ANNUAL REVIEWS

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Endoscopic Approaches to Obesity Management

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Abstract

The field of endoscopic bariatric and metabolic therapy has rapidly evolved from offering endoscopic treatment of weight regain following bariatric surgery to providing primary weight loss options as alternatives to pharmacologic and surgical interventions. Gastric devices and remodeling procedures were initially designed to work through a mechanism of volume restriction, leading to earlier satiety and reduced caloric intake. As the field continues to grow, small bowel interventions are evolving that may have some effect on weight loss but focus on the treatment of obesity-related comorbidities. Future implementation of combination therapy that utilizes both gastric and small bowel interventions offers an exciting option to further augment weight loss and alleviate metabolic disease. This review considers gastric devices and techniques including space-occupying intragastric balloons, aspiration therapy, endoscopic tissue suturing, and plication interventions, followed by a review of small bowel interventions including endoluminal bypass liners, duodenal mucosal resurfacing, and endoscopically delivered devices to create incisionless anastomoses.

INTRODUCTION

The obesity epidemic has continued to increase within the United States, with 42.4% of adults being classified as having obesity in 2018 (1). Furthermore, the burden of obesity was associated with an estimated annual population-wide medical cost of $147 billion in 2008. The majority of this cost is due to obesity-related comorbidities, given the associated increased prevalence of type 2 diabetes mellitus, hypertension and cardiovascular disease (2). The development of these comorbidities is correlated with an average reduction in chronic disease-free life expectancy of 4.6 and 4.5 years in women and men, respectively, between the ages of 50 and 75 years, and an overall reduction in life expectancy of 4.2 and 4.1 years in women and men, respectively, compared to those with normal weight (3).

High-intensity comprehensive lifestyle modification including dietary change, behavioral therapy, and exercise are consistent first-line recommendations for achieving weight loss; however, they generally remain limited to achieving 3–5% and maximum 10% weight loss (4, 5). Furthermore, despite initial success, these strategies are difficult to maintain, with less than 60% of people sustaining these interventions at 2 years (6). Additional weight loss strategies are commonly required to achieve durable outcomes.

Pharmacologic agents have also been recommended for weight loss in patients with obesity [body mass index (BMI) $\geq$ 30 kg/m^2] or overweight (BMI $\geq$ 27 kg/m^2) with increased adiposity complications (5). Although weight loss medication currently offers an adjunctive means to achieve mild weight loss, individuals with BMI $\geq$ 35 kg/m^2 are usually unable to achieve a normal weight.

Therefore, when greater weight loss is required, bariatric surgery is considered for patients who have either BMI $\geq$ 40 kg/m^2 or BMI $\geq$ 35 kg/m^2 with an obesity-related comorbidity (5). The most common bariatric surgery performed in the United States is sleeve gastrectomy (SG), followed by Roux-en-Y gastric bypass (RYGB); these two procedures account for 76.5% and 21.2% of all primary bariatric surgeries performed, respectively (7). Bariatric surgery not only has provided the greatest total weight loss, averaging 25.5% following RYGB and 18.8% following SG at 5 years, but also is associated with remission of obesity-related comorbidities, including hyperlipidemia, type 2 diabetes, hypertension, and obstructive sleep apnea (8). However, among patients eligible for bariatric surgery, only 1.1% undergo these interventions. Furthermore, despite the success of bariatric surgery, 30-day serious adverse events occur in up to 5.6% and 9.4% of patients undergoing SG and RYGB, respectively (8). Additionally, weight regain following these procedures is common and estimated to occur in up to 36% of patients following SG and 41% of patients following RYGB at 10 years (9–12).

Consequently, endoscopic bariatric and metabolic therapies (EBMTs) have emerged as nonsurgical alternatives for patients who are not surgical candidates or do not want to undergo surgical intervention. Historically, EBMTs evolved with the aim to induce weight loss primarily through gastric restriction and/or overall reduction in caloric intake. With increasing experience, there is now recognition of gut hormonal changes that may be associated with improved metabolic parameters beyond weight loss (13–15).

Two primary hypotheses propose to account for these hormonal changes. The foregut hypothesis postulates that bypass of an early short segment of small bowel (i.e., duodenum and proximal jejunum) induces suppression of an unrecognized anti-incretin factor and subsequent reduction in insulin resistance (16). Additionally, various interventions appear to affect the release of ghrelin, a hormone produced by enterochromaffin cells and responsible for increasing hunger prior to meals (17). The hindgut hypothesis proposes that earlier delivery of nutrient luminal contents to the distal small bowel and colon induces the secretion of incretin and appetite suppression hormones such as glucagon-like peptide 1 (GLP-1) and peptide Y-Y (PYY), thereby improving

