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One-year human experience with a novel endoluminal, endoscopic gastric bypass sleeve for morbid obesity

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Abstract

Introduction Here, we report the first series of patients with 1-year implantation of a novel, endoluminal, endoscopically delivered and retrieved gastro-duodeno-jejunal bypass sleeve (GJBS) (ValenTx, Inc. Carpinteria, CA, USA). In this report, we present the safety, feasibility of the device, weight loss, and changes in comorbidities.

Methods and procedures A prospective, single-center, 12-month trial was designed. The patients are morbidly obese individuals who meet the NIH criteria for bariatric surgery. The GJBS is a 120-cm sleeve secured at the esophago-gastric junction with endoscopic and laparoscopic techniques that is designed to create an endoluminal gastro-duodeno-jejunal bypass. The device was implanted and, at the completion of the trial, retrieved with an endoscopic technique. The primary endpoints were safety and incidence of adverse events. The secondary outcomes included the percentage of excess weight loss (EWL) and changes in comorbidities, specifically glucose control, use of antihyperglycemics, and changes in hemoglobin A1C levels.

Results From July 2009 until October 2009, 13 patients were prospectively enrolled for the 1-year trial. The study included five men and eight women with a mean preoperative BMI of 42 kg/m^2. One patient was excluded, at the time of endoscopic evaluation, due to inflammation at the GE junction. Two additional patients required early explantation of the device, within the first 4 weeks, due to patient intolerance. Upon explant of the device, both patients' symptoms improved. In the remaining ten patients, the device was implanted, left in situ for 12 months, and then retrieved endoscopically. Safe delivery of the cuff at the gastro-esophageal junction was seen in all ten patients whom had device implants, without complication. No esophageal leak was seen immediately post-procedure or during follow-up. The sleeve device was well tolerated within the bowel lumen during the 12-month study, specifically, no bowel erosions, ulceration, or pancreatitis was observed. All ten patients reached the 1-year mark. Of the ten, six had fully attached and functional devices throughout the follow-up, verified by endoscopy. The mean percentage EWL, at 1 year, in this group was 54 %. In the remaining four patients, partial cuff detachment was observed at follow-up endoscopy. The percentage EWL was lower in this group. Of the six patients that reached a year with a fully attached device, five were followed at an average of 14-months post-explant (26 months from the time of device implant). These five maintained an average percentage EWL of 30 % at the 14-month post-explant follow-up. Co-morbidites measured included diabetes mellitus, hypertension, hyperlipidemia, and use of antihyperglycemics. Each of the measured comorbidities showed improvement during the 12-month trial.

Discussion The endoluminal, GJBS can be safely placed and retrieved. The short-term data show it is well tolerated with a good safety profile. It achieves excellent weight loss results with over 70 % of all comorbidities resolved or significantly improved.

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Morbid obesity represents a major healthcare problem in the US and worldwide and has significant impact across several different fields within medicine. Up to a third of the US population is considered obese [1]. The burden of this disease on health care is substantial, both from an economic standpoint, as well as through the impact of obesity on other disease processes such as diabetes, cardiovascular disease, increased cancer risks, and many other manifestations of this disease process [2]. Medical and behavior treatments for obesity have limited success, with only modest long-term weight loss results [3]. Surgical intervention has proven to be successful, but has moderate risks and associated morbidity [4].

In attempts to lower the morbidities of bariatric surgery, alternative treatment options, including the use of an endoscopic approach have been developed to improve bariatric surgical outcomes [5–9]. We have previously demonstrated the safety and efficacy of a novel, endoluminal gastro-duodeno-jejunal bypass sleeve (ValenTx, Inc. Carpinteria, CA, USA) and the short-term weight loss results seen with this device [10]. This study was designed to demonstrate the experience with this endoluminal device over a 12-month period following implantation.

