Clinical Gastroenterology and Hepatology 2017;15:37–43

ALIMENTARY TRACT

Endoscopic Sleeve Gastroplasty Alters Gastric Physiology and Induces Loss of Body Weight in Obese Individuals

Barham K. Abu Dayyeh,[*,‡] Andres Acosta,[‡] Michael Camilleri,[‡] Manpreet S. Mundi,[§] Elizabeth Rajan,[*] Mark D. Topazian,[*] and Christopher J. Gostout[*]

*Developmental Endoscopy Unit, Division of Gastroenterology and Hepatology, Department of Medicine; ‡Clinical Enteric Neuroscience Translational and Epidemiological Research, Division of Gastroenterology and Hepatology, Department of Medicine; and §Division of Endocrinology, Department of Medicine, Mayo Clinic, Rochester, Minnesota

BACKGROUND & AIMS: **Although bariatric surgery is the most effective therapy for obesity, only a small proportion of candidates undergo this surgery. Endoscopic sleeve gastroplasty (ESG) is a minimally invasive procedure that reduces the size of the gastric reservoir. We investigated its durability and effects on body weight and gastrointestinal function in a prospective study of obese individuals.**

METHODS: **Twenty-five obese individuals (21 female; mean body mass index, 35.5 ± 2.6 kg/m^2; mean age, 47.6 ± 10 years) underwent ESG with endoluminal creation of a sleeve along the gastric lesser curve from September 2012 through March 2015 at the Mayo Clinic in Rochester, Minnesota. Subjects were followed for a median period of 9 months. We measured changes in body weight and recorded adverse events; patients were assessed by endoscopy after 3 months. Four participants underwent pre-ESG and post-ESG analyses to measure solid and liquid gastric emptying, satiation (meal tolerance), and fasting and postprandial levels of insulin, glucose, and gut hormones.**

RESULTS: **Subjects had lost 53% ± 17%, 56% ± 23%, 54% ± 40%, and 45% ± 41% of excess body weight at 6, 9, 12, and 20 months, respectively, after the procedure ($P < .01$). Endoscopy at 3 months showed intact gastroplasty in all subjects. After ESG, physiological analyses of 4 participants showed a decrease by 59% in caloric consumption to reach maximum fullness ($P = .003$), slowing of gastric emptying of solids ($P = .03$), and a trend toward increased insulin sensitivity ($P = .06$). Three patients had serious adverse events (a perigastric inflammatory collection, a pulmonary embolism, and a small pneumothorax) but made full recoveries with no need for surgical interventions. No further serious adverse events occurred after the technique was adjusted.**

CONCLUSIONS: **ESG delays gastric emptying, induces early satiation, and significantly reduces body weight. ESG could be an alternative to bariatric surgery for selected patients with obesity. ClincialTrials.gov number: NCT 01682733.**

Keywords: BMI; Weight Loss Procedure; Gastric Restriction; Stomach.

See editorial on page 44.

Despite progress in our understanding of the complex neuronal, hormonal, metabolic, and inflammatory mechanisms in obesity, bariatric-metabolic surgery remains the only current treatment of obesity that is effective in the long-term.[1] Lifestyle modification and pharmacologic approaches for the treatment of obesity have failed to address the increasing burden of disease because they are often associated with only modest weight loss that is rarely maintained over time.[2,3]

Gastric restriction is an important component of all bariatric-metabolic surgical procedures. This is accomplished by creation of a small gastric pouch in Roux-en-Y gastric bypass (RYGB), placement of an adjustable gastric band, or removal of 80% of the stomach in sleeve gastrectomy surgery.[4] The importance of the reduction in the gastric reservoir is illustrated by physiological and comparative effectiveness studies showing comparable 5-year weight loss outcomes, similar decrease in dietary intake, and similar changes in gut hormones after RYGB (which has both restrictive and malabsorptive

Abbreviations used in this paper: BMI, body mass index; BTA, botulinum toxin A; ESG, endoscopic sleeve gastroplasty; EWL, excessive weight loss; GLP-1, glucagon-like peptide 1; PYY, peptide YY; RYGB, Roux-en-Y gastric bypass.

