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IMPACT OF SLEEVE GASTRECTOMY ON GASTROESOPHAGEAL REFLUX DISEASE: A SYSTEMATIC REVIEW

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Abstract:

Introduction: Sleeve gastrectomy (SG) has increased in popularity as both a definitive and staged procedure for morbid obesity. Gastroesophageal reflux disease (GERD) is a common comorbid disease in bariatric patients. The effect of SG on GERD has not been well studied, thus the goal of this systematic literature review is to analyze the impact of SG on GERD.

Methods: A systematic literature search was conducted using Medline, EMBASE, the Cochrane Database, Scopus, and the gray literature for the keywords "sleeve gastrectomy," "gastroesophageal reflux," and equivalents.

Results: Fifteen articles were retrieved. Two articles analyzed GERD as a primary outcome, whereas thirteen included GERD as a secondary study outcome. Four studies showed an increase in GERD after SG. Seven studies found reduced GERD prevalence post-SG. Three studies included only the post-operative prevalence of GERD. One study did not include data on prevalence of GERD.

Conclusion: The evidence on the impact of SG on GERD does not consolidate to a consensus. The studies show differing outcomes. Hence, dedicated studies that objectively evaluate GERD after SG are needed to more clearly define the effect of SG on GERD in bariatric patients.

Keywords: Sleeve gastrectomy, Gastroesophageal reflux disease, Systematic review

Introduction

Sleeve gastrectomy (SG) has gained popularity both as a staged and definitive procedure for morbid obesity[1, 2]. The original biliopancreatic diversion with duodenal switch (DS) was designed for high risk bariatric patients. To increase the safety of the overall operation, the operation was broken into two stages, of which SG was the first step. Many patients, however, were losing sufficient weight with SG alone. Consequently, isolated SG is now generally accepted as a definitive bariatric operation[3].

In SG, the stomach is divided vertically, reducing the volume to approximately 25% of the original. This leaves the pyloric valve at the distal end of the stomach intact, and preserves the continuity of the digestive tract. Thus, at first glance, SG appears to be a restrictive procedure. However, on closer study, the fundus is the main source of ghrelin, which is the hormone that regulates appetite and satiety. Thus, the biochemical changes from reducing the source of ghrelin may be a significant weight loss mechanism in SG[4]. Melissas, et. al. suggest that increased gastric emptying and alterations in gut hormones may be the mechanisms responsible for weight loss in SG[5, 6].

Obesity is an independent risk factor for gastroesophageal reflux disease (GERD)[7-9]. DeGrout, *et. al.* reviewed the effect of various lifestyle interventions and bariatric operations on GERD. They found that Roux-en-Y gastric bypass alleviated GERD symptoms, however, there was no change in GERD in vertical banded gastroplasty[10]. The effect of SG on GERD, however, has not yet been well studied. There is differing evidence on whether SG alleviates or causes or exacerbates GERD and whether symptoms diminish with time post-operatively.

The goal of this systematic literature review is to analyze the evidence describing the impact of SG on GERD.

Methods

Search strategy

Medline, EMBASE, the Cochrane Database, and Scopus were systematically searched for articles with the keywords "sleeve gastrectomy," "vertical gastrectomy," "greater curvature gastrectomy," "parietal gastrectomy," or "longitudinal gastrectomy," and "gastroesophageal reflux," "gastro-oesophageal reflux," "GERD," or "GORD". The references of the articles were hand searched.

A search was also performed on the gray literature (ProQuest Dissertations and Theses, Conference Paper Index, OpenSIGLE, New York Academy of Medicine, OCLC Proceedings First, and Google) and ongoing trials (www.clinicaltrials.gov and Current Controlled Trials).

Selection criteria

The studies were ranked based on the Oxford levels of evidence [11, 12]. Prospective and retrospective studies were included, but case reports and expert opinions were not. The articles that were included were both open and laparoscopic SG, studies where patients had no previous bariatric operations, studies comparing SG versus any other type of intervention, and studies where a two stage procedure was planned, but the patient opted out of the second part. Studies that included gross modifications to SG, studies using SG for rescue after a previous failed

operation, or studies combining SG with other operation (e.g. hiatal hernia repair) were excluded from the analysis. Figure 1 shows the flowchart of the literature search.

