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Endoscopic sutured gastroplasty: procedure evolution from first in man cases through current technique

Nitin Kumar, MD¹, Barham K. Abu Dayyeh², Gontrand Lopez-Nava Breviere, MD³, Manoel P. Galvao Neto, MD⁴, Nicole P. Sahdala, MD⁵, Sohail N. Shaikh, MD⁶, Robert H. Hawes, MD⁷, Christopher J. Gostout, MD², Mahesh K. Goenka, MD⁸, Jorge R. Orillac, MD⁹, Alonso Alvarado, MD⁹, Pichamol Jirapinyo, MD¹⁰, Natan Zundel, MD¹¹, and Christopher C. Thompson, MD¹⁰

¹Bariatric Endoscopy Institute, Addison, IL, USA

²Mayo Clinic, Rochester, MN, USA

³Madrid Sanchinarro University Hospital, Madrid, Spain

⁴Gastro Obeso Center, Sao Paulo, Brazil

⁵Universidad Nacional Pedro Henriquez Urena, Santo Domingo, Dominican Republic

⁶Center for Bariatric Endoscopy, Montclair, NJ

⁷Florida Hospital, Orlando, FL

⁸Apollo Gleneagles Hospital, Kolkata, India

⁹Clinica Hospital San Fernando, Panama City, Panama

¹⁰Brigham and Women's Hospital, Boston, MA, USA

¹¹Florida International University Herbert Wertheim College of Medicine, Miami, FL

Abstract

Background—Endoscopic sutured gastroplasty (ESG) has evolved over time. With the advent of full-thickness endoscopic suturing, an efficient technique for ESG was developed and refined.

Methods—This prospective first in man trial started in April 2012, and represents the first use of full-thickness endoscopic suturing for primary obesity therapy. The trial focused on procedure development, reproducibility, safety, and short-term efficacy. The trial was performed at centers in five countries, in three phases. Phase I was evaluation of safety and technical feasibility of various procedure techniques; stitch patterns and sequences were assessed for efficiency, safety, and feasibility. Phase II entailed continued procedure refinement to establish a standardized technique. Phase III *entailed evaluation of technical feasibility and weight loss outcomes in 77 patients*; the procedure was performed using the standardized technique, and there was no procedure development. Data was prospectively collected into a registry.

Corresponding author: Christopher C. Thompson, Director of Therapeutic Endoscopy, Division of Gastroenterology, Brigham and Women's Hospital, 75 Francis St., Thorn 1404, Boston, MA 02115, Phone: 617-525-8266.

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Results—*In Phase I, the procedure was created, and modified to improve time efficiency.* Safety and technical feasibility were established, and short-term weight loss was demonstrated. In Phase II, a number of stitch patterns were attempted, and the stitch pattern was modified and finalized. 22 patients were included, and 1-year total weight loss was $17.3 \pm 2.6\%$. In Phase III, adherence to the final technique was high. 77 patients were included, with mean BMI of $36.1 \pm 0.6 \text{ kg/m}^2$. Mean weight loss was $16.0 \pm 0.8\%$, at 6 months and $17.4 \pm 1.2\%$ at 12 months ($n=44$). Post-procedure nausea, vomiting, and epigastric pain were frequently reported; there were no reported significant adverse events post-procedure or during the follow-up period.

Conclusions—Following a methodical procedure development phase, ESG demonstrated safety and short-term efficacy in this trial. The procedure also achieved meaningful weight loss during the follow-up period.

Keywords

endoscopic sleeve gastropasty; endoscopic sutured gastropasty; endoscopic bariatric; bariatric endoscopy; obesity; bariatric surgery; weight loss surgery

Introduction

Obesity and its comorbidities - diabetes, hypertension, hyperlipidemia, and nonalcoholic fatty liver disease - have become a global epidemic [1]. Dietary modification, exercise, and pharmacologic therapy have been ineffective in arresting the spread of obesity at the population level. Bariatric surgery, which is effective and is utilized by hundreds of thousands of patients each year, can only be performed on a fraction of eligible patients due to the current number of practicing surgeons and economic limitations [2]. A new paradigm is developing in the treatment of obesity and metabolic disease. The concept that endoscopic procedures have the potential to bridge the gap between medical therapy and weight loss surgery is gaining broader acceptance.