Methods

Study design

An IRB-approved, prospective, single-center trial was designed. Patients were enrolled who met the 1991 National Institute of Health guidelines for bariatric surgery, a BMI over 40 kg/m^2 or over 35 kg/m^2 with comorbidities. Further inclusion criteria included age between 18 and 55, a documented failure with non-surgical weight loss methods, a willingness and ability to comply with study procedures and visit schedule, and ability to provide informed consent. Exclusion criteria included pregnancy, abnormal endoscopic findings, such as hiatal hernia, gastric or duodenal ulceration or polyps, GI bleeding, a past history of esophageal or gastric surgery, current steroid use, or other immune-suppressive disease history. The primary endpoints were the safety of the device, including the incidence of any adverse event. The secondary outcomes included the percentage of excess weight loss and changes in comorbidities seen during the trial. Comorbidities monitored included diabetes mellitus type 2, hypertension, and hypercholesterolemia/elevated triglyceride levels. Diabetes mellitus improvements included changes in hemoglobin A1C and fasting glucose levels as well as evaluation of dosage and frequency of antihyperglycemic medications. Hypertension was considered improved if the systolic and/or diastolic pressures had improved or the patient had been able to decrease or eliminate the need for antihypertensive medications. Hypercholesterolemia and elevated triglyceride levels were considered improved if the patient had improvement in fasting laboratory values or experienced a decrease in preexisting medication dose.

All patients provided written, informed consent according to an approved protocol from our institutional review board. All patients had undergone a screening history and physical examination, screening barium upper GI swallow study, and baseline laboratory evaluation. During the trial, data were recorded according to approved study forms. This study was registered with clinicaltrials.gov number NCT01207830.

Technique

The technique used has been described previously [10]. Briefly, after obtaining consent, the patients were placed under general anesthesia in a supine position on the operating room table. The procedure began with placement of a long overtube, extending through the pylorus, into the duodenal bulb. Through this the gastro-duodeno-jejunal bypass sleeve (GJBS) was delivered via a delivery catheter to the level of the first portion of the duodenum.

The sleeve, which is a 120-cm long fluoro-polymer, with an attached polyester cuff on the proximal end, is deployed down through the pylorus using toposcopic delivery technique, utilizing computer regulated pressure and flow monitoring. Fluoroscopic guidance is also utilized to ensure adequate deployment of the sleeve through the duodenum, into the proximal jejunum. Once the sleeve is adequately deployed downstream into the bowel, the delivery catheter is removed, and the overtube is exchanged for a shorter overtube, in preparation for the proximal cuff attachment.

The patient is then repositioned in a supine, lithotomy position, and the abdomen is prepped and draped in standard surgical fashion in preparation for the laparoscopic portion of the procedure. After placement of one 12 mm and three 5 mm trocars, along with a Nathanson liver retractor, the gastroesophageal junction is dissected circumferentially at the level of the diaphragmatic hiatus using ultrasonic dissection and a Penrose drain placed to assist with further gastro-esophageal junction manipulation.

The polyester cuff is then positioned endoscopically at the GE junction. The positioning is completed with the assistance of a removable stent helping to visualize the esophageal lumen at the GE junction. The attachment is performed with eight endoscopically delivered, nitinol

suture anchors, deployed circumferentially, with the assistance of laparoscopic visualization to ensure transmural anchor placement and to avoid any visceral injury. Once the cuff has been anchored, the stent is detached endoluminally and removed, through the overtube, via a drawstring at its proximal end.

Following cuff attachment, the left and right diaphragmatic crura are laparoscopically approximated with suture closure. The Penrose and all trocars are removed, the incisions closed appropriately, and the patient is awoken from anesthesia.

Postoperatively, the patient is monitored in the hospital for 1 day post-procedurally. A gastrograffin swallow study is performed on post-procedure day one to evaluate sleeve and cuff position. Once this is completed, the post-procedure diet is initiated. This consists of a full liquid diet for the first 2 weeks, followed by pureed diet for 2 weeks, and then progressed to regular food, without caloric restriction. The patient is followed with regular appointments and scheduled laboratory evaluation to monitor for anemia, routine chemistries, liver function panels, pancreatic enzyme levels, and strict blood glucose monitoring.