Outcome measurements

Studies were selected if GERD was a primary or secondary study outcome. A broad definition of GERD was accepted for this study due to the limited number of studies available. As a result, GERD outcomes included 24 hour pH measurements, motility assessments, manometry, validated symptom questionnaire, informal symptom reporting, and medication usage.

Quality assessment and data collection and analysis

Two independent reviewers assessed the quality of each study according to a modified checklist from the CONSORT statement[13, 14]. Table 1 summarizes the characteristics of each study.

Results

Literature search results

A total of fifteen articles met the inclusion criteria. There were two articles where GERD was studied as a primary outcome of SG[15, 16]. Thirteen articles studied GERD as a secondary outcome, but the diagnosis and evaluation of GERD was not standardized across the studies[5, 6, 17-27]. Three studies compared LSG with other bariatric operations[20, 21, 24]. Although no randomized control trials were found where GERD was measured as a primary endpoint, one article was a randomized control trial comparing LSG with laparoscopic gastric banding[20].

The duration of follow up ranged from six months to five years. The method for evaluating GERD included manometry (1), questionnaires (4), proton pump inhibitor use (2), and was not stated in eight studies. The studies did not describe study inclusion and exclusion criteria. Any withdrawals were also not included. Each patient acted as his/her own control and thus, there were no control groups. The summary of the results are shown in Table 1.

Results on the impact of sleeve gastrectomy on GERD

The reviewed studies reported differing results on the impact of SG on GERD. Four studies found increased prevalence of GERD post-SG [17, 21, 22, 27]. Seven studies showed reduced prevalence of GERD post-SG [5, 6, 19, 20, 23, 24, 26]. Three studies included only the post-operative prevalence of GERD [16, 18, 25]. A manometry study by Braghetto *et. al.* [15] found reduced lower esophageal sphincter (LES) pressure post-SG, which may result in reflux symptoms. They did note that in their experience (unpublished data) of 250 patients, 15% had positive acid reflux on 24 hour pH measurements. The summary of the results are shown in Table 1.

Discussion

The object of this systematic literature review was to consolidate the evidence on the impact of SG on GERD. More established bariatric operations, have been previously studied for their effect on GERD. Being a relatively new operation, SG has not been well examined in this regard.

Prevalence of GERD post-SG

Fifteen articles retrieved from a systematic literature search on GERD after SG reported diverging results. Four studies [17, 21, 22, 27] found increased prevalence of GERD symptoms post-SG, whereas seven [5, 6, 19, 20, 23, 24, 26] showed reduced prevalence. From the studies where there was an overall reduced prevalence, the authors did note that patients with pre-existing GERD improved, but there were new cases of GERD post-SG [6, 20]. Himpens, et. al. noted that from the patients with pre-exiting GERD, 75% had resolved, however, there were 21.8% new cases at 1 year post-SG [20]. Melissas noted the same trend of reduction in pre-existing GERD, but also had 2 new cases of GERD [6]. However, the studies did not mention the statistical significance of the new cases. The Himpens, ,et. al., Weiner, *et. al*., and Melissas, *et. al.* study found worsening GERD symptoms early post-SG, but resolution at two to three years[20, 23, 5]. Three studies included only the post-operative prevalence of GERD [16, 18, 25]. Though not included in the analysis, it should be noted that the The Second International Consensus Summit for Sleeve Gastrectomy surveyed attendees and reported that their prevalence of post-operative GERD ranged from 0 – 83% (average 6.5%)[3]. Because of the diverging results, it is difficult to synthesize a definite conclusion with numerical data about the effect of SG on GERD. A meta-analysis is impractical at this point given the heterogeneity of the results and the limited number of studies. Despite these limitations, some conclusions may still be drawn, particularly from the discussion of the effect of SG on physiology and anatomy from these studies and comparing the GERD prevalence after SG and other bariatric procedures.