Endoscopic suturing for revision of gastric bypass was first performed in 2004 [3]. Endoscopic sutured gastropasty (ESG) was first performed in 2008 as part of a trial at Brigham & Women's Hospital and the Cleveland Clinic, as an endoscopic analogue to the surgical gastric imbrication [4]. The procedure utilized a series of running sutures incorporating the anterior, greater curvature, and posterior surfaces of the stomach to create a narrow tunnel along the lesser curvature, limiting the ability of the stomach to accommodate large-volume meals (Figure 1A). This was inspired by an earlier abandoned procedure, the endoluminal vertical gastropasty (EVG), performed in Venezuela. EVG involved one running suture along the midline of the stomach, in an attempt to create an endoscopic analogue to vertical banded gastropasty, and did not incorporate the greater curvature (Figure 1B) [5]. These initial cases were performed using a suction-based superficial-thickness suturing device. More recently, the development and broad availability of full-thickness endoscopic suturing has made possible a more effective and durable procedure [6].

The objective of this longitudinal study was to develop an efficient technique for endoscopic sutured gastropasty using full-thickness endoscopic suturing, and to assess the safety and efficacy of this procedure.

Methods

This was a prospective first in man trial - focusing on procedure development, reproducibility, safety, and short term efficacy. The trial was initiated in April 2012 and represents the first use of the OverStitch endoscopic suturing system (Apollo Endosurgery, Austin TX, US) for primary obesity therapy.

This was an international multicenter trial performed at centers in India, Panama, the Dominican Republic, Spain, and the United States. The trial was performed in three phases. Each center obtained ethics review board approval to perform the procedure, clinical follow-up, and data collection, followed by a separate approval to submit data to a central registry. Key physicians were physically present at multiple sites to perform procedures, train clinical teams, and maintain the continuity of procedure development.

The procedure was performed in obese patients with body mass index $> 30 \text{ kg/m}^2$ who had failed attempts at diet and lifestyle modification. Patients were excluded if they had bleeding disorders, gastrointestinal disease, prior gastric surgery, active use of weight loss medication, eating disorders, or uncontrolled or severe psychiatric disease.

Certain procedure characteristics remained constant throughout the trial. A cephalosporin antibiotic was administered prior to the procedure. The patient was placed in a supine position. A wedge under the right side or table tilt were used to create a partial left lateral position. Procedures were performed with general anesthesia and endotracheal intubation. An esophageal overtube was placed to protect the pharynx and the esophagus and to ease endoscope exchanges. The endoscopic suturing system was attached to a double-channel endoscope (GIF-2T160; Olympus, Tokyo, Japan). Patients underwent gastropasty using the Apollo OverStitch and tissue helix (Apollo Endosurgery, Austin, TX). A tissue helix was, which has a corkscrew at the end of a catheter, was driven into the muscularis of the stomach and then retracted toward the device to ensure full-thickness tissue acquisition and to lessen the risk of injury to structures adjacent to the stomach (Helix, Apollo Endosurgery). Routine use of the helix was integrated into the technique over the course of the development process. Antiemetics and dexamethasone were administered prior to extubation. Patients were observed for at least two hours to administer analgesics, antiemetics, and intravenous hydration as needed.

Phase I: Development of a procedure to reduce gastric volume, and technical feasibility

Initial human cases were performed on five patients in India (CCT, RHH, MKG). The aim of this phase was to evaluate safety and technical feasibility of various procedure techniques. A variety of stitch patterns and sequences were studied and iteratively optimized with procedural efficiency in mind. Techniques were assessed, and the preferred method was analyzed and subsequently applied in 23 patients in Panama and the Dominican Republic. In this step, the aim was to determine the time efficiency and clinical outcomes of the refined

technique. During this step, the procedure continued to evolve to a lesser degree, with more subtle modifications.

Phase II: Technique refinement

The multicenter series included 22 patients at two centers in the Dominican Republic and the United States. Patients had nutritional and behavioral evaluation prior to the procedure, and dietary and lifestyle counseling postprocedure. Analysis was performed using prospectively collected registry data.

Phase III: Evaluation of technical feasibility and weight loss outcomes

Phase III included 77 patients in the Dominican Republic, Spain, and the United States. There was no procedure development during Phase III, and the procedure was performed using the standardized technique refined during Phases I and II. The focus was on technical feasibility, ability to adhere to the refined technique, and weight loss outcomes. The diet regimen after the procedure was liquids for two weeks, with a 70 gram daily goal for protein intake. This was followed by gradual introduction of soft food and then solid food over the next four weeks. The fluid intake goal was at least 48 ounces of liquid daily.

The registry was prospectively collected and maintained at Brigham & Women's Hospital. Statistics were performed using STATA 11 (StatCorp, College Station, TX). Means are reported with standard error.