Following completion of the study period, the device removal is performed endoscopically, using standard sedation protocols. This is completed through endoscopic ligation of the eight anchoring sutures. The cuff is then gently mobilized via use of an endoscopic grasper and, after ensuring circumferential detachment, gently slid out of the esophagus along with the attached sleeve. The patients are briefly observed in recovery and discharged.

Results

From July 2009 until October 2009, 13 patients were prospectively enrolled for the 1-year trial. The study included five men and eight women with a mean preoperative BMI of 42 kg/m^2. The mean starting weight was 111.7 kg (range 80.4–144.8 kg), with an average age of 39 years. Ten of the patients (83 %) presented with at least one comorbid condition, four presented with diabetes mellitus (33 %), seven with hypertension (58 %), one with hypercholesterolemia (8 %), and five with hypertriglyceridemia (42 %).

Twelve of the 13 patients underwent successful device implantation during the trial (92 %). One patient was excluded, at the time of endoscopic evaluation, due to significant inflammation at the GE junction. Two of the implanted patients required early explantation of the device (17 %), within the first 2 weeks, due to patient intolerance. Intolerance was due to dysphagia in one patient and due to odynophagia with associated gastritis in the second patient. The explantations were necessary on post-procedural day #13 and #5, respectively, for these patients. Upon endoscopic explantation of the device, both patients' symptoms improved. In the remaining ten patients, the device was implanted, left in situ for 12 months, and then retrieved endoscopically.

Safe implantation of the cuff at the gastro-esophageal junction and delivery of the sleeve was seen in all ten patients whom had device implants, without complication. The mean total implantation time was 1.53 h. All implanted patients had a 2-day hospital stay following the procedure. No esophageal leak was seen immediately post-procedure on the gastrograffin swallow study or during follow-up. The sleeve device was well tolerated within the bowel lumen during the 12-month study, specifically, no bowel erosions, ulceration, bowel obstruction, or pancreatitis were observed.

All ten patients reached 12-month follow-up and had data collected. For these ten patients, the mean percentage excess weight loss was 35.9 %. Of the ten, six had attached and functional devices throughout the follow-up period, as verified on follow-up endoscopy. The mean percentage EWL, at 1 year, in this group was 54 %, as seen in Fig. 1.

The weight loss, when compared with preprocedural, baseline weight was statistically significant for all ten patients in the trial beginning at 1-week post-procedurally. This data can be seen in Table 1 below.

Endoscopic device removal was completed in each patient at the 12-month mark, as planned. There were no complications associated with explantation of the device. Endoscopic retrieval was accomplished with the use of an endoscopic grasper, after ligation of the anchor sutures. No laparoscopic assistance was necessary during this procedure. No cuff ingrowth or adherence was noted at the GE junction, and no adhesions were noted between the sleeve and mucosa in the stomach or small bowel. No significant bleeding, erosion, or esophageal leakage was experienced at the time of explantation. Upon endoscopic inspection, the mucosa appeared healthy and normal.

Comorbidities measured during the trial included diabetes mellitus, hypertension, hyperlipidemia, and use of antihyperglycemics. Four patients had diabetes mellitus (DM) at the time of trial enrollment (33 %), seven enrolled with hypertension (58 %), one with hypercholesterolemia (8 %), and five with hypertriglyceridemia (42 %). At 12 months, the mean improvement in fasting glucose was 28 %. For the four patients with preexisting DM, all had improvements in the fasting blood glucose values with a mean improvement of 38 %, and three of the four patients had over a percentage point drop in their hemoglobin A1C value. The fourth patient with DM had improvement and was off diabetes medication. Of the seven patients with hypertension, five of the seven patients (71 %) had blood pressure values within the normal range and were off all

