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Chapter

Endoluminal Techniques to Treat Obesity

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Abstract

The prevalence of overweight and obesity increased dramatically during the past decades and now affects approximately 30% of people worldwide. Bariatric surgery has proven to be the most effective treatment modality for obesity in the long term. However, current surgical procedures are accompanied by a substantial risk of complications. Several endoluminal techniques have been developed to achieve weight loss in obese patients and claim to be as effective as surgery but safer. This chapter evaluates the efficacy and safety of innovative endoluminal techniques that are already available in clinical practice or in advanced stages of development. This chapter outlines their potential mechanism of action and their safety and efficacy in clinical practice, by reviewing the current literature.

Keywords: endoscopic, endoluminal, laparoscopic, obesity, bariatric

1. Introduction

Overweight and obesity have reached epidemic proportions. The World Health Organization (WHO) estimates that approximately 2.5 billion adults are overweight, and at least 700 million are obese [1]. Overweight and obesity are linked to more deaths worldwide than underweight. As the number of people with obesity rises, the prevalence of obesity-related comorbidities, such as diabetes, hypertension, hyperlipidemia, obstructive sleep apnea, and fatty-liver disease is rising as well. Numerous strategies have been employed in the treatment of obesity; however, most people do not reach or sustain such significant weight loss with lifestyle intervention, composed of diet, exercise, and behavior modification, alone. Bariatric surgery has emerged as the most effective treatment for obesity in the long term and is associated with a significant decrease in obesity-associated comorbidities [2, 3]. However, current bariatric surgical procedures are accompanied by a substantial risk of complications. These potentially serious complications during and following the invasive and irreversible surgical procedures are incontrovertible. In addition, only a small proportion of obese patients actually undergo bariatric surgery. With this in mind, there exists a critical gap in the treatment of obesity for those not qualifying for bariatric surgery or those who do not wish to pursue bariatric surgery because of a multitude of reasons such as the associated risks, morbidity, and costs. Thus, there is a strong need for new and less invasive, safer and preferably reversible alternatives to bariatric surgical procedures. Therefore, new techniques to achieve weight loss in obese patients who claim to be as effective as surgery but safer have been developed. In addition, these therapies may be beneficial earlier on in the

onset of obesity. In this chapter, we aim to present the current state of field regarding investigational procedures in the treatment of obesity that are already available in clinical practice or in advanced stages of development. This chapter outlines their potential mechanism of action and their safety and efficacy in clinical practice, by reviewing the current literature.

2. Malabsorptive procedures

2.1 Gastrointestinal bypass liners

With the success of the Roux-Y Gastric Bypass (RYGB), attempts have been made to develop nonsurgical endoscopic procedures which mimic the attributes of the RYGB. Several companies have come up with gastrointestinal bypass liners which are removable, replaceable, and do not require gastric stapling or permanent changes to the patient's anatomy.

2.1.1 The EndoBarrier

A promising alternative to bariatric surgery is the EndoBarrier (**Figure 1**) (GI Dynamics Inc., Lexington Massachusetts, USA). This device is an endoluminal duodenal bypass liner (DJBL), which mimics the malabsorptive features of the RYGB.

2.1.1.1 Technique

The EndoBarrier consists of a single use endoscopic system including a liner, delivery system, and retrieval system. The liner, a Teflon covered sleeve that is impermeable to nutrients, extends 65 cm into the small bowel and can remain in situ for up to 3–12 months. Under general anesthesia, a capsule containing the liner and its anchor will be placed at the duodenal bulb with fluoroscopic guidance. The device has anchors with barbs of nitinol located at its proximal end, which functions as a self-expandable stent. This allows fixation to the duodenal bulb distal to the pylorus, but proximal to the ampulla of Vater. In this way, the liner is anchored proximally, whereas the distal part extends into the jejunum due to peristalsis of the intestine. The liner is open at both sides, to ensure the passage of chyme from the stomach while bypassing the duodenum. Along the outside of the liner, pancreatic juices and bile will enter from the ampulla of Vater, thereby avoiding contact with gastric contents until these exit the sleeve in the jejunum. In this way, it mimics the malabsorptive effects of the RYGB, without the permanent alterations of the intestinal anatomy and its complications. The device is licensed for 1 year, after which it should be removed. In order to remove the liner, a custom drawstring of the device can be grasped with an endoscope, to which the device will collapse and subsequently can be gently removed from the gastrointestinal tract.

2.1.1.2 Efficacy and safety profile

To date, there have been multiple observational studies and five randomized controlled trials assessing the efficacy of the EndoBarrier [4]. The first post marketing nonrandomized trial was conducted in the United Kingdom, in which 45 obese patients with a mean BMI of 39.9 kg/m^2 were recruited [5]. The study comprised a 12-month period with the EndoBarrier inserted and a 6-month follow-up period after it had been explanted. Average implantation time was 27 min and no procedure-related complications occurred. A total of 31/45 patients completed the

full 12 month-period, whereas 14 patients had a premature removal of the device. In two patients, this was due to a device-related adverse event, namely melena and device migration causing abdominal pain. In the remaining 31 patients, a mean reduction in BMI of 4.9 kg/m^2 was observed at 12 months. In addition, this reduction in weight was maintained 6 months after the removal of the device. In another study, 41 patients with a mean BMI of 49 kg/m^2 were randomized between the EndoBarrier and a low calorie diet [6]. After 12 weeks, the mean excess weight loss (EWL) in the device group versus the control group was 19 versus 6.9%, respectively. In one large multicenter trial carried out in the Netherlands, 73 patients were randomized to either EndoBarrier implantation in combination with dietary intervention or dietary intervention alone [7]. Thirty-five subjects with a baseline BMI of 35 kg/m^2 received the EndoBarrier for a period of 6 months. After 6 months, just before the device removal, the EndoBarrier group had lost 32.0% [22.0–46.7%] of their excess weight versus 16.4% [4.1–34.6%] in the control group ($p < 0.05$). In addition, the EndoBarrier-group demonstrated the impact on diabetic control, with improvements in HbA1c of 1.3% compared to 0.3% in the control group. Only one early device removal was reported due to the blockage of the Endobarrier with food. A recent systematic review and meta-analysis assessing the effect of the EndoBarrier on weight loss and glycemic control in obese patients with type 2 diabetes mellitus concluded that the EndoBarrier induces significant weight loss and improves glycemic control in this population [8]. With regard to safety, the most frequently reported side effect of the EndoBarrier is abdominal pain and nausea, which commonly resolves after the body is used to having the device in situ. More serious complications that have been reported are gastrointestinal bleeding, device migration, and the formation of hepatic abscesses. However, the first international data from the EndoBarrier worldwide registry suggest that the likely benefits of the EndoBarrier far outweigh the risks. The registry, including 403 Endobarrier patients, reported 4 cases of hepatic abscesses, 15 cases of gastrointestinal bleeding, and 8 cases of device migration [9]. In conclusion, the EndoBarrier has shown to be a promising and feasible technique that is able to account for significant weight loss in obese patients and moreover improves glycemic control in those with T2DM. However, while the liner is currently licensed for only 1 year, a vast majority of the patients risk to lose the beneficial effects of the device after removal and subsequently will regain weight. In the study of Forner et al., 72% of the patients regained their weight 6 months postremoval of the EndoBarrier [10]. Future research should be focused on reimplantation strategies or a device that could

