Electrical stimulation of the lower esophageal sphincter to address gastroesophageal reflux disease after sleeve gastrectomy

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Abstract
Background: Laparoscopic sleeve gastrectomy (LSG) can result in de novo and worsen preexisting gastroesophageal reflux disease (GERD). Post-LSG patients with GERD refractory to proton pump inhibitors (PPI) usually undergo more invasive, anatomy-altering Roux-en-Y gastric bypass surgery. Lower esophageal sphincter (LES) electrical stimulation (ES) preserves the anatomy and has been shown to improve outcomes in GERD patients.

Objective: To evaluate the safety and efficacy of LES-ES in post-LSG patients with GERD not controlled with maximal PPI therapy.

Setting: Prospective, international, multicenter registry.

Methods: Patients with LSG-associated GERD partially responsive to PPI underwent LES-ES. GERD outcomes pre- and poststimulation were evaluated based on quality of life, esophageal acid exposure (after 6–12 mo), and PPI use.

Results: Seventeen patients (11 female, 65%), treated at 6 centers between May 2014 and October, 2016 with a median follow-up of 12 months (range 6–24), received LES-ES. Median age was 48.6 years (interquartile range, 40.5–56), median body mass index 31.7 kg/m² (27.9–39.3). All patients were on at least daily PPI preoperatively; at last follow-up, 7 (41%) were completely off PPI, 5 (29%) took PPI on an intermittent basis, and 5 (29%) were on single-dose PPI. Median GERD–health-related quality of life scores improved from 34 (on-PPI, 25–41) to 9 (6–13) at last follow-up (off-PPI, P < .001). Percentage of time with esophageal pH <4 improved from 13.2% (3.7–30.7) to 5.8% (1.1–54.4), P = .01.

Conclusion: LES-ES in post-LSG patients suffering from symptomatic, PPI-refractory GERD resulted in significant improvement of GERD-symptoms, esophageal acid exposure, and need for PPI. Preserving the post-LSG anatomy, it offers a valid option for patients unable or unwilling to undergo Roux-en-Y gastric bypass surgery. (Surg Obes Relat Dis 2018;14:611–615.) © 2018 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Keywords: Electric stimulation therapy; Lower esophageal sphincter; Gastroesophageal reflux; Proton Pump Inhibitors; Quality of life; Sleeve gastrectomy; Bariatric surgery; Esophageal pH; Postgastrectomy syndromes; Prospective studies

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Morbid obesity is recognized as a major public health issue that contributes to serious health risks. Bariatric surgery has been demonstrated to be the most efficacious method to achieve sustainable weight loss and resolution of co-morbidities among the morbidly obese [1,2].

In recent years, laparoscopic sleeve gastrectomy (LSG) has become the most frequently performed bariatric procedure, both as a stand-alone and as a prelude to staged duodenal switch [1,3]. Contributing factors to its widespread acceptance are technical simplicity, low morbidity, and results comparable to Roux-en-Y gastric bypass (RYGB) for weight loss and control of metabolic syndrome [2]. Preservation of anatomy predisposes this procedure for patients in need for access to the biliary tree, stomach, and duodenum. Furthermore, complications associated with RYGB, such as dumping syndrome, small bowel obstruction due to internal hernia, and nutrient deficiencies, are avoided.

The prevalence of gastroesophageal reflux disease (GERD) in bariatric patients is increased; up to 70% of patients have symptomatic GERD and half of patients undergoing bariatric surgery have erosive esophagitis in the preoperative evaluation [4,5]. In contrast to RYGB, there are reports of LSG worsening preexisting GERD or causing new-onset GERD [6–9]. So far, GERD after LSG, not sufficiently controlled by medication, is addressed by conversion to RYGB [10]. As with every revisional procedure, this carries an increased morbidity, but it particularly abrogates the initial intention of LSG as anatomy-preserving procedure [10,11].

Electrical stimulation of the lower esophageal sphincter (LES) is a novel surgical option that has been shown to normalize LES pressure and esophageal acid exposure in GERD patients without altering the anatomy [12–15]. The aim of this study was to evaluate the safety and efficacy of electrical LES stimulation in LSG patients with refractory GERD despite maximum-dose PPI therapy.

