ELSEVIER

Surgery for Obesity and Related Diseases ▮ (2016) 00–00

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

# The effect of sleeve gastrectomy on extraesophageal reflux disease

Catherine Frenkel, M.D.[a], Dana A. Telem, M.D.[a], Aurora D. Pryor, M.D.[a], Maria S. Altieri, M.D.[a], Kenneth R. Shroyer, M.D., Ph.D.[b], Elliot Regenbogen, M.D.[c,*]

[a]*Division of Advanced Gastrointestinal, Foregut, Bariatric and General Surgery, Stony Brook University Medical Center, Stony Brook, New York*
[b]*Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York*
[c]*Division of Otolaryngology-Head and Neck Surgery, Stony Brook University Medical Center, Stony Brook, New York*

Received September 2, 2015; accepted November 2, 2015

**Abstract**

**Background:** Sleeve gastrectomy (SG) has been linked to increased rates of postoperative gastroesophageal reflux.

**Objective:** The aim of this study was to evaluate whether SG is also linked to increased pulmonary extraesophageal reflux disease in a rodent model, based on histologic inflammatory distal airway changes.

**Setting:** University hospital.

**Methods:** Wistar rats (Charles River Institute, Wilmington, MA) were fed a high fat diet (HFD) for 4 months. They were divided into HFD only (n = 25) and SG + HFD (n = 19) groups and euthanized at 12 weeks, and the trachea and lungs were harvested en bloc then preserved for analysis by a blinded board-certified pathologist.

**Results:** Rats who underwent SG were significantly less likely to show postmortem distal airway changes (4.0% versus 31.0%, $P = .03$), had a lower average chronic aspiration pneumonitis grade (.73 versus 1.57, $P = .006$), and had a lower total lung injury score (1.19 versus 2.28, $P = .005$). Alveolar hemorrhage was also less common in the SG + HFD group (37.5% versus 80.0%, $P = .006$).

**Conclusion:** SG is associated with increased incidence of normal lung histology on postmortem examination, less evidence of chronic aspiration pneumonitis and alveolar hemorrhage, and decreased total lung injury score in a rodent model. SG appears to have a protective effect on the pulmonary system. This suggests that SG does not exacerbate extraesophageal reflux effects on the pulmonary epithelium. (Surg Obes Relat Dis 2016;▮:00–00.) 

*Keywords:* Extraesophageal reflux; Sleeve gastrectomy; Morbid obesity; Bariatric surgery

Choosing the best type of bariatric surgical intervention for a patient is complex. Sleeve gastrectomy (SG) for morbid obesity provides equivalent or slightly less weight loss compared with Roux-en-Y gastric bypass [1]. Additionally, many obese patients present with co-morbid gastroesophageal reflux disease (GERD). Roux-en-Y gastric bypass is the bariatric operation most associated with improved reflux, whereas SG has a complex relationship with GERD [2]. A 2011 systematic review found there was inadequate evidence available to clearly define this multifactorial relationship [3]. However, newer single center studies and a national review of the Bariatric Outcomes

Accepted for Poster of Distinction and Presentation, Obesity Week, Boston MA, November 2014.

This study was sponsored by the Stony Brook University School of Medicine 2013 Department of Surgery Small Grant.

*Correspondence: Elliot Regenbogen, M.D., Division of Otolaryngology-Head and Neck Surgery, Health Sciences Center T19-068, Stony Brook Medicine, Stony Brook, NY 11794-8191.

E-mail: Elliot.Regenbogen@stonybrookmedicine.edu

http://dx.doi.org/10.1016/j.soard.2015.11.002

Longitudinal Database (BOLD) strongly support that SG is associated with new or persistent GERD [4–6]. Reflux may be exacerbated or result de novo from transecting lower esophageal sphincter fibers, disrupting the phrenoesophageal ligament or angle of His, resecting cardia sling fibers, or increases in intragastric pressure or gastric compliance, which can lead to proximal sleeve dilation or neofundus [7,8]. Alternatively, reflux may be alleviated or eradicated by weight loss, fundus resection, or decreased acid production. Additionally, there is disagreement regarding whether esophageal pressure and gastric emptying increase or decrease in SG.

