StomaphyX vs a Sham Procedure for Revisional Surgery to Reduce Regained Weight in Roux-en-Y Gastric Bypass Patients: A Randomized Clinical Trial

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IMPORTANCE Revisional laparoscopic surgery after Roux-en-Y gastric bypass (RYGB) has been linked to substantial complications and morbidity.

OBJECTIVE To investigate the safety and effectiveness of endoscopic gastric plication with the StomaphyX device vs a sham procedure for revisional surgery in RYGB patients to reduce regained weight.

DESIGN, SETTING, AND PARTICIPANTS A prospective, single-center, randomized, single-blinded study from July 2009 through February 2011, evaluating revisional surgery using StomaphyX was conducted in patients with initial weight loss after RYGB performed at least 2 years earlier. We planned for 120 patients to be randomized 2:1 to multiple full-thickness plications within the gastric pouch and stoma using the StomaphyX device with SerosFuse fasteners or a sham endoscopic procedure and followed up for 1 year. The primary efficacy end point was reduction in pre-RYGB excess weight by 15% or more excess body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) loss and BMI less than 35 at 12 months after the procedure. Adverse events were recorded.

RESULTS Enrollment was closed prematurely because preliminary results indicated failure to achieve the primary efficacy end point in at least 50% of StomaphyX-treated patients. One-year follow-up was completed by 45 patients treated with StomaphyX and 29 patients in the sham treatment group. Primary efficacy outcome was achieved by 22.2% (10) with StomaphyX vs 3.4% (1) with the sham procedure (P < .01). Patients undergoing StomaphyX treatment experienced significantly greater reduction in weight and BMI at 3, 6, and 12 months (P < .05). There was one causally related adverse event with StomaphyX, that required laparoscopic exploration and repair.

CONCLUSIONS AND RELEVANCE StomaphyX treatment failed to achieve the primary efficacy target and resulted in early termination of the study.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00939055
Roux-en-Y gastric bypass (RYGB) is the most commonly performed bariatric procedure to treat morbid obesity, with weight loss efficacy demonstrated in randomized clinical trials. On average, excess weight loss (EWL) after RYGB is approximately 60% to 70%. Durable weight loss with RYGB, however, is generally considered to be only moderate, although a recent meta-regression study found good durability in mean EWL during a mean follow-up of 3.6 years using pooled data. Studies that followed up patients for 5 to 10 years after RYGB have reported outcome failure due to significant weight regain in 20% to 50% of patients.

Revisinal laparoscopic surgery after RYGB has been linked to substantial complications and morbidity. A minimally invasive technique for revision after RYGB has been tested using the transoral StomaphyX device (EndoGastricSolutions). Gastric plication using StomaphyX has been found to be safe and result in subsequent weight loss in several open-label series with patients who regained weight after previous treatment with RYGB. Thoracic empyema was reported in a single patient after the StomaphyX procedure after previous RYGB.

To our knowledge the current study is the first randomized, controlled, clinical trial to evaluate efficacy and safety of endoscopic gastric plication using the StomaphyX device in adults with weight regain after RYGB. This study was designed to test the hypothesis that at least half of patients treated with gastric plication using the StomaphyX procedure would achieve a clinically significant weight reduction compared with a sham procedure.

Methods

This randomized, single-blinded, sham-controlled trial evaluated StomaphyX for revisional surgery in post-RYGB patients requiring additional intervention due to regained weight. The study was conducted from July 2009 through February 2011 at 2 tertiary university centers in the United States (clinicaltrials.gov Identifier NCT00939055). The study was approved by Western Institutional Review Board and conducted in accordance with guidelines of the International Conference on Harmonization for Good Clinical Practice. Before enrollment, all participants provided written informed consent. This report provides data from 1 of the 2 enrolling centers because data from the other center were not available for inclusion in this report.