Table 1 Endoluminal devices and techniques for the treatment of obesity

Gastric					Small bowel	
Space-occupying	**Remodeling**	**Aspiration therapy**	**Superabsorbent hydrogel**	**Mucosal resurfacing**	**Endoluminal bypass sleeves**	**Magnets**
Orbera IGB	Suturing (i.e., ESG)	Aspire Assist	Plenity	Revita DMR	Endobarrier	Incisionless Magnetic Anastomosis System
ReShape Duo IGB						
Obalon IGB						
Spatz IGB	Plications (i.e., POSE)				ValenTx	
Elipse IGB						
Transpyloric Shuttle (TPS)						

Abbreviations: DMR, duodenal mucosal resurfacing; ESG, endoscopic sleeve gastroplasty; IGB, intragastric balloon; POSE, Primary Obesity Surgery Endoluminal.

glycemic control (18, 19). These mechanisms are leveraged through gastric and small bowel devices, and while most of the experience to date has consisted of gastric-targeted devices, emerging data suggest that small bowel therapies may play an even greater role in targeting metabolic parameters. Future implementation of combination therapy including both gastric and small bowel interventions offers an exciting option to further augment weight loss and help alleviate metabolic disease.

This article discusses the current state of bariatric and metabolic endoscopy through a review of all US Food and Drug Administration (FDA)-approved EBMTs and non-FDA-approved emerging modalities (**Table 1**). Gastric devices and techniques including space-occupying intragastric balloons (IGBs), aspiration therapy, endoscopic tissue suturing, and plication interventions are reviewed first, followed by a review of small bowel interventions including endoluminal bypass liners, duodenal mucosal resurfacing, and endoscopically delivered devices to create incisionless anastomoses.

GASTRIC SPACE-OCCUPYING DEVICES

Gastric EBMTs have been demonstrated to be safe and effective methods to induce weight loss. These interventions were initially designed to work through a mechanism of volume restriction, leading to earlier satiety and reduced total caloric intake. However, increasing data support alterations in gut hormones that may inform the development of future therapies. To date, all FDA-approved endoscopic weight loss devices involve alteration of the gastric lumen.

Intragastric Balloons

Intragastric balloons (IGBs) are temporary space-occupying devices that are placed within the lumen of the stomach (**Figure 1**). Aside from volume restriction, increasing data suggest that IGBs delay gastric emptying, in part due to antral distension inducing enhanced fundic relaxation and possibly a decrease in plasma ghrelin levels (17). Use of IGBs dates back as far as 1984 in Europe and South America, although FDA approval was achieved in 2015 (20). Most recently, the American Gastroenterological Association has recommended IGBs as an intervention that should be offered to patients who have failed conventional weight loss treatment (21).

There are currently three FDA-approved IGBs available in the United States and several other IGBs undergoing pivotal trials. These balloons are FDA-approved for individuals with BMI $\geq$ 30 kg/m^2 and $\leq$ 40 kg/m^2 who have failed to lose sufficient weight through lifestyle modifications. Both fluid- and gas-filled options exist, with fluid-filled balloons more likely to induce greater weight loss (22). The greatest weight loss occurs while the balloon is in place and thus may

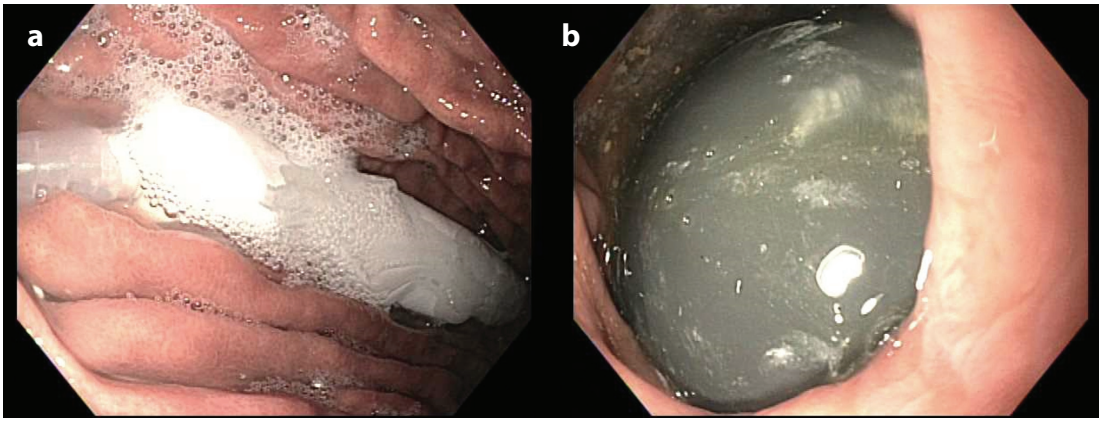

Figure 1

Endoscopic visualization of an intragastric balloon before (*a*) and after (*b*) filling with fluid.

play a valuable role in serving as a bridge to another intervention (23, 24). Weight loss following balloon extraction is variable. Generally, contraindications to IGB placement include the presence of a gastric mass, large hiatal hernia (>5 cm), mucosal inflammation from Crohn's disease or esophagitis, achalasia, cirrhosis, severe coagulopathy, or ongoing alcohol or substance abuse. Five IGB interventions are reviewed in detail below.