Comparison of GERD post-SG with other bariatric operations

Three studies compared SG with other bariatric procedures. Himpens, *et. al.* noted that patients without GERD who underwent gastric banding saw an increase in prevalence of GERD

that continued to increase with time. In contrast, the prevalence of GERD in patients with SG peaked at 1 year and declined by 3 years. Further, the prevalence of GERD in patients with pre-existing GERD reduced by 75% in SG and 83.3% in gastric banding[20]. In contrast, the Omana study showed a non-statistically significant reduction in the prevalence of GERD of only 22% in LSG and 33% in laparoscopic adjustable gastric banding at 15 months[24]. Finally, the Lakdawala, *et. al.* study showed a reduction of prevalence of GERD from 13% to 0% in laparoscopic Roux-en-Y gastric bypass and a reduction from 5% to 0% in the SG group. However, they noted that the incidence of GERD was 9% at 1 year in the SG group (statistical significance was not reported)[21]. Without statistically significant results, it is difficult to draw conclusions, but superficially it appears that SG is at least as good as gastric banding at reducing the prevalence of GERD.

Physiologic and anatomic effects of sleeve gastrectomy on GERD

Several authors commented about the anatomic and physiologic effects of SG and postulated their effect on GERD. Using manometry, Braghetto, *et. al.* demonstrated that the pressure in the lower esophageal sphincter was reduced post-SG, which can cause reflux symptoms and esophagitis[15]. Klaus *et. al.* reasoned that esophageal manometry may be a useful criterion in deciding whether to offer sleeve gastrectomy [28]. Himpens, *et. al*. hypothesized that the lack of gastric compliance and emptying and blunting of the angle of His inherent in SG at 1 year was responsible for the increase GERD symptoms at one year post-SG. They postulated that an increase in gastric compliance and clearance after three years likely accounted for the resolution of GERD symptoms at three years. Finally, they also noted that on barium swallow after three years, the angle of His was restored, which may account for decreased GERD [20].

Hamoui, *et. al.* also noted the alteration in the anatomy of the angle of His and recommended exercising caution when offering open SG to patients with GERD[18]. In contrast to Himpens *et. al.*, Melissas, et. al. noted an acceleration of gastric emptying both in the short term (6 months) and long term (24 months) post-SG[5, 6]. They ventured that weight loss may be the mechanism for improved GERD symptoms, and that surgical division of ligaments around the abdominal esophagus and destruction of the cardioesophageal junction may account for worsening GERD symptoms[5, 6]. Yehoshua, *et. al.* measured and compared the volumes and pressures in the stomach before and after SG. They found that the sleeve was ten times less distensible than the resected section, and also the remaining sleeve had a higher luminal pressure and smaller volume[29]. It is conceivable that these changes in stomach pressure, volume, and distensibility contribute to worsening GERD symptoms in the context of reduced LES pressure. Table 2 summarizes the hypothesized anatomic and physiologic effects of SG on GERD. In conclusion, the relationship between GERD and sleeve gastrectomy is multifactorial. Factors that increase GERD post-SG include reduction of LES pressure (possibly from division of ligaments and blunting the angle of His), reduction of gastric compliance and emptying, increased sleeve pressure, and decreased sleeve volume and distensibility. These GERD exacerbating factors may be countered by accelerated gastric emptying and weight loss. Finally, resolution of GERD in the long term may be accounted for by increased gastric compliance and emptying and restoration of the angle of His three years post-SG.

Modifications to SG

Multiple novel modifications to sleeve gastrectomy have been proposed to resolve the problems of GERD post-SG. Fedenko, *et. al.* proposed an antireflux sleeve gastroplasty, which is

a combination of a vertical gastroplasty and Nissen fundoplication[30]. Alexander, *et. al.* described a banded sleeve gastrectomy, in which a band of processed human dermis was placed around the upper part of the sleeve to prevent late dilatation and weight gain, and improve GERD symptoms[31]. Korwar *et. al.* combined a laparoscopic hiatal hernia repair with a sleeve gastrectomy with good results in controlling GERD symptoms and weight loss.

Limitations

There were multiple limitations to our study. First, the quality of the studies were poor for our purpose. No randomized control trials were available where GERD was the primary outcome measured after SG. Only two studies evaluated GERD as a primary outcome after SG [15, 16]. Second, no studies evaluated GERD using the gold standard pre- and post-operative 24h pH measurements. Third, there was no standardization among the studies of the surgical technique, severity of symptoms, and follow up times. Fourth, there was generally no statistical analysis comparing the prevalence of GERD before and after SG. Fifth, the studies generally did not include the inclusion and exclusion criteria for entering into the study. Sixth, there were no long term studies available beyond five years. As a result of these limitations, there is a high risk of bias in this review.

