which referred to the presence of esophageal mucosal injury visible in EGD, but without typical or atypical GERD symptoms. Therefore, we can assume that EE may be underestimated in one in three patients post-LSG.

In terms of the known evolution of esophagitis, high-grade esophagitis evolving to Barrett's esophagus occurs in 5–15% of patients [20] and with this group, 0.3% subsequently developed into adenocarcinoma [21]. There is recent published data from Braghetto et al. showing that confirmed histological evidence of Barrett's esophagus was found in 1.2% of their patients at 5 years post-LSG [22]. This is especially worrying for three important reasons: (1) LSG is the most common bariatric procedure worldwide (75,359 cases in 2013). (2) LSG is carried out in relatively young patients with mean age of 38 years in our study. (3) We do not yet understand if the progression of esophagitis to Barrett's esophagus and adenocarcinoma is similar to patients without LSG. Therefore, many young patients in this population may be exposed to unnecessary risk.

Most of the bariatric programs do not offer routine postoperative upper endoscopy unless patients are symptomatic. This is worrying as our study clearly indicates that erosive esophagitis symptomology does not correlate with endoscopic evidence of disease. Given this, we are afraid that erosive esophagitis maybe profoundly underdiagnosed in this patient population.

One of the interesting findings in our study was the increased finding of erosive esophagitis with a sleeve diameter (diameter of the remnant stomach) of more than 2 cm. Pathologically, we correlate erosive esophagitis with acid reflux. Physiologically, we would have predicted that a wider sleeve diameter would have translated to a lower intra-gastric pressure and therefore less acid refluxing retrograde into the esophagus. But study by Francois et al. countered our belief with high-resolution impedance manometry (HRIM) showed no significant correlation between the intra-gastric pressure and reflux impedance episodes or sleeve volume on 3-D CT scan [23]. On the other hand, eight studies consisting of 123 patients using scintigraphy [24–31] showed that removal of the majority of the body and fundus during sleeve gastrectomy markedly reduces receptive capacitance of the stomach which by default projects nutrients directly to the antrum, at a comparatively more rapid rate. Specifically, a weighted average of these studies demonstrates a reduction in the T½ of gastric emptying for a semisolid meal from 65.7 to 48.6 min after sleeve gastrectomy [32]. Interestingly, if comparing the T½ of gastric emptying and bougie size between those studies. The larger bougie size (48 Fr) used associated with longer gastric emptying compared to the smaller one (32–36 Fr) (Table 3). Hence, a smaller sleeve diameter has a smaller receptive capacitance compared to a larger one and therefore likely promotes faster gastric emptying, hence less acid reflux into the esophagus.

Another possible explanation is that a larger sleeve diameter means more acid producing parietal cells in the remaining stomach, and this in turn may result in larger amount of acid available for refluxing into the esophagus. We also postulate, that over time, as a consequence of over eating and sleeve dilatation occurs leading to chronic volume reflux which

Table 3 Review of studies showing correlation between Bougie size and gastric emptying post sleeve gastrectomy

	Patients	Bougie size (F)	Buttress or oversewing	Post-op T½	Year
Braghetto et al. [26]	20	32	None	38.3 ± 18.77	2009
Burgerhart et al. [22]	13	34	None	40.6 ± 10.0	2014
Burgerhart et al.	7	34	None	34.4 ± 9.3	2014
Melissas et al. [23]	21	34	Oversewing	49.1	2012
Michalsky et al. [24]	4	36	None	32.3	2013
Bernstine et al. [27]	21	48	Oversewing	56.79 ± 18.72	2009

may induce erosive esophagitis. Braghetto et al. [28] reported data on 15 LSG patients undergoing CT scan gastric volumetry on post-operative day 3 and, repeatedly, at 24–36 months after surgery, and found that the mean gastric volume had increased from 108 to 250 ml.

Limitations to this study include the retrospective nature of the study as well as the small sample size. Other limitations include operator biasness in the use of endoscopy to determine the sleeve diameter and the grade of esophagitis. Although the exclusion rate was 35.1% in the study, this is comparable to study by Tai et al. (31.1%) and Genco et al. (30.9%) [18, 19]. Even with these limitations, sleeve gastrectomy is currently the most commonly performed surgical treatment for obesity and metabolic syndromes in the world. We cannot ignore the increase in reporting of erosive esophagitis at 1 year, which exposes the young patient to a lifetime risk, which is still ill-defined. Therefore, even with this limited study we recommend early upper endoscopy in patient following sleeve gastrectomy and aggressively treat erosive esophagitis if present. With regard to the correlation between erosive esophagitis with wide sleeve diameter, further studies are required to confirm this association.

Compliance with Ethical Standards

Conflict of Interest Statement Author 1, author 2, author 3, author 4, author 5, author 6, author 7 & author 8 have nothing to disclose.

Ethics Approval Statement For this type of retrospective study, formal consent is not required.

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