Study Participants

Study candidates were recruited from established patients at a university bariatric program where this study was conducted. Eligible participants were adults 18 to 65 years old who had previously undergone RYGB at least 2 years before enrollment. Candidates were required to have achieved an initial weight loss after RYGB of 60% or more of excess body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) and a BMI of 35 or less followed by regaining 20% or more of the pre-RYGB excess weight. The percentage of excess BMI loss (EBL) was calculated as (pre-RYGB BMI - current BMI)/(pre-RYGB BMI - 25). At the time of the study, participants were required to have a BMI of 35 to 40 (class II and III obesity) and report stable weight or a continued failure to lose weight for at least 3 months before enrollment. A baseline BMI of 35 to 40 is similar to previously identified mean BMI in other studies (eg, BMI of 33-40). A recent systematic review of endoluminal revision for gastric bypass (including StomaphyX) concluded that more studies are needed to help identify appropriate treatment populations by standardizing criteria for identifying failure. Use of the limited BMI range in the current study will help to refine whether patients are appropriate for revisional surgery when they are in class II and III obesity categories. Inclusion criteria also required demonstration of an enlarged gastric pouch (>30 mL) and/or stoma (>15 mm) based on esophagogastroduodenoscopy (EGD), barium radiography, or the patient’s self-reported ability to eat more than 1 cup of solid food at a meal. Participants were also required to have normal levels of vitamin D, iron or ferritin, calcium, and magnesium within 1 year before screening and a serum albumin level of 3 g/dL or higher (to convert to grams per liter, multiply by 10).

Study candidates were excluded if they previously underwent revisional bariatric surgery after RYGB, had an esophageal stricture or other anatomical condition that precluded passing the StomaphyX into the gastric pouch, or had causal factors for weight regain other than pouch and/or stoma enlargement. Patients were also excluded if they had an eating disorder, type 1 diabetes mellitus, inflammatory bowel disease, gastrojejunostomy anastomosis ulceration, portal hypertension, a coagulation disorder or long-term use of anticoagulants, active substance abuse, serious peri- and post-RYGB complications (eg, leaks, fistula, incisional hernia, ulcers, pulmonary embolism, or deep venous thrombosis), a life expectancy of less than 1 year, or an American Society of Anesthesiologists classification greater than 3 (representing severe systemic disease). Patients were excluded if they were using immunosuppressant drugs, planned to discontinue smoking during the next 12 months, used weight loss prescription drug therapy within 3 months before the screening, or intended to start weight loss therapy. Women were excluded if they were pregnant or were planning conception in the next 12 months.

Intervention

Patients were randomized to StomaphyX or sham procedure using 2:1 randomization, stratified by the treating surgeon, using dynamic balancing techniques. Treatment assignment was generated by an electronic data capture system. All patients underwent EGD while under general anesthesia. During the endoscopy, anatomical landmarks of the pouch were identified. For patients randomized to treatment with the StomaphyX, multiple full-thickness plications within the gastric pouch and/or stoma were created using the StomaphyX device with SerosFuse fasteners (EndoGastricSolutions). The endoscope was inserted through the StomaphyX shaft and introduced through the patient’s mouth into the pouch under continuous visualization. Intrapouch device position was main-
Assessments

Body weight and height were recorded at baseline to calculate BMI. Additional baseline assessments included medical and nutritional history and quality of life using the Impact of Weight on Quality of Life–Lite Questionnaire (IWQOL-Lite)\(^1\) and the Three-Factor Eating Questionnaire.\(^2\) Both EGD and barium radiography were used to assess the anatomy and geometry of the gastric pouch and gastrojejunal anastomosis.\(^3\)

A pouch was considered to be enlarged when the volume was 30 mL or more, using the following equation: volume = \(3.14 \times (0.5 \text{ width})^2 \times \text{length}\). An anastomosis was considered to be dilated when the diameter was 1.5 cm or larger. Pouch size was verified on barium radiograph plates.\(^4\)

Follow-up assessments for weight, EBL, and IWQOL were conducted with in-office assessments at months 1, 3, 6, 9, and 12. Adverse events (AEs) were recorded at each visit and during telephone call assessments at months 2, 4, 5, 7, 8, 10, and 11.

