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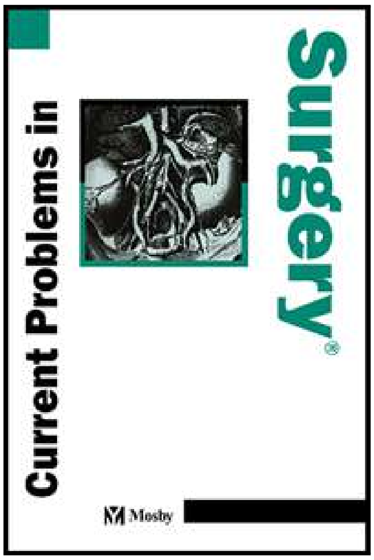

Evolving Procedural Options for the Treatment of Obesity

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Evolving Procedural Options for the Treatment of Obesity

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INTRODUCTION

The field of bariatric surgery is constantly evolving. Patients and providers are seeking procedural options with improved risk profiles, durability, and outcomes for both weight loss and mitigation of obesity related co-morbidities. The last decade has seen a dramatic decrease in laparoscopic adjustable gastric banding (AGB) and increase in sleeve gastrectomy (SG). Laparoscopic Roux-en-Y gastric bypass (RYGB) and SG are now the most commonly performed bariatric procedures. We have also seen the introduction of novel endoscopic therapies and technical modifications of existing surgical options. Herein, we review the new and evolving procedural options for the treatment of obesity.

BALLOON THERAPY

In 1985 the United States Food and Drug Administration (FDA) approved the Garren-Edwards Gastric Bubble (GEGB) as the first endoscopically implanted gastric balloon for the treatment of obesity.[1] In an era where procedures such as the RYGB and vertical banded gastroplasty (VBG) predominated, the GEGB provided a novel, reversible, and less invasive alternative to complex bariatric surgery. Although the adoption of the first intragastric balloon

(IGB) was widespread across the world, the outcomes were less than optimal.[2-4] Weight loss was minimal and the frequency of serious complications such as gastrointestinal (GI) obstruction and gastric ulceration were notable, leading to discontinuation of the device in 1988.[2-4] Around the same time, different IGBs were introduced (none of which were approved for use in the US), such as the Taylor balloon (Mill-Rose Technologies, Cleveland, Ohio 1985) and the Ballobes bubble (DOT ApS Company, Denmark 1988). These devices varied in synthetic material (polyurethane vs. silicone), fill substance (air vs. saline), shape, size, and implantation duration. Despite these variations, weight loss outcomes remained suboptimal and similar complications to the GEGB were reported.[5-8] The disappointing clinical results of IGBs set the stage for the convergence of international experts in a scientific meeting (the "Obesity and the Gastric Balloon: A Comprehensive Workshop") in 1987 aiming to identify a patient population that would benefit most from IGBs and to design the ideal balloon.[9] The conclusion of the conference set the standard for the ideal balloon, which would be spherical in shape, designed from silicone, filled with saline rather than air, and filled to a volume of 400 to 500 mL. Importantly, prior gastric surgery was to remain a contraindication to balloon insertion and the device would be kept in place for 4 to 6 months.

The clinical application of IGBs was also established at the "1987 Obesity Congress", and these indications remain today. The balloons were to be used: (1) in patients with a body-mass index (BMI) between 30 and 35 kg/m^2 as an adjunct to conservative weight loss measures, primarily in the form of diet and exercise, (2) in patients with a BMI greater than 40 kg/m^2 or a BMI greater than or equal to 35 kg/m^2 with at least 1 obesity-related comorbidity who lack reasonable access to a bariatric center or are excluded based on increased intraoperative risk secondary to cardiovascular disease or other severe obesity related comorbidities, and (3) in patients who are super-obese (BMI > 50 kg/m^2) as a bridge to bariatric surgery to reduce surgical morbidity.

FDA Approved Intragastric balloons (IGBs)

After the withdrawal of the Garren-Edwards Gastric Bubble from the US market in 1992, it took more than 20 years until the FDA approved another IGB in the US. The Bioenteric Balloon (BIB), now referred to as the ORBERA® balloon, was developed in 1991. Although not approved for clinical application in the US or Canada at the time, utilization across Europe, South America, and Eastern hemisphere spread quickly. By the time the FDA had approved the ORBERA® device in 2015, roughly 200,000 devices had been inserted in more than 80 countries.[10] The ORBERA® balloon is a single saline-filled silicone balloon which is filled to a volume of 400 to 700 mL and left in place for a maximum of 6 months. The pivotal FDA study was a multi-center, randomized, trial of 448 subjects to evaluate the safety and efficacy of the IGB. Additionally, weight change and obesity-related comorbidities were compared in patients randomized to ORBERA® IGB for 6 months and behavioral modification versus patients who underwent behavior modification alone. The ORBERA® group was found to have a higher percentage total body weight loss (TBWL) at 6 months (10.1% vs. 3.3%), 9 months (9.1% vs. 3.4%), and 12 months (7.6% vs. 3.1%). Obesity-related comorbidities were similar between the 2 groups. The incidence of device and procedure-related serious adverse events was 10%, although there were no deaths. Numerous studies reported superior weight loss with the ORBERA® IGB in conjunction with behavior modification versus lifestyle modification alone.[10-15]

A randomized clinical trial by Courcoulas and colleagues showed a significantly higher TBWL (10% vs 3.3%, P<0.001) in patients who had placement of the ORBERA® balloon as an adjunct to lifestyle changes.[10] Furthermore, a separate study suggested that long-term management of obesity at 1 year, insulin sensitivity, and triglyceride levels were improved in patients with BMI>30 treated with a combination of the ORBERA® IGB and behavior modification.[16]

The success of the ORBERA® balloon laid the foundation for alternative IGBs that varied in design or insertion technique, but mechanistically worked in the same fashion. Two IGBs that were both developed in California, the ReShape™ Duo Integrated Dual Balloon System (ReShape Medical Inc, San Clemente, CA, USA) and the Obalon Gastric Balloon® (Obalon Therapeutics Inc, Carlsbad, CA, USA), were both approved for clinical use by the FDA in 2015. The REDUCE Pivotal Trial was a prospective, sham-controlled, double-blinded randomized multicenter study in patients with a BMI of 30 to 40 kg/m2, that demonstrated improved outcomes in subjects treated with the ReShape™ balloon plus diet and exercise versus sham endoscopy with diet and exercise alone.[17] At 24 weeks, intent-to-treat mean percent excess weight loss (EWL) was 25.1% in the treatment group and 11.3% in controls. The secondary endpoint, weight maintenance at 24 weeks after device removal, was not met.

The Obalon Gastric Balloon® is unique in that it is the first FDA approved balloon that does not require endoscopic insertion. The swallowable intragastric device was investigated in the 2016 SMART clinical trial.[18] This was a multicenter trial involving 15 US institutions that evaluated the efficacy of this new intragastric device in 387 patients. One Half of these patients received 3 Obalon balloons, which were subsequently inflated and the other half served as the control group and their balloons were not inflated. After 24 weeks of treatment, the Obalon group reported a TBWL of 6.81 ± 5.1% and the control group reported a 3.59 ± 5.0% TBWL. Similarly to the Reshape trial, the utilization of the Obalon intragastric devices provided a near double TBWL as compared to control groups. Furthermore, in a recent prospective analysis of 1343 patients with a BMI ≥ 25 who were treated with the Obalon® balloon in the first year of its commercialization, the device was found to have a lower incidence of serious adverse events (0.15% vs. 0.30%) and increased weight loss compared to the results of the SMART trial.[19] The most effective weight loss was seen in patients treated with 3 balloons (n=1103 patients; 9.8 ± 9.5 kg, 9.9 ± 9.7% TBWL, and 42.3 ± 35.2% EWL). Still, long-term data on weight loss outcomes following IGB removal is scant.

Mechanisms of Weight Loss and Effect on Metabolism

Bariatric surgery induces weight loss through various physiologic mechanisms including gastric restriction, malabsorption, and alterations in gut-induced neurohormonal pathways controlling hunger and satiety. The weight loss effects of IGBs are less understood although likely function through similar pathways. As expected, IGBs predominantly stimulate gastric restriction. The inflated balloon functions as an artificial bezoar preloading the stomach and subsequently reducing the size of the gastric lumen to stimulate early satiety.[20] Additionally, the presence of the balloon within the stomach may delay the gastric emptying time.[21] The effect of surgical manipulation of the GI tract on gut neurohormonal pathways has been well documented.[22-25] The effect of IGBs on gut hormones and peptides remain inconclusive and are likely short-lived. Despite this, some studies have demonstrated a decrease in plasma ghrelin[21], transient decrease in leptin levels[26], and decreased cholecystokinin levels[27] in obese patients following treatment with IGBs.

The potential to stimulate weight loss provides an opportunity to repair the metabolic derangements associated with obesity. Obesity-related comorbidities including metabolic syndrome are vastly prevalent in the bariatric population and treatment with IGBs may ameliorate these conditions. In a study of 142 obese patients, the incidence of metabolic syndrome decreased from 34.8% to 14.5% at the time of balloon removal, and continued to decrease at 1 year following balloon removal despite weight regain.[28] A significant reduction in the incidence of hypertriglyceridemia, type II diabetes mellitus (DM-2), and non-alcoholic steatohepatitis have been reported in other studies.[29-31]

Limitations and Adverse Events

The American Society of Gastroenterology (ASGE) Bariatric Endoscopy Task Force performed a systematic review and meta-analysis of more than 8000 ORBERA® implantations in 1683 patients which demonstrated significant weight loss at 6 months with weight maintenance at 1 year.[32] A consensus review of 40,000 balloon implantations (with many devices including some which are not approved for use in the US) in Brazil reported similar weight loss outcomes with 11% to 15% TBWL which was maintained at 1 year.[33] Despite the ability of IGB devices to aid in short-term weight loss and improvement of obesity-related comorbidities, its long-term durability is limited. After balloon removal, the majority of patients experience a steady decline in weight loss and ultimately weight regain. Thus the role of lifestyle modification, pharmacotherapy, and behavior modification becomes increasingly important for long-term weight loss maintenance and should be stressed.

IGBs are generally well tolerated in the majority of patients. Common adverse events associated with balloon implantation include nausea, vomiting, and abdominal pain. To aid in management of typical postoperative symptoms a treatment protocol including anti-emetics, proton-pump inhibitors, and close patient monitoring is recommended. Although IGB placement is a relatively low risk procedure, rare major complications including gastric perforation, hemorrhage, bowel obstruction, and pancreatitis have been reported.[34-36] The FDA issued an updated alert to providers documenting 5 deaths between the period of 2016 through 2017 due to intestinal obstruction, gastric perforation, and esophageal perforation all within 1 month of IGB placement.[37] Subsequent studies have demonstrated a low mortality rate associated with IGB implantation. In a systematic review of mostly fluid filled IGBs, the rates of gastric perforation and mortality were 0.1% and 0.05%, respectively.[35] In February, 2017 the FDA issued an updated alert reporting the phenomena of spontaneous balloon over-inflation and pancreatitis shortly following IGB placement. Appropriately detailed clinical knowledge and advanced training is imperative to minimize complications associated with insertion and removal of IGBs.

Future of Intragastric balloons (IGBs)

IGBs provide a novel non-operative approach to the management of obesity. Short-term weight loss outcomes using both single and double balloons appear to be good and overall major complications are rare. Although maintenance of long-term weight loss with IGBs is unlikely without the addition of pharmacotherapy, and both dietary and lifestyle modification, its utility as a bridging therapy should not be overlooked. Laparoscopic bariatric surgery in extremely obese individuals is technically challenging, and poses increased morbidity and mortality. The use of IGBs to induce preoperative weight loss as a bridge to definitive bariatric surgery may help mitigate these risk factors. As the technology of IGBs continue to evolve, its safety profile improves, and its optimal role is elucidated, it remains an effective tool in the armamentarium of the bariatric surgeon.

ENDOSCOPIC SLEEVE GASTRECTOMY

Bariatric surgery is the current gold-standard therapeutic modality for moderate and severe obesity. Several studies have shown long-lasting weight loss and improvement or resolution of related comorbidities.[38,39] However, surgery is not free from adverse events. The mortality rate is less than 1% for most bariatric procedures but non-fatal adverse events are far more common.[40] A recent systematic review showed an overall adverse events rate of 17% (11%-23%), and a reoperation rate of 7% (3%-12%).[41] Along with high costs, limited access, and patient avoidance, such risks restrict considerably the spread of bariatric surgery.[42]

In this setting, the endoscopic sleeve gastroplasty (ESG) has arisen as an interesting alternative, especially for mild obesity. It creates gastric sleeve-like anatomy through endoluminal full-thickness suturing. The first report on ESG was published by Abu Dayyeh and colleagues in 2013. Since then, many technical modifications have been made to the initial technique and several studies have demonstrated the efficacy and safety profile of the procedure. In this section, we aim to review technical aspects, clinical outcomes, and future perspectives on the use of ESG at treating obesity.

TECHNICAL ASPECTS OF THE ENDOSCOPIC SLEEVE GASTROSTOMY

Several different devices have been employed trying to suture or plicate the stomach, thus mimicking surgical procedures.[43-46] However, the term ESG refers mainly to the suturing of the greater curvature with the Apollo OverStitch™ device (Apollo Endosurgery, Austin, Texas, USA). This is a disposable device that is attached to a double-channel gastroscope. The OverStitch™ handle is mounted on the control handle of the endoscope while the distal end - the needle driver – is attached to the tip of the scope. An anchor exchange catheter is used in one of the working channels to manage the passing of the suture while a tissue helix is used through the secondary channel for atraumatic tissue grasping (Fig. 1). After the stitching is completed, a single-use cinch (Fig. 2) provides knotless fixation, thus keeping the traction of the suturing.

Abu Dayyeh and colleagues first described ESG in a series of 4 patients in 2013.[47] The initial stitching pattern consisted of two parallel rows of interrupted sutures, creating apposition of the anterior and posterior wall (Fig. 3A). Stitching patterns were later refined in a multicenter international collaboration.[48]

For the initial technique, 2 longitudinal dotted target lines were created from the antrum to the gastroesophageal junction using argon plasma coagulation (APC) to orient stitching. Suturing started at the fundus then worked distally towards the antrum. Suction was routinely employed for tissue grasping. Initial cases were performed using running stitches in a triangular fashion (anterior wall, greater curvature, and posterior wall). Each stitch entailed 6 to 12 tissue purchase sites (Fig. 3B).

In time, the APC demarcation lines were felt no longer needed since they were not consistently located throughout the procedure. The tissue helix started being employed for all stitches, aiming to assure full-thickness suturing. The stitching pattern was inverted to an antrum-fundus progression but kept a small fundal pocket that was expected to help delay gastric emptying. Finally, reinforcing interrupted stitches were added just medial to and in-between the running suture lines to increase durability without excessively increasing the operative time (Fig. 3).[48] This is currently the most commonly employed ESG technique[49-51], despite slight particularities between centers such as the number of sutures per stitch.[52,53] Typically, the final appearance of the ESG shows a sleeve-like anatomy in the gastric body and an evident fundal pocket (Figs. 4–6).

PHYSIOLOGICAL ASPECTS

Several studies showing the efficacy of the ESG at treating obesity have already been published (discussed below). However, few articles investigate the physiological alterations leading to weight loss in this setting. Currently, delayed gastric emptying seems to be a central factor.

The most reliable evidence was published by Abu Dayyeh and colleagues in 2017.[54] Four patients underwent different tests to assess the metabolic and physiological effects of the ESG. The authors planned pre- and postoperative (3-month) measurement of satiation by nutrient drink test, gastric emptying for liquids and solids, and fasting and post-prandial glucose, insulin, leptin, active ghrelin, peptide YY (PYY), and glucagon-like peptide 1 (GLP-1). The first and most significant finding was related to gastric emptying of solids at 3 months: an increase in time for 50% (T50) by 90 minutes (*p*=0.03). Accordingly, 32% of the meal was still retained 4 hours after ingestion versus 5% pre-ESG. On the contrary, no significant delay was found in the emptying of liquids (*p*=0.05). Gastric scintigraphy showed that the majority of retained food remained within the fundal remnant. These findings corroborate the beneficial role of the fundal pocket. Regarding the satiation parameters, 35.2 ± 9.9 minutes were needed for termination of the meal in the pre-ESG period compared to 11.5 ± 2.3 minutes post-ESG (*p*= 0.01). Correspondingly, there was a 59% decrease in caloric intake to reach maximum fullness in the nutrient drink test (*p*=0.003). Such data suggest that restriction is an important factor to promote weight loss after ESG. Moreover, the authors found no significant changes in the gut hormones (ghrelin, PYY, GLP-1, and leptin). This information endorses the poor or no action at all of the GI hormones on weight loss following ESG, thus rendering delayed gastric emptying and restriction central factors. Finally, there was a trend toward an improvement in the Fasting Homeostatic model assessment for Insulin Resistance (HOMA-IR) score (p= 0.06). Hypothetically, a larger sample could demonstrate such difference as statistically significant. The area under the curve (AUC) for insulin did not change significantly (decreased by 34%, *p*=0.17) but the AUC for post-prandial glucose had a significant improvement (decreased by 36%, *p*=0.005). Currently, there is still no full understanding of the mechanism behind such improvement but data firmly suggest that the ESG improves insulin sensitivity.

In a series published by Sharaiha and colleagues, the endoscopists measured the length of the stomach pre-ESG and immediately after the procedure.[49] The mean size from the pylorus to the gastroesophageal junction decreased from 34.8 cm to 20.4 cm (p<0.001). These data also suggest restriction as an important physiological pathway through which the ESG promotes weight loss.

CLINICAL OUTCOMES

Weight loss

Non-comparative studies

Kumar N and colleagues published a multicenter series enrolling 77 patients with a mean age of 41.3 ± 1.1 years undergoing ESG with the current technique.[48] The mean baseline BMI and weight were 36.1 ± 0.6 kg/m^2 and 99.4 ± 1.8 kg, respectively. The mean absolute loss (AWL) and TBWL were 16.4 ± 0.9 kg and 16.0 ± 0.8%,respectively at 6 months. At 12 months, they were 18.9 ± 1.5 kg and 17.4 ± 1.2%, respectively. Nausea, vomiting, and abdominal pain were often reported during the first week after the procedure. There were no serious adverse events during the study.