Most current article

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2015.12.030

anatomic components) and sleeve gastrectomy (which has only a restrictive component).[5–7]

Despite the positive impact of bariatric-metabolic surgery, only 1% of qualified patients receive surgery because of limited access, patient preference, risks, and cost of surgery.[8] Because of this low utilization rate of surgery and limited efficacy of lifestyle and pharmacologic interventions, a significant gap exists in our current approach to obesity, which contributes to unprecedented rates of the disease and escalation of comorbid conditions resulting in an enormous economic burden on our health care system.[9,10]

Endoscopic bariatric therapies can potentially offer effective weight loss intervention at lower cost and higher patient acceptability, potentially bridging the current obesity management gap. We have previously reported the feasibility of a novel endoscopic approach to obesity that reduces the size of the gastric reservoir by creation of an endoscopic sleeve gastroplasty (ESG) by using a full-thickness endoscopic suturing device.[11] Here we report prospective mid-term outcomes, adverse effects, and physiological alterations after ESG. In addition, to assess the reproducibility of our results, we compared our outcomes with those of Spanish investigators who have been performing ESG since our initial feasibility report.[11,12]

Methods

Participants

Twenty-five consecutive adult patients with body mass index (BMI) between 30 and 40 kg/m^2, stable weight for 3 months before the procedure, and no contraindication to ESG (anticoagulation, previous gastric surgery, gastric ulceration, hiatal hernia $\geq$5 cm, or pregnancy) were included in this prospective study. All patients underwent ESG between September 2012 and March 2015 and completed a median of 9 months (range, 5–20) follow-up after the procedure. The first 10 procedures were performed under institutional review board protocol (12-003195) registered with ClinicalTrials.gov (NCT 01682733) by using a commercially available endoscopic suturing device (Overstitch; Apollo Endosurgery, Austin, TX). Once we had demonstrated the feasibility and safety of the procedures in this pilot study, we opened the protocol to acquire clinical experience and appraise outcomes in open label fashion with the same prospective follow-up in 15 more patients. Finally, we assessed the reproducibility and generalizability of the procedures by comparing our outcomes with those from a 30-patient series from Spain.[12] All authors had access to the study data and had reviewed and approved the final manuscript.

Endoscopic Sleeve Gastroplasty

ESG was performed on an outpatient basis. A standard upper endoscope (GIF-H180; Olympus America, Center Valley, PA) was used to examine the esophagus and stomach for any anatomic contraindications. After placement of an esophageal length overtube (US Endoscopy, Mentor, OH), we mapped 3 parallel (anterior, greater curvature, and posterior) suture placement sites by using argon plasma coagulation starting at the incisura and extending proximally to the gastroesophageal junction. Five of the first 10 patients were randomly selected to have 10 U botulinum toxin A (BTA) (Botox; Allergan, Irvine, CA) injected at suture sites in the body of the stomach before suture placement to evaluate whether BTA enhances ESG durability, which was assessed by endoscopy at 3 months. BTA injections were then abandoned after this pilot trial showed lack of impact on ESG durability. Thus, only 5 of 25 patients received BTA injections in addition to ESG.

ESG was created by using an interrupted triangular suture pattern that invaginates the greater curvature of the stomach for creation of a narrow sleeve that reduces the functional capacity of the stomach by 80% (Figure 1). A second layer of sutures was placed over the length of the central sleeve in an interrupted pattern to further reduce the gastric volume and reinforce the sleeve. Each suture was intended to be full thickness enabled by a tissue screw that captures the muscularis propria, thereby avoiding gastric wall layer delamination (Helix; Apollo Endosurgery). The suturing sequence is described in detail in our previous feasibility report.[11]

All procedures were performed with patients under general anesthesia in an outpatient endoscopy unit by

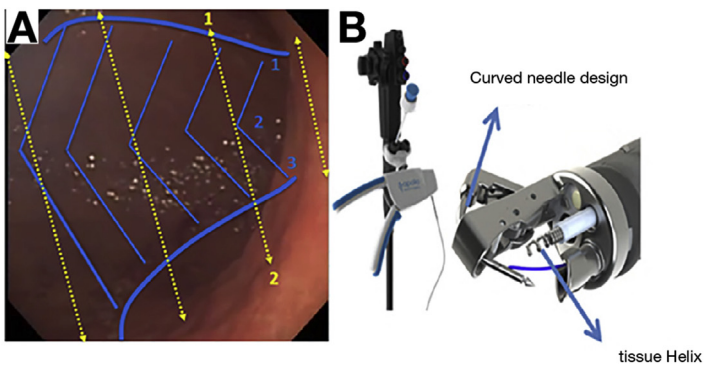

Figure 1. (*A*) Suturing pattern used to create the ESG. (*B*) The full-thickness endoscopic suturing device used to create the ESG. (*C*) A longitudinal section depicting the invagination of the greater curvature of the stomach for creation of a narrow sleeve reducing the functional capacity of the stomach by 80%.