Figure 1.
The EndoBarrier.

remain in situ for longer, thereby providing a more permanent solution. A recent study already demonstrated implantation of a new prototype for up to 3 years in two obese subjects with T2DM, but high frequency and severity of AE's still preclude the use of the device for a period longer than 1 year [11]. Efforts are made to kick start further development to combat these issues.

2.1.2 ValenTx

Another novel endoluminal gastro duodenal-jejunal bypass liner which has been introduced is the ValenTx (**Figure 2**) (ValenTx, Inc. Carpinteria, CA, USA) [12]. It is designed to reproduce the restrictive and malabsorptive features of the RYGB, by creating a gastric, duodenal, and biliopancreatic bypass. This gastro duodenal-jejunal bypass liner is an implantation device which is delivered endoscopically, but other than the EndoBarrier, requires laparoscopic assistance.

2.1.2.1 Technique

The procedure starts with an overtube placed through the pylorus at the level of the duodenal bulb. The liner, a 120-cm long fluoropolymer, is then delivered through this overtube via a delivery catheter up till the first portion of the duodenum. The liner, which has a polyester cuff attached to its proximal end, is deployed using computer-regulated pressure and flow monitoring under fluoroscopic guidance to ensure deployment of the liner into the proximal jejunum. Hereafter, the delivery catheter will be removed, and the overtube will be replaced for a shorter one leading up to the proximal cuff attachment. After this step, the laparoscopic part of the procedure will take place. After the placement of one 12-mm and three 5-mm trocars together with a Nathanson liver retractor, the gastroesophageal (GE) junction is dissected circumferentially at the level of the diaphragmatic hiatus. With an endoscope, the polyester cuff will then be positioned at the level of the Z-line of the GE junction and anchored with full-thickness sutures deployed in a circumferential manner. Full-thickness suture placement is secured under laparoscopic visualization. After cuff attachment, the final step in the procedure is approximation of the left and right diaphragmatic crura through laparoscopically placed sutures to prevent iatrogenic hiatal hernia. In order to remove the device, one has to circumferentially detach the cuff by endoscopic ligation of the eight anchoring sutures. The cuff can then be gently mobilized with an endoscopic grasper and subsequently be removed via the esophagus together with the attached sleeve.

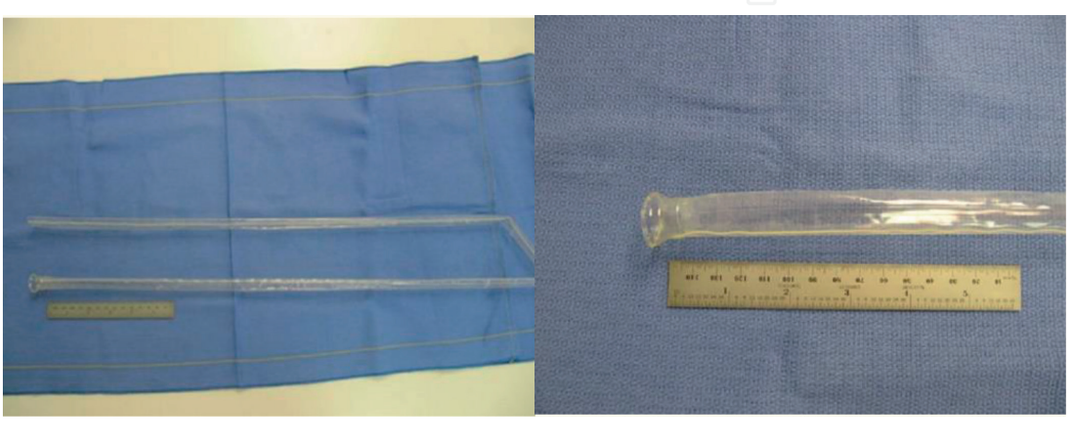

Figure 2.
The ValenTx gastro duodenal-jejunal bypass liner ([12], with permission).

2.1.2.2 Efficacy and safety profile

The first human experience with the ValenTx was gained during a single-center prospective trial among 24 morbidly obese individuals who met the National Institutes of Health (NIH) criteria for bariatric surgery [12]. In 22 patients, with a mean preoperative BMI of 42 kg/m^2, the liner was successfully implanted. One patient got excluded because of noncompliance with the preoperative liquid diet, and another patient suffered from significant inflammation at the GE junction to which the investigators decided to halt the procedure. A total of 5 out of the 22 implanted patients underwent the removal of the liner before the 12-week scheduled explantation, because of dysphagia presumably due to a too high placement of the cuff. This complaint completely resolved after explantation of the liner. After 12 weeks, the average % EWL in the successfully implanted patients was 39.7% (27–64%), which corresponded with an average total weight loss of 16.8 kg (8.6–30.8 kg). Moreover, the device demonstrated effective glycemic control during the trial. Except for the patients requiring premature explantation, no other adverse events took place. Therefore, the same research group designed a consecutive 1-year trial in which 13 patients with a mean BMI of 42 kg/m^2 were enrolled [13]. In 10 patients, the device was successfully implanted and left in situ for 12 months. All 10 patients completed the 1-year follow-up without major complications resulting in a mean % EWL of 54% after 1-year and significant improvement of all comorbidities. Partial cuff detachment was observed in four patients during follow-up endoscopy, which indicates that the redesign of the anchoring mechanism is needed before further research can be done. While showing to be safe and able to achieve significant weight loss, further research is focused on a purely endoscopic deployment of this device. Unfortunately, further development and research on this device is currently hampered due to investment problems.