Another multicenter series enrolled 112 patients from 3 centers in the United States and Australia.[52] At baseline, the mean age and BMI were 45.1 ± 11.7 years and 37.9 ± 6.7 kg/m^2, respectively. At 6 months, the AWL and TBWL were 16.4 ± 10.7 kg and 14.9 ± 6.1%, respectively. Four out of 5 patients achieved greater than 10% TBWL at a 6-month follow-up. Higher baseline weight, male gender, and no previous endoscopic bariatric therapy were predictors of greater AWL at 6 months. As to the safety profile, there were no intraprocedural complications. All patients were discharged on the day of the procedure despite frequent mild epigastric pain, nausea, and vomiting. There were 3 serious adverse events (2.7%) managed conservatively: 2 cases of upper GI bleeding and 1 case of peri-gastric fluid collection.

In 2016, Lopez-Nava and colleagues published a single-center study assessing predictive factors for weight loss.[50] Twenty-five patients (5 men, 20 women) undergoing ESG were followed for 1 year. The mean baseline BMI was 38.5 ± 4.6 kg/m^2. At 12 months, the mean BMI reduction and TBWL were 7.3 ± 4.2 kg/m^2 and 18.7 ± 10.7, respectively (n=22). No related serious adverse events were recorded. The linear regression analysis showed that the number of psychological and nutritional contacts were predictive of better weight loss results.

In a subsequent study, Lopez-Nava and colleagues reported the results of a 24-month follow-up of 248 patients undergoing ESG.[51] In this multicenter series, procedures from 3 centers - 2 in the United States and 1 in Spain - were recorded. The mean age and baseline BMI were 44.5 ± 10 years and 37.8 ± 5.6 kg/m^2, respectively. The loss to follow-up rate was 13% at 6 months and 38% at 2 years. The average TBWL at 6 and 24 months was 15.17% [95% CI 14.2–16.25] and 18.6% [95% CI 15.7–21.5], respectively, and was similar among participating centers. The linear regression analysis demonstrated that the weight loss at 6 months highly predicted weight maintenance and weight loss at 24 months. Therefore, it was pointed out as a central early predictor of poor long-term outcome, thus allowing further additional interventions to avoid long-term failure. Five (2%) serious adverse events were reported: 1 pulmonary embolism; 2 peri-gastric fluid collections treated with percutaneous drainage and antibiotics; 1 self-limited extra-gastric bleeding requiring transfusion; and 1 pneumoperitoneum and pneumothorax that required chest tube placement. None of these patients required surgery.

Recently, Alqahtani and colleagues published the largest series to date: 1000 consecutive patients undergoing ESG from a single center in Saudi Arabia.[55] The mean baseline BMI and age were 33.3 ± 4.5 kg/m^2 and 34.4 ± 9.5 years, respectively. The mean TBWL at 6, 12, and 18 months was 13.7 ± 6.8% (n=369/423), 15.0 ± 7.7% (n=216/232), and 14.8 ± 8.5 (n=54/63), respectively. As for obesity-related comorbidities, all 28 cases of hypertension, 13 of 17 cases of DM-2, and 18 of 32 cases of dyslipidemia presented complete remission by the third month. Ninety-two percent of patients complained of postoperative mild abdominal pain and nausea which were easily controlled with oral medications. Regarding adverse events, 8 patients reported severe abdominal pain, 3 requiring ESG reversal; 7 developed post-procedure bleeding, 2 requiring blood transfusions; 4 had peri-gastric collections with pleural effusion, 3 of whom needed percutaneous drainage; and 5 patients developed post-procedure self-limited fever. There were no mortalities or emergency interventions. During 18 months of follow-up, 8 cases of ESG were revised to sleeve gastrectomy, and give with weight regain underwent redo-ESG.

Of note, Graus-Morales and colleagues employed a different stitching pattern to perform the ESG: instead of the standard triangular pattern, the authors reported 4 rows of parallel longitudinal running “Z”-pattern sutures.[56] Despite this technical detail, the final anatomy – assessed with upper endoscopy, oral contrast studies, and contrast-enhanced computed tomography (CT) – was indistinguishable from the standard technique. The authors performed the ESG in 148 patients who were followed for 12 months. A subgroup of 72 individuals also had an 18-month assessment. The average age was 41.53 ± 10 years, and the mean baseline weight and BMI were 35.11 ± 5.5 kg/m^2 and 98.7 ± 17 kg, respectively. The TBWL was 17.53 ± 7.57 at 1 year and 18.5 ± 9% at 18 months. Interestingly, a subgroup analysis demonstrated that patients with BMI less than 35kg/m^2 almost reached the ideal weight, that is, presented an average EWL of 98.6%. Regarding adverse events, again most patients experienced mild abdominal pain, nausea, or vomiting during the first days after the procedure. Two major adverse events were recorded: 1 case of refractory pain, and 1 case of GI bleeding treated with sclerotherapy. None required further interventions.

Comparative studies

The first comparative study was published in 2017 by Ruiz and colleagues [57] The authors compared ESG to Laparoscopic Greater Curvature Plication (LGCP) and SG. This retrospective non-matched cohort included 357 patients (253 ESG, 38 LGCP, and 66 SG) from 4 different centers. Both surgical groups had greater weight loss compared to the ESG group, even though the final BMI was equivalent among groups (29.96, 29.57, and 28.51 kg/m^2). This can be explained by the lower baseline BMI of the ESG group (37.29 vs 39.95 and 40.23 kg/m^2), suggesting that it could be a good option to treat non-morbid patients. Interestingly, the overall adverse event rate was lower and length of stay was shorter for the endoscopic group.

Later, Novikov and colleagues performed a single-center retrospective cohort study comparing 3 bariatric procedures: Laparoscopic Sleeve Gastrectomy (LSG), Laparoscopic Adjustable Gastric Banding (LAGB), and ESG.[58] The authors included 278 patients (120 LSG, 67 LAGB, and 91ESG). As expected, the surgical group had a significantly higher baseline BMI (47.2 ± 7.84 *vs* 44.9 ± 6.4 *vs* 38.6 ± 6.9, $p<0.05$) and significantly more obesity-related comorbidities, namely, diabetes, hypertension, hyperlipidemia, and obstructive sleep apnea. The multivariate analysis showed LSG to be associated with the greatest weight loss at 12 months (*p*<0.001). However, for patients with BMI less than 40kg/m^2, there was no significant difference in percentage TBWL at 1 year when comparing the 3 techniques (*p*=0.21). Additionally, the length of stay of the ESG group was significantly shorter than LSG and LAGB (0.34 ± 0.73 days *vs* 3.09 ± 1.47 days *vs* 1.66 ± 3.07 days, *p*<0.01). Finally, both surgical groups presented higher overall complication rates than the endoscopic group (9.1% for LSG, 8.9% for LAGB, 2.2% for ESG, *p*<0.05). None of the adverse events with ESG required emergency surgery but 5 (4.1%) and 2 (3%) patients undergoing LSG and LAGB, respectively, underwent reoperation in the shortterm. Despite the retrospective design, these data suggest that ESG is less invasive and has comparable outcomes to well-established bariatric procedures for obese individuals with BMI less than 40kg/m^2.

Fayad and colleagues recently published another study comparing ESG (n=54) to LSG (n=83).[59] In this single-center cohort, baseline age, gender distribution, and BMI were similar. However, the endoscopic group had less obesity-related comorbidities. At 6 months, 35% and 15% of patients from the ESG and LSG groups, were lost to follow-up, respectively. The authors found that the surgical group had a significantly higher TBWL at 6 months (23.6% ± 7.6 vs 17.1% ± 6.5, *p*<0.001). Again, the difference between groups in TBWL sharply diminished for the subset of patients with BMI <40 kg/m^2 although there was still a borderline superiority of LSG over ESG (*p*=0.05). Interestingly, the surgical group had higher rates of new-onset post-procedure GERD (1.9% *vs* 14.5%, p<0.05). Again, the authors demonstrated a significantly lower overall rate of adverse events with ESG (5.2% vs 16.9%, *p*<0.05). This study also supports ESG as a minimally invasive alternative to standard bariatric procedures for mildly obese patients or for those who refuse surgery.

Metabolic improvement

As to obesity-related comorbidities, a study from Sharaiha and colleagues assessed the impact of ESG on improvement and remission rates.[49] In this single-center series enrolling 91 consecutive patients (mean baseline BMI = 40.7 ± 7kg/m^2), the average TBWL was 14.4%, 17.6% and 20.9% at 6, 12, and 24 months, respectively. The authors found a significant overall reduction in levels of hemoglobin (Hb) A1c (6.1% ± 1.1 *vs* 5.5% ± 0.48, p=0.05) at 1 year. For patients previously diagnosed with pre-diabetes or diabetes, the reduction was even more distinct (6.6 % ± 1.2 v. 5.6 % ± 0.51, p=0.02). Additionally, there were significant reductions in systolic blood pressure (p=0.02), waist circumference (p<0.001), alanine aminotransferase (p<0.001), and serum triglycerides (p=0.02). On the contrary, the low-density lipoprotein did not decrease considerably (p=0.79).

FUTURE PERSPECTIVES

Currently, there are 2 ongoing open-label randomized trials investigating the efficacy and safety of ESG. The first is a Chinese trial (NCT03124485) enrolling 37 patients allocated either to standard LSG or ESG. Aside from weight loss outcomes, the authors intend to assess physical, functional, and hormonal changes. The second study is the denominated MERIT Trial (NCT03406975) and is the most awaited study regarding ESG. This RCT is a multicenter open-label trial comparing ESG to lifestyle intervention for 1 year. The enrollment goal is 200 nonmorbidly obese patients (BMI ≥30 and ≤40kg/m^2) at 8 centers across the United States. Worldwide, endoscopists and bariatric surgeons expect this study to reveal central information to help better support ESG, further improving the treatment of obesity and related comorbidities.

DUODENAL MUCOSAL RESURFACING

The increased incidence of DM-2 and weight related comorbidities has increased the number of bariatric procedures performed in the United States. A significant decrease in hyperglycemia has been noted following bypass surgery in diabetic morbidly obese patients.[60] Bypassing the proximal small bowel, especially the duodenum, has been directly related with glucose metabolism.[61] The duodenal mucosal layer is believed to play a key part in metabolic homeostasis and has increasingly been recognized as a key player in regulating insulin action and insulin resistance states.[62-65] Therefore, analysis of duodenal mucosa has shown abnormal hypertrophy and endocrine hyperplasia in the presence of diabetes.[66,67] Based on this concept, new endoscopic interventions have been explored to alter the duodenal mucosa with effects on glucose homeostasis similar to bypass surgery. Duodenal mucosal resurfacing (DMR) is a novel, minimally invasive approach that elicits a clinically significant improvement in hyperglycemia in patients with DM-2.[60,61,66-69]

PROCEDURE

DMR is a superficial endoscopic procedure that aims to mechanically disrupt the duodenal mucosa.[61,66] A wire-guided balloon catheter is passed through the upper scope and is placed in contact with the target duodenal mucosal segment (Figs. 7 and 8). The treatment segment stretches post-papilla to the proximal jejunum, usually involving a 9 to 10 cm segment. A circumferential mucosal lift separates the mucosa from deeper layers.[61,66-68] This is accomplished by creating a submucosal lift with normal saline injections, creating a submucosal aqueous buffer to protect the deeper layers from the hydrothermal ablation. Discrete 10-second hydrothermal ablations at 90°C are applied until the entire segment has been completed (Fig. 9). Ablation length correlates with diabetic and hepatic indices. The advantage of using hydrothermal ablation over other ablating technologies, is that this is non-desiccating. The duodenal mucosa gets coagulated and it later sloughs off, alleviating the bleeding risk, and it also provides better control of ablation depth preventing deeper injury.[61,66-68]

Re-epithelialization of the duodenum with normal mucosa is stimulated and starts immediately postoperatively.[66] Limitations of the procedure are the need of an advanced surgical endoscopist, able to perform the procedure in the duodenum safely.

MECHANISM AND OUTCOMES

Insulin resistance is the underlying cause of DM-2 and fatty liver disease. The duodenum has been recognized as a signaling center that regulates insulin metabolism.[62,66,69] Preventing direct contact between nutrients and duodenal mucosa improves insulin sensitivity and β-cell function.[61,66] This has been a recently noted additional benefit of bariatric surgery. The current standard of care for the treatment of DM-2 is lifestyle modification and pharmacologic therapy targeted to reduce insulin resistance, despite evidence suggesting many struggle to adhere to these over time.[66]

The addition of oral hypoglycemic agents has shown that these medications' pathways alter not only glucose metabolism, but also lipid metabolism and blood pressure control, among others.[66] Thiazolidinedione (TZD), biguanide, glucagon-like peptide 1 receptor (GLP-1R) antagonists and, sodium/glucose cotransporter 2 (SGLT2) inhibitors have all demonstrated significant insulin sensitization effects. Exercise, weight loss and diet are the pillars of lifestyle modifications.[70] Despite the significant improvements seen with intense medical therapy, it has been difficult to engage patients to comply with the rigorous life-style modifications and to adhere to the medical therapy. Inability of patients to adhere to regular dosing of these medications has resulted in significant side effects such as GI intolerance, edema, and heart failure.[66] For this reason, bariatric - now referred to as metabolic - surgery continues to gain popularity in the long-term treatment of obesity patients with diabetes.[62,66,70]

Bypassing the first portion of the small bowel has a significant metabolic effect on insulin sensitivity resulting in better glucose control.[63,67,70] These dramatic effects are seen immediately after surgery and they are reversed if the normal anatomy is restored.[63] Animal studies where the proximal small bowel is isolated from direct contact with nutrients have shown similar results. The duodenal-jejunal bypass sleeve (or EndoBarrier GI liner [GI Dynamics, Inc, Boston, MA]), where a sleeve device is implanted to the duodenal bulb preventing contact between the food bolus and the mucosa, induced weight loss and glucose homeostasis in diabetic obese patients. These studies opened the gate for more endoscopic, minimally invasive, and novel procedures to remodel and bypass the duodenal mucosa.[66,71] In human studies, the infusion of nutrients at 3 different starting points in the small bowel (duodenum, proximal jejunum, and mid-jejunum) through a balloon catheter resulted in an approximately 50% increase in insulin sensitivity in patients with and without DM-2.[72]

DMR (Revita DMR system [Fractyl Laboratories, Inc, Lexington, MA]) uses a catheter that produces superficial tissue ablation producing an exchange of the duodenal surface with subsequent regrowth of normal tissue which does not have the alterations in signaling that regulates insulin metabolism.[61,66] This novel approach avoids surgery and the implantation of a foreign body. Interestingly, animal studies have shown that the improvement in glucose control was not seen in normal rats or non-diabetic rats.[60,61] This proves that the procedure itself is not responsible for glucose improvements; instead, resetting the mucosal alterations encountered in obese diabetic patients may be responsible.

Two human studies have been published (Table 1).[60,66,68] The first was a 6-month safety and efficacy trial from a single-arm, open-labeled, nonrandomized study. Forty-four patients with poorly controlled DM-2 on at least 1 medication were enrolled from a single South American institution. Enrolled patients ranged in age from 38 to 65 years, had DM-2 for less than 10 years and an average BMI of 30.8 kg/m^2. At 6 month follow-up, there was significant improvement in HbA^1 levels (-1.8%), lower fasting glucose level and homeostatic model assessment for insulin resistance (HOMA-IR), and improvement in transaminases. There was greater glycemic improvement in patients with a longer length ablation area. This first-in-human study showed significant improvements in glycemia in DM-2 patients up to 24 weeks after DMR.[68]

More recently, an international multicenter, prospective, open-labeled study was published. Forty-six patients were enrolled in the study. Inclusion criteria included patients with a BMI 24 to 40 kg/m^2 and DM-2 on stable oral glucose-lowering medication, which remained stable for at least 24 weeks after DMR. Eighty percent of patients underwent complete DMR; the remaining patients were excluded due to technical issues during the procedure. A significant difference was observed 24 weeks post-procedure in patients' HbA1c (0.9% lower compared to baseline), fasting plasma glucose, HOMA-IR, weight loss, and hepatic transaminase levels. Results were maintained for 12 months.[60]

Both human studies showed similar results with improvement in the metabolic state of patients with DM-2 and fatty liver disease.[60,61,66] Currently, a multicenter FDA clinical trial is being conducted for approval in the United States.[73] A clinical study in which DMR is combined with GLP-1 and lifestyle intervention is also under way.

SUMMARY

DMR is a novel endoscopic approach that obtains durable glycemic control in DM-2 and improves other comorbidities related to insulin resistance. In the current DM-2 treatment algorithm, DMR may have a role as an adjuvant or alternate approach to pharmacologic therapy. Studies have shown this to be a safe and feasible procedure in experts' hands. Further investigations are needed to fully comprehend the critical effects the duodenal mucosa has over metabolic homeostasis.

DUODENAL-JEJUNAL BYPASS LINER

The most effective treatment for obese patients with DM-2 is metabolic bariatric surgery, mainly Roux-en-Y gastric bypass (RYGB), with remission rates greater than 50% and sustained weight loss.[74-77] However, disadvantages include the invasive and irreversible nature of the procedure and the non-negligible morbidity and mortality rates.[78-80] Furthermore, bariatric surgery is limited to less than 2% of patients who fit the criteria for the procedure. The reasons for this are multifactorial and likely include high surgical risk, morbidity, costs, access, and patient preference.[78,81,82]

As a result, there is a drive to develop less invasive, reversible, and cost-effective therapies to combat this obesity and diabetes epidemic. Endoscopic therapies that focus on weight loss are important since they are more effective than pharmacologic treatments and lifestyle changes and present lower adverse event rates compared to bariatric surgery.[83,84] The Duodenal-jejunal Bypass Liner (DJBL) (Endobarrier® Gastrointestinal Liner, GI Dynamics, Lexington, MA, USA) is a minimally invasive and fully reversible procedure with a growing body of evidence to support its use in this patient population.[85-87]

DEVICE AND PROCEDURE

The DJBL is a single-use endoscopic device, composed of a nitinol anchor for fixation and a 62 cm long fluorine polymer liner, which impedes mixing of chyme with bile and pancreatic secretions prior to the proximal portion of the jejunum (Fig. 10).