using carbon dioxide (CO_2) insufflation. Procedures were performed by 3 endoscopists (B.A., C.G., M.T.). All subjects were placed on a postprocedural diet consisting of liquid protein shakes for 4 weeks, followed by 2 weeks of a pureed diet before transitioning to a regular diet. The postprocedural diet was designed to provide 70 g protein and 1000–1200 calories per day. In 9 sequential participants repeat upper endoscopy was performed at 3 months to evaluate ESG durability and safety. Weight outcomes and side effects of ESG were prospectively recorded every 3 months. Percentage excess body weight loss (%EWL) was calculated by using BMI 25 kg/m^2 as ideal body weight. All subjects were counselled to follow a standardized healthy lifestyle modification program,[13] although this was not monitored or enforced during the duration of the study.

Physiological Testing

Four sequential patients participated in a pilot substudy (Institutional Review Board 12-003383) to assess the metabolic and physiological alterations that occur in response to ESG. On separate days (once within 2 weeks before ESG and once 3 months after ESG), participants attended the Mayo Rochester Clinical Research Unit after fasting overnight ($\geq$8 hours) on separate days for measurement of gastric emptying of solids and liquids, satiation by nutrient drink test, and fasting and postprandial insulin, glucose, active ghrelin, leptin, glucagon-like peptide 1 (GLP-1), and peptide YY (PYY) levels. These tests are described in detail in our previous publications and in the Supplementary Methods.[14–16]

Comparative Analysis

To assess the reproducibility of ESG results, we used a fixed effect meta-analysis to assess the degree of heterogeneity between our findings (25 patients) and published results from Spain (30 patients).[12] Statistical heterogeneity was evaluated by means of I^2 statistics and Q values. An I^2 value greater than 50% was considered to indicate high statistical heterogeneity. The comprehensive meta-analysis software (Comprehensive Meta Analysis, Version 2.2; Biostat Inc, Englewood, NJ) was used for this analysis.

Statistical Analysis

The paired *t* test was used to assess statistically significant differences among continuous variables. Area under the curve was calculated for pre and post glucose, insulin, ghrelin, leptin, GLP-1, and PYY levels. Analyses were performed by using SAS version 9.3 software (SAS Institute, Cary, NC) and MedCalc v15.6.1. Data in the article are presented as mean $\pm$ standard deviation or median (range).

Results

Patient Demographics and Procedural Details

There were 25 participants including 21 women, mean age was 47.6 $\pm$ 10 years with 88% white ethnicity, mean baseline BMI was 35.5 $\pm$ 2.6 kg/m^2, and 5% of the cohort had type II diabetes managed with oral hypoglycemic agents. The average number of sutures used to create the sleeve was 16 $\pm$ 5. Procedural times significantly decreased from 217 $\pm$ 17 to 98 $\pm$ 4 minutes, when comparing the first 5 cases with the last 5 cases, respectively ($P \leq .01$).

Weight Loss Outcomes

Median follow-up was 9 months (range, 5–20), and weight outcomes on 8 of 10 patients who reached 20 months of follow-up were available. Figure 2 shows changes in BMI and %EWL after ESG and number of eligible patients available at each time point. The %EWL was 53% $\pm$ 17%, 56% $\pm$ 23%, 54% $\pm$ 40%, and 45% $\pm$ 41% at 6, 9, 12, and 20 months after ESG, respectively ($P < .01$) (Figure 2). Five of 8 available participants (62.5%) with 20 months of follow-up had an excellent durable response to ESG with %EWL of 72% $\pm$ 21.8% (median, 78.7%), and 3 of 8 (37.5%) regained all the weight lost at 20 months.

Endoscopic Sleeve Gastroplasty Durability

Repeat upper endoscopy was performed at 3 months in 9 sequential patients to evaluate integrity of the ESG. Six of 9 (67%) had a durable, intact ESG with formation of fibrotic bridges (Figure 3). Three of 9 (33%) had a partially intact ESG with opening of the proximal body and fundus. Two of the 3 non-responders to ESG at 20 months had only partially intact ESG at the 3-month