**Methods**

*Data collection*

Anonymized data of post-LSG patients with a follow-up of >6 months and GERD treated with LES stimulation therapy (EndoStim, BV, Nijmegen, the Netherlands [currently filing for Food and Drug Administration approval]) were extracted from a prospective, web-based, international multicenter registry tracking symptomatic and objective outcomes, registered at the clinical trials registry of the National Institutes of Health (NCT 02441400). Patient symptoms, medication use, and esophageal tests pre- and post-LES stimulation therapy were analyzed.

*Surgical technique and LES stimulation*

Two electrodes were sewn into the esophageal wall laparoscopically 1 cm apart in the LES region (Fig. 1), the lead body was exteriorized through one of the laparoscopic ports and the pulse generator was implanted in a subcutaneous pocket in the left upper abdomen. Small hiatal hernias (<2 cm) were addressed with hiatoplasty (posterior or combined anterior and posterior) hiatoplasty at the surgeons’ discretion. Preoperative bigger hiatal hernias were a contraindication. LES stimulation was initiated during the implant procedure; PPI therapy was discontinued 3 to 4 weeks later. Patients with residual or recurrent symptoms despite optimization of their stimulation parameters were treated with rescue GERD medications.

The standardized stimulation pulse (215 μs wide and nominally 5 mA in amplitude) is monophasic followed by a charge-balancing phase. The stimulation pulse is delivered at a rate of 20 Hz and continues for a period of 30 minutes. Up to twelve 30-minute sessions are delivered per day. Electrical stimulation can wirelessly be optimized to tailor the delivery to individual needs by adjusting amplitude and electrode polarity to address suboptimal symptom or pH response beginning 6 months after the procedure.

*Symptom assessment and pH monitoring*

GERD symptoms were assessed using the validated GERD–health-related quality of life questionnaire, which provides a composite score of maximum 50 points [16]. Assessment was carried out at baseline (before implantation) with the patient on PPI therapy and at every follow-up (every 6 mo in the first 2 yr, then yearly). Esophageal acid exposure was assessed at baseline and after 6 to 12 months of LES stimulation therapy using 24-hour esophageal pH-metry. Sensors were positioned in the esophageal body 5 cm above the manometric upper border of the LES with the patient off PPI therapy for at least 5 days. Furthermore, use of PPI medication and anthropometric parameters were recorded at each follow-up visit.
Descriptive statistics were used for demographic variables. Data were compared using 2-tailed Student’s t test, Friedman test, or Wilcoxon signed-rank test. A 2-sided P value of < .05 was considered significant. Data were reported as medians with interquartile range (IQR) unless otherwise stated.

Results

Seventeen patients (11 female, 65%), treated at 6 centers between May 2014 and October 2016 with a median follow-up of 12 months (minimum 6 to maximum 24), were included. No patient was lost to follow-up. Median age was 48.6 years (IQR, 40.5–56), median body mass index at time of implantation was 31.7 kg/m² (27.9–39.3), and there was no significant decrease during the follow-up (after 6 mo 28.5 kg/m² [23.9–34.8], after 12 mo 29.8 kg/m² [23.6–35], P = .2). There were no serious adverse events related to the device or procedure, and there were no reoperations or device removals within the follow-up.

Preoperatively, all patients were using daily double- or higher-dose PPI (single dose defined as 40 mg pantoprazole or equivalent). At their last follow-up, 5 patients (29%) were on single dose, 7 (41%) completely off PPI, and 5 (29%) took PPI on an intermittent basis.

All patients reported improvement in their GERD symptoms after initiation of LES stimulation. Median GERD–health-related quality of life scores (Figs. 2a, 2b) at baseline (on-PPI) were 34 (25–41), which improved to 9 (6–13) at last follow-up (off-PPI, P < .001).

Evolution of median esophageal acid exposure is depicted in Fig. 3. Percentage of time with pH < 4 improved from 13.2% (3.7–30.7) to 5.8% (1.1–54.4), P = .01; normalization (<4% of esophageal pH < 4) was observed in 7 (41%) and worsening in 2 patients (12%). Yet, in both patients, GERD–health-related quality of life improved and both were responsive to PPI therapy.