Endoscopic implantation is performed under general anesthesia or sedation. First, a guidewire is placed in the jejunum, then the device is introduced over the wire, under fluoroscopic guidance. The fluorine polymer liner is advanced to overlay the duodenum and the proximal portion of the jejunum. After correct positioning is confirmed on fluoroscopy, the anchoring system is released and fixed at the duodenal bulb. Finally, a contrast infusion is performed to verify correct placement of the device and the absence of obstruction within the liner.

Device removal is typically performed under general anesthesia. A foreign body hood is placed at the tip of the endoscope, and the device is removed by securing the anchor system with a procedure-specific grasping device.

MECANISMS OF ACTION

This procedure is analogous to the RYGB (Fig. 11). During the RYGB, the stomach is divided into a small pouch and a larger remnant stomach. The pouch is connected to the jejunal Roux limb, bypassing the gastric remnant, duodenum, and proximal jejunum.[88]

Bypass of the small intestine is thought to have a significant role in the weight loss and metabolic benefits experienced after certain bariatric surgeries. Studies suggest that duodenal exclusion and accelerated arrival of biliopancreatic secretions and partially-digested meals to the mid-jejunum and ileum are partially responsible for the favorable effects of RYGB in DM-2 and obesity.[89]

The DJBL prevents ingested nutrients from contacting the mucosa of the proximal small bowel, allowing food to pass from the stomach into the sleeve and then directly into the jejunum without contacting the duodenum.[88-90]

A recent systematic review and meta-analysis of the DJBL[91] showed gut hormone changes, suggesting mechanisms similar to RYGB. This review showed a decrease in glucagon-dependent insulinotropic polypeptide (GIP), with an increase in glucagon-like peptide-1 (GLP-1) and peptide YY (PPY). However, an increase in ghrelin levels was also noted, which is in contradiction to the RYGB findings.[92] A potential explanation for this is that ghrelin is predominantly released from P1/D1 cells in the upper stomach and fundus, a part of the GI tract which is unaffected by the DJBL implant, unlike in RYGB. Additionally, the rise in ghrelin could be a physiologic response to dieting or in response to weight loss induced by the device.[93]

The use of DJBL demonstrated an increase of GLP-1 post-prandially, likely due to undigested nutrients rapidly reaching the distal small bowel increasing stimulation of L-cells. The decrease in GIP may be due to limited contact of food with the proximal intestine where most of K-cells are located. GLP-1 stimulates insulin secretion from the pancreas, increases insulin sensitivity, and inhibits glucagon, thus reducing gluconeogenesis and hepatic glucose output. GLP-1 is also an anorexigenic hormone that acts centrally to increase satiety and reduce appetite. GIP has various physiological effects including postprandial secretion of insulin and glucagon release during hypoglycemia.[94,95] Some studies suggest that the blunting of GIP contributes to the antidiabetogenic effect of the proximal small bowel exclusion.[93,96,97]

The PPY is an anorectic gut hormone secreted postprandially from L cells in the distal ileum and colon. It is associated with delayed gastric and intestinal transit, inhibits food intake and promotes satiety.[98] Also, a delay in gastric empty was found in patients with DJBL when compared to the baseline group.[99] No studies analyzed gut microbiota after DJBL placement.[93]

The similarities between DJBL and RYGB are summarized in Table 2.

EFFICACY AND SAFETY

In this review we focus on randomized controlled trials (RCT)[90,92,100-102] and meta-analyses, to provide the most rigorous evidence[85,91].

Efficacy

All 5 RCT[90,92,100-102] demonstrated that the DJBL is effective in promoting weight loss. Gersin and colleagues showed significantly more weight loss in the DJBL group compared to the sham group (8.2 ± 1.3 kg *vs* 2.0 ± 1.1 kg).[101] At 3 months, Tarnoff and colleagues reported 22% EWL for the DJBL group compared to 5% EWL of the control group.[100] After 12 weeks, Schouten and colleagues demonstrated a BMI decrease favorable to the DJBL group, with a decrease of 5.5 kg/m^2 *vs* 1.9 kg/m^2 in the control group.[102]

All RCT[90,92,100-102] also showed a decrease in HbA1c after treatment. Rodriguez and colleagues comparing DJBL with sham, showing a decrease by 2.4% vs 0.8% in favor of the DJBL group.[90] An additional study confirmed the superiority of the DJBL (pre: 8.8±1.7%; post: 7.7±1.8%) compared to the control group (pre: 7.3±0.1%; post: 6.9±0.6%).[102]

All RCTs had shorter (12-24 weeks) follow-up compared to the available open label prospective studies (52 weeks).[86,103] At 1 year follow-up, Escalona and colleagues, showed weight loss of 22.1 ± 2.1 kg or 47.0% ± 4.4% EWL, and BMI decline of 9.1 ± 0.9 kg/m^2.[103] Waist circumference decreased significantly, from 120.5 ± 6.8 cm to 96.0 ± 2.6 cm. Statistically significant improvements were also reported in blood pressure, HbA1c, cholesterol, low-density lipoprotein, triglycerides, and prevalence of metabolic syndrome. Another prospective study also demonstrated statistically significant reductions in fasting blood glucose (- 30.3±10.2 mg/dL), fasting insulin (-7.3±2.6 lU/mL), and HbA1c (-2.1±0.3%).[86]

A recent systematic review and meta-analysis, including RCT and cohort studies of only obese patients with DM-2, confirmed the efficacy of the DJBL.[91] At explant, HbA1c decreased by 1.3% [95%CI 1.0, 1.6] and HOMA-IR decreased by 4.6 [2.9, 6.3]. Compared with control, DJBL had greater HbA1c reduction by 0.9% [0.5, 1.3]. Six months after explant, HbA1c remained lower than baseline by 0.9% [0.6, 1.2]. At explant, patients lost 11.3kg [10.3, 12.2], corresponding to a BMI reduction of 4.1 kg/m2 [3.4, 4.9], total weight loss of 18.9% [7.2,30.6], and EWL of 36.9% [29.2,44.6]. The amount of weight loss remained significant at 1 year after explantation. This review also evaluated the hormones related to obesity, and showed that DJBL decreased the GIP, whereas GLP-1, PYY, and ghrelin increased. A previous meta-analysis focusing on a different patient population with either obesity or DM-2 also demonstrated favorable results for the DJBL.[85] This analysis demonstrated a significant mean differences in body weight and EWL of 5.1 kg [95%CI 7.3, 3.0] and 12.6% [95%CI 9.0, 16.2], respectively, compared with diet modification. The mean differences in glycated hemoglobin (−0.9%; 95% CI −1.8, 0.0) and fasting plasma glucose (−3.7 mM; 95% CI −8.2, 0.8) among subjects with DM-2 was also favorable for the DJBL group, however no statistical significance was found.

Safety

As with any other endoscopic device placed into the GI lumen, the most commonly reported adverse events (AE) are abdominal pain, nauseas, and emesis. These symptoms usually resolve as the patient acclimates to the device. However, some patients are unable to tolerate these symptoms, leading to early removal. Other AE include GI bleeding, migration, and device obstruction. Less common AE such as pancreatitis and liver abscess were also reported. The last will be discussed later in this section.

In the US trial from 25 randomized patients, implantation was successful in 21.[101] Four DJBL placements failed due to a short duodenal bulb. The majority of AE were mild or moderate. No pancreaticobiliary events or migration were reported. From the 21 patients, 7 patients had early removal due to AE related to the device. Three of these patients removed the device due to GI bleeding with a decrease in hemoglobin. The other 4 early removals were related to abdominal pain, nausea, and vomiting. The other RCT comparing the DJBL with a sham group showed similar AE, including vomiting and abdominal pain.[90] From 12 DJBL, 3 were explanted early due to symptoms related to migration or twisting of the liner. Additionally, 2 more migrations without symptoms were diagnosed at the time of removal. All the other RCT[100,1002] presented similar results, except one by Koehestanie and colleagues [92] which did not report any early removal.

The ENDO Trial Investigational Device Exemption was a multicenter, double-blinded, and randomized trial performed in the US to evaluate the safety and efficacy of the DJBL on glycemic control. In March, 2015, however the company stopped the trial due to the development of 7 liver abscesses (3.5%), which was higher than anticipated. These were all managed conservatively with intravenous antibiotics and in some cases percutaneous drainage. The cause for these liver abscesses is unclear, but there are several theories including alteration in microbiome, high dose PPI use, and that the DJBL anchors may create a nidus of infection which may spread to the liver bed. Postmarket surveillance data show an incidence of 1%, which is also supported by the data from a worldwide registry established by the Association of

British Clinical Diabetologists in 2017.[104] From 492 patients, there were 6 reported cases of liver abscess. Additionally, in this study, rates of early removal due to GI bleeding, device migration, and device obstruction were 4%, 3%, and 0.3%, respectively.

DISCUSSION

The DJBL is the first endoluminal device bypassing the duodenum and proximal jejunum with favorable results in weight loss and DM-2 control mimicking the clinical and physiological effects of RYGB. Currently, the implantation period for the DJBL is 1 year. There is a paucity of data available related with longer follow-up. The RCTs published with longer follow-up report data for 24 weeks[90,92] and the observational studies report follow-up up to 52 weeks.[103,105,106] One study analyzed 6-month follow-up after DJBL removal and reported 74% of subjects had weight regain.[107] However, this study did not report the follow-up program such as diet or exercises. To prevent remission, reimplantation of the device or development of a prototype that can remain in situ for longer than 1 year could provide a more permanent solution for these patients. However, strategies to combat the unwanted side effects associated with having a duodenal sleeve implanted for a long period are needed. A recent non-randomized study showed favorable results in terms of weight loss and DM-2 in a series including 80 patients, with follow-up to 3 years.[108] At 1-year (71 patients), 2-year (40 patients) and 3-year (11 patients) follow-up, the mean percentage EWL was 44 ± 16%, 40 ± 22%, and 39 ± 20%, respectively. The baseline HbA1c was 7.1 ± 1.6%, and significantly decreased to 6.0 ± 0.9% at 12 months and 5.7 ± 0.7% after 24 months. The diabetic patients who completed 36 months of follow-up maintained a HbA1c below 6%. Despite efficacy of the DJBL, the study reported 9 serious adverse events (SAE), including upper GI bleeding, liver abscess, acute pancreatitis, and cholangitis. Most SAE occurred after 12 months of follow-up. The authors conclude that this device should not be left in place for longer than 1 year.

In summary, the DJBL provides good weight loss results and is associated with improved glycemic control, even in patients who have failed medical therapy. It is a promising device for the management of obesity and DM-2. In its current form the device is unlikely to replace RYGB for the treatment of metabolic disease, however it may be a viable alternative for many of these patients. Future work in this field should focus on developing a device that offers longer treatment duration while also improving its safety and tolerability.

SINGLE ANASTOMOSIS GASTRIC BYPASS (SAGB)

Single Anastomosis Gastric Bypass (SAGB) continues to generate controversy in the United States. Despite the widespread use and consistent growth in international popularity, SAGB always generates lively discussions and fosters emotional debates. Surgeons passionate in their belief that the time has come to endorse the operation are split from those insisting that more research needs to be completed.[109] The operation known originally as the Mini Gastric Bypass (MGB), rebranded as the One Anastomosis Gastric Bypass (OAGB), the Omega Loop Gastric Bypass (OLGB) and the SAGB, generates controversy fanned by concerns that bile reflux will trigger neoplastic changes in the distal esophagus.[110] Surprisingly, questions regarding the long-term safety of SG following reports of Barrett's esophagus developing after SG, has not generated nearly the level of concern that persists surrounding SAGB operations.[111-

[113] Despite new and growing reports regarding Barrett's esophagus, its association with SG, and a possible carcinogenic potential[114], sleeve gastrectomy remains an endorsed procedure by the American Society for Metabolic and Bariatric Surgery (ASMBS). Gastric bypass procedures using a single anastomosis still remain an ASMBS designated investigational operation, one that requires IRB approval for MBSAQIP centers performing this operation.

As the issue of SG-related reflux and Barrett's esophagus raises questions about the future of SG, increasing numbers of American surgeons are taking a new interest in the SAGB operation as both a primary and revisional operation.

HISTORY OF SINGLE ANASTOMOSIS GASTRIC BYPASS PROCEDURES

In 2001 Rutledge published an article in the Journal Obesity Surgery reporting results for 1,274 cases utilizing a single anastomosis version of a gastric bypass.[115] He described a simplified version of a traditional RYGB. Rutledge described using a loop of jejunum measured 175 to 200 cm past the ligament of Treitz and anastomosing it to a long, narrow, gastric pouch created off the lesser curve of the stomach in a vertical rather than horizontal fashion (Fig. 12). He called this approach the "mini gastric bypass." Over the 18 years following that paper, SAGB operations have achieved results similar to the already established and well accepted RYGB.[116] Skeptical criticism regarding a single anastomosis approach to gastric bypass surgery is based largely on concerns that bile reflux complications seen following Edward Mason's attempts with a loop gastrojejunostomy might repeat themselves.[117] The initial loop gastric bypass created by Mason 30 years prior to Rutledge's report was a very different operation than the current SAGB, OAGB, or MGB procedures. The Mason loop gastroplasty often resulted in uncontrolled bile reflux injuring the distal esophagus and occurred due to its extremely short length and horizontal gastroplasty. Fifty years after Mason first described his looped gastric bypass, the concerns of biliopancreatic reflux reaching the distal esophagus from the afferent limb of a loop gastrojejunostomy remains a heated topic of discussion among bariatric surgeons.

Recently, SG has seen reports that as many as 17% of patients undergoing vertical sleeve gastrectomy may develop distal esophagitis and Barrett's changes.[114] There are no reports that this kind of progression occurs in patients undergoing SAGB operations and the etiology of esophageal adenocarcinoma related to any duodenal-pancreatic bile reflux plays is an ongoing debate.[118-120] Some investigators have found no relationship between gastric procedures and adenocarcinoma of the esophagus.[121,122]

Although SAGB has been slow to gain traction in the United States, the opposite has been true in Europe, Asia, and the Middle East. More than 16,000 patients have been included in peer reviewed publications reporting on SAGB outcomes. The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) position statement published on March 29, 2018 recommended that the "One Anastomosis Gastric Bypass become a recognized bariatric/metabolic procedure and should not be considered investigational."[123,124] The IFSO task force was composed of a multinational group of 22 recognized and accomplished bariatric surgeons. The United States was represented by 2 former ASMBS presidents. The IFSO task force reported findings of 52 studies with 16,546 patients and concluded that the safety and efficacy of SAGB procedures warranted the support of IFSO and the society's endorsement.

SINGLE ANASTOMOSIS GASTRIC BYPASS (SAGB)

Reproducible weight loss outcomes combined with a technically easier operation has contributed to the popularity of SAGB. It is easier than RYGB or biliopancreatic diversion with duodenal switch as it eliminates entirely the Roux limb and its associated complications. Bleeding, intussusception, internal hernia, and leakage from the second anastomosis are avoided in SAGB.

SAGB is a cost-efficient operation that can be performed as an outpatient procedure.[125] With reduced operative time and a simplified, less expensive operation, the ability to expand the number of facilities able to offer bariatric surgery has occurred internationally. SAGB appears to be a source of increasing popularity and may result in improved access to care.

The operative technique for SAGB procedures has evolved into 2 similar but slightly different approaches. The first operation described in 2001 by Rutledge was a long narrow gastric pouch based on a lesser curve staple line and an end-to-side anastomosis between the gastric pouch and the loop gastrojejunostomy (Fig. 12). The operative dissection created 1 to 2 cm below the crow's foot utilized a vertical staple line extending towards the angle of His along the lesser curve body of the stomach. The subsequent gastric pouch is rather wide, staying lateral to the angle of His as the stomach is transected and separated into 2 separate structures. The end-to-side anastomosis between the pouch and the jejunum utilizes the full length of a 45 mm stapler and the jejunum is measured typically between 180 and 220 cm distal to the ligament of Treitz. Rutledge called the operation the "mini gastric bypass" and that term is still in wide use around the world today. There is no consensus regarding the measured length of the afferent loop distal to the ligament of Treitz.[126] Lengths of the afferent loop used to create the gastrojejunostomy are reported in a wide range from 180 cm to 250 cm to more than 300 cm depending on the age, eating habits, and comorbid conditions of the patient.[127] (Fig 12)

An alteration to the original procedure described in 2001 using a side-to-side (lateral-to-lateral) anastomosis between the jejunal loop and the gastric pouch was described by Carbajo in 2001 [128] (Fig. 13). This modification was designed specifically to minimize associated bile reflux which could theoretically occur between the afferent loop and the gastric pouch. Carbojo and Caballero described the operation as a "One Anastomosis Gastric Bypass" (OAGB) vs Rutledge's "mini gastric bypass". Their technique utilized this variation of the anastomosis and lengthened the distance between the Ligament of Treitz and the gastrojejunostomy to between 250 and 350 cm.

Most of the operative techniques preferred by individual surgeons performing SAGB are based on opinions and personal experience. Anastomotic techniques of the gastrojejunostomy vary between practices and there are no comparative studies evaluating these differences in operative technique with respect to complications and therapeutic outcomes. What is clear is that experience with laparoscopic suturing and anastomosis is essential when performing SAGB. Complications that can develop following a poorly performed anastomosis can result in intractable reflux, outlet obstruction, afferent loop syndrome, and bile leakage. The most common consensus agreement between various authors appears to be that the creation of a long, relatively narrow gastric tube which extends at or below the crow's foot of the lesser curve is the primary way to protect against duodeno-esophageal reflux from the biliopancreatic limb [129] (Fig. 14).