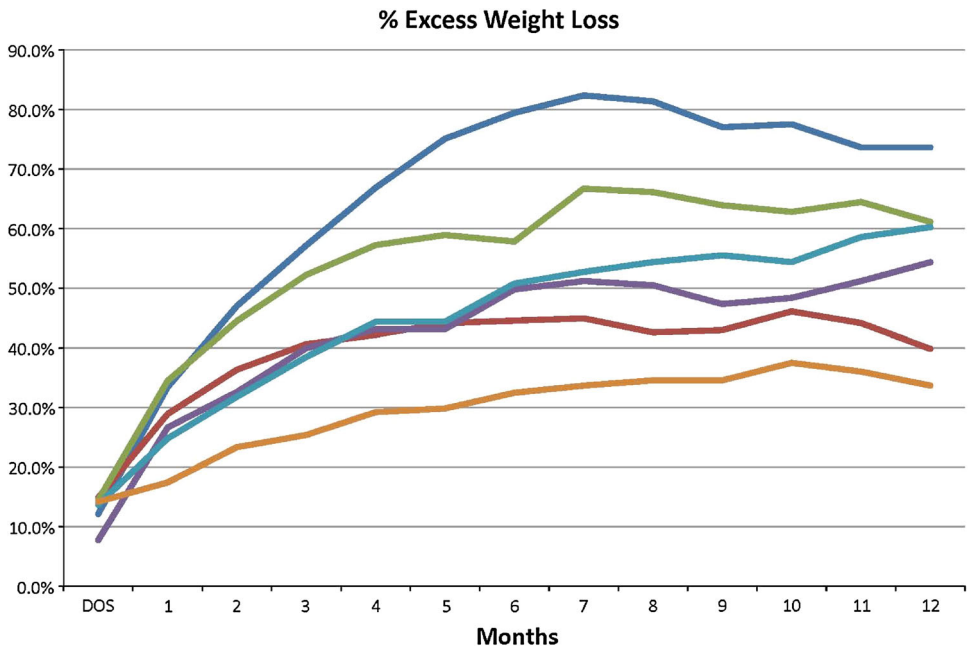

Fig. 1 Weight loss for the 6 patients with fully-attached sleeves throughout the 12 month trial

Table 1 Average monthly weight and EWL of all 10 patients who completed the 12 month trial

Total weight	Weight (kg)	Weight loss (kg)	*p* value
Baseline	111.70	0.00	
1 Wk Post Op	106.13	−5.57	<0.0001
2 Wk Post Op	104.54	−7.16	<0.0001
3 Wk Post Op	102.80	−8.90	<0.0001
1 M Post Op	101.96	−9.74	<0.0001
2 M Post Op	98.98	−12.72	<0.0001
3 M Post Op	97.02	−14.68	<0.0001
4 M Post Op	95.48	−16.22	<0.0001
5 M Post Op	95.26	−16.44	<0.0001
6 M Post Op	94.26	−17.44	<0.0001
7 M Post Op	94.14	−17.56	<0.001
8 M Post Op	94.24	−17.46	<0.001
9 M Post Op	95.28	−16.42	<0.001
10 M Post Op	95.40	−16.30	<0.001
11 M Post Op	95.54	−16.16	<0.001
12 M Post Op	96.84	−14.86	0.0029

antihypertensive medication. The other two had significant improvement in hypertension but were still on medication. The mean change in blood pressure for all ten patients was a 15 % decrease. The one patient with hypercholesterolemia had complete resolution of this comorbid condition at 12 months and was off all medication for this medical problem. Lastly, of the five patients with hypertriglyceridemia, four patients (80 %) had measurements within the normal range and were off all medication for the condition. The overall change for the ten patients was a 26 % decrease in triglyceride levels.

Safety monitoring during the trial consisted of routine clinical evaluation, on a weekly basis during the early trial period and then on a monthly basis after the first month. Routine examination, including vital sign check and lab work, including CBC, electrolytes, and chemistries were completed on all patients and were within normal range throughout the follow-up period.

Following explant of the device, the six patients who had fully attached anchors at explant were contacted for a follow-up at 14 months following the device explant. Five of the six returned for the follow-up and were evaluated for weight, adverse events, and survey information. The five patients had maintained a mean EWL of 30 % compared to 52 % for the same group of five at the time of device explant. Upon survey, all of the patients indicated they would have the procedure again. There were no post-explant adverse events seen.