3. Restrictive procedures

Restrictive procedures limit food intake, creating a small gastric reservoir with a narrow outlet to delay gastric emptying, thereby stimulating an earlier sense of satiety with reduction of caloric intake.

3.1 Gastric remodeling techniques

3.1.1 TOGA system

Transoral gastroplasty (TOGA) with the use of the TOGA system (Satiety Inc., Palo Alto, CA) creates a vertical gastroplasty along the lesser curvature of the stomach performed through a transoral endoscopy [14]. The created gastric pouch limits the amount of food or liquids that the patient can eat, with an accompanying feeling of early satiety.

3.1.1.1 Technique

The TOGA is an incision free procedure performed under general anesthesia creating a restrictive pouch in the stomach using a set of flexible staplers which are introduced endoscopically. Using suction, tissue from both the anterior and posterior wall of the stomach is positioned together into two vacuum pods inside the device. Hereafter, 3 rows of 11 titanium staples create a serosa to serosa transmural suture, connecting the anterior and posterior gastric walls from the angle of His

to the lesser curvature. This step is repeated until one has created a sleeve of the desired length. The sleeve outlet is then narrowed using the TOGA restrictor.

3.1.1.2 Efficacy and safety profile

The first human study assessing the safety and efficacy of the TOGA system took place in 2008, in which 21 morbidly obese individuals with a mean BMI of 43.4 kg/m^2 were enrolled [15]. After 6 months, patients had an average EWL of 24.4%. No serious adverse events (SAE) were reported. However, at 6 month follow-up endoscopy, gaps in the staple line were observed in 13 out of 21 patients. After technical improvements of the device, a second human pilot study enrolled 11 patients who met criteria for bariatric surgery [14]. Average BMI decreased significantly from 41.6 kg/m^2 before treatment to 33.1 kg/m^2 at 6 month follow-up. The same results were seen in a multicenter trial with 1-year outcome, which involved 67 patients with a mean BMI of 41.5 kg/m^2, which dropped to 33.1 kg/m^2 at 6 months after the TOGA procedure [16]. A small case study evaluating the effect of TOGA on insulin sensitivity and secretion even demonstrated an amelioration of insulin sensitivity with subsequent reduction of the insulin secretion [17]. Compared to the more effective laparoscopic gastric bypass and biliopancreatic diversion, the TOGA system reached a good therapeutic outcome in terms of weight loss and showed no complications [18]. Based on the evidence available, TOGA has showed to be a feasible and effective procedure to treat obesity with a promising potential for the future. However, a multicenter randomized FDA trial was terminated secondary to lack of efficacy, whereafter the company dissolved, and future applications remain uncertain.

3.1.2 Endoscopic sleeve gastroplasty (ESG)

Another system to create a restrictive sleeve is the Overstitch system (Apollo Endosurgery, Austin, Texas, USA). Contrary to the TOGA system, it applies full-thickness running sutures alongside the greater curvature of the stomach. This results in a reduction of the functional capacity of the stomach by up to 70%, a size comparable to the reduction of the gastric lumen in laparoscopic sleeve gastrectomy (LSG) [19]. This device is currently commercially available in the United States.

3.1.2.1 Technique

The Overstitch system (**Figure 3**) consists of a double-channel endoscope equipped with a mounted suturing platform. To ensure full-thickness suture placement, a tissue grasper device is used to mobilize and capture the desired location of the suture at the gastric wall, whereafter the tissue is retracted into the suturing arm of the device [20]. As the evolution of the ESG evolved over time, different

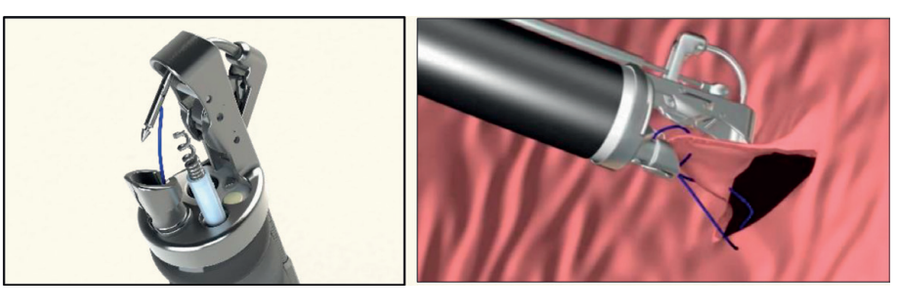

Figure 3.
The Overstitch system and full-thickness suture placement (from ApolloEndosurgery®, with permission).

techniques of suture placement have been tried, and therefore vary between studies [21]. A recent study showed good effect of a modified running suture following a Z-pattern, to provide a homogenous distribution of the disruptive force on the suture among all stitch points [22].

3.1.2.2 Efficacy and safety profile

After the Mayo Clinic first demonstrated the clinical safety and feasibility of this technique in early 2013, multiple studies have confirmed the safety and efficacy of this procedure. A multicenter study among 3 centers, including 248 subjects with a baseline BMI of 37.8 ± 5.6 kg/m^2, showed a total body weight loss (TBWL) of 15.2% [95%CI 14.2–16.3] and 18.6% [15.7–21.5], at, respectively, 6 and 24 month follow-up [23]. Five (2%) serious adverse events occurred: two patients presented with peri-gastric inflammatory fluid collection which resolved with percutaneous drainage and antibiotics, one patient presented with self-limiting hemorrhage due to marginal splenic laceration, one patient with a pulmonary embolism 72 h postoperative, and one patient required placement of a chest tube to treat concomitant pneumoperitoneum and pneumothorax caused during the procedure. All patients recovered without the need of surgical intervention. A recent retrospective analysis among 112 obese patients (baseline BMI 37.9 ± 6.7 kg/m^2) who underwent ESG using the Overstitch device reported comparable and consistent findings of approximately 15% TBWL and 50% EWL at 6 month post-ESG [24]. In the prospective study of Sharaiha et al., ESG accounted for a reduction in markers of hypertension, diabetes, and hypertriglyceridemia in addition to sustained total body weight loss after a period of 24 months [25]. ESG appears to be safe and effective in obese patients, but future randomized research is needed before incorporation into clinical practice can take place.