Surgeons who create a short pouch by beginning their dissections above the Crow's foot put their patients at risk of developing biliopancreatic reflux. The Mason loop gastric bypass was susceptible to large amounts of biliopancreatic reflux largely due to the combination of a short horizontal gastric combined with a loop reconstruction.[130] Our preferred technique in performing SAGB involves beginning the peri-gastric dissection 1 to 2 cm below the crow's foot (Fig. 14). Our preferred bougie is a 40 Fr and unlike a SG, the goal when creating the gastric pouch is to avoid hugging the bougie and to create a pouch in which the stapler is positioned a bit wider and lateral to the bougie. (Figs. 15–17)

REVERSAL OF SAGB

Postoperative complications following SAGB procedures are a rare but recognized reason for considering reversal of the procedure. Malnutrition, excessive weight loss, severe lower extremity edema, and motor deficits can present as a refractory malnutrition syndrome after any malabsorptive procedure. Genser and colleagues reported on a series of 2934 patients who had undergone MGB over a 10-year period.[131] Of the 2934 patients, 26 were identified as having developed severe and refractory malnutrition syndrome which responded to reversal of MGB to normal anatomy.

Reversal of SAGB can be accomplished via 2 approaches. Complete anatomic reversal requires simple transection of the gastrojejunostomy on the jejunal side of the anastomosis followed by creation of a gastro-gastrostomy between the gastric pouch and the gastric remnant. Alternatively, functional reversal of the SAGB can be accomplished by simply reconnecting the stomach to the gastric remnant while leaving the gastrojejunostomy intact.

BENEFITS OF A SINGLE ANASTOMOSIS PROCEDURE: AVOIDING MESENTERIC DEFECTS

Mesenteric defects are a reality with RYGB and are the etiology of internal hernia, bleeding, and bowel obstruction. Internal hernia following gastric bypass is the cause of intestinal obstruction in up to 41% of cases.[132] RYGB requires 2 intestinal anastomoses and the anastomosis between the biliopancreatic limb and the alimentary limb creates a potential site for internal hernia. Antecolic RYGB has 2 potential sites for internal hernia and retrocolic RYGB creates 3 mesenteric defects at risk for internal hernia. Herniation of bowel through any of these defects creates a surgical emergency. Closure of mesenteric defects can reduce the risk of internal hernia from 3.3% to 1.2% but cannot eliminate the risk.[133] SAGB eliminates 2 of the 3 potential sites of internal herniation seen in RYGB and as a result the potential for internal hernia is lower in SAGB than in RYGB. Internal hernia following SAGB is a rare complication.[132-140]

Decreasing the number of mesenteric defects associated with RYGB resulted in a decrease in the rate of internal hernia.[135,136] Morbidity and mortality from internal herniation was reduced, making RYGB a safer operation.[137,138] SAGB utilizes an antecolic loop and reduces the risk of internal hernia to only 1 potential site. The incidence of internal hernia following SAGB is lower than the risk associated with RYGB and the single defect between the mesentery of the efferent limb and the mesentery of the transverse colon is easily closed at the time of initial operation (Fig. 18).

The internal hernia rates following RYGB are well reported. Iannelli and colleagues reported findings of 11,918 patients following RYGB. Internal herniation was discovered in 300 patients for an internal hernia rate of 2.51%.[138] Internal herniation occurred at the level of the transverse colon in 69% of cases, at the level of the Petersons defect in 18% of cases and at the enteroenterostomy in 13% of cases. Internal hernia reported with SAGB are relatively rare compared to the incidence reported with RYGB and 82% of the cases of internal hernia with RYGB occur at defects not associated with SAGB.[140]

THE ISSUE OF BILE REFLUX

The most contentious, widely discussed topic surrounding SAGB has been the issue of potential bile reflux. The topic remains controversial and potential concerns regarding Barrett's esophagus and possible esophageal cancer continue to be debated. Despite the large number of SAGB publications and low reported incidence of reflux related revisions, this controversy continues to persist. There is a noticeable absence of any significant clinical data demonstrating progression to Barrett's following SAGB. The theoretical issue concerning bile reflux and SAGB has directly resulted in a delay of acceptance of single anastomosis bariatric procedures in the United States. Symptomatic GERD is unusual following SAGB and unlike SG, most authors report an improvement in GERD symptoms following SAGB.[141] Postoperative reflux related symptoms following SAGB can occur and may require revision to either RYGB or implementation of Braun's anastomosis distal to the gastrojejunostomy of the single anastomosis of the gastrojejunostomy.[142]

Despite positive published results regarding weight loss and improvement of obesity-related co-morbidities, the concerns surrounding biliary reflux gastritis and esophagitis following SAGB procedures remain.[143] Specifically, questions regarding the risk of esophageal cancer due to chronic biliary reflux is in many surgeons' opinion unanswered, as well as any role bile reflux might play in neoplastic progression.[144] Despite the more than 20 years of data following the introduction of OAGB/MGB operations, there are still no prospective or randomized data to suggest that there is any legitimate concern that gastroesophageal reflux following SAGB could progress to Barrett's esophagus or cancer.

OUTCOMES: Single Anastomosis Gastric Bypass vs. Sleeve Gastrostomy – POSTOPERATIVE REFLUX

Tolone and colleagues evaluated 15 patients (5 men/10 women) who had undergone SAGB.[145] At 1 year of follow-up, the median weight was 81.2 kg (72–111), the median BMI was 31 kg/m^2 (28-42), and EWL was 63% (56–69). The SAGB was compared to a control group of 25 adult patients who underwent SG. The SG group had similar clinical outcome results 1 year postoperatively. The median BMI had decreased to 34.7 kg/m^2 and patients experienced EWL of 56%. The outcomes, however, differed with respect to preoperative and postoperative reflux. In this study the SAGB group (15 patients) reported no symptoms of reflux prior to surgery. Following SAGB, none of the 15 patients reported reflux/GERD symptoms and there was no esophagitis or evidence of silent reflux or bile reflux on endoscopic examination. This was not the case with the group that underwent SG.

Using high-resolution impedance manometry and 24-hour pH-impedance monitoring, Tolone discovered a significant reduction in esophageal acid exposure as well as reflux episodes in all patients undergoing SAGB. The control group of patients undergoing SG developed an increase in both esophageal acid exposure and reflux episodes.

RESOLUTION OF COMORBIDITIES FOLLOWING SINGLE ANASTOMOSIS GASTRIC BYPASS

Major co-morbid conditions associated with morbid obesity include diabetes, hypertension, obstructive sleep apnea, hyperlipidemia, and joint pain. Improvement in all these co-morbid conditions comparable to that seen with RYGB has been demonstrated 5 years after SAGB. Bruzzi and colleagues published a series of 126 patients with 72% follow-up at 5 years.[146] Percent excess BMI lost was an impressive 71%. Complete remission of DM-2 occurred in 82% of patients. Fifty-two percent of patients with hypertension and 81% of patients with hyperlipidemia were able to stop medications at 5-year follow-up. Sleep apnea resolved in 50% of patients.

The largest UK study showing safety and acceptable results for metabolic syndrome and obesity co-morbid conditions following SAGB procedures was published in 2019.[147] The DM-2 remission rate was 83% and 70% at 1 and 3 years, respectively. Hypertension resolution was 61%, 58%, and 58% at 1, 2 and 3 years postoperatively. Ninety-nine percent of patients with sleep apnea improved symptomatically and went off their CPAP machines. The study reported on the outcomes of 527 SAGB patients.[147] Multiple additional authors report similar results with comorbidity resolution following laparoscopic SAGB.[146,148-151]

OUTCOME COMPARISON: ROUX-EN Y GASTRIC BYPASS VS. SLEEVE GASTROSTOMY VS. SINGLE ANASTOMOSIS GASTRIC BYPASS

Ruiz-Tovar and colleagues published one of the most recent prospective randomized series comparing long-term results between RYGB, SG, and SAGB.[152] This report adds to the already growing and well established body of literature reporting improved clinical results in comparison studies between SAGB and other established bariatric operations. Ruiz-Tovar prospectively randomized 600 patients undergoing primary bariatric operations into 3 groups: SG, RYGB, and SAGB. Five-year follow-up in the 3 groups was 91%, 92%, and 90%, respectively. Significantly greater excess BMI loss was achieved in the SAGB group versus that achieved in the SG and RYGB groups at 5-year follow-up. Similarly, the SAGB group achieved greater remission of DM-2, hypertension, and dyslipidemia than RYGB or SG. The prospective results confirm findings observed with previous studies demonstrating the safety and efficacy of the SAGB operations.

SUMMARY

SAGB/MGB remains a polarizing bariatric operation. There are now thousands of procedures published in the world's literature yet there remain concerns surrounding the single anastomosis approach to gastric operations. Bile reflux continues to persist as a theoretical concern based largely on rat and animal models.[153,154] In the more than 2 decades that SAGB operations have evolved, the technical simplicity of the operation, short learning curve, standardized approach, and relative ease with which the operation can be reversed or revised has convinced many surgeons to advocate for this operation. SAGB procedures are at least comparable to RYGB in the treatment of obesity. The single anastomosis approach to gastric bypass can be performed in less time than RYGB, utilizes less resources, and has a very low complication rate. The controversy, debate, and discussion surrounding SAGB will continue, perhaps one day resulting in more widespread adoption among American surgeons as a safer alternative to RYGB.

SINGLE ANASTOMOSIS DUODENO-ILEOSTOMY WITH SLEEVE (SADI-S)

The search for the ideal bariatric procedure has remained elusive and an area of diverse opinion and limited consensus. There are many reasons. To begin, bariatric surgery is a controlled abnormality and there are evolutionary reasons that the stomach is kidney shaped and can relax to receive a food bolus prior to a rise in intra-gastric pressure. Additionally, procedures that prospered were designed based on observations of weight loss following gastrectomy or intestinal resections for medical reasons. Recently, there has been a better understanding regarding the effects of bariatric surgical procedures. Besides mechanical factors such as limiting stomach size and reducing the absorptive capacity of the small bowel, surgical manipulation alters the production of gut hormones, the gut-brain neurologic connections, and interactions throughout the body. Fat is not a dormant storage tank of excess energy, but an endocrine organ that sends signals to all organs. An additional barrier for designing the ideal bariatric procedure is that there are no uniform metrics to measure success. Procedures that offer the greatest weight loss and lowest recidivism also have the highest rates of anemia, risk of bone loss, and micronutrient deficiency. Furthermore, even procedures labeled with the same name can be vastly different. A RYGB can have alimentary limbs, enzymatic limbs, and common channels that vary greatly.

The purpose of this section is to explain the physiologic rationale and the advantages of a titrated single anastomosis duodenal switch (SADS) or, as called by many, SADI-S (Single

Anastomosis Duodeno-ileostomy with Sleeve). We have been reluctant to use the I, as the ileum is the very distal part of the intestine. To date, the majority of reported cases have utilized either a 250 cm (Spain) or 300 cm (United States, Cottam and Roslin) efferent limb.[155-161] As total intestinal length is often 6 meters, in many the attachment is in the jejunum. Additionally the ideal length that would optimize weight loss without increasing micronutrient deficiency remains to be determined.

Duodenal switch (DS) procedures have represented a minority of bariatric procedures for several reasons. A major cause is lack of familiarity and concern about dissecting in the area of the pancreas and duodenum. Another major factor is the perception that the classic DS is equated to malabsorption. It is important that physicians realize that the length of bowel limbs determines the degree of malabsorption, not the post-pyloric reconstruction. In theory, preservation of the pylorus regulates gastric emptying, thus limiting rapid emptying into the intestine. Therefore, a distal gastric bypass that empties into the small bowel is more likely to provoke diarrhea than a DS with similar bowel lengths.

Whereas the attraction for many to DS procedures is the greater average weight loss, lower recidivism, and better resolution of DM-2, our journey to these procedures was different. An early area of interest was weight regain following gastric bypass. An attractive approach was to reduce the gastric outlet with an early endoscopic suturing device, the Bard Endocinch. Our early results, and the work of Dr. Christopher Thompson led to the RESTORE trial. During that time, we had a chance to interview multiple trial enrollees. They reported intra-meal hunger and fatigue following the ingestion of carbohydrates. Essentially, they were describing reactive hypoglycemia. This was paradoxical as the teaching at that time was that RYGB was the preferential procedure for sweet eaters as the symptoms of dumping would deter carbohydrate ingestion. This led to a study where we assessed the impact of glucose challenge on gastric bypass. It was demonstrated that abnormal glucose tolerance was common following RYGB. Although average glucose was normal, patients became hyper- and hypoglycemic. These results have now been confirmed by continuous glucose monitoring. Rather than deterring carbohydrate ingestion, those with weight gain would often eat to relieve fatigue and low sugar only to have the cycle repeat.

As a parallel, the dietary causes of obesity were undergoing transition. When familiar bariatric procedures were designed, many believed that fat was the culprit. After all, the heart health hypothesis suggested that avoidance of cholesterol and fat limited heart disease. Fat was more calorically dense. Since fat was considered the enemy, short common channels that prevented the majority of fat absorption were logical. Fast forward to today and our current understanding. Many believe that a major factor for rising obesity is when fat consumption was reduced, it was replaced with an abundance of simple carbohydrates that provoke insulin secretion. The advice of most weight loss dieticians is to eat foods that have a low glycemic index or load. This minimizes insulin secretion and glucose fluctuations. Other current trends include paleo diets, ketogenic diets, and intermittent fasting. All are designed to lower glucose and prevent insulin spikes.

The summation is whether an operation that preserves the pyloric valve to theoretically control gastric emptying and limit glucose fluctuations, and lengthens common channel length to avoid severe fat malabsorption would improve bariatric outcome. Our design of SADS is based on these observations.

TECHNICAL DETAILS

The SADS consists of a gastric and intestinal component. A vertical gastrectomy is created similar to primary LSG. However, the sleeve is generally larger. In the United States we have recommended a 40 to 44 Fr bougie as a guide, at a minimum. In Spain, a 54 Fr bougie is used. The point is that the resulting pouch allows for adequate intake to handle the intestinal bypass and not be so restrictive to prevent adequate protein intake. There are several potential benefits for a larger sleeve. Recent data has shown that leak rates for sleeves that are larger are lower. The risk of stricture should also be reduced. Additionally, the wider diameter may minimize GERD symptoms which are becoming a significant issue following primary LSG.

The duodenum is then divided 3 to 4 cm past the pyloric valve. It is this portion of the procedure that causes trepidation for many surgeons. Although, with proper training and in patients without previous surgery to this area, this is truly a rather simple dissection. We recommend to continue the dissection along the greater curvature of the stomach, coming past the pyloric valve. All posterior attachments of the stomach should be divided and the lesser sac cleanly entered. The pylorus is elevated and just above the gastroduodenal artery, the duodenum is encircled (Fig. 19).

The intestinal component consists of locating the ileo-cecal valve and measuring 2.5 to 3 m of intestine. This is attached to the post-pyloric duodenum (Fig. 20).

A major question for those reading is whether there is need for another bariatric procedure and what that procedure will be. The choice of bariatric procedure has always been an area of debate. Prior to the laparoscopic era, the debate was RYGB vs vertical banded gastroplasty (VBG). Advocates for VBG argued that bypassing the proximal intestine would be associated with greater likelihood of anemia and bone hunger. Alternatively, the RYGB supporters highlighted greater weight loss and reduced recidivism. With the advent of laparoscopic RYGB in 1994 by Wittgrove and Clark,[162] along with articles highlighting patient dissatisfaction with VBG,[163] RYGB became the gold standard bariatric surgical procedure. As a result, in many minds there are already appropriate surgical options. If a gastric only procedure is preferred, SG is the choice. For those that believe that adding the intestine improves long-term weight loss and metabolic control, a RYGB meets that need.

Proponents of SADS believe that there are many advantages compared to RYGB. The differences include resection of the entire fundus and no remnant, preservation of the pyloric valve, and a single post pyloric attachment. These alterations highlight the critical questions to be analyzed to determine what the best design for a bariatric procedure is.

1) should the remnant be resected or preserved?
2) what are the advantages or disadvantages of attaching the intestine above or beneath the pyloric valve?
3) is there any advantage to a Roux reconstruction as compared to a loop or Billroth II? As a corollary, is there a difference above or below the pyloric valve?

Pouch Resection

The advantages of pouch resection include the ability to preserve the pyloric valve, perform a pouch that resembles a SG, and reduce acid secretion and marginal ulcer formation. DS, SADS, and SIPS reports highlight an absence of multiple anastomotic complications such as ulcer formation and strictures. The post-pyloric position that potentially reduces acid and the impact of resection are possible reasons for these results. Additionally, removing the fundus is associated with the resection of the secretion of certain hunger hormones such as ghrelin.

A major disadvantage of resection is the taking of the blood supply of the greater curvature of the stomach. In VSG there have been reports of new onset GERD and Barrett's esophagus.[164] Although first line therapy is ablation, if there was progression to carcinoma, the stomach could no longer be a conduit for reconstruction.

It is interesting to point out that VSG is part of DS. There are no reports of increased risk of esophageal cancer following DS with long-term follow-up from multiple centers. An important difference is potentially that these sleeves were intentionally of larger diameter than primary VSG. As a result, there is a lower pressure gradient and this difference may be important. It is conceivable that a larger sleeve with an intestinal bypass may be a better long-term option for more than weight loss. Another area that requires further investigation is the significance of bile diversion. In DS, the bile is diverted. With VSG, a certain amount of bile refluxes above the pylorus. Although there was little initial concern, increased reports of de novo Barrett's esophagus are concerning.

If there is a resection and preservation of the pylorus, the intragastric pressure is increased. In comparison, a gastrojejunostomy attaches the stomach to the low-pressure small bowel, and therefore reduces reflux symptoms. Whether a high-or low-pressure system is best is an unanswered question. Certainly, for those with severe reflux symptoms, a low-pressure system is preferable. In contrast, a high-pressure system may be better for satiety and lasting fullness.

Is The Pylorus Important?

The function of the pylorus is to control the emptying of solid food. Thus, logic would dictate that if the goal is to allow food to remain in the stomach and prevent rapid hunger and have controlled release of solids, then preserving the pylorus is beneficial. The issue is that how the pylorus functions following resection of the fundus and part of the antrum is difficult to decipher. Making things more complex is the suggestion that rapid, as opposed to delayed, emptying activates intestinal gut peptides.