The Orbera™ balloon. The Orbera™ balloon (Apollo Endosurgery, Austin, Texas, USA) is a fluid-filled balloon that is placed and removed endoscopically. It was initially designed for a 6-month dwell time, but a 12-month option known as Orbera365™ is now available. Depending on desired weight loss, symptom tolerance, and patient anatomy, the balloon is filled with a volume of 450 to 750 mL.

The Orbera™ balloon achieved FDA approval shortly following a pivotal multicenter (IB-005) prospective comparative study that randomized 448 patients to either a 12-month behavioral modification program with the Orbera™ balloon (6 months with balloon in place; 6 months following balloon removal) or 12 months of behavioral modification alone (25). The Orbera™ group achieved a significantly greater percent of total body weight loss (TBWL) at 6 months in comparison to the control group (mean TBWL 10.2% versus 3.3%; $p < 0.001$). This was followed by a large retrospective study of 321 patients that demonstrated a mean TBWL of 11.8% at 6 months (26). A meta-analysis of 17 studies including 1,683 patients who underwent placement of an Orbera™ balloon demonstrated a TBWL of 12.3%, 13.16%, and 11.27% at 3, 6, and 12 months after implantation, respectively (27). Data outside of the United States have demonstrated even greater weight loss of up to 18.4% (28). Early device removal due to intolerance has been reported to be as high as 18.8% (29). The most common adverse events include nausea, vomiting, balloon hyperinflation, spontaneous deflation, and gastric ulcer formation.

The Reshape Duo™ balloon. The Reshape Duo™ (Reshape Medical, Inc., San Clemente, California, USA) is an endoscopically placed and removed fluid-filled dual-chamber balloon system. Each chamber is filled to 450 mL (900 mL total) (30). This balloon is FDA-approved for a maximum dwell time of 6 months.

The original pivotal study (REDUCE Trial) investigating the Reshape Duo™ balloon was a randomized double-blinded prospective sham-controlled multicenter study including 330 patients (30). The balloon remained in place for 6 months, followed by 6 months of monitored diet and

exercise. At 6 months, the mean percentages of TBWL were 7.6% and 3.6% in the treatment and sham groups, respectively. A subsequent retrospective study of 202 patients demonstrated a mean TBWL of 4.8%, 8.8%, 11.4%, 13.3%, and 14.7% at 1, 3, 6, 9, and 12 months, respectively (31). Although adverse events were uncommon, esophageal mucosal tears requiring no intervention were seen in 8.4% of device placements. Furthermore, 6.4% of patients required balloon removal prior to the completion of the 6-month treatment period. Gastric ulcers were initially seen in 35% of placements; however, this was reduced to 10% following device modification (30).

The Obalon™ balloon. The only FDA-approved gas-filled balloon system available is the Obalon™ balloon (Obalon Therapeutics, Carlsbad, California, USA) which contains a nitrogen-gas mixture. These balloons have a smaller maximum inflation of 250 mL per balloon, and up to three can be deployed simultaneously for a total space-occupying volume of 750 mL (32). These balloons are swallowed sequentially every 2–3 weeks and ultimately removed endoscopically at 6 months. The original system required radiographic confirmation following device swallowing; however, advancements have now permitted balloon placement without this need.

The Obalon™ balloon was originally studied in 2013 in a small cohort of patients who underwent sequential balloon placement and achieved a mean weight loss of 5.0 kg at 3 months (33). This was followed by the Six-Month Adjunctive Weight Reduction Trial (SMART) in 2018. In this study, 387 patients were randomized to 6 months of either Obalon™ ($n = 198$) or sham capsule placement ($n = 189$), followed by an additional 6 months of monitored diet and exercise (32). At 5.5 months, TBWL was 6.6% and 3.4% in the Obalon™ balloon and sham groups, respectively.

The Spatz™ balloons. The Spatz3™ balloon (Spatz Medical, Fort Lauderdale, Florida, USA) is placed and removed endoscopically and provides the first adjustable IGB option, as it contains a curved catheter attached to a silicone balloon to allow easy endoscopic access following deployment (34). It can be filled with between 400 and 800 mL of fluid, and this volume can be either increased or decreased during the dwell time. This device is currently under evaluation with the FDA but been utilized outside the United States for a dwell duration of up to 12 months.

The original pilot Spatz™ study in 2011 contained two generations of the device, the later of which incorporated a modified design due to complications of the first generation (34). This study was followed by a larger prospective study using the modified device, which included 73 patients followed for 12 months (35). Mean TBWL was 19% with 21 early removals required due to balloon intolerance or adverse events. When compared to nonadjustable IGB options using the modified Spatz™ model, the adjustable balloon achieved similar weight loss despite an increased rate of adverse events (36, 37). The newest iteration of the device is Spatz3™, currently awaiting FDA approval.

The Elipse™ balloon. The Elipse™ (Allurion Technologies, Natick, Massachusetts, USA) is an IGB that is placed and removed without the need for endoscopic intervention. The balloon has a fill volume of 550 mL of fluid and is swallowed by the patient, obviating the need for endoscopy. Removal of the balloon occurs through natural expulsion via the gastrointestinal tract at around 4 months. This device is currently under FDA evaluation.