Discussion

Morbid obesity remains a major health concern throughout the world with many serious long-term health concerns. Conservative treatments, via medication administration or via lifestyle intervention yield limited success and require extensive effort, from both the patient and the healthcare provider, to maintain success over the long-term [11]. Surgical options typically have improved weight loss success, when compared with non-surgical treatments, but

these approaches have an associated morbidity viewed by some as prohibitive. The long-term sequelae can also be substantial, when these procedures are considered early in adult life, or in some severe cases, even as adolescents [12]. As standard bariatric procedures involve moderate GI tract manipulation, via a surgical approach, many potential patients view this as a prohibitive feature, preventing a more widespread application. Natural orifice surgery and endoluminal approaches to common disease processes have the potential to create an alternative means of accomplishing similar end results, traditionally seen with surgical approaches, but without the complications seen with surgery. These novel approaches may help generate a wider acceptance of treatment of morbid obesity and thus help limit the disease prevalence.

This study of an endoluminal device to treat morbid obesity, and the mid-term follow-up data seen in this 1-year trial shows that this device is safe and effective when used to treat morbid obesity. The device is designed to mimic the therapeutic mechanisms of a Roux-en-Y gastric bypass surgery, but with a less invasive, endoscopically placed, implantable, and removable device. Like the bypass procedure, considered by many to be the gold-standard surgical treatment for morbid obesity in the US, the endoluminal sleeve provides a restriction of food intake, exclusion of the stomach and proximal bowel, and a presentation of undigested food to the distal bowel.

Of the 12 devices implanted by the three surgeons in this trial, 10 were in place for the full 12-month duration. Device tolerance and safety were excellent, as only two early explantations were seen. No other significant adverse sequelae were encountered during the year follow-up period, showing the safety of leaving the device in place for up to a year's duration. The implantation was technically successful in all 12 patients in whom it was attempted (100 %) and no significant postoperative complications were seen during the peri-procedural hospitalization. The two early explantations were necessary due to dysphagia or odynophagia, which completely resolved upon device removal. There were no further intolerances noted during the 12-month follow-up period. Removal of the device was not complicated. All device explantations were performed by the endoscopists in the trial, without any need for surgical intervention. There was no adherence of the device noted at either the GE junction or distally between the polymeric sleeve and the stomach or bowel wall. No erosions or ulcerations were observed in the GI tract upon removal of the device.

Weight loss was substantial throughout the entire trial period. There was statistically significant weight loss seen at 1 week following device implant, and this significance was maintained throughout the entire 12-month follow-up period for all patients. The device function was better, with improved weight loss, in the subset of patients whom maintained full cuff attachment during the follow-up period. The small subset of patients in whom partial cuff detachment was seen, maintained weight loss throughout the follow-up, but this was less than that seen in the fully attached subset. No patients gained weight with the device in place during the trial.

The co-morbidity improvements during the trial were significant and persistent throughout the duration of the trial. The improvement in diabetes mellitus was demonstrated by >1 % decrease seen in hemoglobin A1C values in three of the four patients with diabetes mellitus, a finding supported further by the similar improvement in fasting glucose values for the four diabetic patients in the trial. Hypertension was also significantly improved though the device trial, as five of the seven hypertensive patients had resolution of this disease during the trial and were off antihypertensive medications. Similar substantial improvements were noted in the lipid profiles of patients with preexisting hypertriglyceridemia and hypercholesterolemia.

Patients reported a very high level of satiety with the device. Appetite was minimized between meals, and a sensation of restriction was reported after eating. With small portions, the patients reported a feeling of fullness. The patients were not given special dietary restrictions, but were counseled to chew food thoroughly and to eat slowly. No instances of food obstructions in the sleeve were noted during the study. While some epigastric pain was reported in the immediate postoperative period, this was minimal and qualitatively less than that associated with other laparoscopic bariatric procedures such as banding and gastric bypass. Following the perioperative period, pain was not observed in the study group. Quality of Life surveys (IWQOL; © Duke University, 1995) were administered during the postoperative period, and improvements were noted in all categories, the most pronounced being Personal, Health, Food/Diet, and Physical Activity.