3.1.3 Primary obesity surgery endoluminal (POSE)

The POSE procedure is an approach in which a reduction of the gastric fundus is created, using a peroral incisionless operating platform (USGI Medical. San Clemente, CA, USA) [26]. During this procedure, transmural plications are placed at eight to nine locations in the gastric fundus with an additional three plications in de distal part of the stomach. The notion behind this is to mechanically and physically restrict the surface to which ingested food comes in contact with the stomach. Moreover, it is assumed that the plications in the gastric fundus limit the capacity to accommodate food, and therefore, activation of gastric stretch receptors in response to food is more rapidly induced.

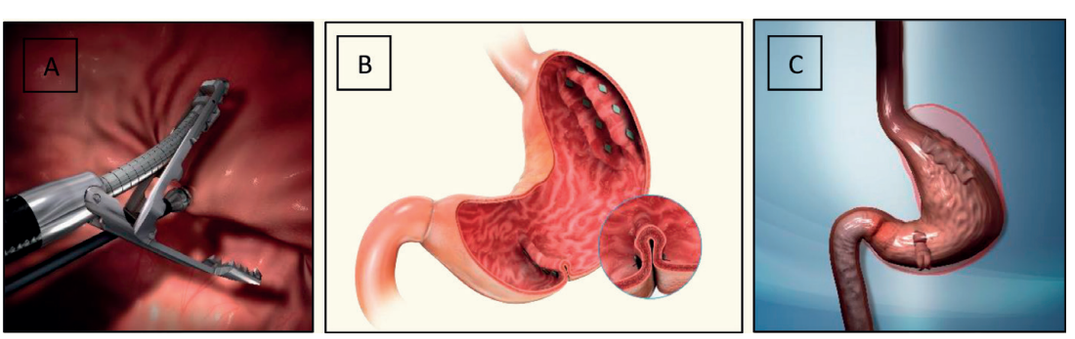

Figure 4.
The g-Prox EZ® Endoscopic Grasper (A), transmural plications at the gastric fundus and distal part of the stomach (B), and stomach after POSE procedure (C) (from USGI Medical®, with permission).

3.1.3.1 Technique

In order to create full-thickness serosa-to-serosa plications, a special overtube-style platform, the Transport Endoscopic Access Device (USGI medical) is used at the operative site [26]. It has four working channels through which an endoscope and three additional instruments can be introduced. The g-Prox EZ® Endoscopic Grasper, a flexible shaft with a gripper at the tip to mobilize and capture target tissue (**Figure 4A**); the g-Lix™ Tissue Grasper, a flexible probe which is designed to assist the g-Prox in capturing the desired tissue; and the g-Cath EZ™ Suture Anchor Delivery Catheter which is equipped with a needle at its distal tip, and facilitates the creating of plications by penetrating the mobilized tissue with a pair of pre-loaded suture anchors. This ensures anchoring of the fold until there is serosal fusion.

3.1.3.2 Efficacy and safety profile

Current literature on the efficacy and safety of this device consists of two-open label prospective single-arm trials and two randomized controlled trials [26–29]. In a multicenter randomized controlled trial in the United States, 221 patients received the POSE procedure combined with low-intensity lifestyle interventions for a period of 12 months [29]. They achieved a TBWL of 4.95 ± 7.04%, in comparison to 1.38 ± 5.58% in the control group, consisting of 111 patients who received low-intensity lifestyle intervention alone. Reported SAE were 4.7% (1.9% vomiting, 1.6% nausea, and 0.4% pain), which often occurred within the first week post-procedure and required extended hospital stay. In addition, 0.4% extra gastric bleeding and 0.4% liver abscess occurred which required, respectively, open surgery and per-cutaneous drainage [29, 30]. In another multicenter randomized controlled trial, POSE-treated subjects showed 30% TBWL after 12 months compared to 5.9% in the control group [28]. Furthermore, the POSE procedure has demonstrated to result in a significant improvement in satiation [31]. In conclusion, the POSE procedure is a promising option for the bariatric patient, but still requires further development.

3.1.4 Endomina system

The Endomina system (EndoTool SA [SST], Gosselies, Belgium) reduces gastric volume by creating an endoscopic gastroplasty alongside the greater curvature of the stomach [32].

3.1.4.1 Technique

By using an over-the-scope triangulation platform attached to an endoscope, anterior-to-posterior greater curvature plications are applied. While introducing a 5F needle preloaded with suture into the flexible arm of the platform, the stomach wall is mobilized and pulled back with a forceps. Under visual control, the needle pierces the stomach wall at the designated site, and a first tag, attached to the suture and a pre-tied knot, is released. The needle is retracted, the first plicature is released, and a second plicature can be made with the same action.

3.1.4.2 Efficacy and safety profile

A single-center, phase 1, prospective cohort study was initiated in May 2015, which demonstrated 11% TWBL after 6 months. No major adverse event was observed in the 10 patients who underwent the procedure [32]. In a multicenter prospective trial with 1-year follow-up, EWL and TBWL at 1 year were 29%

(SD 28) and 7.4% (SD 7), respectively, for the whole cohort (45 patients). At follow-up gastroscopy, 88% of sutures were still in place (30 patients). No SAE were observed [33]. A randomized controlled trial comparing the Endomina combined with diet to diet alone is currently underway.

3.1.5 Articular circular stapling device (ACE)

The articular circular stapling device (**Figure 5**) (BaroSense, Redwood City, CA; Boston Scientific Corp., Marlbourough, MA) is an investigational device which applies full-thickness transmural plications of the stomach wall aided by vacuum and stapling.