The primary efficacy end point was achieving EBL reduction from pre- to post-StomaphyX of 15% or greater and BMI of 35 or less at 12 months after the procedure. The weight criterion is based on the Reinhold classification for a good or excellent result after gastric bypass\(^5\) and has been used in previously published gastric bypass trials.\(^6,7\) The secondary efficacy end point was clinically significant quality-of-life improvement defined as an improvement in IWQOL-Lite total score from baseline to 12 months of 10 or greater.\(^8\)

Statistical Analysis

Sample size was determined using a power analysis based on retrospective EBL data at 4 (n = 38) and 13 months (n = 20) after StomaphyX (Endogastric Solutions, 2007 through 2008). On the basis of these data, the proportion of patients with EBL of 15% or greater and a BMI less than 35 at 12 months was expected to be at least 55% (25) with StomaphyX and 15% (5) with sham intervention. A total of 135 patients (90 in the StomaphyX group and 45 in the sham group) would be needed to provide the power to detect a statistically significant difference at a 2-sided .02 level by the Fisher exact test of approximately 0.997. Assuming a 10% dropout rate, the planned population for this study was 150 participants, with approximately 120 participants planned at the center described in the current report and approximately 30 participants at the other enrolling center.

Throughout the analysis, categorical variables are summarized by frequencies, continuous variables with normal distributions as mean (SD), and continuous variables with nonnormal distributions as median (interquartile ranges [IQR]). Demographics and outcomes were evaluated using descriptive statistics. Baseline and 12-month between-treatment differences were assessed using independent sample t tests, Wilcoxon-Mann-Whitney tests, \(\chi^2\) tests, and Fisher exact tests, as applicable, with significance set at \(P < .05\).

Results

Enrollment was closed prematurely in June 2011 because of preliminary data analysis that indicated failure to achieve the primary end point of clinically meaningful weight loss in at least 50% of patients after treatment with StomaphyX. Follow-up was modified for patients currently enrolled in the study at that time to include assessment of 12-month weight and the occurrence of AEs only.
At the time of study closure, 90 patients had been randomized, with the 12-month assessments completed by 74 patients (Figure 1). Demographic features for patients initiating intervention were generally similar (Table 1). Most patients were white (n = 83) (91.9%), with no between-treatment differences in race. No significant differences were found in prevalence of common comorbid conditions between patients assigned to StomaphyX and sham interventions, respectively: hypertension (41.8% and 35.5%), depression (37.0% and 41.9%), gastroesophageal reflux disease (22.2% and 38.7%), hypercholesterolemia (16.7% and 12.9%), sleep apnea (10.9% and 20.0%), asthma (10.9% and 12.9%), type 2 diabetes (10.9% and 6.7%), and hypertriglyceridemia (11.1% and 3.2%). Median procedure length was 40.8 (IQR, 34.1-50.4) minutes with the StomaphyX and 30 (IQR, 29.8-31.2) minutes with the sham procedures.

**Efficacy**

The primary efficacy end point (pre- to post-StomaphyX decrease of ≥15% EBL and BMI <35) was achieved at month 12 by 10 of 45 patients (22.2%) after the StomaphyX and 1 of 29 patients (3.4%) after the sham procedures (P < .01).

At the 12-month assessment, the mean (SD) BMI was 34.9 (3.5) with the StomaphyX and 36.8 (2.9) with the sham procedures. Mean (SD) EBL was 7.8% (10.7%) and 2.0% (8.5%) in the StomaphyX and sham groups, respectively. Significant between-group differences were noted for