Conclusions

This review aimed to present a systematic assessment of the best available evidence on the impact of SG on GERD. Four studies showed an increase in prevalence, but seven showed reduced prevalence of GERD post-SG. Given the poor quality of the evidence, it is impossible to consolidate the data into a consensus. However, in light of the limitations of this study, some

useful conclusions may still be drawn. The relationship between GERD and sleeve gastrectomy is multifactorial. Sleeve gastrectomy may promote GERD by reducing LES pressure (possibly from division of ligaments and blunting of the angle of His). Further, the inherent properties of the sleeve (reduced gastric compliance and emptying, increase gastric pressure, and decreased volume and distensibility) may worsen GERD. Factors that reduce GERD in SG are accelerated gastric emptying and weight loss. Resolution of GERD in the long term may be accounted for by increased gastric compliance and emptying and restoration of the angle of His three years post-SG.

Undoubtedly, dedicated studies that objectively evaluate GERD after SG would more clearly define the effect of SG on GERD and contribute to the understanding of the physiologic and anatomic effects of SG. A definition of GERD such as based on the Montreal consensus would aid in standardization [32]. De Groot, *et. al.* recommended validated questionnaires and objective measurements such as 24h pH measurements or LES manometry at different time points post-SG to quantify the course of GERD post-SG[10]. Screening patients with manometry before offering SG may or may not be helpful – further studies are required. Patients with GERD who are possible candidates for SG should be informed of the equivocal evidence on the impact of sleeve gastrectomy on GERD.

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Table 1: Characteristics of studies and summary of results

Authors	Level of evidence	No. Patients	Pre-op BMI (kg/m^2)	Reflux evaluation	Follow-up	Pre-op GERD	Post-op GERD	Conclusions of outcome on GERD	Bougie size
GERD prevalence decreased									
Cottam, et. al.	2b	126	65.3	Informal symptom reporting	1 y	36%	70% resolved, 8% improved		*46-50Fr*
Han, et. al.	2b	60	37.2	Informal symptom reporting	12 mo	8.30%	0%	Comorbidities improved with weight loss (including GERD).	*48Fr*
Himpens, et. al.	2b	80 (40 LSG)	39	Medication usage	3 y	20%	Pre-existing 5%; New cases 21.8% (1y), 3.1% (3y)	GERD at 1 year may be due to lack of gastric compliance and emptying seen at 1 year. Increased gastric compliance and clearance and restoration of angle of His at 3 years may account for improving GERD.	*34Fr*
Melissas, et. al. (2008)	2b	14	49.46	Motility assessment, Informal symptom reporting	24 mo	35%	22.7%; 2 new cases		NS
Melissas, et. al. (2007)	2b	23	47.2	Motility assessment, Informal symptom reporting	12 mo	14%	35.7% (6m), 7% (24m)	Reduced GERD symptoms were likely due to weight loss. Worsening or new GERD symptoms may be due to surgical division of ligaments around abdominal esophagus and destruction of cardioesophageal junction.	*34Fr*
Omana, et. al.	2b	123 (49 LSG)	52	Informal symptom reporting, Medication usage	15 mo	18%	14%	Rates of resolution of GERD symptoms was not statistically significantly different for LSG vs. LAGB.	*46Fr*
Weiner, et. al.	2b	120	60.7	Informal symptom reporting	5 y	35%	15%	There was increased GERD during the first post-op month, followed by decrease in pre-existing GERD 2 years post-op.	*32-44Fr*
GERD prevalence increased									
Arias et. al.	2b	130	43.2	Informal symptom reporting	24 mo	0%	2.10%		*40Fr*
Frank, et. al.	2b*	119	not stated	Medication usage	not stated	29.4% (35/119, 17/35 used PPI)	13/17 still using PPI, 12 new cases	RYGB is more effective than DS to treat GERD after SG.	NS
Lakdawala, et. al.	4	100 (50 LSG)	46	Informal symptom reporting, Medication usage	1 y	5%	9%	GERD worsened at 1 year post-LSG, but all symptoms resolved in LRYGB.	*36Fr*
Nocca et. al.	2b	163	45.9	Informal symptom reporting	2 y	6.10%	11.80%		*36Fr*
Change not determined									
Braghetto et. al.	2b	20	38.3	Manometry	6 mo	n/a	not stated	SG reduces LES pressure, which can cause GERD. GERD symptoms was an exclusion criterion.	*32Fr*
Hamoui, et. al.	2b	118	55	Not stated	24 mo	not stated	12.70%	GERD post-SG may be due to alteration of angle of His. Exercise caution when offering open SG to patients with GERD.	NS
Keidar, et. al.	2b, 4	706	Not stated	Validated symptom questionnaire	not stated	not stated	1%	GERD post-LSG ranges in severity. Contrast swallow showed wide, dilated fundus with narrow mid-stomach.	NS
Menenakos, et. al.	2b	261	45.2	Informal symptom reporting, Medication usage	12 mo (mean)	not stated	25%	Symptoms of GERD were common especially in the first few months. Symptoms were responsive to PPI.	*38Fr*