For many years, it has been suggested that dumping is a beneficial component for success following gastric bypass. It is argued that the negative symptoms provoked following the intake of efficiently absorbed carbohydrates would deter consumption of these foods that have been linked to obesity. To date, there has never been a study that has correlated weight loss and dumping. In contrast, the opposite can also be argued. RYGB allows for the rapid entry of food from the small pouch into the intestine. When foods are eaten that are easy to absorb such as carbohydrates and alcohol, they rapidly enter the bloodstream. When the source is a sugar or starchy vegetable, there is a rapid rise in glucose level, precipitating a rapid rise in insulin, followed by a rapid decline. As a result, RYGB increases glucose variability.[165] Since the pylorus regulates gastric emptying, recent research has demonstrated that there is less of this variability following DS and SADS procedures. The clinical importance remains to be proven. However, a primary goal of medical weight loss is preventing glucose fluctuations by encouraging the replacement of high glycemic index or load foods with alternatives that are more complex to absorb and less efficient in causing a glucose rise.

Another potential advantage is that preserving the pyloric valve allows for a greater proportion of the intestine to be bypassed, without the risk of diarrhea. Although most believe that DS or SADS result in a greater amount of malabsorption than RYGB, the principle reason is that more intestine is bypassed in these procedures. Although there is great variation in limb lengths amongst surgeons, the majority of RYGB procedures performed have short biliopancreatic limbs (50 to 100 cm) and slightly longer Roux limbs (75 -150 cm). In contrast, for DS and SADS the BP limb is often more than 3 m. That means far less bowel comes into contact with food. This probably accounts for the greater weight loss. It is hypothesized that preservation of the pylorus allows for this and alleviates the risk of too frequent bowel movements. The point is that cm to cm preservation of the pylorus probably reduces malabsorption.

Another extremely important factor is data suggesting a reduced risk of marginal ulcer and anastomotic stricture. Pooled data from many contributors who have performed SADS procedures demonstrate that these complications are exceedingly rare to absent. This information cannot be understated. The lifetime risk, especially of marginal ulcer following RYGB has been estimated to be as high as 5% to 10 %. Although generally this can be treated with medical therapy and the avoidance of caustic materials, complications such as bleeding, perforation, and intractable pain are not uncommon. Again, there is no single mechanism that can account for these results. The longitudinal resection of the stomach reduces acid production. Additionally, the preservation of the small duodenal cuff secreting bicarbonate acts as a protective buffer

Antagonists would state that the role of the pylorus when other aspects of the GI tract have been surgically manipulated is unknown and relatively inconsequential. They highlight the minimal differences seen in pyloric sparring Whipple procedures and the high number of RYGB and SAGB procedures that have bypassed the pylorus with successful outcomes. In our opinion, although clearly the longitudinal gastrectomy has an impact on gastric emptying, an innervated pyloric valve still contributes a regulatory component.

Single or Double?

Perhaps the most contentious debate is whether it is appropriate to abandon the Roux construction and perform a loop or single anastomosis. Although the majority of bariatric surgeons feel that the Roux limits bile gastritis, it was actually added to the gastric bypass and the biliopancreatic diversion to potentially reduce the rate of marginal ulceration. Several important historical points are required. First, not only were proton pump inhibitors not available, but histamine 2 blockers such as Tagamet and Pepcid were not yet on the market. Additionally, rather than the longitudinal pouches of today that promote forward flow and exclude the fundus, the staple lines were horizontal. Finally, rather than longer biliopancreatic limbs placed in a dependent position, they were often proximal and attached to the proximal fundus.

For multiple reasons the Roux-en-Y became standard for gastric bypass. Its use in duodenal switch is also interesting. The duodenal switch was first described as a treatment for bile reflux gastritis by DeMeester.[166] It was adopted for bariatric surgery by Hess who added a longitudinal gastrectomy.[167] What is interesting about SADS is that it in all probability reduces susceptibility to bile reflux more than VSG or normal anatomy. Bile enters the second portion of the duodenum and frequently will reflux into the stomach. With single anastomosis DS, bile must travel down several meters of small bowel where it is diluted and partially absorbed before coming to the area of the anastomosis. There, the bile would have to reflux through the anastomosis and through the pylorus into the pouch, in lieu of traveling down the small bowel that has normal peristalsis and has not had the enteric pacemaker divided. Thus, the concern that bile reflux could cause gastric dysplasia and esophageal cancer is especially remote as compared to SAGB.

Several other potential advantages exist for single anastomosis variations. There is only 1 anastomosis that can leak, stricture, or obstruct. The number of variables is reduced. No additional mesenteric defect is created and the small bowel is not divided cutting the enteric pacemaker. Although each of these things may seem minor it is our belief that collectively, their importance is being overlooked. In 8 years of clinical performance of SIPS or SADS we have yet to admit a patient with small bowel obstruction as a primary case. Midgut volvulus following RYGB is a tragic complication.[168] Although still a possibility (the first case in which a Peterson's hernia was described was following a Billroth II reconstruction following a gastrectomy), the incidence is reduced and minimized.[169]

Another potential advantage of the Roux is that it allows for a longer alimentary limb and shorter common channel. Advocates for classic DS or BPD feel that this is essential for lasting weight loss. To review, sugars are easily absorbed in the alimentary limb, as are most proteins. The common channel is needed for fat absorption and perhaps certain complex starches. Again, a historical perspective is important. These operations were designed when the majority felt that fat was the culprit causing obesity. Few believe that fat is the major cause of obesity today. It is carbohydrates that are easily absorbed in the Roux limb and stimulate insulin production. Furthermore, a common concern with DS is that there will be frequent bowel movements and nutritional deficiencies. Logic would suggest that lengthening the common channel would alleviate some of these concerns. Short common channels also can lead to subtle deficiencies in fatty acids that are rarely measured. There can be subtle central nervous system changes that are not clinically apparent. Therefore, do we really want or need a short common channel? In the days that BPD and DS were first described, common channels of 50 to 75 cm were standard; today, 100 cm is the shortest common channel suggested by most authorities.

In gastric bypass procedures, single anastomosis versions have been far more popular outside the United States. In the United States, they have been strongly discouraged. It is possible that many of these strong viewpoints are based on an original proponent of the procedure who aggressively marketed it as a mini gastric bypass.[170] At this point it is hard not to account for the favorable data reported throughout the world. The single randomized trial demonstrated a small advantage for the single anastomosis version as compared to the Roux. In the single anastomosis versions, weight loss appears to be greater, incidence of small bowel obstruction lower, and incidence of diarrhea higher. To date, there have not been reports of an increased incidence of gastric cancers. Recently, IFSO position statements endorsed single anastomosis versions of gastric bypass and duodenal switch.

For single anastomosis DS, the biggest concern is that it will not be as robust or effective as the Roux version. To counter, it has already shown 30% greater weight loss than VSG which is the most popular weight loss procedure in the world. Presently, there has been considerable data published from the United States and Europe that show that the early and intermediate results demonstrate fewer anastomotic and small bowel complications than RYGB, with the suggestion of greater weight loss.[161] What is clearly apparent from both the US and international experience is that there has been no sentinel issue. There is certainly no medical evidence that a Roux configuration is safer. In general, many are confusing familiarity and tradition with proven and evidence-based medicine. A randomized trial would require a countless number of patients over an extended period and still may not provide an answer.

Intestinal Length

Perhaps this is the area with the least objective information. First, there is probably no precise method to measure bowel. Additionally, at times bowel is dilated and other times collapsed. Furthermore, it is not truly understood whether absolute length is more important, or the percentage of bowel bypassed. Interestingly, in the vast majority of RYGB procedures performed, the biliopancreatic limb and Roux limb are measured. This means that the common channel and the total length of bowel that is exposed to food is variable.

Despite these limitations there are historical precedents. The majority of Roux BPD or DS operations have suggested an alimentary to limb distance of 150 cm. Less attention has been given to the BP limb. Yet, weight loss varies directly with the length of the BP limb. This makes complete sense as this is the portion of bowel not exposed to food. Operations with longer BP segments, DS, SADS, SIPS, SADI-S, SAGB (200 cm afferent limb) have higher average weight loss. Often in RYGB, the BP limb is made short and the Roux longer. Longer BP limbs may potentially improve weight loss and metabolic outcomes.

Besides diversity of opinion about the ideal limb length, the total length of the bowel is highly variable and can range from 6 to 10 m. There is no technique to accurately measure bowel length. Another disputable issue is whether limb lengths should be proportional to the total bowel length and vary in each individual.

There is little definitive science to guide us. Brolin demonstrated that expansion of the Roux limb shows slightly more rapid weight loss in the super obese, but with time, similar weight loss.[171] Torres reported that weight loss varies directly with the BP limb.[172] Lebel and colleagues have recently reported similar weight loss with a tendency for lower micronutrient deficiencies with a 200 cm common channel in DS, as opposed to 100 cm.[173] Sanchez and Torres initially performed SADI with a 200 cm efferent limb.[174] Because of a high incidence of diarrhea, they increased to 250 cm with excellent long-term results. For SIPS, Cottam and Roslin have suggested a slightly smaller sleeve with a 300 cm efferent limb [175] (Fig. 21). Weight loss seems identical to SADI. In a multicenter registry awaiting publication, there was a 37% TBWL at 1 year with no protein deficiency and increasing levels of vitamin A and D.

Although there is no consensus, several rules are apparent. Total alimentary limb length should never be less than 250 cm, including the Roux limb and common channel. Common channels shorter than 100 cm are risky. Furthermore, the results reported above make us question the need for significant fat malabsorption. Stimulation of the distal gut resulting in physiologic changes is probably more important than the mechanical impact of calories passing into the fecal stream.

Staged vs Single Procedures

An increasing school of thought is to start with VSG on all patients who do not have Barrett's esophagus or severe reflux and convert to another procedure such as SADS only for inadequate weight loss, weight regain, or ineffective resolution of co-morbid conditions. It is argued that there is less subjection to the risks of vitamin deficiency. Additionally, the interval time period allows for assessment of behavior and determination of patients most likely to comply with supplement regimens. Finally, there are several publications that suggested similar results with staging and the weight loss appears to be additive.

Alternatively, one-stage advocates would state their ability to perform these procedures with short operative times and little to no increased risk. The concept of staged surgery is potentially more attractive than the reality, where it is difficult to obtain insurance approval. Furthermore, many policies are instituting one procedure per life benefits. As a result, many patients may not get the therapy they require. This can be most difficult for patients who regain weight, but when the subsequent BMI is less than 40. Furthermore, it ignores data which have told us for which patients VSG will be ineffective. The vast majority of patients with BMI greater than 50 prior to VSG will still have class III obesity 3 to 5 years following surgery.

It is our practice pattern to perform SADS in the majority of cases in a single stage. Our operative times are generally less than 90 minutes and the vast majority of patients are discharged on the first postoperative day. Rather than intentionally staging, our philosophy is to preform primary VSG in patients that we have a strong reluctance to add an intestinal component such as patients with extensive prior lower abdominal surgery, indigent patients living in public shelters with poor access to supplements, and those taking multiple psychiatric medications. We believe that indications shift with level of experience and comfort with the procedure.

EXPECTED RESULTS

At this point the weight loss results from the multiple centers in the United States and Spain that have been performing this procedure have been remarkably consistent. The multi-center US trial demonstrated an average weight loss of 21 BMI units at 1 year. Maximum weight loss is approximately at 14 months. In a recent study that we are preparing for publication, there is a 30% increase in weight loss as compared to LSG. Interestingly, in the majority of patients there is rise in fat soluble vitamin levels. What has been most striking is the low level of medium-term complications. Of course there can be peri-operative leaks and GI bleeding; however, bowel obstructions, strictures, and ulcers have been very rarely encountered. In our facility, the most common issue requiring medical attention is frequent diarrhea. Interestingly, the rate that we have encountered is 1% to 2% and the majority of patients have 1 to 3 bowel movements daily. When we have had to correct, the bowel has been measured correctly. The exact cause is unknown and can be an acquired hypersensitivity to an agent in the diet that we do not diagnose or possibly a degree of underlying pancreatic insufficiency. Most often, nutritional parameters can be maintained and the indication for surgery is quality of life. These few cases have been handled by moving the loop more proximally. In general, this leads to marked improvement, but still more frequent bowel movements than average. This again indicates an underlying mechanism that is unrecognized.

WHERE ARE WE GOING AND WHAT DOES THIS MEAN?

In the last 5 years we have seen the disappearance of the lap band, a significant decline in RYGB, and VSG becoming the most popular procedure worldwide. A lesson to remember is that the stomach gets weight off and the intestine keeps it off. As a result, weight loss failures and weight regain are becoming an increasingly common clinical issue. Furthermore, for those with the highest BMI's and super morbid obesity, the VSG may not be adequate long-term therapy. This means that there will be an increasing need for malabsorptive procedures that involve the intestine.

It is estimated that RYGB now represents only 17% of the total of primary bariatric procedures performed. Historically, once a procedure declines it generally means that public and physician perception has changed and there rarely is recovery. Thus, the question is what comes next. There are many possibilities. The most likely circumstance is that single anastomotic procedures such as SAGB or SADS will rise in popularity. The goal of this section is to highlight why we believe that SADS is the best option. It has effective weight loss and the post-pyloric construction reduces glucose variability and minimizes anastomotic issues. Lengthening of the common channel mitigates against frequent bowel movements and nutrient deficiencies. However, it does require operating in an area less familiar for many surgeons and most commonly a hand sewn anastomosis. SAGB will be simpler for many to adapt. Unfortunately, it will have a higher risk of marginal ulcer and a much greater risk of the negative impact of bile reflux gastritis. Although not supported by clinical data, studies in laboratory animals suggest an increased risk of gastric cancer. Perhaps another possibility will be that the robot will allow a fresh new look at RYGB and new instrumentation combined with elongating the BP limb will improve results and offer a new-age perception.

It is our contention that for multiple physiologic reasons, SADS offers the best approach. Further work needs to be done to find the ideal intestinal length and whether this should be altered in different patients. Currently, the ASMBS labeling the procedure investigational and suggesting IRB approval for its performance is curtailing growth. In our opinion this is most unfortunate. Countless surgeons have attended courses and seminars and have strong interest. Initially, they hope to convert VSG patients that require increased therapy to the procedure. It is our expectation that as surgeons become more comfortable that this will become a commonly performed primary procedure. With RYGB numbers, the era of single anastomosis cases is ready to commence. SADS will be a key player in the next 5 years.

ENDOSCOPIC MANAGEMENT OF COMPLICATIONS

INTRODUCTION

Alongside the increasing incidence of obesity, there has also been an increase in bariatric surgical procedures performed annually, with an estimated 216,000 bariatric procedures performed in 2016.[176] These procedures have generally demonstrated a reliable safety profile and are largely being performed in experienced centers, however bariatric surgical procedures place patients at risk for several perioperative and delayed complications. These have a wide range in both timing and severity from the acute endoluminal staple-line bleed to the chronic fistula after an anastomotic leak. Where appropriate, flexible endoscopy has emerged as a key management tool in the arsenal of the surgical endoscopist to prevent, diagnose, and treat many of the complications observed in bariatric procedures. It should be noted that many advocate for the routine use of intraoperative endoscopy in bariatric procedures in an effort to reduce the incidence of complications and reintervention, however practice patterns continue to vary.[177] In the following sections, we outline the endoscopic management of some of the most common complications after laparoscopic AGB, SG, and RYGB.

BLEEDING

Acute bleeding after bariatric procedures has a reported incidence of 0.1% after AGB, 0% to 8% after SG, and 1% to 5% after RYGB.[178] General principles of initial management parallel those of all GI bleeds, with prompt resuscitation, reversal of potential causes, and localization. Nonoperative management is feasible in most cases for hemodynamically stable patients. Upper endoscopy can be used to determine if the source is endoluminal and potentially endoscopically treatable. Manifestations often include hematochezia, melena, and even obstruction-like symptoms. Although infrequent, endoluminal bleeding sites are most commonly found at the gastric staple line in SG. After RYGB, the most common site of endoluminal bleeding is at the gastrojejunostomy staple line, however other sources include the gastric pouch staple line, the jejunojejunostomy, and from the gastric remnant. Once encountered endoscopically, endoluminal bleeding sources can be treated by standard hemostatic methods including bipolar energy application, mechanical endoscopic hemostatic clips (Fig. 22), and epinephrine injection, with up to 80% success rate.[179] Double-balloon endoscopy (DBE) may be employed for deep endoscopic access to the gastric remnant or the jejunojejunostomy, although data are lacking for the efficacy of these methods. Although an uncommon presentation, marginal ulceration after RYGB (Fig. 23) may manifest with bleeding and successful endoscopic suturing of an early bleeding ulcer has been described.[180]

STRICTURE OR STENOSIS

Stricture devlops in 3.7% to 7.8% of cases following RYGB and is most commonly found at the gastrojejunostomy.[181] Endoscopy is a key diagnostic modality and although no formal definition exists, most surgical endoscopists define the presence of a stricture by the inability to pass a standard diameter endoscope (9.5 mm) in the setting of dysphagia and other common symptoms. Although rigid dilation with bougies has demonstrated efficacy, endoscopic balloon dilation is considered by many the preferred treatment modality for stricture after reversible causes have been addressed. Through-the-scope (TTS) balloon dilation (Fig. 24) allows for the exertion of radial forces on the stenotic site under direct visualization, with high success rates and acceptably low rates of perforation (2%-3%).[182,183] Most patients respond to a single dilation session, however up to 13% of cases can require 4 to 5 dilation sessions and can be treated safely with injected steroids at the site in an effort to reduce post-dilation fibrosis.[181] Severely refractory cases can be managed with endoscopic stent placement, however due to the anatomy of the small gastric pouch, these cases will often require stenting of the lower esophageal sphincter leading to severe symptoms and potential for complications such as stent migration.[184]

Symptomatic stenosis can also be seen following SG, usually secondary to a mechanical and functional narrowing at the level of the incisura angularis. Patients with a short segment stenosis may be somewhat responsive to continuous radial expansion (CRE) TTS balloon dilation, however Zundel and colleagues have described successful treatment of these patients with pneumatic dilation.[185] We believe successful therapy often requires pneumatic dilation and possible early stenting. This allows for realignment of the stomach and remodeling of the fibrotic region at the incisura. A review of 857 SG patients found that 26 (3.0%) patients developed a subsequent symptomatic stenosis (most at the incisura) and reported successful endoscopic treatment in all cases using CRE balloons with pneumatic dilation and/or temporary self-expandable metal stent (SEMS) placement in refractory cases.[186]

LEAK

Perhaps the most feared complication following bariatric procedures involves leakage from the alimentary tract, typically from an anastomosis or staple line. Large efforts have been undertaken to understand patient and technical factors that may predispose patients to this rare but morbid and costly complication. Endoscopy plays a valuable role in the diagnosis and treatment of these leaks. It allows for the delineation of the unique anatomy while also determining the optimal subsequent therapeutic plan.