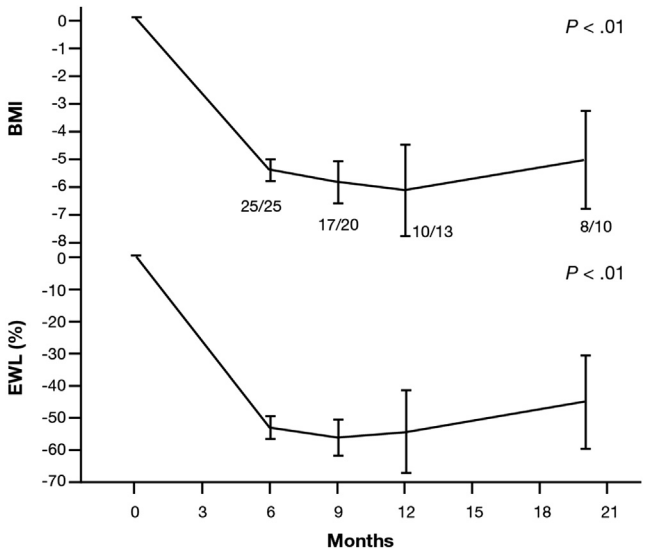

Figure 2. Changes in BMI and %EWL after ESG. Means and standard errors are presented. Number of eligible patients available for analysis at each time point is presented.

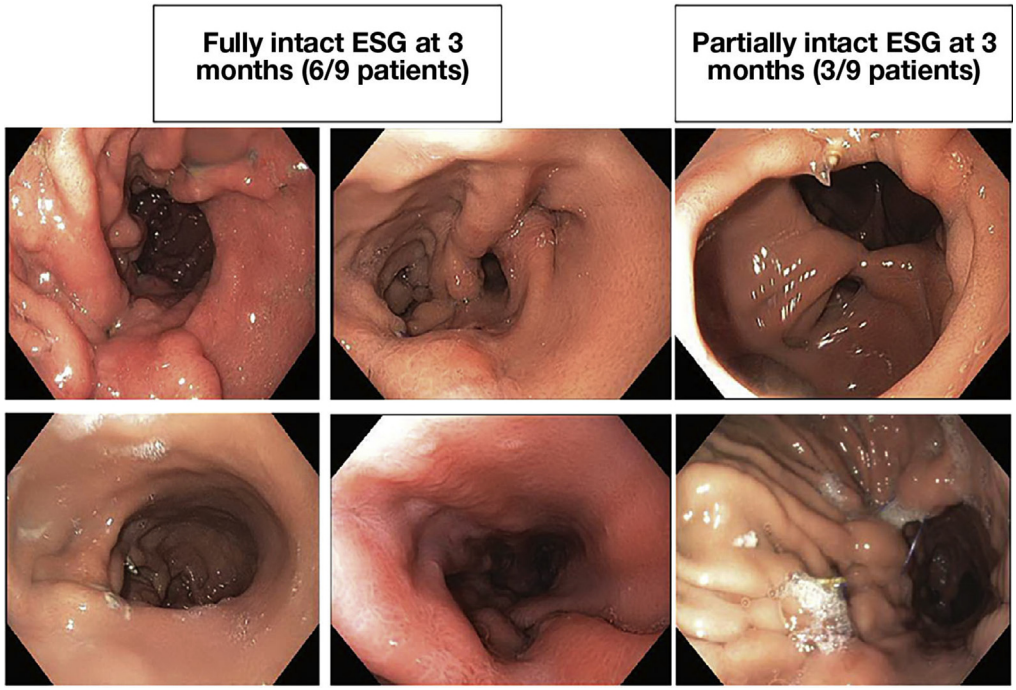

Figure 3. Endoscopic evaluation of ESG durability at upper endoscopy 3 months after ESG creation.

endoscopy. None of the patients had evidence of esophagitis on repeat upper endoscopy.

Adverse Events

Seventeen patients (68%) remained outpatients after ESG and received a short course of oral narcotics and antiemetic medications to treat acute post-ESG pain and nausea. Eight participants required hospitalization for pain and/or nausea for a median of 1.5 days (range, 1–4). Three serious immediate adverse events occurred; one participant developed a perigastric inflammatory serous fluid collection (adjacent to the fundus) that resolved with percutaneous drainage and antibiotics, another developed a pulmonary embolism 72 hours after the procedure, and a third developed pneumoperitoneum and pneumothorax requiring chest tube placement. All 3 patients required hospitalization but had full recovery with no need for surgical interventions. No longer-term adverse events were reported.

Reproducibility of Body Weight Loss After Endoscopic Sleeve Gastroplasty (Meta-analysis)

Overall, the mean %EWL at 6 and 12 months among 55 patients receiving ESG (25 in Rochester, Minnesota and 30 in Madrid, Spain) was 53 (95% confidence interval, 47.7–58.6) and 56.4 (95% confidence interval, 45–67.8), respectively. The degree of heterogeneity in weight loss outcomes calculated by a fixed effect meta-analysis was minimal ($I^2 = 0$), indicating reproducible ESG outcomes in independent centers (Figure 4).