**Table 1. Baseline Characteristics of the Study Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>StomaphyX (n = 55)</th>
<th>Sham (n = 31)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), y</td>
<td>51 (43-56)</td>
<td>50 (43-55)</td>
<td>.67</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>54 (98.2)</td>
<td>29 (93.6)</td>
<td>.29</td>
</tr>
<tr>
<td>Time since RYGB, median (IQR), y</td>
<td>6.4 (5.0-7.5)</td>
<td>7.2 (6.4-9.0)</td>
<td>.01</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At time of RYGB, mean (SD)</td>
<td>47.1 (4.6)</td>
<td>47.2 (3.8)</td>
<td>.91</td>
</tr>
<tr>
<td>Nadir BMI, mean (SD)</td>
<td>29.2 (2.9)</td>
<td>29.5 (2.4)</td>
<td>.60</td>
</tr>
<tr>
<td>Baseline BMI median (IQR)</td>
<td>36.6 (35.0-38.3)</td>
<td>36.5 (35.4-39.2)</td>
<td>.31</td>
</tr>
<tr>
<td>Baseline weight, mean (SD), kg</td>
<td>96.8 (11.0)</td>
<td>98.2 (8.7)</td>
<td>.54</td>
</tr>
<tr>
<td><strong>Anatomy, median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anastomosis diameter, mm</td>
<td>25.0 (20.0-30.0)</td>
<td>20.0 (20.0-30.0)</td>
<td>.40</td>
</tr>
<tr>
<td>Pouch length, cm</td>
<td>4.0 (3.0-5.0)</td>
<td>4.0 (3.0-5.0)</td>
<td>.75</td>
</tr>
<tr>
<td>Pouch width, cm</td>
<td>6.0 (5.0-8.0)</td>
<td>5.5 (4.5-8.0)</td>
<td>.00</td>
</tr>
<tr>
<td>Pouch volume, mL</td>
<td>98.1 (62.8-150.7)</td>
<td>98.1 (58.9-150.7)</td>
<td>.98</td>
</tr>
<tr>
<td><strong>IWQOL-Lite score, mean (SD)</strong></td>
<td>62.8 (19.5)</td>
<td>60.7 (48.4-75.0)</td>
<td>.63</td>
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<td><strong>TFEQ scores</strong></td>
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<td></td>
<td></td>
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<td>Cognitive restraint, median (IQR)</td>
<td>50 (38.9-61.1)</td>
<td>50 (38.9-61.1)</td>
<td>.57</td>
</tr>
<tr>
<td>Uncontrolled eating, mean (SD)</td>
<td>39.6 (18.4)</td>
<td>37.5 (19.2)</td>
<td>.61</td>
</tr>
<tr>
<td>Emotional eating, median (IQR)</td>
<td>55.6 (44.4-77.8)</td>
<td>55.6 (44.4-66.7)</td>
<td>.28</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range; IWQOL, Impact of Weight on Quality of Life–Lite Questionnaire; RYGB, Roux-en-Y gastric bypass; TFEQ, Three-Factor Eating Questionnaire.
weight change and EBL at months 3, 6, and 12 (Figure 3 and Figure 4). None of the within-group changes in weight, BMI, or EBL from baseline to end point in the sham group were significant.

The IWQOL-Lite data were available for 52 of 74 patients (31 in the StomaphyX group and 21 in the sham group) at 12 months, with a median change of 14.5 (IQR, 4.8-23.4) with the StomaphyX and 5.6 (IQR, −1.2 to 17.3) with the sham procedures. Clinically meaningful quality-of-life improvement (IQWOL-Lite change ≥10) was achieved by 58.1% of StomaphyX-treated patients and 40.0% of patients in the sham treatment group (P = .01).

**Adverse Events**

Most AEs were mild or moderate in severity (Table 2). Few AEs were considered to be causally related to the study device or intervention. The one AE considered to be causally related to the StomaphyX procedure was a serious gastric perforation that required laparoscopic exploration and repair, followed by full recovery.

**Discussion**

To our knowledge, this is the first randomized controlled trial to evaluate outcome of endoscopic gastric plication using the StomaphyX device in adults with weight regain after RYGB. On the basis of retrospective data, we anticipated that 50% or more of the patients would achieve a clinically significant reduction in regained weight (≥15% EBL and BMI <35) after StomaphyX; however, this was achieved by 22.2% after StomaphyX vs 3.4% after a sham procedure. Among patients regaining weight after RYGB, StomaphyX did not result in satisfactory weight reduction. These data parallel a recent retrospective report of 53
patients undergoing StomaphyX plication (mean baseline BMI, 36.1), with a mean 6-month weight loss of 3.6 kg. A single patient in the current study experienced a StomaphyX procedure-related serious complication that required additional intervention (laparoscopic procedure to repair a gastric leak). A previously published retrospective report of similar size revealed no major complications with the StomaphyX procedure. Testing in larger samples is necessary to confirm safety.