This study reflects our early experience with implantation of this device, and the placement technique and instruments evolved significantly over the course of the trial. Technique learning with regard to anchor placement location, spacing, and uniformity were significant over the course of the trial, and not surprisingly, the patients with best results were those implanted toward the end of the implant experience as the technique matured. Subsequent analysis showed that the causes of partial cuff detachment were due to poor positioning and spacing of the anchors. Placement as such leads to disproportionately higher forces on certain anchors. No cuffs or sleeves became completely detached during the study. Partial cuff detachment allows foods and liquids to pass around the cuff and sleeve, limiting the device effectiveness and leading to inferior weight loss when compared with the fully attached subset.

Well-placed, even, and uniform anchors yielded the best results in terms of attachment and performance of the device in terms of weight loss and co-morbidity resolution. Improved device delivery tools and placement techniques have been developed and are expected to minimize or eliminate this issue moving forward. The device and cuff implantation technique used in this patient trial is a combined endoscopic and laparoscopic deployment procedure that has a definite learning curve, which improved over the course of the trial. Device and technique improvements as well as switch to a fully endoscopic procedure may lead to shorter procedure times, as the laparoscopic surgical intervention may be eliminated. Fully endoscopic suturing tools, with elimination of the laparoscopic surgical manipulation, will also help to achieve better anchor placement and spacing, as the native gastro-esophageal position will not be altered during the procedure. With elimination of the laparoscopic dissection in the future, it may be possible to re-implant, endoscopically, the device following endoscopic removal, but this is an area for further investigation and was not considered for this early trial.

This early device trial has several strengths and weaknesses. A strength of this early device trial is its prospective nature, designed to evaluate the safety of the device; there was no need for additional surgical interventions, after the initial device implantations and all device removals were accomplished endoscopically. This trial was a single-center, prospective trial, not a randomized or a multi-centered trial, which is a weakness of the trial, but future trial design with this device may address these issues.

Conclusions

The 1-year data for this unique endoluminal gastro-duodeno-jejunal bypass sleeve show that it is an effective and safe device for weight loss in morbidly obese individuals. The device is safe and relatively well tolerated in the majority of patients in whom it is implanted. Significant weight loss is seen quickly with the device, as early as 1 week following implantation, and weight loss continues as long as the device is in situ. Weight loss is sustained following explantation in most patients who reach 1-year with a fully attached device, although this is only an early, short-term result, and morbid obesity is a chronic disease. Resolution of metabolic diseases such as type-2 diabetes, hypertension, and hyperlipidemia was observed in the majority of patients presenting with those conditions. The endoluminal nature of the device makes the procedure completely reversible once the device is removed, a beneficial feature some consider important when considering bariatric surgery. This feature is also important, as device intolerance, while infrequent, may necessitate removal, which allows for resolution of the associated symptoms. The short-term weight loss at 1 year seen with this device and improvement in related metabolic disorders are similar to those seen with more conventional bariatric surgical techniques such as roux-en-Y gastric bypass. Evolution of delivery tools and techniques, enabling a fully trans-oral, endoscopic procedure, is underway and will be the subject of future clinical studies. Continued clinical evaluation, including long-term data and device durability information, is important in establishing the effectiveness of this device in the treatment of morbid obesity.

Disclosures Bryan J. Sandler, Roberto Rumbaut, Gustavo Torres, Luis Morales, and Lizcelly Gonzales have served as consultants for ValenTx Corporation. Santiago Horgan and C. Paul Swain have served as consultants for and have an equity interest in ValenTx Corporation. Sarah Schultz, Mark A. Talamini, and Garth Jacobsen have no conflicts of interest or financial ties to disclose.

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