Discussion

This study reports the outcome of post-LSG patients with refractory GERD addressed with electrical stimulation of the LES over a median follow-up of a year (range, 6–14 mo). This treatment led to a significant improvement of GERD symptoms, esophageal acid exposure, and reduction in GERD medication use.

Morbid obesity is associated with GERD and esophageal motility disorders; the prevalence is estimated up to 70% [4,5,17–19]. There is a linear relationship not only between body mass index and GERD, but also between central obesity and GERD [20]. Yet, central obesity complicates bariatric procedures and is one of the main reasons— together with the resulting co-morbidities—for the popularity of LSG [21]. Morbid obesity increases the intraabdominal pressure having an effect on intragastric pressure and the gastroesophageal pressure gradient, and leads further to a higher rate of hiatal hernias and postprandial transient LES relaxations [22]. Furthermore, LES pressures are lowered, and there is high incidence of ineffective esophageal motility [23,24].
The effects of LSG on GERD are controversially discussed, yet the vast majority of studies report a worsening of preexisting and a substantial rate of de novo GERD [8,25–27].

Depending on duration of follow-up, measures to detect GERD, and operative technique, the incidence of de novo post-LSG GERD ranges up to 47% in symptoms and 63.5% endoscopically [7,8,19,26]. Also troubling is a high rate of asymptomatic GERD in bariatric patients of so far unknown importance and an association of worse outcome after LSG with GERD regarding weight loss and resolution of comorbidities [8,28,29]. Post-LSG Barrett’s esophagus has a high incidence and occurs unrelated to symptoms [30]. In addition, with rising numbers of LSG, this problem might be exacerbated in the near future as most studies describe a selected patient group with less GERD; so far, most patients with preexisting higher-grade GERD are denied the benefits of LSG and proposed RYGB instead [31].

A multitude of factors have an influence on post-LSG GERD after LSG [27]. Technical factors such as proximity of the staple to the LES have an impact on its function; disruption of sling fibers lead to a decrease of LES pressure and shortening of LES, as showed by manometric pre- and postoperative evaluation [5,24]. LSG results in decreased gastric compliance provoking a possible increase of transient LES relaxations [22]. Furthermore, another study showed a high rate of ineffective esophageal peristalsis after LSG [23].

Electrical stimulation of the LES leads to a sustained reduction of GERD symptoms and improvement of esophageal acid exposure in the majority of patients [12–14]. It is a procedure with minimal morbidity, also in the small group reported here. The underlying mechanisms have yet to be elucidated in detail; it has a positive impact on LES pressure and length and may improve esophageal motility and reduce the frequency of transient LES relaxations [15]. In the context of post-LSG GERD, it offers the distinctive advantage of preserving the anatomy. This study shows it to be safe and technically feasible. It offers a significant improvement of esophageal acid exposure, with normalization in almost half of patients. A longer follow-up might lead to an even higher rate, as the maximum effect has to be expected after 9 months, yet the median objective follow-up in this study was 6 months. Symptomatic control, in terms of PPI use and standardized questionnaires, was excellent and comparable to RYGB. Even more, the patient population included was nonresponsive to PPI and had a rather high esophageal acid exposure.

There are limitations to this study. It is an open-label, multicenter design with a small sample size, including a heterogeneous patient population from a self-reported patient registry. Postbariatric patients are different than other GERD patients with different co-morbidity profiles and probable different reasons for GERD. These data are preliminary; a larger sample size with a longer follow-up in a prospective, randomized, double-blind, sham-controlled design is needed to validate these results.

Conclusions

Electrical stimulation of LES in post-LSG patients suffering from symptomatic GERD refractory to medication led to a significant improvement of GERD-symptoms, esophageal acid exposure, and overall decrease of need for PPI. Preserving the post-LSG anatomy, it offers a valid option for patients unable or unwilling to undergo RYGB.

Disclosures

Y.B. received travel reimbursements from Endostim, all other authors declare that they have no conflicts of interest.

References