An open-label trial in 2017 demonstrated safety and efficacy (38) of the Elipse™ balloon. Among 27 patients included in analysis, there was a 10.0% TBWL at 4 months without serious adverse events (38). This was followed by a prospective series of 135 patients that demonstrated 15.1% TBWL at 4 months. Three patients required early removal due to intolerance, and three other patients experienced early spontaneous balloon deflation (39). Notably, one additional patient required laparoscopic balloon removal due to onset of small bowel obstruction.

Another study of 112 patients demonstrated a 10.9% TBWL at 6 months and a 7.9% TBWL at 12 months following device excretion (40).

The Transpyloric Shuttle™

The Transpyloric Shuttle™ (TPS; BAROnova, Inc., San Carlos, California, USA) provides a mechanism similar to IGB therapy with easy reversibility. It was FDA-approved in 2019 for individuals with BMI between 30 mg/kg^2 and 40 mg/kg^2 and for a dwell time of 12 months. The device contains a space-occupying balloon in addition to a flexible silicone catheter that connects to a smaller bulb designed to intermittently advance through the pylorus to induce gastric outlet obstruction.

The initial TPS feasibility study, published in 2014, included 22 patients evaluated over 6 months. This study demonstrated a TBWL of 14.5% (41). The randomized controlled TPS pivotal study (Endobesity II Study) was completed in 2019 and contained 302 patients; 270 TPS placements were compared to 32 sham procedures. Overall TBWL was 9.8% at 12 months compared to 2.8% in the control group (42). There were few adverse events, including one esophageal rupture and four gastric impactions. This device is not yet commercially available.

GASTRIC REMODELING PROCEDURES

Endoscopic Sleeve Gastroplasty

Endoscopic sleeve gastroplasty (ESG) has recently provided an alternative to laparoscopic SG while leveraging a similar mechanism of inducing early satiety and reducing gastric emptying (43). This procedure is performed using the Apollo OverStitch endoscopic suturing system (Apollo Endosurgery, Austin, Texas, USA). There are two iterations of the device, which attach to either a single- or double-channel endoscope, and each is composed of a curved suture arm and an anchor exchange that is deployed through the channel. With activation of the handle, the suture arm propels the needle through the gastric tissue and passes the needle to the anchor exchange. Opening of the handle then releases the tissue. The anchor then can be passed back to the suture arm in anticipation of additional stitch placement.

Although variable suturing patterns have been reported (44), stitches are generally placed in either a U-stitch or Z-configuration along the anterior, greater curvature, and posterior gastric walls to create a tubular configuration and reduce gastric volume (**Figure 2**).

While gastric restriction is well recognized, underlying gut hormonal and physiologic changes are incompletely understood. Whereas there appears to be a significant decline in leptin secretion and a trend toward decreased serum insulin levels, changes in GLP-1 or PYY secretion have not been demonstrated (14), potentially discouraging the hindgut hypothesis of action.

ESG is typically implemented in individuals with BMI $\geq$ 30 kg/m^2, although practices vary. One of the first pilot trials in 2018 included 44 patients and demonstrated a mean TBWL of 17.4% at 12 months. No serious adverse events were reported, although postprocedure nausea, vomiting and epigastric pain were common (45). One early multicenter retrospective study of 248 patients found a mean TBWL of 18.6% at 24 months, and >50% of patients achieved ≥10% TBWL at this time point. The strongest predictor of weight loss at 24 months was TBWL at 6 months (46). There was no difference in weight loss between the centers reported.

This study was followed by a larger single-center study that included 1,000 patients and demonstrated a mean TBWL of 14.8% at 18 months with resolution of diabetes, hypertension, and hyperlipidemia in a large percentage of patients (47). Furthermore, this series demonstrated safety of the procedure, with <1% of patients being readmitted with pain, bleeding, perigastric fluid collection, or fevers (47). More recently, ESG has proven to achieve durable weight loss; one