Many different techniques have been described to manage post RYGB leaks endoscopically. In most cases following RYGB, after initiation of conservative therapies, early endoscopy may allow for correction of distal strictures that can contribute to leak or failure to heal. Leaks after RYGB are most commonly encountered at the gastrojejunostomy anastomosis, followed by the gastric pouch and jejunojejunal anastomosis.[187] Principles of therapy regardless of approach include resuscitation, correction of potential causes, drainage (internally is preferred), diversion when necessary, and distal enteral access if needed. Covered or partially covered stents have been widely used with success rates ranging from 65% to 95%, however in delayed cases with a formed abscess cavity, either internal or external drainage is necessary.[188] One case series found improved closure results when leaks were managed endoscopically with over-the-scope clips (OTSC, Fig. 25) and covered stents, compared to those treated surgically with reoperation.[189] Many stent types and deployment systems exist, however the most commonly used stents after bariatric surgery leak are the partially or fully covered self-expanding metal stents.[190] Endoscopic closure has also been described using fibrin sealants and OTSC with mixed results.[188] Trans-fistulary endoscopic debridements have been reported, as well as treatment with endoluminal vacuum sponge therapy. [191,192]

After SG, leaks are encountered in less than 0.5% of non-revisional cases, however when present they are almost always encountered at the proximal sleeve staple line near the gastroesophageal junction.[193] This phenomenon is poorly understood but is proposed to be due to elevated intraluminal pressure developed proximal to stenosis at the incisura angularis. Although many advocate for surgical management of early leaks (within 4 days), endoscopic techniques are commonly employed for delayed leaks. Gagner and colleagues have proposed an algorithm based on leaking site size, where stents are utilized in large leaks, while those with fistulous sites smaller than 10 mm are managed with double-pigtail internal drainage of cavities (Fig. 26) for 6 to 8 weeks followed by OTSC (Ovesco Endoscopy, Germany) if needed.[194] Some centers have employed the use of endoluminal vacuum therapy using custom fashioned sponges attached to nasogastric tubing (Fig. 27) with successful resolution of sleeve leaks.[195]

FISTULA

Fistulous connections from upper GI bariatric surgical sites to many different locations have been described, representing another category of chronic complications that present a challenge to the surgical endoscopist. Gastrogastric fistula (GGF) following RYGB has a diverse range of proposed etiologies including technical failures, anastomotic leaks, foreign body erosion, and other tissue injuries.[196] At this time, successful endoscopic closure using fibrin sealants, endoscopic suturing, and endoscopic clips have been reported in small series, however high long-term recurrence and complication rates hinder the routine use of endoscopy to definitively manage GGFs. Gastrocutaneous, gastropleural, and gastrocolic fistulas after SG have complex courses often requiring surgical reintervention with interposed omentum, however internal or external drainage along with endoscopic stenting plays an important role in initial management.[193] Campos and colleagues reported successful management of 14 of 15 (93.3%) gastrobronchial fistulas using multiple endoscopic sessions using balloon dilation, stricturotomy, or septoplasty (Fig. 28), endoscopic stent, or fibrin glue.[197]

FOREIGN BODY

Various foreign materials have been used in the history of bariatric surgery, primarily for gastric restriction, with the most common being the AGB. Although it is now less commonly performed, hundreds of thousands of AGBs have been inserted worldwide in the past couple decades.[198] The most clinically significant complication arising from these foreign body insertions involves band erosion in to the gastric wall (Fig. 29), usually after band slippage. Endoscopic removal of these intragastric erosions have been described by many centers, typically utilizing a combination of polypectomy snares, endo-shears, biopsy forceps, and even specifically designed endoscopic gastric band cutters.[198] Although primary laparoscopic management is also commonly performed, the endoscopic treatment is viable primarily due to the natural capsule formed surrounding the band which allows gastric contents to be contained.

As with the AGB, non-adjustable banding materials have been used in weight loss procedures which can also lead to erosion. Silastic bands, for example, are technically easier to remove due to the lack of incorporation with surrounding tissues that is seen in other materials such as marlex mesh. Additional challenges arise when gastric tissue has incorporated into the foreign body, however techniques such as argon beam coagulation have been used to divide remaining gastric tissue.[199] Other miscellaneous foreign bodies that can be managed endoscopically include suture erosion, or staple line reinforcement erosion, which can be managed similarly.

CONCLUSION

Endoscopy continues to play a vital role in the management of the obese patient. General endoscopic management principles must be applied to any surgical patient when dealing with foreign bodies, obstructions, early and late leaks, and bleeding. Complications can often be successfully managed non-operatively and therapeutic endoscopic techniques continue to aid and evolve in this area.

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FIGURE LEGENDS

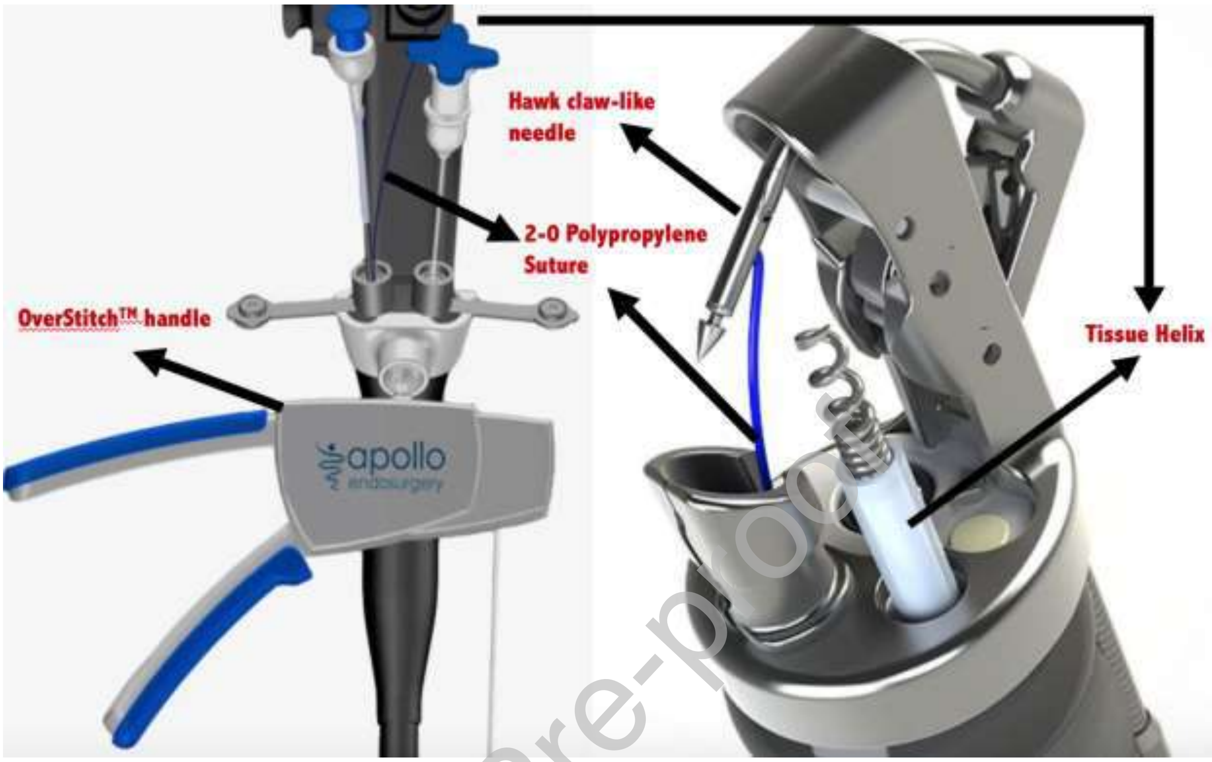

Fig 1. Details of the Apollo OverStitch™ device. Available from: https://apolloendo.com/overstitch/

Fig 2. Single-use cinch that provides knotless fixation of the suture. Available from: www.overstitch.com

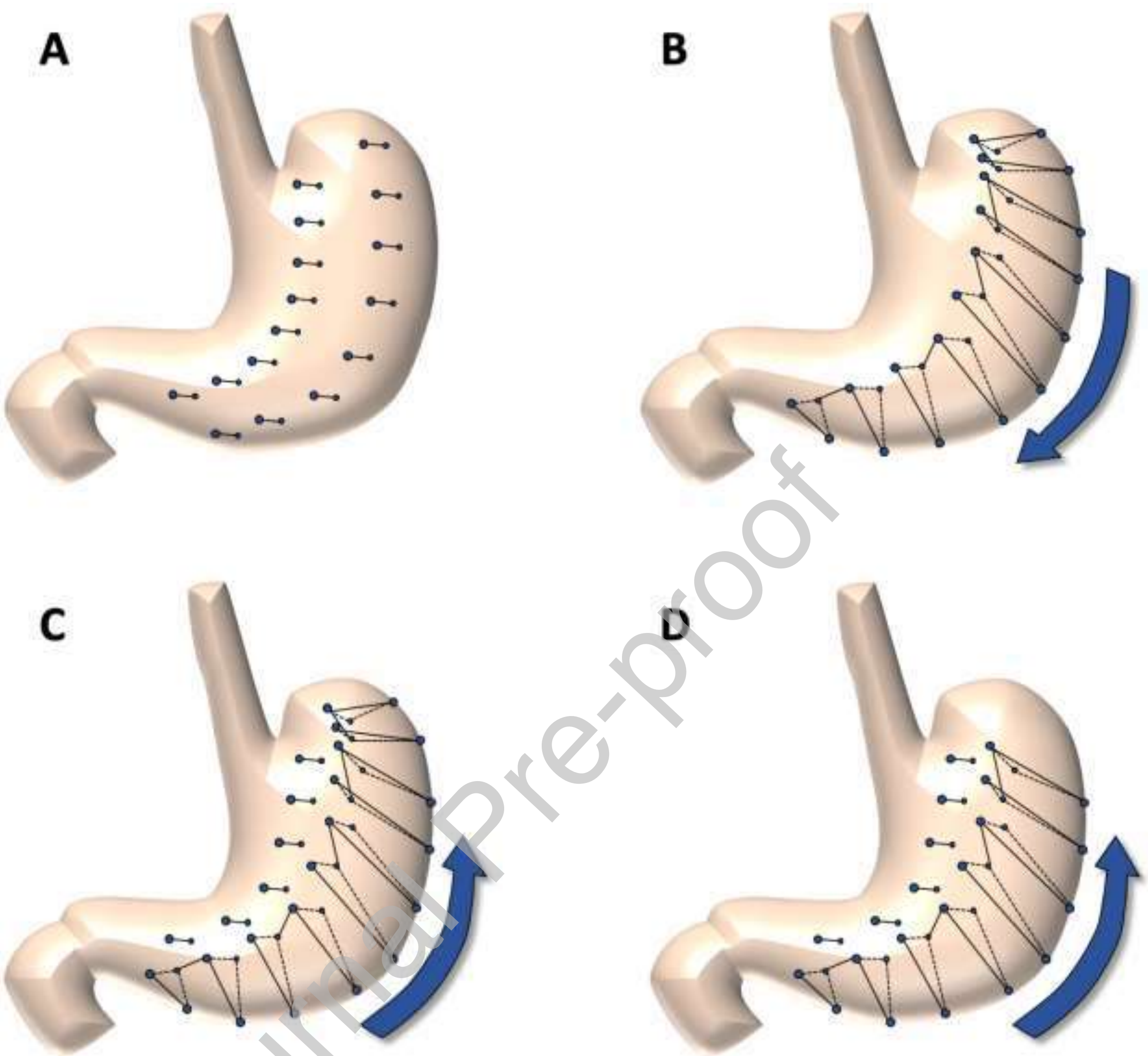

Fig 3. Schematics of the refinement over time of the ESG technique. A – First description by Abu Dayehh et al.[47]; B – Technique of the initial procedures from the multi-center series published by Kumar N et al.[48]; C and D – Progressive technical improvements, namely adding a second row of interrupted stitches and not suturing the fundus, to reach the current technique (D).

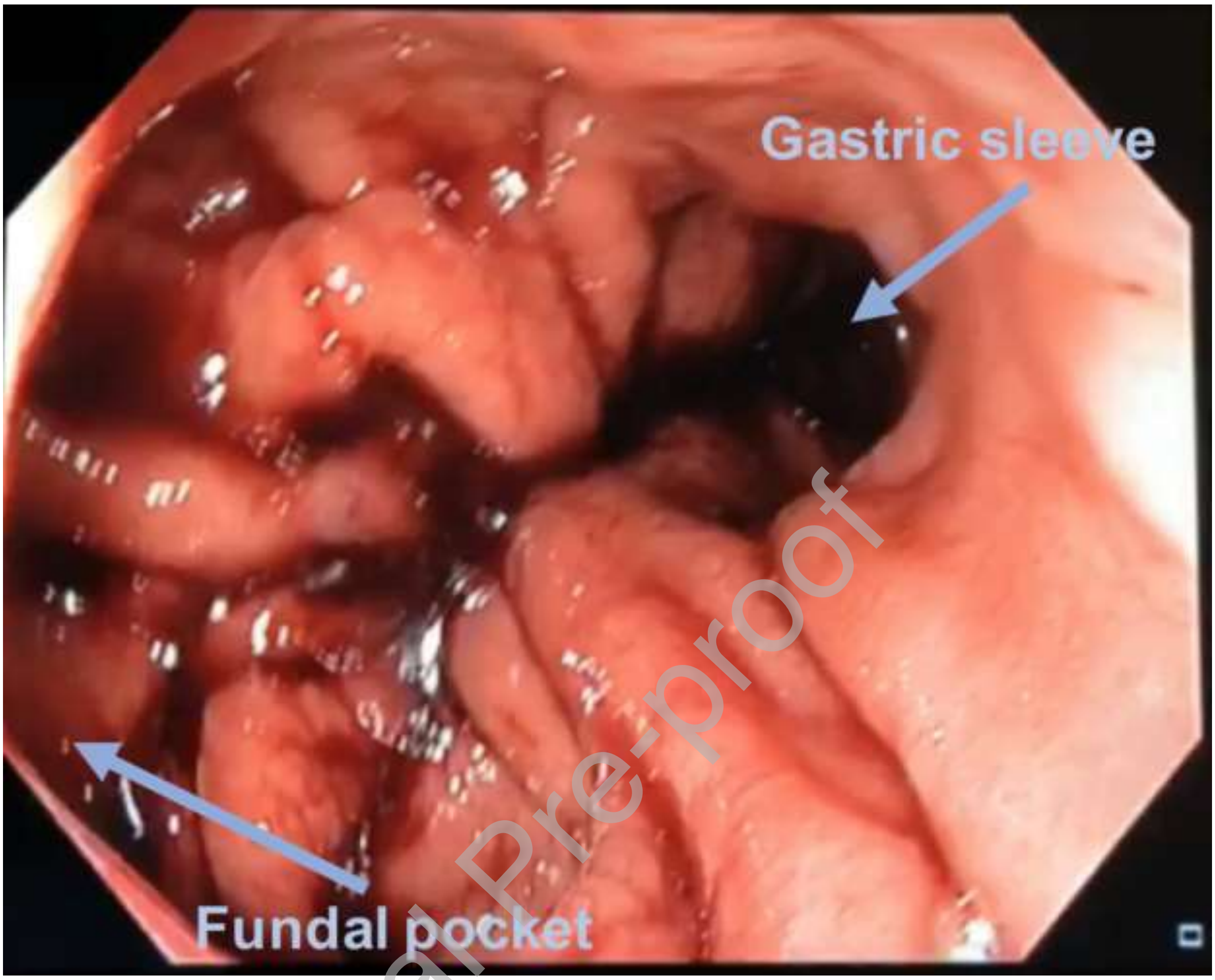

Fig 4. The immediate endoscopic result of the current technique.

Fig 5. Schematic of the final anatomy of the current endoscopic sleeve gastrostomy (ESG) technique.