Physiological Alterations as a Result of Endoscopic Sleeve Gastroplasty

Gastric emptying. ESG significantly alters gastric emptying and satiation. Figure 5*A* demonstrates a significant delay in gastric emptying of solids 3 months after ESG compared with before ESG, with an increase in time for 50% emptying of solid (T50) by 90 minutes ($P = .03$). Four hours after solid meal ingestion, 32.25% of the meal is retained in a small gastric fundus cap after ESG compared with 5.25% before (Figure 5*B–D*). There is no significant change in gastric emptying of liquids after ESG ($P = .5$).

Satiation by nutrient drink test and appetite regulatory hormones. ESG significantly increased satiation with 59% ($P = .003$) decrease in caloric intake to reach maximum fullness on a meal tolerance test, leading to earlier termination of a meal at 11.5 ± 2.3 minutes after

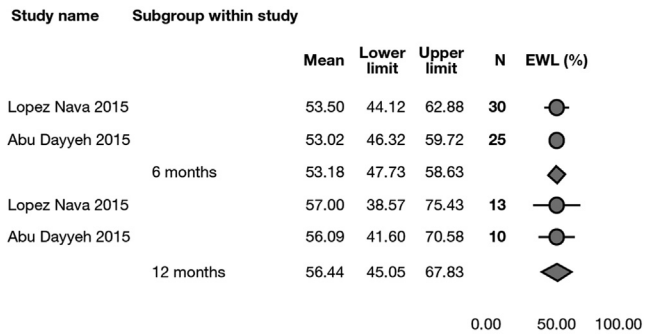

Figure 4. Forest plot depicting pooled %EWL at 6 and 12 months after ESG by using a fixed effect meta-analysis from 2 independent centers to evaluate the reproducibility of the technique.