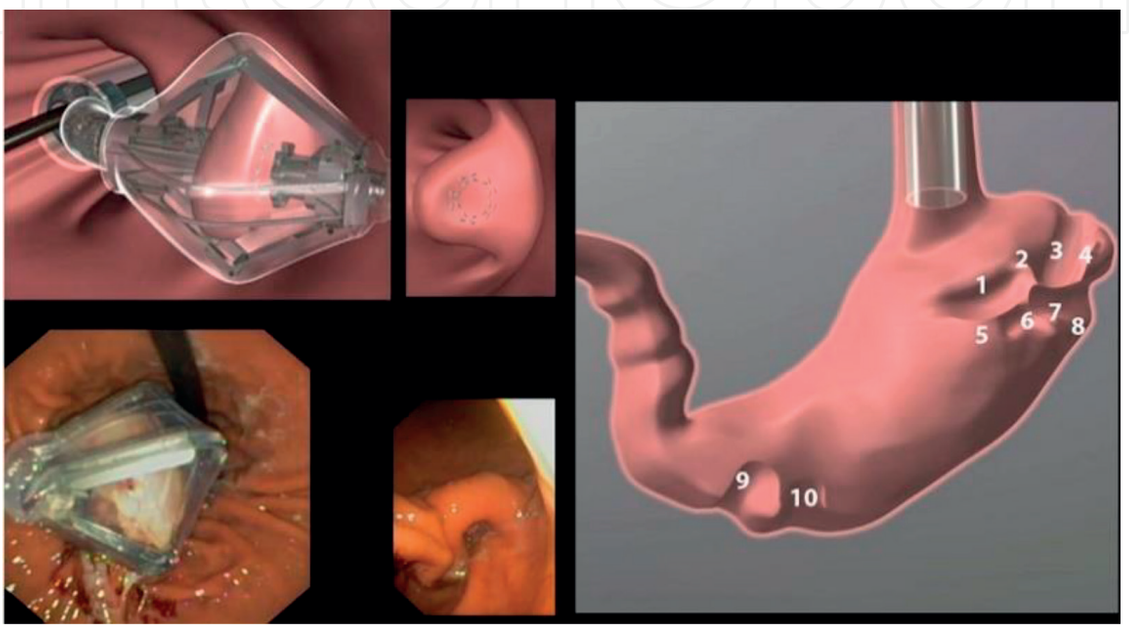

Figure 5.
The ACE stapler: after the tissue is acquired by vacuum, plications are made with a circular staple ring in 10 locations in the stomach (from [34], with permission).

3.1.5.1 Technique

With an outer diameter of 16 mm, the device has a built-in channel for a 5-mm endoscope. The stapler head, located at the distal part of the device, is able to rotate 360° and orientate into complete flexion or retroflexion. When introduced into the stomach, it is able to create a vacuum inside its silicone cover, to capture the desired amount of stomach tissue. After ensuring an adequate amount, the acquired piece of stomach tissue will be compressed by a 10-mm plastic ring with eight titanium staples, thereby creating a large, full-thickness transmural plication. After pre-loading the system with a new staple cartridge, creation of new plications can be continued in the same fashion. After a maximum of eight plications in the fundus together with an additional two in the antrum of the stomach, reduction of stomach volume alongside the greater curvature is completed. The two extra plications in the antrum of the stomach are believed to delay gastric emptying.

3.1.5.2 Efficacy and safety profile

This first reported human phase 1 study enrolled 17 patients with a median BMI of 40.2 kg/m^2 who underwent the ACE procedure [34]. Adverse events involved gastric pain (n = 7), sore throat (n = 4), diarrhea (n = 4), nausea (n = 3), and

constipation (n = 4), but resolved with conservative treatment within 15 days after surgery. No SAE occurred. Patients demonstrated a median % EWL of 34.9% (IQR 17.8–46.6) in the first year. This phase 1 study showed that the ACE stapler is safe and effective in humans. The study was funded by Barosense until sufficient funds could no longer been raised and further research was discontinued. However, randomized controlled trials and long-term follow up are needed to determine its place in the treatment of obesity. With acquisition by Boston Scientific Group, follow-up research on the ACE procedure may be on the horizon in the near future.

3.1.6 The incisionless magnetic anastomosis system

The incisionless magnetic anastomosis system (IMA) manufactured by GI Windows (Boston, MA) is a compression anastomosis technology used to create a dual-path enteral bypass in the small bowel with the use of octagon shaped self-assembling magnets.

3.1.6.1 Technique

Under fluoroscopic guidance, self-assembling magnets are delivered in the proximal jejunum and ileum by simultaneous upper and lower endoscopy. After deployment and coupling due to the magnetic field, the tissue in between will be pressed against each other causing necrosis. The necrotized tissue induces remodeling of the surrounding tissue, leading to the formation of a jejunal-ileal anastomosis. After the anastomosis has been established, the coupled magnets will be expelled by the feces.

3.1.6.2 Efficacy and safety profile

Ten patients with a mean BMI of 41 kg/m^2 underwent the procedure in the first human pilot study [35, 36]. In this pilot, laparoscopy assistance was used to ensure adequate magnet coupling and verify limb lengths. The anastomosis was formed in approximately 1 week, and magnets were expelled without pain or obstruction. All anastomoses were patent at 2- and 6-month follow-up endoscopy. After 6 months, subject demonstrated a TBWL of 10.6%. After 1 year, EWL was 40.2%, and all anastomosis remained patent. No SAE occurred and reported nausea and diarrhea were self-limiting [37]. More investigations and applications of this promising procedure are underway [38].

3.2 Gastric occupying devices

3.2.1 Transpyloric shuttle

The TransPyloric Shuttle (TPS) (BAROnova Goleta, CA, USA) is a gastric occupying device that is designed to delay gastric emptying and induce early and prolonged satiety [20]. The device consists of a spherical silicone orb that tapers into a tail tethered to a smaller cylindrical orb. After the device is delivered into the stomach through an overtube using a transluminal endoscopic procedure, the TPS moves freely in the stomach without the attachment to the tissue. Due to the physiological peristalsis, the small cylindrical orb will be pulled through the pylorus and reside in the duodenum. Because the base of the greater orb is compliant, it will self-position across the pylorus creating an intermittent seal intended to delay gastric emptying. Device removal is performed endoscopically, in which standard endoscopic graspers are used to unlock and retrieve the locking mechanism. Once unlocked, a standard endoscopic polypectomy snare can be used to retrieve the device.