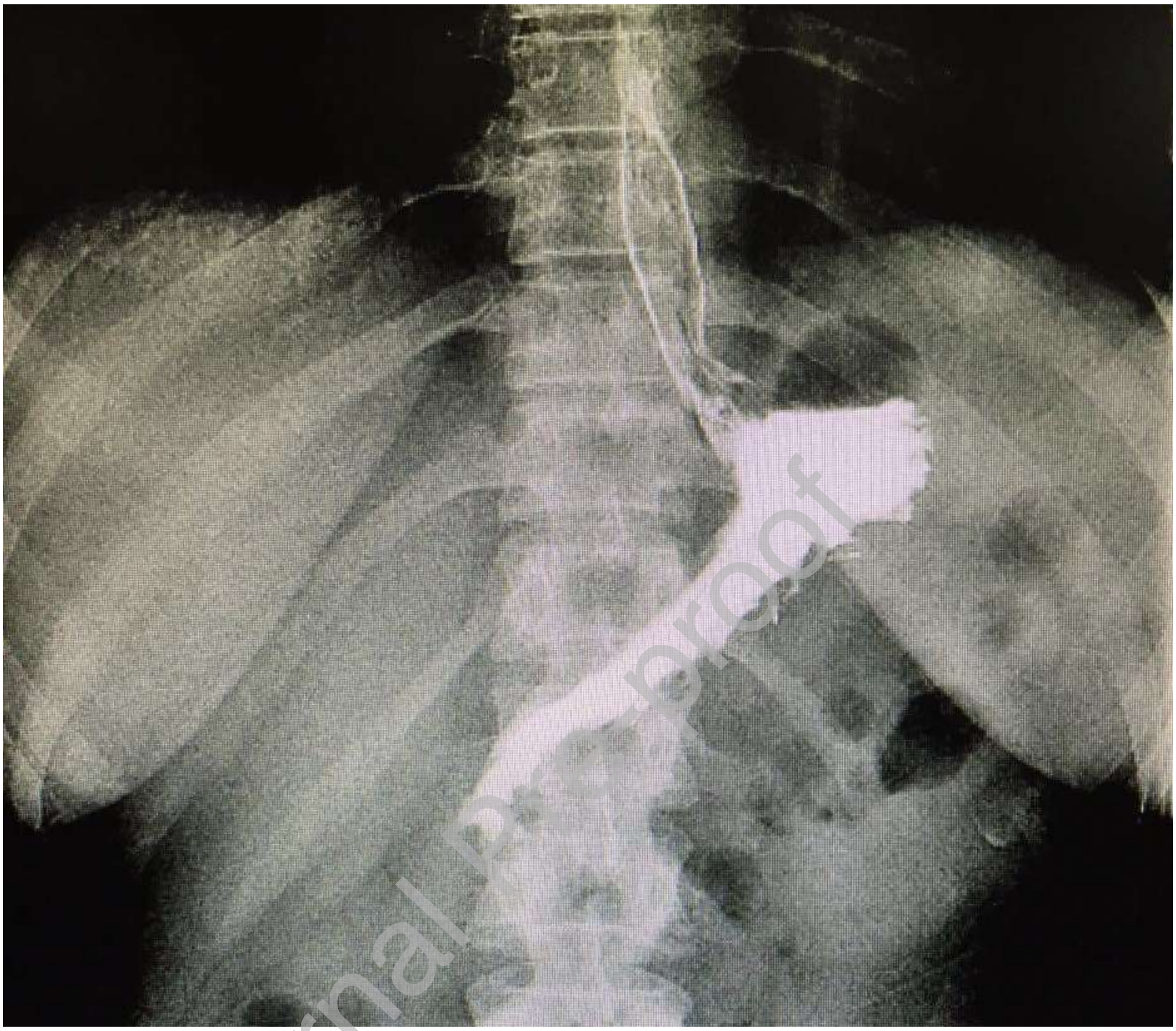

Fig 6. Upper GI series of an endoscopic sleeve gastrostomy (ESG) at 3-month follow-up. Courtesy of Dr. Thiago Ferreira de Souza.

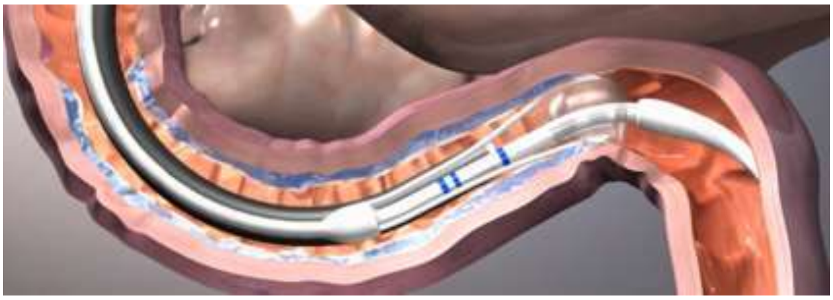

Fig 7. Demonstration of the DMR catheter (Fractyl Laboratories, Inc, Lexington, MA) within the duodenum.[61]

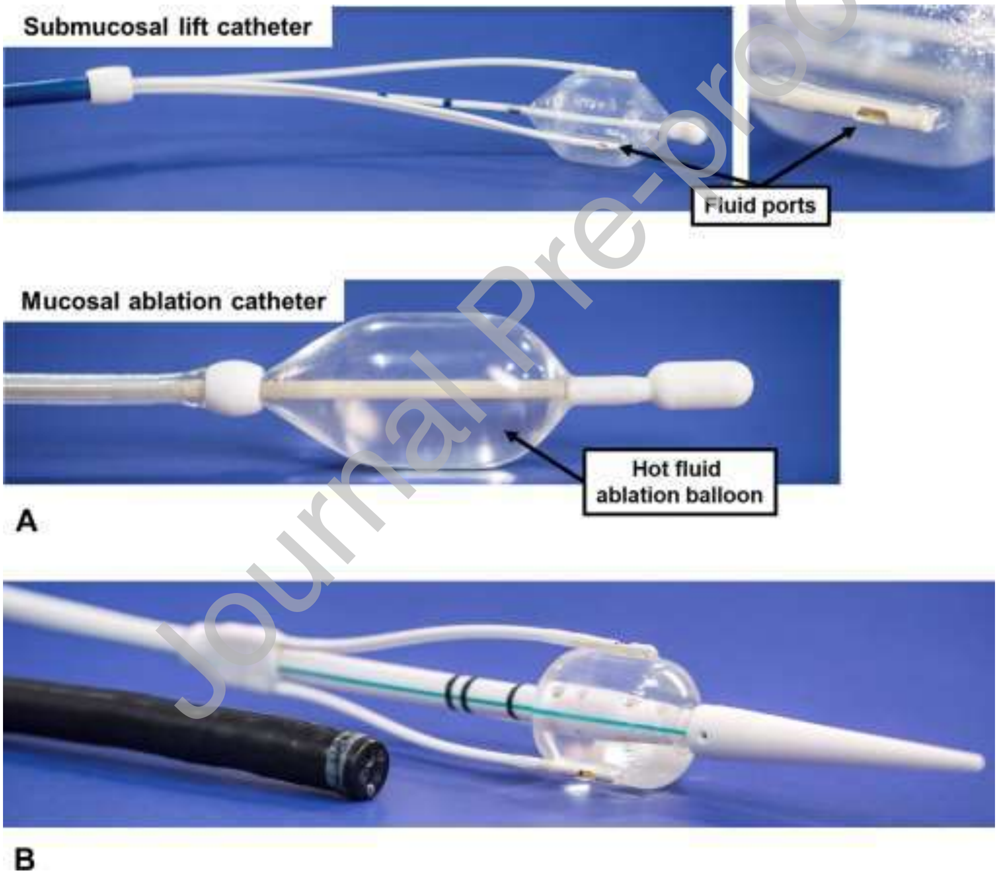

Fig 8. Demonstration of the duodenal mucosal resurfacing (DMR) catheter progression from a 2 catheter system to a single catheter system (B). The single catheter system provides both a submucosal lift and hydrothermal ablation functions.[61]

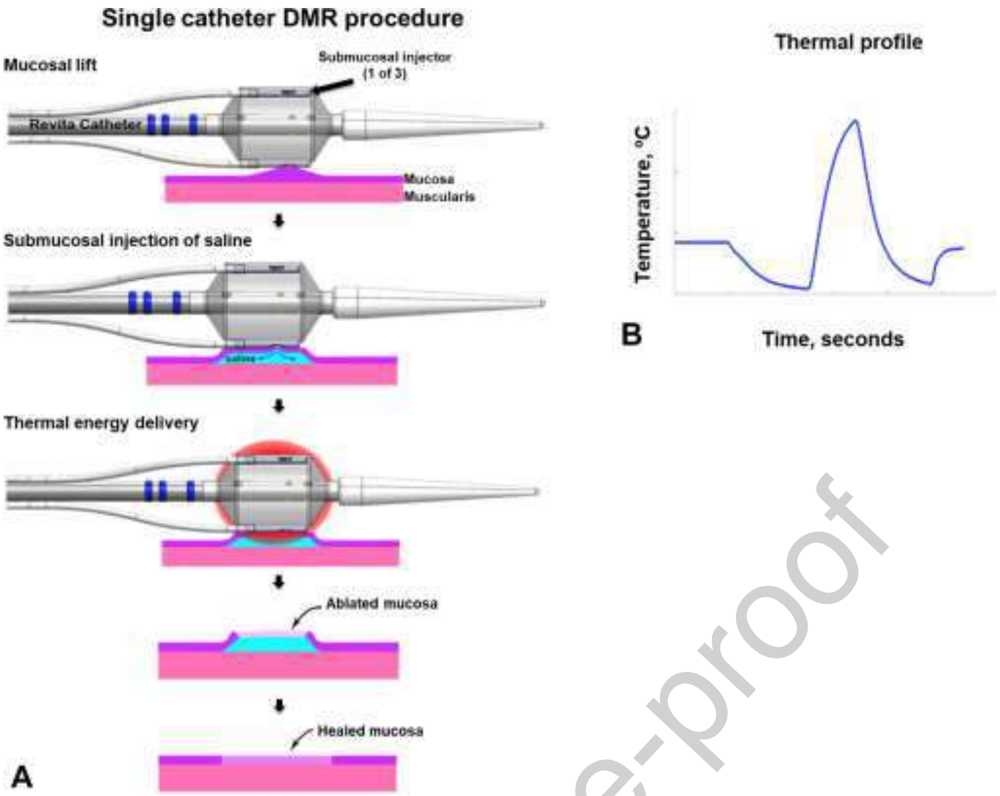

Fig 9. Demonstration of the single catheter duodenal mucosal resurfacing (DMR) system. A balloon (2 cm in length) with 3 submucosal injectors with a port used to draw a vacuum when placing the saline solution during the mucosal lifting portion of the procedure. During mucosal lift, tissue is drawn into the needle port and saline solution is injected in the submucosal space through the needles resulting in a circumferential lift of the mucosa. The ablation cycle is then started with hot water circulated into the balloon to complete an ablation of the lifted tissue. The balloon is then deflated and the catheter is advanced distally for the next segment treatment.[61]

Fig 10. Duodenal-jejunal bypass liner.

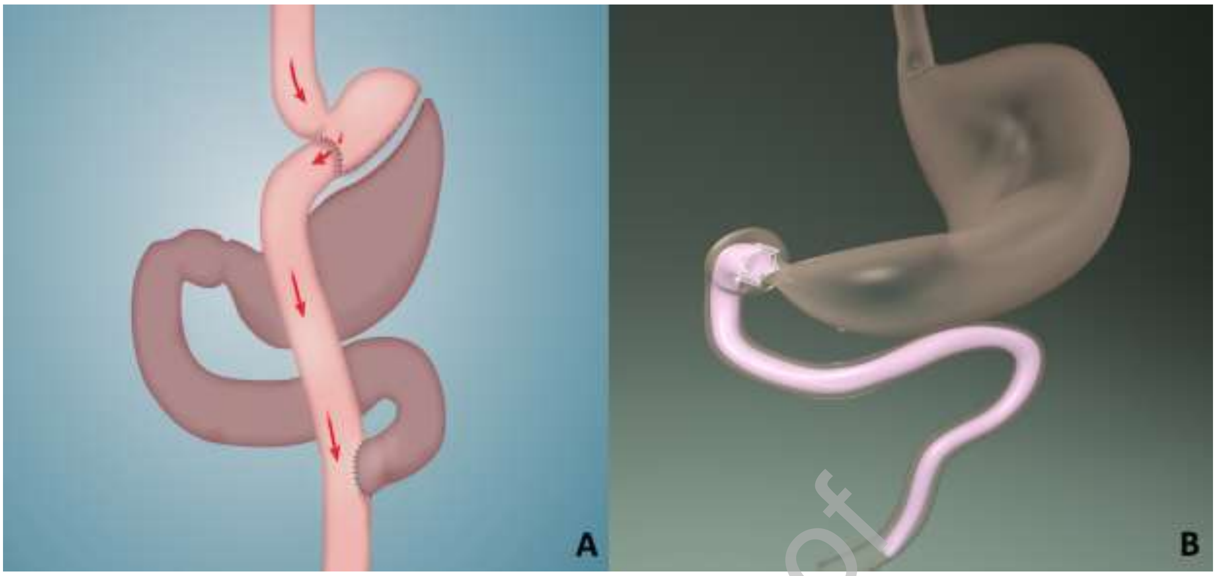

Fig 11. Analogous procedures. A. Roux-en-Y gastric bypass; B. Duodenal-jejunal bypass liner.

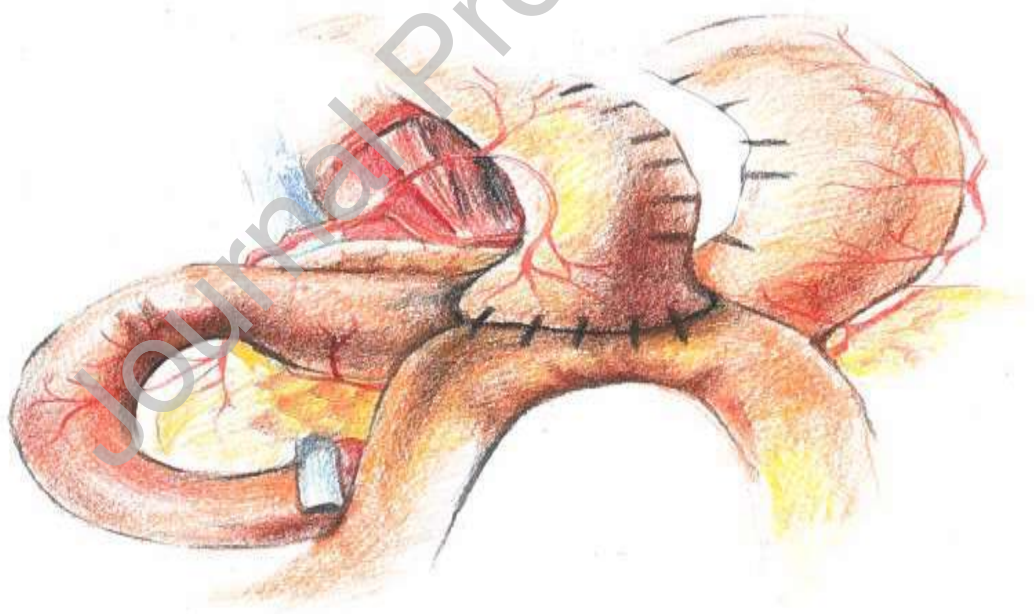

Fig 12. Single anastomosis gastric bypass (SAGB) as described by Rutledge (Mini Gastric Bypass, MGB).

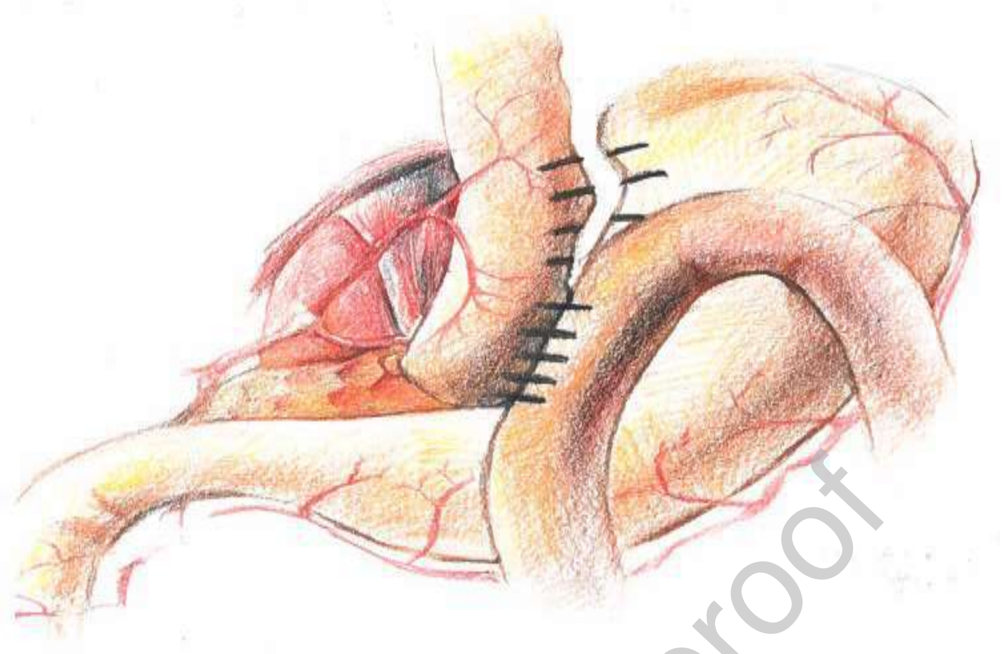

Fig 13. Single Anastomosis Gastric Bypass (SAGB) as described by Carbajo.

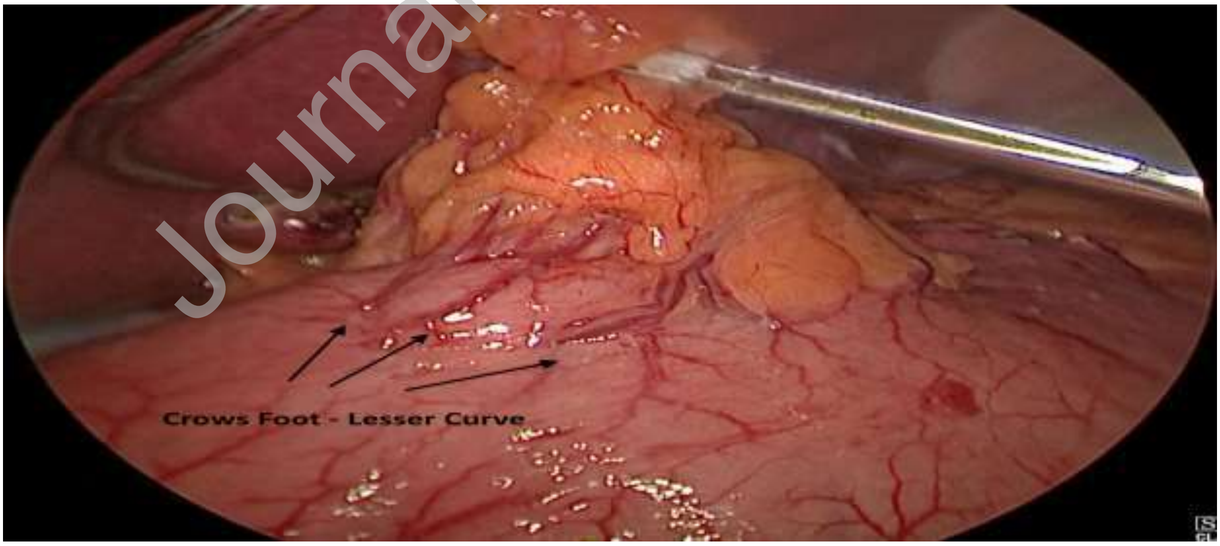

Fig 14. Identification of the proper and precise location of the crows foot is essential to performing the single anastomosis gastric bypass.