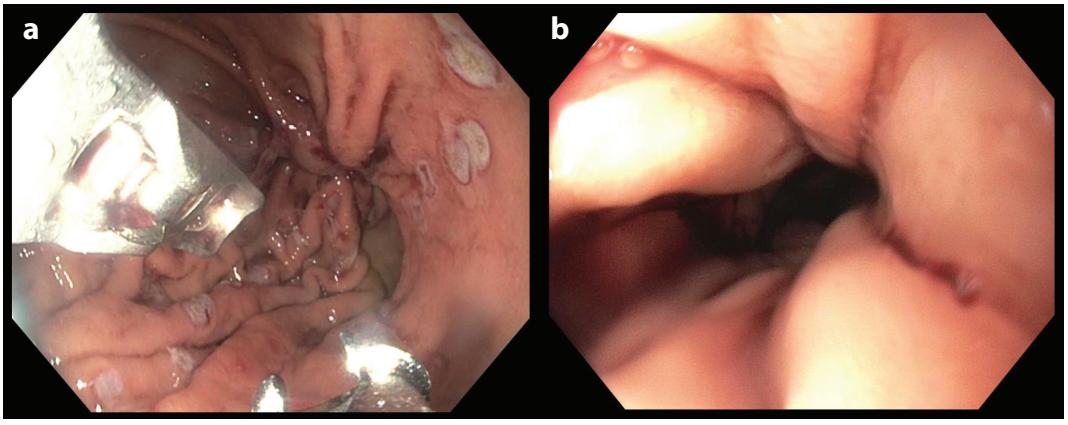

Figure 2

Endoscopic sleeve gastroplasty with initial marking of the anterior, greater curvature, and posterior wall with argon plasma coagulation to delineate suture (*a*) and eventual completion of the procedure demonstrating considerable gastric restriction (*b*).

study, containing 216 patients (68 of whom were followed for 5 years), demonstrated a TBWL of 15.9% at 5 years. Consistent with prior literature, a low adverse event rate of 1.3% was reported without any serious adverse events (48).

Subsequent studies have also suggested reversibility of ESG, in addition to safety and efficacy in surgical conversion if required (49). In one retrospective analysis comparing ESG to surgical SG, ESG was associated with significantly lower TBWL (6.5% versus 17.1%, $p < 0.01$). However, compared to SG, ESG was also associated with significantly fewer adverse events at 6 months (5.2% versus 16.9%, $p < 0.05$), significantly lower rate of new-onset gastroesophageal reflux disease (1.9% versus 14.5%, $p < 0.05$), and decreased length of stay (0.3 versus 3.1 days, $p < 0.001$) (50).

Primary Obesity Surgery Endoluminal

Endoscopic plication techniques using the Incisionless Operating Platform (IOP; USGI Medical, San Clemente, California, USA) also lead to tissue apposition and provide an alternative to endoscopic suturing (**Figure 3**). The IOP was initially FDA-approved in 2007 for tissue apposition. Primary Obesity Surgery Endoluminal (POSE) is a procedure in which tissue plications are placed in the gastric lumen as a primary therapy for weight loss. The device consists of a large 54-Fr transport that contains four working channels to accommodate a slim endoscope, tissue approximator, and tissue helix. Whereas endoscopic suturing is somewhat reversible, the IOP places polypropylene anchors with baskets cinched on either end of tissue folds and is designed for permanent remodeling. Early experience demonstrates a mean TBWL for POSE of 13.0%–15.1% at 12 months (51, 52). Although adverse events are uncommon, potential risks include infection, bleeding, gastric stenosis, perforation, and injury to surrounding intraabdominal organs.

ASPIRATION THERAPY

Aspiration therapy provides a unique alternative mechanism for weight loss. The AspireAssist device (Aspire Bariatrics, Inc., Exton, Pennsylvania, USA) was FDA-approved in 2014 for adult patients over 22 years of age with a BMI between 35 kg/m^2 and 55 kg/m^2. The primary

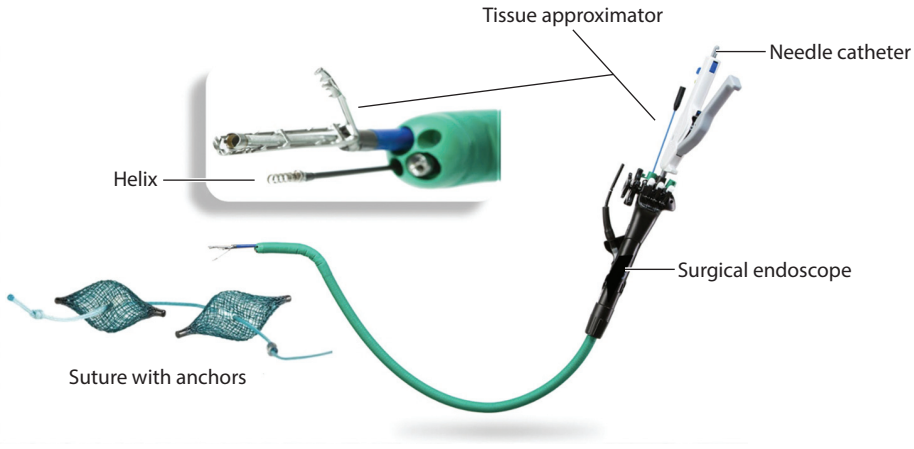

Figure 3

The plication technique creates full-thickness tissue folds through the delivery of Snowshoe® Suture Anchors, which are inserted through a proprietary overtube. The overtube has four working channels, which accommodate an ultraslim endoscope, tissue approximator, and up to two tissue graspers. Adapted from Reference 53.

mechanism is overall reduction in caloric absorption through the gastrointestinal tract via direct aspiration from the gastric lumen through the abdominal wall following meals. The system contains an A-tube, which is a percutaneously placed tube, much like a percutaneous endoscopic gastrostomy (PEG) tube, that is connected to a gravity flow director system (**Figure 4**). This device is designed to be activated by the patient 20–30 min postprandially. Aspiration removes approximately 30% of meal content to be discarded in a waste receptacle or toilet.