3.2.1.1 Efficacy and safety profile

To date, only one feasibility study has investigated the safety and efficacy of the TPS [39]. Around 20 patients with a mean BMI of 36 kg/m^2 were randomized to TPS placement with treatment periods of either 3 or 6 months. Patients lost an average of 25.1 ± 14.0% of EWL in the 3-month group and those who had the device for 6 months lost an average of 41 ± 21.1%. Early device removal occurred in two patients because of acute onset of epigastric pain after 10.5 weeks and 5.5 months, respectively. After device removal, the complaints resolved immediately. No SAE were reported, and TPS insertion and removal procedures went without any problems. Gastric ulcer, localized in the antrum, occurred in 10 patients and was resolved by medication. The majority of adverse events reported were periprocedural and mild or moderate. However, the incidence of gastric ulcers prompted changes in the design of the TPS, with the new prototype now being studied in a multicenter randomized sham-controlled trial in the United States [40].

3.2.2 Full sense bariatric device

The Full Sense Bariatric Device (BKFW LLC, Grand rapids, MI, USA) is another gastric occupying device that comprises an esophageal stent connected to a gastric disk. It is hypothesized that it aids weight loss by placing direct and continuous pressure on the distal esophagus and cardia portion of the stomach, thereby inducing satiety. The pressure should provide continuous gastric nerve stimulation and hormonal feedback mechanisms that signals a feeling of fullness to the brain, even when there is no food present.

3.2.2.1 Efficacy and safety profile

In unpublished data with three human subjects, the device reportedly showed a 28% EWL after 46 days. During a 6-month trial in an unknown number of subjects, the device demonstrated a median EWL of 80%. However, no peer-reviewed data are currently available to determine its safety and efficacy [20].

4. Bariatric pacing and gastric electrical stimulation

4.1 Bariatric pacing

As early as 1980, the vagal system gained attention as a possible target in obesity treatment. Patients with peptic ulcer disease temporarily lost weight after truncal vagotomy [41, 42]. Only 10–20% of the vagal nerve fibers are composed of efferent fibers that control stomach activity, whereas the remaining 80–90% consist of afferent fibers that send signals regulating satiety and satiation [43]. With this in mind, application of electrical current to the stomach vagus nerve alters gastric myoelectrical activity. While the exact mechanism of action remains to be elucidated, bariatric pacing poses a new frontier in the treatment of severe obesity.

4.1.1 Maestro rechargeable system

Vagal blocking therapy (VBloc therapy) has been suggested as a new approach to tackle morbid obesity. Instead of performing a permanent truncal vagotomy, it blocks the vagal nerves in an intermittent manner using electrical pulses generated by the Maestro Rechargeable System (Enteromedics, St Paul, MN).

4.1.1.1 Technique

The maestro rechargeable system is an FDA approved implant device that is implanted with minimally invasive laparoscopic techniques. The system is provided with two leads which are placed around both the anterior and posterior vagal trunks at the level of the esophageal junction. Each lead delivers high-frequency, low energy, intermittent electrical pulses to its respective intra-abdominal vagal trunk for a predetermined period each day. This intermittent interruption of vagus nerve signaling leads to delayed gastric emptying which reduces feelings of hunger and promotes satiety [44]. A rechargeable neuroregulator is placed subcutaneously on the thoracic wall.

4.1.1.2 Efficacy and safety profile

Several feasibility studies have shown that VBloc therapy has a desirable safety profile and results in clinically important weight loss [45]. However, in the first randomized controlled trial comparing VBloc therapy with sham control, results were disappointing [46]. VBloc therapy was regarded safe, but weight loss was no greater in treated compared to control patients. Authors reported that the system electrical safety checks could have accounted for the weight loss in the control group. Another randomized controlled trial demonstrated 24.4% EWL in the VBloc group compared to 15.9% in the sham control group after a period of 12 months [47]. An open label follow-up study of the VBloc arm showed maintenance of weight loss in the majority of patients [48]. Adverse events were more frequently reported in the VBloc group and mostly involved heartburn or dyspepsia. Stronger evidence is needed to determine the place of VBloc therapy in the treatment of obesity.

4.2 Gastric electrical stimulation

Based on growing knowledge about gastrointestinal physiology, gastric electrical stimulation (GES) has been identified as a potential treatment modality for obesity [49, 50]. As early as 1995, the concept of GES was demonstrated in a series of animal experiments [51]. The exact mechanism of action of GES is still relatively unknown. However, it is thought that GES impairs gastric electrical activity, induces gastric distension, reduces gastric accommodation, and inhibits stomach peristalsis, thereby leading to delayed gastric emptying and increased satiety [52].

4.2.1 The transcend implantable gastric stimulator

A novel gastric electrical stimulator is the Transcend Implantable Gastric Stimulator (IGS, Transneuronix Inc., Mt Arlington, NJ, USA).

4.2.1.1 Technique

The device consists of one lead with two electrodes which is laparoscopically implanted on the lesser curvature near the pes anserinus and approximately 6 cm away from the pylorus. Proximally, the lead is fixed using an endostitch suture, and distally fixation is secured with the use of two clips. One electrode is positioned near the pes anserinus, while the other is placed near the esophagogastric junction. After adequate lead and electrode placement, the electrical pulse generator, which is connected to the lead, is implanted in a supra-fascial pocket and anchored with two sutures. Intraoperative gastroscopy is used to diagnose iatrogenic gastric perforation. After implantation, the device will be in off-mode for a period of 30 days, to allow the gastric tissue to heal before stimulation is initiated.

4.2.1.2 Efficacy and safety profile

A safety and feasibility study of the Transcend IGS implanted in 12 patients demonstrated a technically feasible and safe procedure [53]. In 25% of the patients, lead dislodgement occurred which required replacement. After 9 months, patients had lost a mean weight of 16 ± 12 kg. Another study conducted in 2002, in which 20 patients with a mean BMI of 40.9 kg/m^2 received the device, showed a % EWL of 10.6 ± 1.8 at 1 month, 1.5 ± 3.5 at 6 months, and 23.8 ± 5.0 at 10 months. Three intraoperative gastric penetrations were observed by gastroscopy. No further adverse events or complications were reported during the study period [54]. However, in a prospective double-blinded randomized sham-controlled trial, no difference was observed between the treatment and control group after a treatment period of 12 months [55]. Contributing to this was an investigator-initiated sub-study designed to assess whether IGS affects plasma levels of ghrelin and peptide YY which resulted in the conclusion that IGS does not prevent increase in fasting plasma levels of ghrelin that are associated with weight loss [56]. In conclusion, further studies are needed to determine whether changes in technology can provide meaningful weight loss and maintenance.