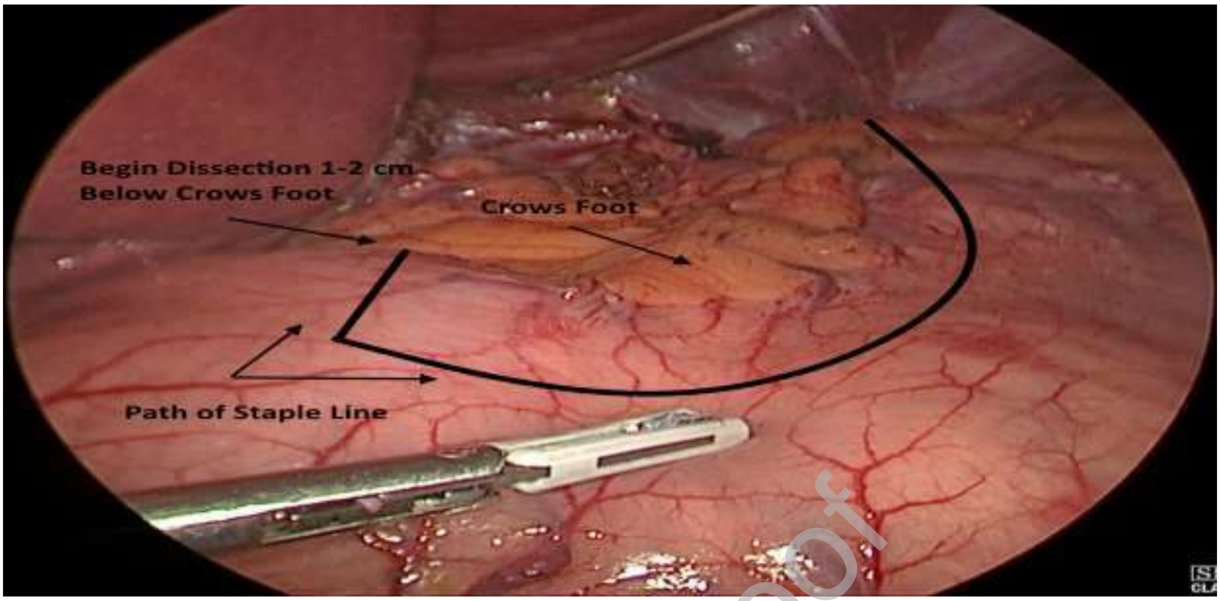

Fig 15. Ideal path of dissection for single anastomosis bypass (SAGB). Dissection begins 1-2 cm below the crows foot and using a 34-40 Fr bougie continues with a staple line until the angle of His near the fundus is transected.

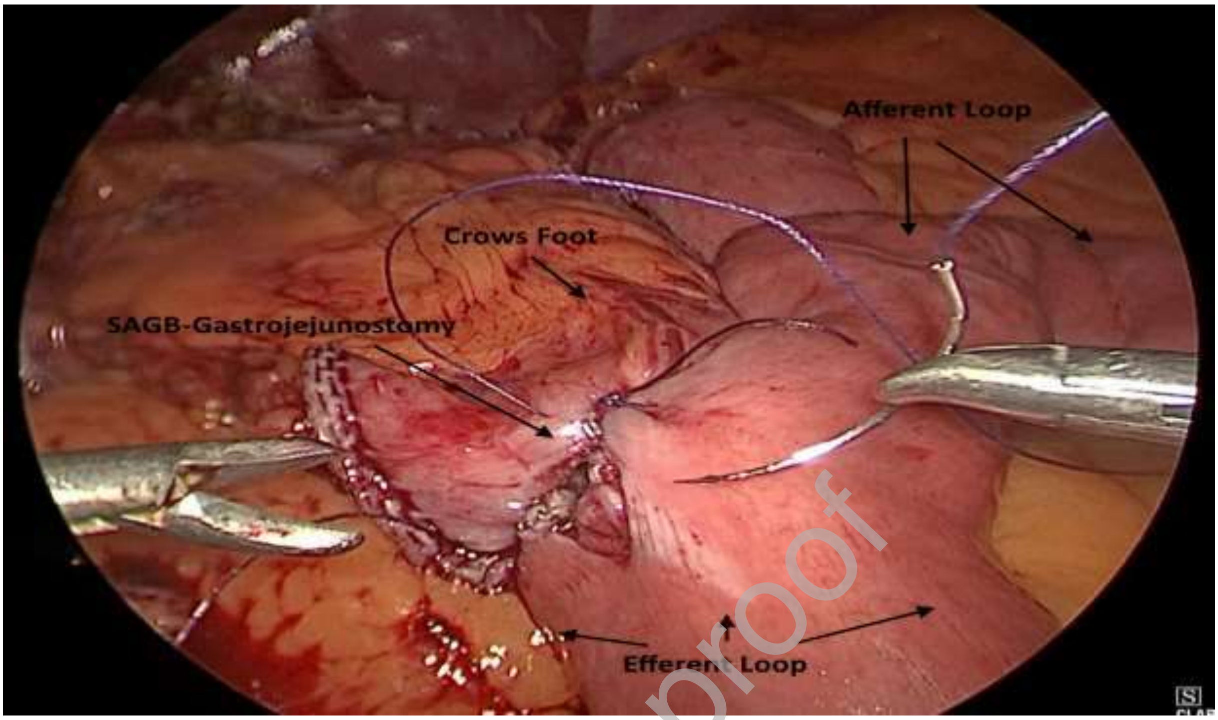

Fig 16. The gastrojejunostomy as described by Carbajo. A side-to-side anastomosis using a 5-6 cm "anti-reflux" stitch to approximate the mesenteric border of the loop anastomosis to the gastric pouch

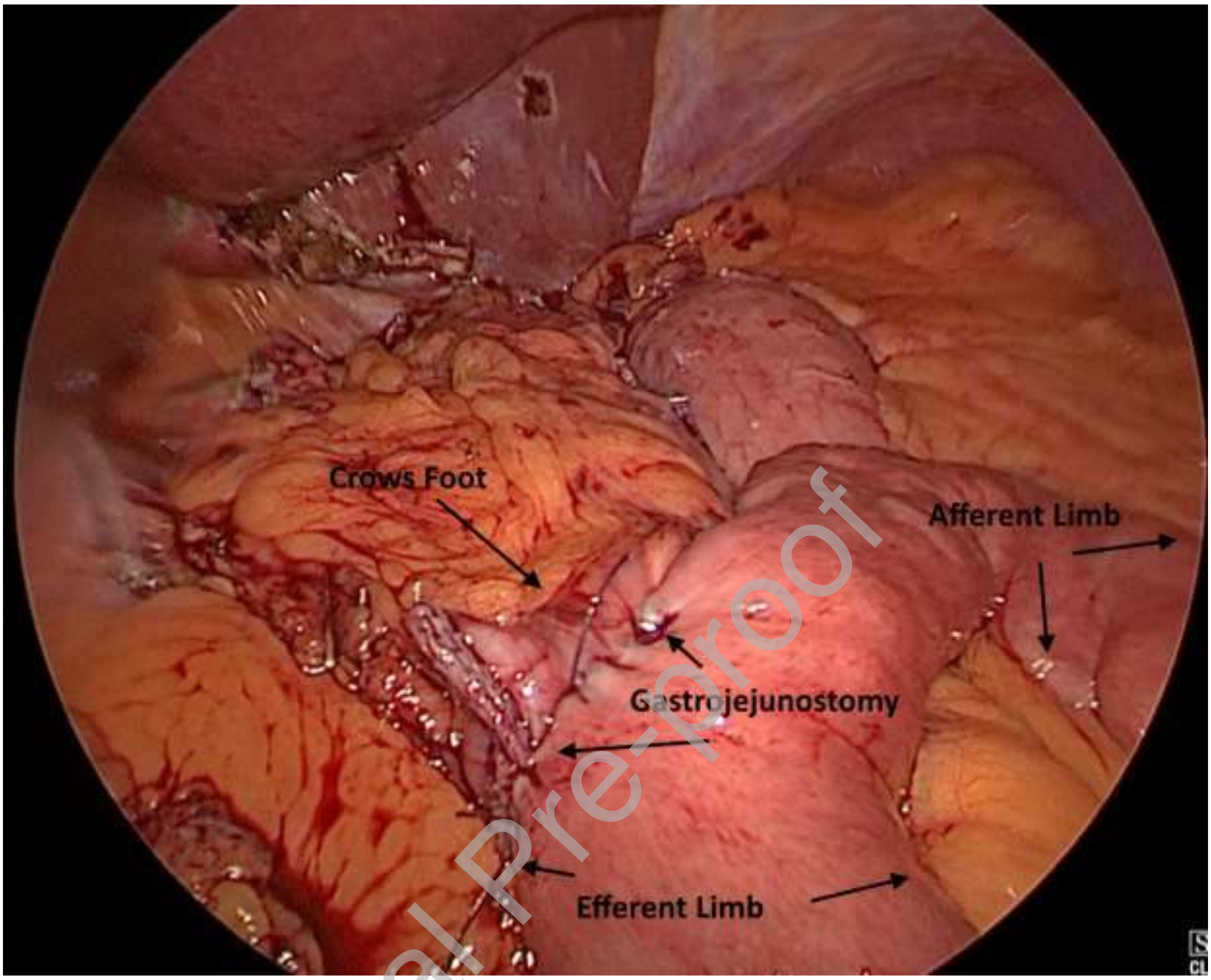

Fig 17. Completed single anastomosis gastric bypass.

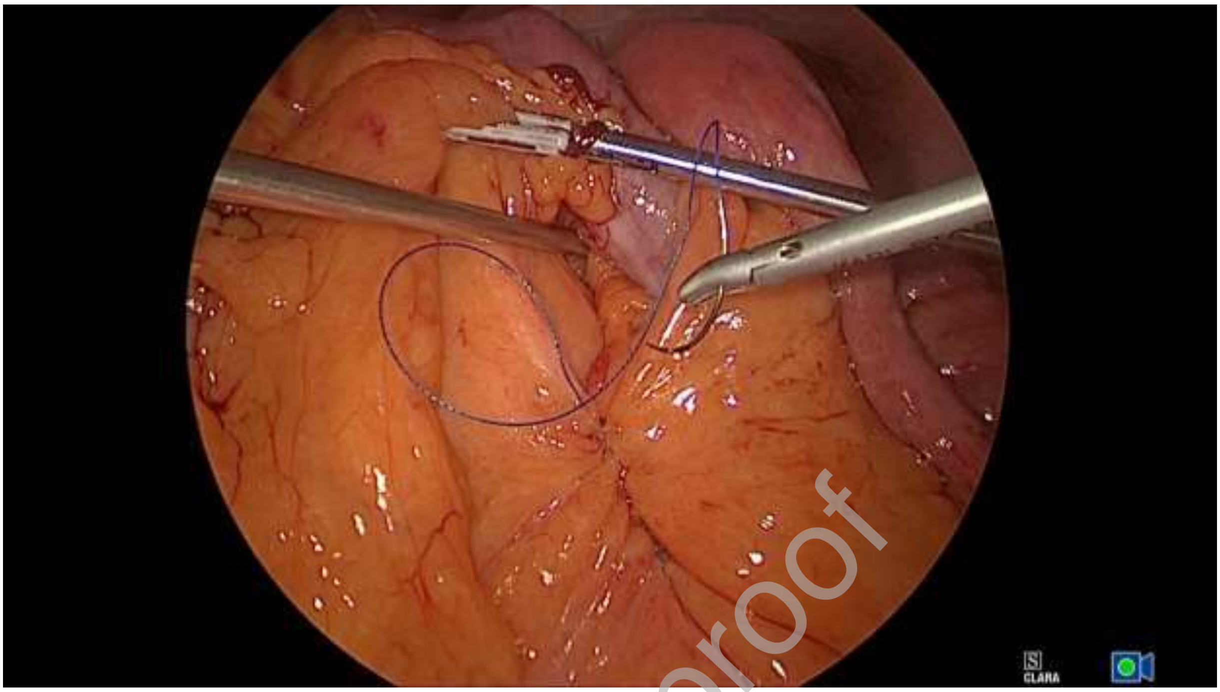

Fig 18. Closure of the mesenteric defect. Non-absorbable suture is used to close the defect created by the antecolic path of the loop over the transverse colon to reach the gastrojejunostomy.

Fig 19. The stomach is elevated, revealing the gastroduodenal artery below. Directly above, the duodenum is encircled and divided.

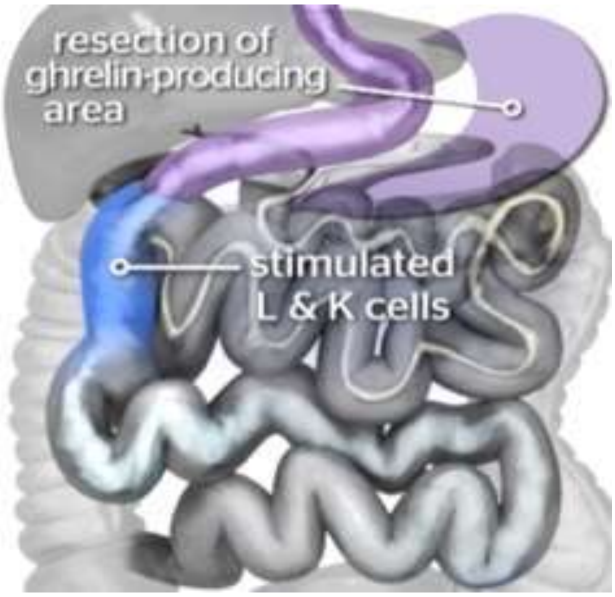

Fig 20. A segment of intestine 250-300 cm from the ileo-cecal valve is anastomosed to the duodenal cuff attached to the sleeved stomach.

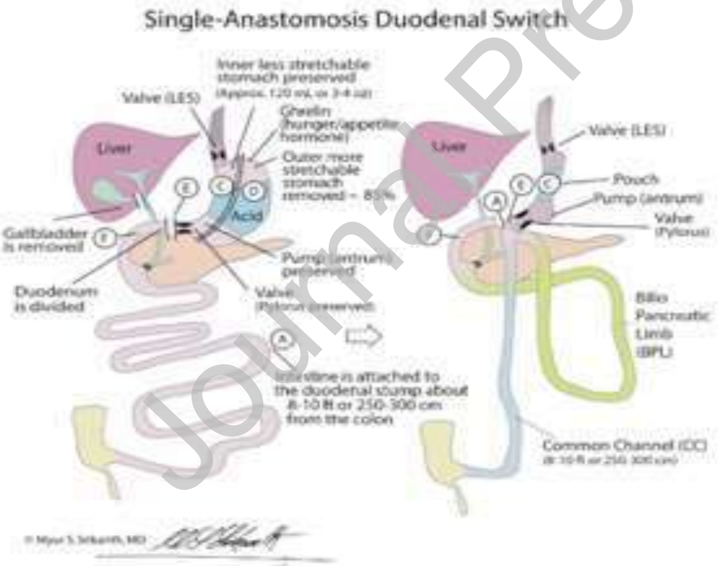

Fig 21. In the single-anastomosis duodenal switch, the stomach is sleeved, the duodenum is divided just distal to the pylorus, and a 250-300 cm common channel is created via a single anastomosis.

Fig 22. typical endoscopic hemostatic clip.

Fig 23. Marginal ulceration at gastrojejunostomy following RYGB.

Fig 24. Balloon dilation of gastrojejunostomy stricture .

Fig 25. Over the scope clip (OTSC) device placed at leak site after gastric sleeve.

Fig 26. Double pigtail catheter.

Fig 27. Endoscopic vacuum therapy setup (A)and placement (B).

Fig 28. Septoplasty.

Fig 29. Eroded Non-adjustable Gastric Band

Table 1. Human studies.

<table>
<tr><td colspan="9">Table 1. Human studies</td></tr>
<tr><td></td><td>No of patients enrolled</td><td>Preoperative BMI</td><td>Preoperative HbA1C</td><td colspan="2">Length of DMR</td><td colspan="2">HbA1C reduction</td></tr>
<tr><td rowspan="5">Rajagopalan et al, 2016[66]</td><td rowspan="5">39 (LS 28; SB 11)</td><td rowspan="5">31 kg/m²</td><td rowspan="5">9.5%</td><td rowspan="5">LS ~9.3cm</td><td rowspan="5">SS ~3.4cm</td><td colspan="2">Overall at 6 months 1.2%</td></tr>
<tr><td colspan="2">At three months</td></tr>
<tr><td>LS → 2.5%</td><td>SS → 1.2%</td></tr>
<tr><td colspan="2">At six months</td></tr>
<tr><td>LS → 1.4%</td><td>SS→ 0.7%</td></tr>
<tr><td>van Baar et al, 2019[60]</td><td>36</td><td>31.6 km/m²</td><td>8.5%</td><td colspan="2">9-10cm</td><td colspan="2">0.9 +/- 0.2%</td></tr>
<tr><td colspan="8">BMI: body mass index; HbA1C: hemoglobin A1C; LS: Long segment ablation; SS: short segment ablation</td></tr>
</table>

Table 2. Similarities between Duodenal-Jejunal Bypass Liner and Roux-en-Y Gastric Bypass

Mechanisms	RYGB	DJBL
Isolation of the cardia	✓	X
Partial vagotomy	✓	X
Exclusion of distal stomach	✓	X
Exclusion of duodenum and proximal jejunum	✓	✓
Exposure of small intestine to undigested nutrients	✓	✓
Delay in gastric empty	NA	✓
GLP-1	↑	↑
GIP	↓	↓
Peptide YY	↑	↑
Ghrelin	↓	↑