Data from the current study support results from research evaluating endoscopic gastric plication for revision after RYGB using the revision obesity surgery endoscopic (ROSE) procedure to reduce gastric pouch and/or stoma size. A small study of the ROSE procedure in 5 patients demonstrated a mean weight loss after 3 months of 7.8 kg, with no major complications. A larger series of 20 patients undergoing the ROSE procedure reported technical success in 17 patients, with a mean 3-month weight loss of 8.8 kg among those having a successful procedure. Long-term data for 116 patients treated with the ROSE procedure revealed a mean weight loss of 6.5 kg at 6 months and 5.9 kg at 12 months. In the current study, weight loss was slightly less, with a similar decrease in achieved weight reduction during 1-year follow-up. The technique in the current study focused on pouch rather than stoma reduction, which may be an important factor that affects weight loss after revisional surgery. A previous study using the ROSE procedure, for example, achieved a 65% reduction in stoma diameter, a 36% reduction in pouch length, and a resultant mean weight decrease of 8.6 kg at 3 months. In addition, restricting baseline BMI to 40 or less may have limited weight loss because a previous study (mean baseline BMI, 50) found that greater weight regain after RYGB was a predictor of more favorable outcome after endoscopic sclerotherapy. Other reasons for reduction in weight loss over time are likely to be multifactorial and were not evaluated in the current study. Future studies that investigate StomaphyX for revision plication should include a broader patient sample (eg, including patients with higher BMI) and include measurements of stoma size reduction determination as a procedure success in addition to pouch size reduction. Future studies may also want to evaluate larger patient samples to identify patients more likely to benefit from the StomaphyX procedure and investigate the role of postprocedural interventions (eg, ongoing behavioral support) to assist in both initial and maintained weight loss.

Interpreting data from the current study is limited by several factors. First, early study termination resulted in a smaller than planned treated patient group. In addition, dropouts were substantial in the active treatment group, with 12-month data unavailable for 18% of patients (8) treated with StomaphyX. Early study termination also limited the type of data obtained from participants, with only 24-month weight and AE data collected for patients in follow-up after the date of enrollment termination. Attrition during long-term follow-up after weight loss surgery has been variable among other studies, with attrition after the StomaphyX procedure reported at 33% to 81% for 6 months and 85% at 1 year. Although one study using a Veterans Affairs hospital population reported that only 5% of patients undergoing bariatric surgery were lost to follow-up after 1 year, another sample of patients undergoing laparoscopic adjustable gastric banding reported that 45% of patients were lost to follow-up during their 3- to 7-year follow-up. A meta-analysis of laparoscopic banding and bypass operations for obesity reported high attrition at 2 years (50%-75%) and greater than 3 years (83%-89%) of follow-up. A recent French study prospectively evaluating gastric banding and not included in the previous meta-analysis reported only 14% of patients were lost to follow-up. This latter study used a target for attrition of less than 20%, which was achieved in the current sample. One study that investigated predictors of high attrition after bariatric surgery identified young age as a factor linked with higher attrition, without additional factors identified. The current study was not designed to identify potential factors linked with attrition. Furthermore, although attempts were made to ensure approximation of pouch size, good tools are not available to estimate pouch size objectively, which limits the reproducibility of results. Finally, this study did not monitor for potential clinical benefits associated with small amounts of weight reduction, which may be relevant because regaining weight after initially successful RYGB has been linked to reemergence of important comorbid conditions, such as type 2 diabetes.

The greater early weight reduction that decreased during the ensuing months in both the ROSE trial and our study raises the possibility that lack of durability of endoscopic sutures may contribute to weight regain. It is possible that the full-thickness plications created during the procedure may not have been reliable or durable, reducing long-term weight loss. This was not evaluated in the current study. Future studies may want to include follow-up evaluations with endoscopy to verify maintenance of pouch or stoma reduction and explore the benefits of using more durable suturing mechanisms. Preliminary evidence of follow-up endoscopy after the ROSE procedure, however, revealed good durability of anchors and tissue fold for up to 12 months after revision, with superior weight loss linked to stoma reduction. Future work may also be needed to identify whether weight reduction maintenance is differentially affected when these interventions focus on reducing pouch vs stoma size. Additional interventions that may also improve weight loss maintenance might include routine regular follow-up to address behavioral issues and dietary and lifestyle modifications important for weight reduction maintenance. Finally, future work may wish to explore the benefits of addressing the gastric outlet as a potential cause for the loss of restriction in gastric bypass patients.

Conclusions

One year after gastric plication using the StomaphyX procedure for regained weight after RYGB, clinically meaningful weight reduction was not achieved by at least half of treated patients.
after short- and long-limb gastric bypass in patients: a meta-regression study.