There is a scarcity of data regarding the effects of SG on extraesophageal reflux disease (EERD). EERD manifests as cough, hoarseness, asthma, pulmonary fibrosis, or other laryngopharyngeal/respiratory symptoms and results in significant healthcare expenditure [9]. It can be a result of GERD via direct reflux of acid, pepsinogen, bile salts, or particulate matter into the oropharynx or tracheobronchial tree [10]. These structures might be more susceptible to acid-peptic injury than the esophagus. Unlike postoperative GERD, EERD may be more refractory to medical management with proton pump inhibitors [11–14]. The purpose of this study was to examine whether SG in a rodent model produces airway and lung changes consistent with EERD.

## Methods

A diet-induced obesity rodent model was selected based on previous validated SG models for weight loss [15]. After Institutional Animal Care and Use Committee (IUCUC) approval (Protocol 450722-7), healthy 10-week old Wistar Rats (Charles River Institute, Wilmington, MA; initial weight 187.81 ± 29.5 g) were fed ad libitum a high fat diet (HFD) consisting of 59% fat (3.24 kcal/gm), 27% carbohydrate (1.43 kcal/gm), and 14% protein (.82 kcal/gm; diet F3282, Bio-Serv, Frenchtown, NJ). At 4 months, animals had reached their target weight, which was double their initial weight. At this time, 25 animals continued on the high fat diet (HFD) and 38 animals underwent SG based on equal total weights among the groups by using MATLAB 8.0 and Statistics Toolbox 8.1 (The Mathworks, Inc., Natick, MA). The program was used to sort the rats into different groups according to their weight such that the mean of each group was nearly identical with similar coefficients of variation. The 2 groups were (1) HFD alone (n = 25; animals were fed an HFD without surgical intervention or related surgical preparation, such as general anesthesia and were measured at the time of randomization and before sacrifice) and (2) SG and HFD (HFD + SG) (n = 19; animals were fed an HFD, underwent an SG, and were continued on an HFD).

All animals were fasted 8–16 hours before the procedure (the operative technique is described later). General anesthesia was induced with 4% vaporized isoflurane administered in an oxygen mixture. After induction, the abdomen was shaved and disinfected with 70% ethanol and betadine, and weight-based antibiotic prophylaxis was administered. Anesthetized animals were placed in supine position with anesthesia maintenance of 2.5% vaporized isoflurane provided via a nosecone. Operations were performed via sterile technique.

### *Sleeve gastrectomy*

SG was performed as previously established in rodent models [16]. An upper midline laparotomy was performed. The splenic and hepatic connections to the stomach were released along the greater curvature. The greater omentum was ligated and divided to the level of the pylorus to adequately expose the stomach. After mobilization of the stomach, a SG was performed with the goal of reducing gastric volume by 70%. The thoracoabdominal linear stapler (Proximate Reloadable Stapler, product code TX 60 B) with 3.5 mm cartridge (Ethicon Endosurgery, Cincinnati, OH) was used to construct the gastric tube. Stapling was started 3-4 mm from the pylorus. After gastric resection, the staple line was reinforced with a hand sewn, running 4-0 Vicryl suture (Ethicon Endosurgery). The laparotomy incision was closed using a running 2-0 poldioxanone suture (Ethicon Endosurgery) for the peritoneum and aponeurotic muscle planes and 4-0 monocryl suture (Ethicon Endosurgery) for the skin. Thirty-eight animals were fed a HFD and underwent SG. Mortality of the procedure was 50%. This was higher than anticipated and occurred mostly in the initial phase of the study, likely as a result of a significant learning curve with the sleeve operation. The animals in this group died early, within the first 3 days of the postoperative period. All animals were autopsied, and postoperative hemorrhage or gastric leak was identified. These animals were excluded from the analysis, and the remaining 19 animals were considered.

After surgery, animal weights and HFD intake were recorded on a weekly basis. Animals were sacrificed 12 weeks after the surgery. This time period was based on reflux rodent models, which found that esophagojejunostomy leads to Barrett's esophagus within this time frame. Necropsy was performed, assessing integrity, morphology, and volume of the gastric tube in animals. The trachea and lungs were harvested en bloc and preserved for histopathologic analysis. Three SG specimens could not be sectioned and were excluded from analysis, thus leaving 16 samples.

After hematoxylin and eosin staining, cross-sections were analyzed by a pathologist blinded to the animal treatment group. Extraesophageal reflux was characterized by the presence of acute or subacute inflammation, emphysema, alveolar hemorrhage, interstitial thickening, and atelectasis. The degree of epithelial damage and infiltration of inflammatory cells was qualified, ranging from mild to severe, focal, or diffuse [17]. Lung injury secondary to chronic