4.2.2 Tantalus gastric electrical stimulatory device

The Tantalus Electrical Stimulatory Device (Metacure, Israel) is a pulse generator accommodated with three bipolar leads. The device is designed to create an early activation of physiological satiety by enhancing physiological signals of gastric distensions and contractions. The system is capable of delivering gastric contractility modulation (GCM) signals triggered by food. The device senses spontaneous electrical activity of the smooth muscles and then delivers signals to enhance them. With the use of a specialized algorithm of electro-mechanical parameters in the gut, the system can detect the onset of a meal. It is hypothesized that enhancing of spontaneous gastric contractions in a very early stage of the meal, before reaching full gastric distension, induced early satiety by stimulation of stretch receptors. These elicit an increased input to the CNS, thereby promoting a feeling of fullness.

4.2.2.1 Technique

The system is implanted with the use of a laparoscope, whereby the three bipolar leads are placed in the sub-serosa of the gastric wall. One lead is placed in the fundus area to detect the intake of food, while the other two are positioned in the antrum for slow-wave detection and signal delivery. Nonabsorbable sutures and two clips are to ensure proper fixation at, respectively, the proximal and distal part of the lead. The procedure is carried out under both laparoscopic and gastroscopic visualization to prevent perforation of the gastric wall. After successful lead placement, the leads are connected to the implantable pulse generator which is placed in a subcutaneous pocket at the left side of the abdomen.

4.2.2.2 Efficacy and safety profile

In the first open-label single center trial, 12 patients with a mean BMI of 43.2 kg/m^2 underwent the implantation with the Tantalus system [57]. After 6 weeks of "off"-mode, the system got activated, which resulted in 17.6 ± 4.3% of EWL after a period of 20 weeks. Furthermore, a significant decrease in hunger, assessed with the three-factor eating questionnaire (TFEQ), was observed. Apart from two SAE including one case of rhabdomyolysis and one case of pulmonary

embolism, the therapy was well tolerated. Both cases resolved completely without the need of surgical intervention, and patients were able to complete the study. In a study assessing the performance of the system, the algorithm was able to detect 73% of meals consumed with a false stimulation rate of 28% [58]. The majority of studies have also demonstrated a good improvement on glucose control in addition to weight loss [50, 59, 60].

5. Conclusion

New advancements in the field of bariatric endoscopy offer a promising entity to bridge the gap between lifestyle counseling, pharmaceutical treatment, and major surgical interventions in the treatment of obesity. Most of the procedures demonstrate the unique ability to be reversible or can be repeated throughout life for continued management of this disease. Besides, they have been proven to be not only effective in weight loss but also in the reduction of comorbidities associated with obesity. The results of these innovative techniques are very encouraging, and further clinical studies will likely occur in the near future. As we gain more evidence through well-designed conducted research, these treatment modalities can become an inherent part of everyday clinical practice.

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Conflict of interest

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References

[1] WHO. Obesity and Overweight Factsheet. 2018. Available from: http://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

[2] Ribaric G, Buchwald JN, McGlennon TW. Diabetes and weight in comparative studies of bariatric surgery vs conventional medical therapy: A systematic review and meta-analysis. Obesity Surgery. 2014;**24**(3):437-455

[3] Sjostrom L. Bariatric surgery and reduction in morbidity and mortality: Experiences from the SOS study. International Journal of Obesity. 2008;**32**(Suppl 7):S93-S97

[4] Ruban A, Ashrafian H, Teare JP. The EndoBarrier: Duodenal-jejunal bypass liner for diabetes and weight loss. Gastroenterology Research and Practice. 2018;**2018**:7823182

[5] Patel N, Mohanaruban A, Ashrafian H, Le Roux C, Byrne J, Mason J, et al. EndoBarrier(R): A safe and effective novel treatment for obesity and type 2 diabetes? Obesity Surgery. 2018;**28**(7):1980-1989

[6] Schouten R, Rijs CS, Bouvy ND, Hameeteman W, Koek GH, Janssen IM, et al. A multicenter, randomized efficacy study of the EndoBarrier Gastrointestinal Liner for presurgical weight loss prior to bariatric surgery. Annals of Surgery. 2010;**251**(2):236-243

[7] Koehestanie P, de Jonge C, Berends FJ, Janssen IM, Bouvy ND, Greve JW. The effect of the endoscopic duodenal-jejunal bypass liner on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. Annals of Surgery. 2014;**260**(6):984-992

[8] Jirapinyo P, Haas AV, Thompson CC. Effect of the duodenal-jejunal bypass liner on glycemic control in patients with type 2 diabetes with obesity: A meta-analysis with secondary analysis on weight loss and hormonal changes. Diabetes Care. 2018;**41**(5):1106-1115

[9] Ryder REJ, Munro L, Mcmaster JJ, Bessell J, Bascomb JM, Collins JE, et al. First risk-benefit data from the worldwide endobarrier registry. Diabetes. 2018;**67**(Supplement 1)

[10] Forner PM, Ramacciotti T, Farey JE, Lord RV. Safety and effectiveness of an endoscopically placed duodenal-jejunal bypass device (EndoBarrier(R)): Outcomes in 114 patients. Obesity Surgery. 2017;**27**(12):3306-3313

[11] Quezada N, Munoz R, Morelli C, Turiel D, Hernandez J, Pimentel F, et al. Safety and efficacy of the endoscopic duodenal-jejunal bypass liner prototype in severe or morbidly obese subjects implanted for up to 3 years. Surgical Endoscopy. 2018;**32**(1):260-267

[12] Sandler BJ, Rumbaut R, Swain CP, Torres G, Morales L, Gonzales L, et al. Human experience with an endoluminal, endoscopic, gastrojejunal bypass sleeve. Surgical Endoscopy. 2011;**25**(9):3028-3033

[13] Sandler BJ, Rumbaut R, Swain CP, Torres G, Morales L, Gonzales L, et al. One-year human experience with a novel endoluminal, endoscopic gastric bypass sleeve for morbid obesity. Surgical Endoscopy. 2015;**29**(11):3298-3303

[14] Moreno C, Closset J, Dugardeyn S, Barea M, Mehdi A, Collignon L, et al. Transoral gastroplasty is safe, feasible, and induces significant weight loss in morbidly obese patients: Results of the second human pilot study. Endoscopy. 2008;**40**(5):406-413