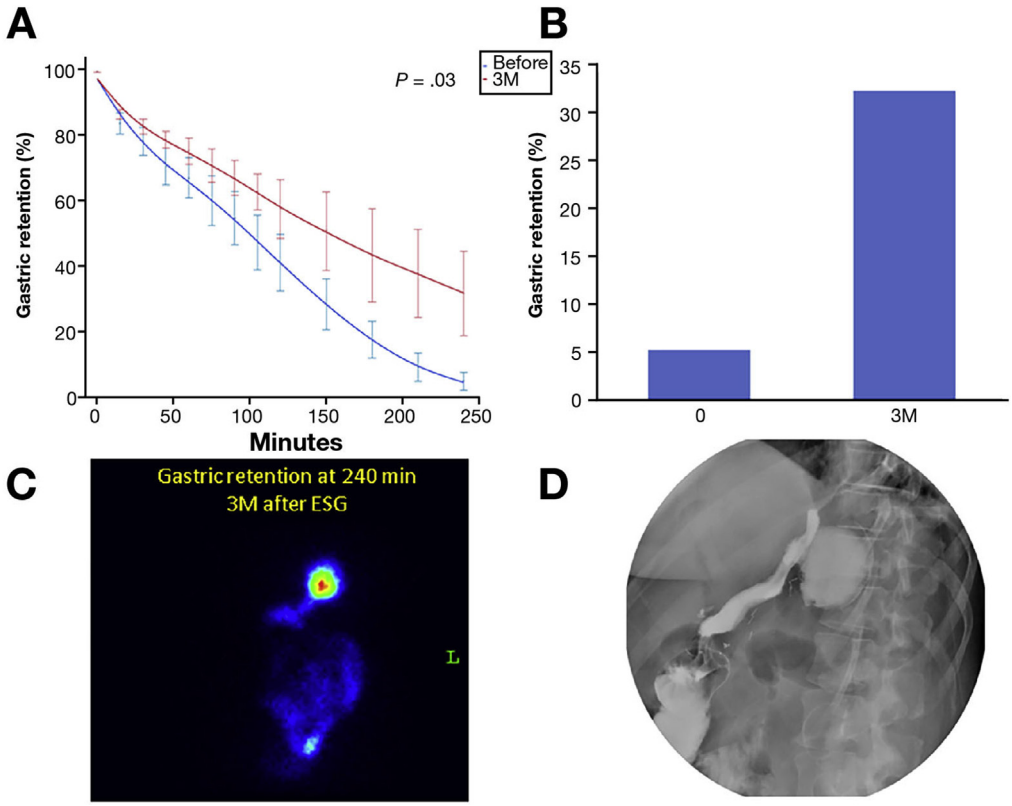

Figure 5. (*A*) Changes in gastric emptying of solids before and 3 months after ESG. Means and standard errors are presented. (*B*) Percent gastric retention of a solid meal at 240 minutes before and 3 months after ESG. (*C*) Gastric scintigraphy image at 240 minutes after a solid meal ingestion depicting retained solid meal in a small gastric fundus cap after ESG. (*D*) Upper gastrointestinal series with a radiopaque contrast demonstrating a sleeve effect with a small fundus cap.

ESG compared with 35.2 ± 9.9 minutes before ESG ($P = .01$). Despite significant weight loss, active fasting and postprandial ghrelin levels decreased by 29.4% ($P = .1$) 3 months after ESG. There were no statistically significant changes in leptin, GLP-1, and PYY levels.

Insulin sensitivity. ESG significantly improved insulin sensitivity. Fasting homeostatic model assessment for insulin resistance score improved ($P = .06$), and area under the curve for postprandial glucose and insulin decreased by 36% ($P = .005$) and 34% ($P = .17$), respectively (Figure 6).

Discussion

In this study we demonstrated the efficacy of ESG as a minimally invasive endoscopic intervention for obesity. ESG produced similar %EWL at 1 year to laparoscopic adjustable gastric band surgery but less than laparoscopic sleeve gastrectomy and RYGB, which produce between 60% and 90% EWL at 1 year.[17] In addition to weight loss, ESG is associated with impairment of gastric emptying, increased satiation, and metabolic effects that are potentially important to control the metabolic dysregulation associated with obesity.

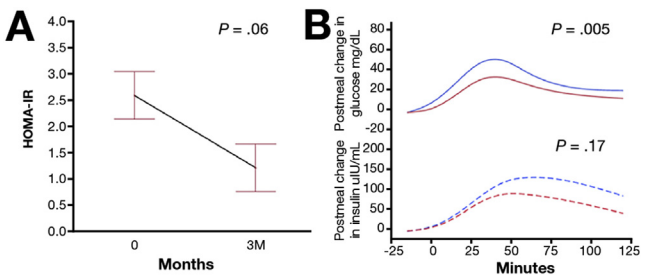

Figure 6. (*A*) Change in homeostatic model assessment for insulin resistance (HOMA-IR) score after ESG. (*B*) Changes in postprandial glucose and insulin levels after ESG.

For an endoscopic bariatric therapy to have a meaningful impact on obesity, it should reach a certain threshold of efficacy that is balanced with the risks and cost of the intervention. ESG was well-tolerated as an outpatient intervention, requiring less than 2 hours of endoscopy time after a short initial learning curve, and was performed by using standard "off the shelf" endoscopic tools as opposed to specific weight loss devices or platforms. Recovery period after ESG was short, with the majority of patients returning to a fully functional status within 1–3 days after the intervention. Coupled with the significant weight loss observed, reproducibility of the results among independent centers, and the anatomic durability of the intervention, this suggests that ESG is a cost-effective intervention for obesity. Although not tested in this study, ESG is potentially a reversible and repeatable procedure.

We did observe 3 serious adverse events in the study, and in response we have changed our clinical protocols. To decrease the risk of pulmonary embolism, intermittent pneumatic compression devices are now placed on patients' lower extremities during the procedure, and a dose of prophylactic subcutaneous heparin is given during the endoscopic procedure. Because of the

full-thickness nature of the endoscopic suturing device, a small pneumoperitoneum is expected as a result of CO_2 leaking during suture placement. This is usually clinically inconsequential; however, to decrease the risk of potential complication such as pneumoperitonuem, CO_2 insufflation is minimized during suture placement, and the abdomen is closely monitored for distention during the procedure. Finally, the posterior aspect of the gastric fundus is the most vulnerable location for a post-procedure leak because of its thin wall and tension exerted by sutures in this location that approximate the fundus anteriorly to the gastroesophageal junction. On the basis of our gastric emptying studies demonstrating a potentially beneficial role of the fundus cap in enhancing the satiety effect of the procedure by acting as a food reservoir for many hours after meal ingestions, we no longer attempt to reduce the gastric fundus. Since adopting these changes, no serious adverse events have occurred.