*conference abstract

DS = duodenal switch; GERD = gastroesophageal reflux disease; LAGB = laparoscopic adjustable gastric banding; LES = lower esophageal sphincter; LRYGB = laparoscopic roux-en-y gastric bypass; LSG = laparoscopic sleeve gastrectomy; NS = not stated; PPI = proton pump inhibitor; RYGB = roux-en-y gastric bypass; SG = sleeve gastrectomy.

Table 2: Anatomic and physiologic factors affecting GERD

Factors worsening GERD	Factors improving GERD
Decreased gastric emptying	Accelerated gastric emptying
Lower LES pressure	Weight loss
Blunting angle of His	Reduced acid production
Decreased gastric compliance and volume	Removal of fundus (source of relaxation waves to lower esophageal sphincter)
Increased gastric pressure	Reduced wall tension (LaPlace's law)

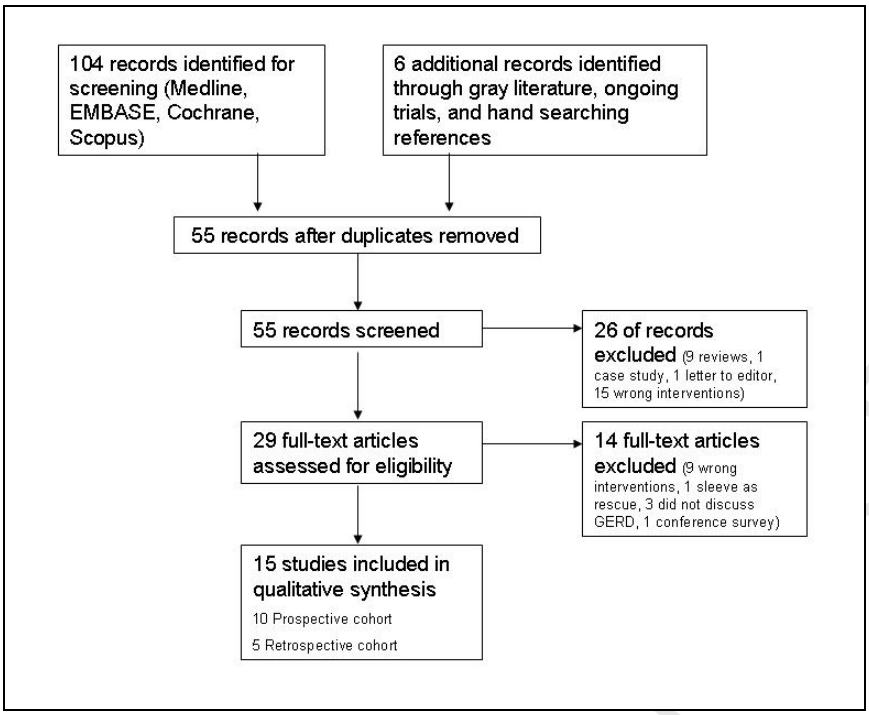

Figure 1: Flowchart of literature search