A pivotal trial published in 2017 compared aspiration therapy to lifestyle counseling and demonstrated a mean excess body weight loss of 31.5% at 12 months with aspiration therapy compared to 9.8% with lifestyle counseling (54). Adverse events occurred in 3.4% of patients, the most common of which were similar to risks associated with PEG tube placement and included peristomal bleeding/irritation, infection, pain, nausea, vomiting, and abdominal discomfort. Four-year data reported TBWL of 18.7% in addition to durable improvement in cardiometabolic parameters (i.e., hemoglobin A1c, blood pressure, dyslipidemia, and transaminase elevation). The additional risk of persistent enterocutaneous fistula formation requiring surgical repair following A-tube removal was reported in this study (55).

SUPERABSORBENT HYDROGEL

Plenity™ (Gelesis, Boston, Massachusetts, USA) is a novel gastric-targeted mechanism currently under investigation. It is composed of a three-dimensional superabsorbent hydrogel consisting of cellulose and citric acid, which modifies gastric contents following ingestion. The hydrogel is ingested in capsular form and expands within the gastric lumen to promote early satiety. Although it is not yet FDA-approved, FDA clearance was achieved for individuals with a BMI of 25–40 kg/m^2 in 2019, after early experience suggested a 6.4% weight loss at 6 months (56). Associated side effects are predominantly gastrointestinal, including diarrhea, bloating, constipation, nausea, and flatulence. Plenity™ offers an appealing approach for patients seeking mild weight loss via a natural mechanism. Full FDA approval is anticipated in the near future, and further study is warranted to evaluate effectiveness over longer use.

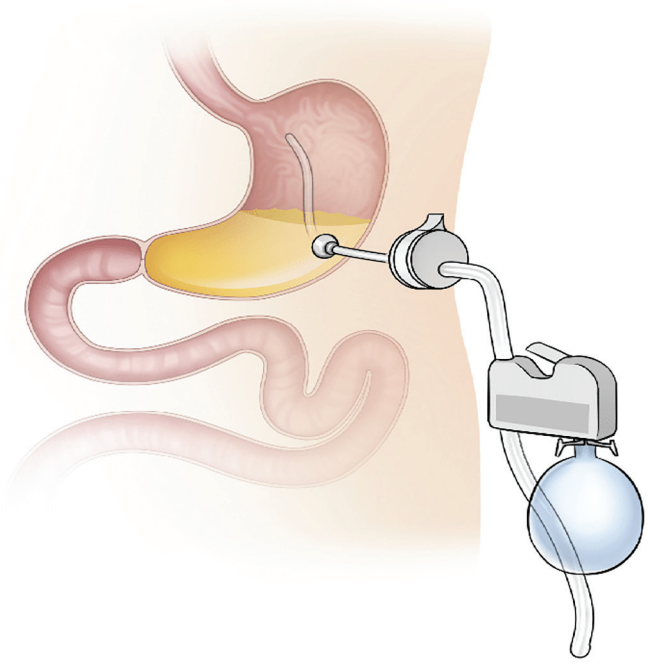

Figure 4

Aspiration therapy. The system contains an A-tube, which is a percutaneously placed tube, much like a percutaneous endoscopic gastrostomy tube, connected to a gravity flow director system. Reprinted from Reference 53 without alteration under the Creative Commons Attribution-Non-Commercial Unported 3.0.

SMALL BOWEL DEVICES

As the foregut and hindgut hypotheses have evolved, research focus has shifted to include investigations of small bowel EBMTs that may have a greater role in gut hormonal changes associated with weight loss than their gastric predecessors. This approach is predicated on the fact that bariatric surgical interventions that bypass nutrient contact from the duodenum, such as RYGB and biliopancreatic diversion, have demonstrated improvements in glycemic control in patients with type 2 diabetes and other comorbidities. Although no small bowel EBMTs are currently FDA-approved, there are multiple investigative trials with anticipated approval soon.

Duodenal Mucosal Resurfacing

Revita duodenal mucosal resurfacing (DMR)^{TM} (Fractyl Laboratories, Inc., Lexington, Massachusetts, USA) is a small bowel EBMT designed to treat type 2 diabetes in addition to promoting weight loss. This technology utilizes heat therapy applied to the duodenal intestinal barrier and results in surface change that subsequently impacts metabolic pathways to decrease insulin resistance. Although incompletely understood, the mechanism likely leverages the foregut pathway to simulate a bypass of nutrients beyond the duodenum, enhancing an incretin effect.

Initial FDA approval for investigational use was achieved in 2016, and subsequent studies have demonstrated significant improvement in glycemic indices (57, 58); however, significant weight changes have not been consistently reported. One of the first reports of 36 patients undergoing DMR found a reduction in hemoglobin A1c of 10 mmol/mol, which was sustained at 12 months

(58). DMR is also being studied for treatment of other metabolic comorbid disorders including nonalcoholic fatty liver disease. The first multicenter randomized controlled trial demonstrated that compared to sham controls, European patients treated with DMR had significant improvements in hemoglobin A1c at 5.5 months and liver fat density at 3 months (59). These promising early results will soon be supplemented with larger, longer studies, including data from within the United States.