Results

Phase I: Procedure development

The esophagus, stomach, and duodenum were examined with an upper endoscope. Two longitudinal dotted target lines were made from the antrum to the gastroesophageal junction using end-firing argon plasma coagulation at 30 Watts. The lines were made to the greater curvature side of both the anterior and posterior gastric walls. This was intended to guide stitch placement and to allow for intraprocedural re-orientation. Initial cases were started in retroflexion, reducing the fundus, and working distally towards the antrum. Suction was used to acquire tissue for the majority of stitches, however, the tissue helix was occasionally employed. Initial cases were performed using running stitches, with 6–12 tissue purchase sites, placed in a triangular fashion at the anterior wall, greater curvature, and posterior wall (Figure 2). The stitches were placed by acquiring tissue, rotating the endoscope and moving distally, and then acquiring the next stitch. Once 6–12 stitches were placed in this fashion, the suture was pulled to appose the tissue, and a cinch was placed to secure the plication. The abdomen was monitored for distension by palpation during the procedure. Chest X-rays did not reveal free air beneath the diaphragm. In the initial 5 cases, procedure time was 3.5 ± 0.5 hours. BMI decreased from 37.4 ± 1.9 kg/m² at the time of the procedure to 34.8 ± 1.5 kg/m² after 5 months. The following 23 patients (19 females) had mean age of 37.7 ± 1.9 y. A median of 8 running sutures, each with 6–12 tissue purchases, was used per procedure. Average procedure time was 120 min (range 95–240 min). Patients had mean BMI of 34.2 ± 1.1 kg/m² at the time of the procedure. Weight loss at 1 month was 8.0 ± 0.5 kg; weight loss at 6 months was 14.5 ± 2.2 kg and BMI had decreased to 28.9 kg/m²; weight loss at 1

year was 13.1 ± 1.3 kg and BMI had decreased to 29.4 kg/m^2 . There were no reported significant adverse events during the procedure or during the follow-up period.

Phase II: Technique refinement

Several technical points were learned from Phase I and applied during Phase II. It was felt that the APC target lines were felt to no longer be necessary because they tended to move with the procedure and were not in a consistent position. Due to endoscopic appearance and lack of free air under the diaphragm on imaging, it was felt that the sutures were not full thickness during Phase I. As such, the tissue helix was used to place all stitches in Phase II. In Phase I, working in retroflexion was felt to be cumbersome and time-consuming. In later cases, we reverted to a stitch pattern more consistent with that used in the TRIM trial (Figure 1D). Suturing from the antrum to the fundus was felt to be more efficient and resulted in shortening of the stomach with the fundus being pulled down, making tissue acquisition less arduous. In Phase II, all procedures were performed moving from antrum to fundus. In Phase I, it was felt that placing more than 6 stitches per suture increased tension and procedure complexity. Thus, in Phase II, a maximum of 6 stitches were allowed per running suture. The fundus was sutured to the lower esophageal sphincter. This phase included 22 patients (20 females) with mean age of 39.2 ± 1.6 y. A median of 9 running sutures, each with 6 tissue purchases, was used per procedure. Patients had mean BMI of $34.3 \pm 1.0 \text{ kg/m}^2$ at the time of the procedure. Weight loss at 6 months was 15.5 ± 1.2 kg, or $17.3 \pm 1.7\%$. In patients achieving 1-year follow-up ($n=20$), weight loss was 15.6 ± 2.4 kg, or $17.3 \pm 2.6\%$. The procedure was well tolerated, without intraoperative complications. After the procedure, nearly all patients were found to have air under the diaphragm on chest x-ray. This was not clinically consequential in any of the cases, and was attributed to the full-thickness nature of the suturing. Post-procedure nausea was routinely reported; transient epigastric pain and vomiting were frequently reported. Epigastric pain and nausea were frequently reported during the first post-procedure week. However, there were no reported significant adverse events post-procedure or during the follow-up period.

Further procedure refinement

In Phase II, due to the full-thickness nature of the suturing and the consistent presentation of free air under the diaphragm, the procedure was modified to use carbon dioxide insufflation. Additionally, during the early US experience (BKAD, CJG), we found that interrupted stitches were durable, yet time-consuming to place (Figure 1C). Therefore, reinforcing interrupted stitches were added just medial to the running suture lines in an effort to increase durability without excessive increase in procedure duration.

Phase III: Evaluation of technical feasibility and weight loss outcomes

Phase III included 77 patients (59 female) with mean age of 41.3 ± 1.1 y. At the time of ESG, mean weight was 99.4 ± 1.8 kg, and mean BMI was $36.1 \pm 0.6 \text{ kg/m}^2$. Mean weight loss was 16.4 ± 0.9 kg, or $16.0 \pm 0.8\%$, at 6 months. Of patients reaching 12-month follow-up ($n=44$), mean weight loss was 18.9 ± 1.5 kg, or $17.4 \pm 1.2\%$. In patients with a BMI below 35 kg/m^2 , mean weight loss was $15.2 \pm 1.9\%$; in patients with BMI of $35\text{--}40 \text{ kg/m}^2$, mean weight loss was $17.6 \pm 2.1\%$; in patients with BMI of 40 kg/m^2 , mean weight loss was $19.2 \pm 2.1 \text{ kg/m}^2$. Adherence to the final procedure technique was high: a sleeve was created

in all patients with limit to 6 tissue acquisitions per suture, and use of the tissue helix for each tissue acquisition (Figure 3). Longitudinal guidelines marked with APC were used in some cases, at the discretion of the endoscopist. No significant adverse events were reported during the procedures or during the follow-up period, although epigastric pain and nausea were frequently reported during the first week after the procedure. During the early months of the study, most patients were admitted to the hospital after the procedure for 24 hours. Patients generally resumed daily activities in 1–3 days. Overall weight loss results for Phase II and III are shown in Table 1.