Studies have demonstrated a multitude of compensatory physiological adaptations in the homeostatic mechanisms involved in body weight regulation in response to restrictive diets alone, resulting in weight cycling "yo-yo dieting" that paradoxically promotes a net weight gain.[18] In humans, weight loss that is based on caloric restriction through dieting resulted in significant increase in appetite with increase in orexigenic gut hormones such as ghrelin and decrease in anorexigenic gut hormones such PYY.[19–22] This suggests that the high rate of relapse among obese patients after restrictive diets has strong physiological basis. In contrast, despite significant weight loss after ESG, satiation is increased with a decrease in ghrelin and delay in gastric emptying, especially at 4 hours. This is a finding of significant physiological importance in light of the association between obesity and accelerated gastric emptying and the fact that delayed gastric emptying of solids at 4 hours is a determinant of fullness and satiation in humans.[16,23] This suggests that the physiological perturbations produced by ESG are sufficient to overcome the compensatory responses that lead to weight regain after restrictive diets. We believe that these effects on gastric reservoir volume and gastric emptying both contribute to the increased satiation and result in a more significant and durable weight loss.

Limitations to our study include its small sample size, lack of a control group, limited long-term follow-up, and evaluation of ESG anatomic durability and physiology in only a subset of patients, potentially leading to a type II error. These limitations reflect the novelty of this technique. The current study addresses proof of concept and the mechanisms associated with the weight loss after ESG. Randomized controlled studies with longer follow-up are needed.

In conclusion, ESG is a minimally invasive and cost-effective weight loss intervention. ESG slows gastric emptying, increases satiation, and improves the metabolic profile of obese persons. ESG may have a role in the treatment of obese persons who do not undergo bariatric surgery, including those with moderate obesity, and those who require a bridge to surgery, including super-obese individuals. ESG offers a paradigm shift in our management of obesity that targets current gaps in therapy and may allow us to gain ground in our losing battle against obesity.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at http://dx.doi.org/10.1016/j.cgh.2015.12.030.

References

1. Sjostrom L. Review of the key results from the Swedish Obese Subjects (SOS) trial: a prospective controlled intervention study of bariatric surgery. J Intern Med 2013;273:219–234.
2. Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity 2014;22:5–13.
3. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. JAMA 2014;311:74–86.
4. Acosta A, Abu Dayyeh BK, Port JD, et al. Recent advances in clinical practice challenges and opportunities in the management of obesity. Gut 2014;63:687–695.
5. Moize V, Andreu A, Flores L, et al. Long-term dietary intake and nutritional deficiencies following sleeve gastrectomy or Roux-En-Y gastric bypass in a mediterranean population. Journal of the Academy of Nutrition and Dietetics 2013;113:400–410.
6. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med 2012;366:1567–1576.
7. Peterli R, Steinert RE, Woelnerhanssen B, et al. Metabolic and hormonal changes after laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy: a randomized, prospective trial. Obes Surg 2012;22:740–748.
8. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient: 2013 update—cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. Surgery for Obesity and Related Diseases 2013;9:159–191.
9. Cawley J, Meyerhoefer C. The medical care costs of obesity: an instrumental variables approach. Journal of Health Economics 2012;31:219–230.
10. Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA 2014; 311:806–814.
11. Abu Dayyeh BK, Rajan E, Gostout CJ. Endoscopic sleeve gastroplasty: a potential endoscopic alternative to surgical sleeve gastrectomy for treatment of obesity. Gastrointest Endosc 2013; 78:530–535.
12. Lopez-Nava G, Galvao MP, Bautista-Castano I, et al. Endoscopic sleeve gastroplasty: how do I do it? Obes Surg 2015; 25:1534–1538.
13. Pi-Sunyer FX, Bouchard C, Carleton RA, et al. Clinical guidelines on the identification, evaluation, and treatment of overweight

and obesity in adults: executive summary—Expert Panel on the Identification, Evaluation, and Treatment of Overweight in Adults. Am J Clin Nutr 1998;68:899–917.