Endoluminal Bypass Sleeves

Small bowel bypass liners have garnered interest as an easily reversible mechanism that bypasses the early small bowel (i.e., duodenum and proximal jejunum) and therefore likely leverages components of both the foregut and hindgut pathways. These devices remain in the investigational phase; however, multiple randomized controlled trials are underway, and FDA approval is anticipated in the near future.

The Endobarrier™ sleeve. The Endobarrier™ (GI Dynamics, Boston, Massachusetts, USA) is a 60-cm sleeve composed of ultraslim Teflon with proximal anchors designed to be implanted within the muscularis propria of the duodenal bulb (**Figure 5**). Construction simulates the biliopancreatic limb of Roux-en-Y anatomy as a result of bypassing the duodenum and biliopancreatic systems. The device has an intended implantation duration of 12 months.

Although early experience demonstrated no significant weight differences detected at 4 years after a 12-month device dwell time (61), there was a significant 12.0% reduction in weight following a 24-month dwell time (62). Side effects were predominantly gastrointestinal in nature, with risks of hepatic abscess formation and tissue ingrowth at the duodenal anchor sites. Both studies demonstrated a trend of improvement in hemoglobin A1c. A recently published meta-analysis showed a durable reduction in hemoglobin A1c of 0.9% at 6 months following device explantation (63). Prospective data from within the United States are lacking, but the device is currently being studied with new data expected in the near future.

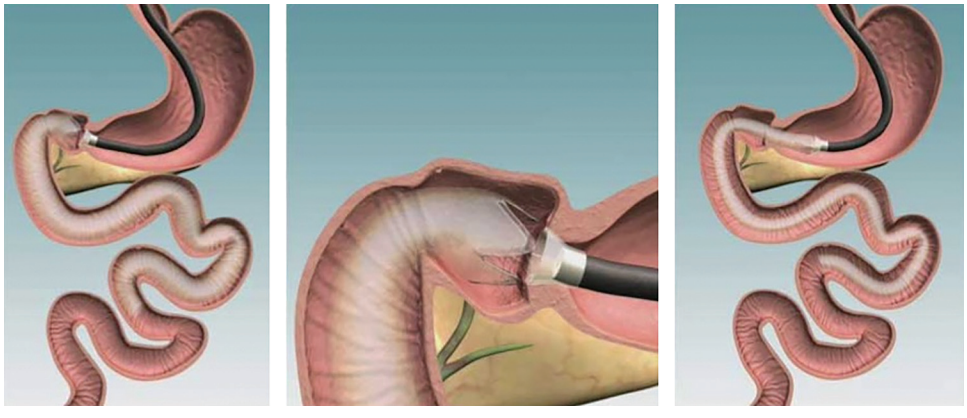

Figure 5

The duodenal-jejunal bypass liner is positioned with anchors in the duodenal bulb attached to a 60-cm fluoropolymer sleeve (*left* and *center* panels). The sleeve is impermeable and therefore inhibits nutrient absorption through the initial 60 cm of small bowel (shown in *right* panel). Following a duration of 12 months, endoscopic removal is required (*right*). Reprinted from Reference 60 without alteration under the Creative Commons Attribution-Non-Commercial Unported 3.0.

The ValenTx sleeve. The gastro-duodeno-jejunal bypass sleeve (ValenTx Inc., Maple Grove, Minnesota, USA) is another small bowel bypass device similar to Endobarrier™ except that it anchors within the distal esophagus. Owing to a length of 120 cm, this sleeve terminates within the jejunum. Similar to the Endobarrier™, this device emulates the biliopancreatic limb of an RYGB (64). While published literature to date demonstrates TBWL at 12 months of 17.6%, side effects are common; a high frequency of reflux, heartburn, nausea and vomiting, and device dislodgement limits clinical applicability (65).

Incisionless Magnetic Anastomosis System

Another mechanism under investigation that accords with the hindgut hypothesis is the incisionless magnetic anastomosis system (GI Windows, West Bridgewater, Massachusetts, USA). This system involves the deployment of two self-assembling "smart" magnets into octagonal rings. Placement in two adjacent loops of small bowel allows for controlled fistulization and subsequent formation of a partial jejunal diversion. This alteration in anatomy allows for more rapid exposure of intraluminal nutrients to the distal small bowel and colon, thereby increasing activation of GLP-1 and PYY. A pilot study with follow-up duration of 12 months demonstrated not only a 14.6% TBWL but also an average 1.9% reduction in hemoglobin A1c among patients with type 2 diabetes (66).