Discussion

A number of endoscopic therapies are emerging to address obesity. These procedures, such as intragastric balloon placement and aspiration therapy, can be more effective than conservative methods such as diet and exercise, while being invasive than bariatric surgery.

This series details the development of ESG, including initial human cases with technique modification to a more efficient and reproducible procedure, followed by evaluation of technical feasibility, safety, and weight outcomes. The primary aims of the study were achieved. Following a methodical procedure development phase, ESG demonstrated safety and short-term efficacy in this trial. There were no significant adverse events and most patients were discharged the same day. Additionally, these multicenter results demonstrate meaningful weight loss during the follow-up period in the setting of dietary and lifestyle counseling. Most of the weight loss occurred during the first 6 months, and weight loss was largely maintained at 12 months. The procedure worked well across the BMI spectrum, with similar results in patients with BMI below 35 kg/m² (as low as 27 kg/m²), BMI 35–40 kg/m², and BMI over 40 kg/m² (up to 48 kg/m²). Long-term durability remains to be determined, and is being assessed in ongoing studies. ESG is of value for patients who desire greater efficacy and durability than available medical weight loss therapies can provide. The technique described here has subsequently gained broad acceptance [7–9].

The mechanisms by which ESG induces weight loss are not fully clear. Abu Dayyeh et al have suggested that impairment of gastric emptying and retention of food in the fundic pouch are important elements to the procedure's mechanisms of action, however more information is needed regarding neurohormonal changes both in the short term, and in the longer term after postprocedural weight loss occurs [7]. Additionally, the potential metabolic effects on comorbidities warrant further investigation. These effects would likely be derived from weight loss, in contrast with procedures that address the small intestine that may have a more direct metabolic effect.

Although ESG and the prior EVG have been compared to surgical sleeve gastrectomy, and are similar in name, the procedures differ in important ways. No significant post-procedure reflux was reported in this series, perhaps due to gaps in the lateral portion of the suture line, or incomplete closure of the fundus. Additionally, the procedure remodeled the gastric anatomy rather than altering its structure. This results in lower invasiveness, and may also allow reversibility. However, sleeve gastrectomy removes ghrelin-producing tissue, which is not performed with ESG. Thus, a better analogue is gastric imbrication.

The procedure was improved during Phase I and Phase II, and was found to be reproducible. Although it remains technically demanding and with relatively long procedure times, the device and the procedure continue to evolve. Experience in endoscopic suturing prior to performing ESG is advisable. Furthermore, it is important to perform this technique in the setting of a multidisciplinary weight management program [10]. Endoscopic sutured gastroplasty has the potential to help a large number of patients who have failed diet and lifestyle therapy, but are not sufficiently advanced to qualify for bariatric surgery.

There are limitations to this study. The series was performed across a number of centers by a number of providers, with various diet and follow-up regimens. However, this affirmed the broad applicability of the final technique. It also demonstrated the success of the procedure regardless of the specific type of diet regimen or follow-up schedule. Additionally, long-term follow-up was limited in this initial cohort of patients.

The OverStitch endoscopic suturing device has been approved for broad indications, and may be applied in a variety of ways, and used to perform a variety of stitch patterns. Although the final technique described in this manuscript is now performed at a number of centers, we feel that it is important to detail the procedure development process and earlier less optimal techniques, so that these are not repeated in practice, or as the procedure evolves. Nevertheless, we do anticipate that further device and procedure refinement will continue, with the goal of improving procedural efficiency.

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Figure 1.

(A) Endoluminal vertical gastroplasty (B) TRIM procedure (C) ESG with interrupted stitches (D) Final ESG technique

Figure 2.
Stitch pattern for sleeve formation

Figure 3.
Sleeve formation

Figure 4.
(A) Upper gastrointestinal series after ESG, and 3 months after ESG (B) Upper gastrointestinal series after ESG, and 10 months after ESG

Table 1

Overall weight loss, Phase II and III

	Weight change (kg)	Total weight loss (%)
6 months	-16.3 ± 0.8	16.2 ± 0.7
12 months	-17.9 ± 1.3	17.4 ± 1.1