14. Chial HJ, Camilleri C, Delgado-Aros S, et al. A nutrient drink test to assess maximum tolerated volume and postprandial symptoms: effects of gender, body mass index and age in health. Neurogastroenterol Motil 2002;14:249–253.
15. Vazquez Roque MI, Camilleri M, Stephens DA, et al. Gastric sensorimotor functions and hormone profile in normal weight, overweight, and obese people. Gastroenterology 2006;131:1717–1724.
16. Acosta A, Camilleri M, Shin A, et al. Quantitative gastrointestinal and psychological traits associated with obesity and response to weight-loss therapy. Gastroenterology 2015;148:537–546 e4.
17. Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. Cochrane Database Syst Rev 2014;8:CD003641.
18. Dulloo AG, Montani JP. Pathways from dieting to weight regain, to obesity and to the metabolic syndrome: an overview. Obes Rev 2015;16(Suppl 1):1–6.
19. Sumithran P, Prendergast LA, Delbridge E, et al. Long-term persistence of hormonal adaptations to weight loss. N Engl J Med 2011;365:1597–1604.
20. Cummings DE, Weigle DS, Frayo RS, et al. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. N Engl J Med 2002;346:1623–1630.
21. Keim NL, Stern JS, Havel PJ. Relation between circulating leptin concentrations and appetite during a prolonged, moderate energy deficit in women. Am J Clin Nutr 1998;68:794–801.
22. Essah PA, Levy JR, Sistrun SN, et al. Effect of weight loss by a low-fat diet and a low-carbohydrate diet on peptide YY levels. Int J Obes 2010;34:1239–1242.
23. Delgado-Aros S, Camilleri M, Castillo EJ, et al. Effect of gastric volume or emptying on meal-related symptoms after liquid nutrients in obesity: a pharmacologic study. Clin Gastroenterol Hepatol 2005;3:997–1006.

Reprint requests
Address requests for reprints to: Barham K. Abu Dayyeh, MD, MPH, 200 First Street SW, Rochester, Minnesota 55905. e-mail: abudayyeh.barham@mayo.edu; fax: (507) 538-5820.

Conflicts of interest
These authors disclose the following: Dr Abu Dayyeh is a consultant and received research support from Apollo Endosurgery. Dr Gostout is the chief medical officer and holds equity in Apollo Endosurgery. The remaining authors disclose no conflicts.

Funding
This study was partially funded by a grant from Apollo Endosurgery and career development and innovation awards by the Mayo Department of Medicine to Dr Abu Dayyeh.

Supplementary Methods

Gastric Emptying of Solids and Liquids

Gastric emptying of solids and liquids was measured by means of a scintigraphic method that used a dual-labeled solid liquid meal (296 kcal, 32% protein, 35% fat, 33% carbohydrate). A 99mTc-sulfur colloid (0.75 mCi) was added to 2 raw eggs during the scrambling and cooking process. The eggs were served on 1 slice of bread with 240 mL 1% milk labeled with 111In-diethylenetriamine pentaacetate (0.05 mCi). Anterior and posterior gamma camera images were obtained immediately after radiolabeled meal ingestion, every 15 minutes for the first 2 hours, and then every 30 minutes for the next 2 hours (total, 4 hours after the radiolabeled meal). Geometric means of decay-corrected counts in anterior and posterior gastric regions of interest were used to estimate the proportion of 99mTc or 111In emptied at each time point (gastric emptying).

Satiation by the Nutrient Drink Test

A standardized nutrient drink test to measure satiation and postprandial symptoms was used. While drinking a liquid nutrient (Ensure, Abbott Labs; 1 kcal/mL, 11% fat, 73% carbohydrate, 16% protein), participants measured satiation by using a scale that combines verbal descriptors and numbers (0 = no symptoms, 5 = maximum or unbearable fullness/satiation). Participants scored the time needed to reach each level of fullness by using a digital timer. Nutrient intake was stopped when subjects reached a score of 5. The nutrient drink volume needed to achieve maximum satiation was recorded and, hence, calorie intake. Postprandial fullness and symptoms of nausea, bloating, and pain were measured 30 minutes after the meal was completed when there is full satiation by using a 100-mm horizontal visual analogue scale. The words *none* and *worst ever* anchored the visual analogue scale at the left and right ends of the lines for each symptom, respectively.

Blood Samples

Six blood samples were obtained for measurement of serum levels of insulin, glucose, active ghrelin, leptin, GLP-1, and PYY during the nutrient drink test. The schedule for the blood samples was as follows: 0 (before meal ingestion), 15, 30, 45, 60, and 120 minutes. Details of the immunochemical assays used can be found in a previous publication.[1,2]

References

1. Vazquez Roque MI, Camilleri M, Stephens DA, et al. Gastric sensorimotor functions and hormone profile in normal weight, overweight, and obese people. Gastroenterology 2006; 131:1717–1724.
2. Acosta A, Camilleri M, Shin A, et al. Quantitative gastrointestinal and psychological traits associated with obesity and response to weight-loss therapy. Gastroenterology 2015; 148:537–546 e4.