ENDOSCOPIC REVISION OF BARIATRIC SURGERY

Despite the rapidly expanding arsenal of primary EBMTs available to endoscopists, among their most commonly performed procedures are endoscopic revisions of prior bariatric surgery. The most common indication for endoscopic revision is weight regain, as up to two-thirds of patients regain at least 20% of their maximal weight lost at 5 years following their initial bariatric operation (67). Although weight regain following bariatric surgery is often multifactorial, involving behavioral, medical, and psychosocial factors (68–70), anatomic causes such as dilated gastrojejunal anastomosis (GJA) following RYGP or dilated sleeve following SG are targets for endoscopic revision.

Transoral Outlet Reduction

The most commonly performed endoscopic revision for weight regain is the transoral outlet reduction (TORe), which aims to strengthen tissue and reduce the diameter of a dilated and incompetent GJA. Increased GJA size has been shown to correlate with increased risk for weight regain following RYGB, particularly when diameter exceeds 25 mm (71). Various endoscopic revisional techniques are currently available, including thermal techniques such as argon plasma coagulation (72–74), cryotherapy (75, 76) or radiofrequency ablation (77); endoscopic suturing (**Figure 6**) and endoscopic submucosal dissection followed by endoscopic suturing (78–80); endoscopic plication techniques; and cap-mounted clip placement (81). Formerly, sclerotherapy was performed surrounding the GJA using the sclerosant sodium morrhuate (82–85); however, due to reduced availability and safety concerns, this is no longer performed.

The technique employed when performing endoscopic revision is typically determined based on patient anatomy and endoscopist experience (86). Among available techniques, the majority of literature focuses on argon plasma coagulation and endoscopic suturing. The most effective and durable approach regarding weight loss is TORe with endoscopic suturing using a purse-string suture pattern, with studies demonstrating an 8.6% and 8.8% TBWL at 12 months and 5 years, respectively (87, 88). When this TORe procedure is combined with the endoscopic submucosal dissection technique, weight loss has been shown to increase to 12.1% TBWL at 12 months (89).

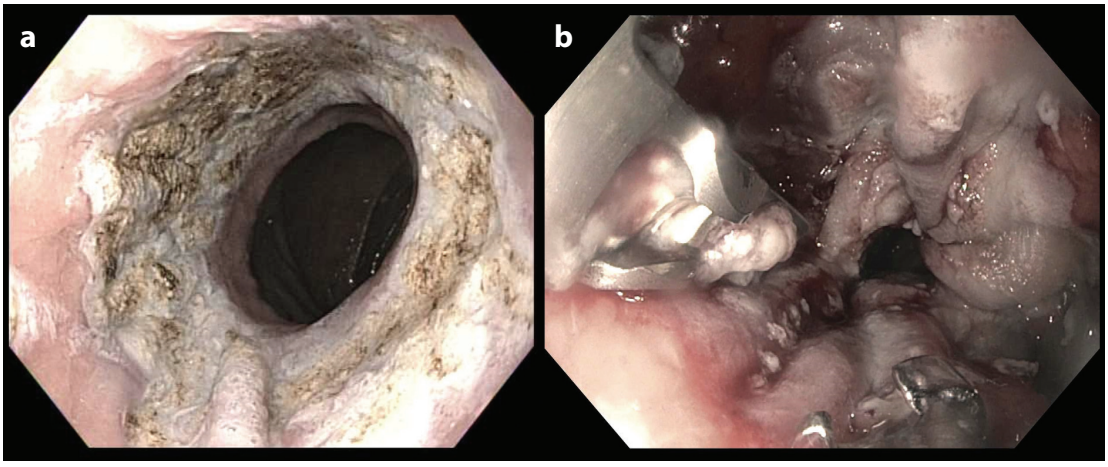

Figure 6

Endoscopic visualization of transoral outlet reduction with argon plasma coagulation applied to the gastric side of the gastrojejunal anastomosis (*a*) prior to endoscopic suturing (*b*).

Sleeve-in-Sleeve

Endoscopic revision for weight regain following SG, commonly referred to as sleeve-in-sleeve, is not as widely performed as TORe; however, sleeve-in-sleeve, using either a suturing or plication technique, is a well-recognized option for these patients, with initial studies suggesting efficacy. One study demonstrated that endoscopic revision using a suturing approach was associated with a mean TBWL of 18.3% weight loss at 12 months (90). Given that SG has become the most commonly performed bariatric surgical procedure and has a rising prevalence, the frequency of sleeve-in-sleeve endoscopic revision is anticipated to increase (91).

DISCUSSION

EBMT is an exciting and rapidly expanding field. As the field continues to evolve, it will emphasize improvement not only in effecting weight loss but also in treating obesity-related comorbidities such as diabetes and nonalcoholic fatty liver disease. There is an expectation of additional therapies with an emphasis on leveraging gut hormone alterations akin to small bowel EBMTs. Furthermore, combination therapy including both gastric and small bowel intervention may improve weight management and treatment of metabolic syndrome. Similar to combination therapy seen in hypertension or diabetes management, a combination between gastric and small bowel therapies may allow providers to tailor therapies according to patient profiles, individualize therapy, and optimize metabolic parameters.

DISCLOSURE STATEMENT

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