[15] Deviere J, Ojeda Valdes G, Cuevas Herrera L, Closset J, Le Moine O, Eisendrath P, et al. Safety, feasibility and

weight loss after transoral gastroplasty: First human multicenter study. Surgical Endoscopy. 2008;**22**(3):589-598

[16] Familiari P, Costamagna G, Blero D, Le Moine O, Perri V, Boskoski I, et al. Transoral gastroplasty for morbid obesity: A multicenter trial with a 1-year outcome. Gastrointestinal Endoscopy. 2011;**74**(6):1248-1258

[17] Chiellini C, Iaconelli A, Familiari P, Riccioni ME, Castagneto M, Nanni G, et al. Study of the effects of transoral gastroplasty on insulin sensitivity and secretion in obese subjects. Nutrition, Metabolism, and Cardiovascular Diseases: NMCD. 2010;**20**(3):202-207

[18] Nanni G, Familiari P, Mor A, Iaconelli A, Perri V, Rubino F, et al. Effectiveness of the transoral endoscopic vertical gastroplasty (TOGa(R)): A good balance between weight loss and complications, if compared with gastric bypass and biliopancreatic diversion. Obesity Surgery. 2012;**22**(12):1897-1902

[19] Fayad L, Adam A, Dunlap M, Badurdeen DS, Hill C, Ajayi T, et al. Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy: A case-matched study. Gastrointestinal Endoscopy. 2018

[20] Bazerbachi F, Vargas Valls EJ, Abu Dayyeh BK. Recent clinical results of endoscopic bariatric therapies as an obesity intervention. Clinical Endoscopy. 2017;**50**(1):42-50

[21] Jain D, Bhandari BS, Arora A, Singhal S. Endoscopic sleeve gastroplasty—A new tool to manage obesity. Clinical Endoscopy. 2017;**50**(6):552-561

[22] Graus Morales J, Crespo Perez L, Marques A, Marin Arribas B, Bravo Arribas R, Ramo E, et al. Modified endoscopic gastroplasty for the treatment of obesity. Surgical Endoscopy. 2018;**32**(9):3936-3942

[23] Lopez-Nava G, Sharaiha RZ, Vargas EJ, Bazerbachi F, Manoel GN, Bautista-Castano I, et al. Endoscopic sleeve gastroplasty for obesity: A multicenter study of 248 patients with 24 months follow-up. Obesity Surgery. 2017;**27**(10):2649-2655

[24] Sartoretto A, Sui Z, Hill C, Dunlap M, Rivera AR, Khashab MA, et al. Endoscopic sleeve gastroplasty (ESG) is a reproducible and effective endoscopic bariatric therapy suitable for widespread clinical adoption: A large, international multicenter study. Obesity Surgery. 2018;**28**(7):1812-1821

[25] Sharaiha RZ, Kumta NA, Saumoy M, Desai AP, Sarkisian AM, Benevenuto A, et al. Endoscopic sleeve gastroplasty significantly reduces body mass index and metabolic complications in obese patients. Clinical Gastroenterology and Hepatology. 2017;**15**(4):504-510

[26] Espinos JC, Turro R, Mata A, Cruz M, da Costa M, Villa V, et al. Early experience with the Incisionless Operating Platform (IOP) for the treatment of obesity: The Primary Obesity Surgery Endolumenal (POSE) procedure. Obesity Surgery. 2013;**23**(9):1375-1383

[27] Lopez-Nava G, Bautista-Castano I, Jimenez A, de Grado T, Fernandez-Corbelle JP. The Primary Obesity Surgery Endolumenal (POSE) procedure: One-year patient weight loss and safety outcomes. Surgery for Obesity and Related Diseases. 2015;**11**(4):861-865

[28] Miller K, Turro R, Greve JW, Bakker CM, Buchwald JN, Espinos JC. MILEPOST multicenter randomized controlled trial: 12-month weight loss and satiety outcomes after pose (SM) vs. medical therapy. Obesity Surgery. 2017;**27**(2):310-322

[29] Sullivan S, Swain JM, Woodman G, Antonetti M, De La Cruz-Munoz N, Jonnalagadda SS, et al. Randomized sham-controlled trial evaluating efficacy and safety of endoscopic gastric plication for primary obesity: The essential trial. Obesity. 2017;**25**(2):294-301

[30] DeAsis FJ, Denham W, Linn JG, Haggerty SP, Ujiki MB. Primary obesity surgery endoluminal. Surgical Endoscopy. 2017;**31**(2):951

[31] Espinos JC, Turro R, Moragas G, Bronstone A, Buchwald JN, Mearin F, et al. Gastrointestinal physiological changes and their relationship to weight loss following the POSE procedure. Obesity Surgery. 2016;**26**(5):1081-1089

[32] Huberty V, Ibrahim M, Hiernaux M, Chau A, Dugardeyn S, Deviere J. Safety and feasibility of an endoluminal-suturing device for endoscopic gastric reduction (with video). Gastrointestinal Endoscopy. 2017;**85**(4):833-837

[33] Huberty V, Machytka E, Boskoski I, Barea M, Costamagna G, Deviere J. Endoscopic gastric reduction with an endoluminal suturing device: A multicenter prospective trial with 1-year follow-up. Endoscopy. Dec 2018;**50**(12):1156-1162

[34] Verlaan T, Paulus GF, Mathus-Vliegen EMH, Veldhuyzen EAML, Conchillo JM, Bouvy ND, et al. Endoscopic gastric volume reduction with a novel articulating plication device is safe and effective in the treatment of obesity (with video). Gastrointestinal Endoscopy. 2015;**81**(2):312-320

[35] Machytka E, Buzga M, Ryou M, Lautz DB, Thompson CC. 1139 endoscopic dual-path enteral anastomosis using self-assembling magnets: First-in-human clinical feasibility. Gastroenterology. 2016;**150**(4):S232

[36] Machytka E, Buzga M, Lautz DB, Ryou M, Simonson D, Thompson CC. 103 A dual-path enteral bypass procedure created by a novel incisionless anastomosis system (IAS): 6-month clinical results. Gastroenterology. 2016;**150**(4):S26

[37] Machytka E, Buzga M, Zonca P, Lautz DB, Ryou M, Simonson DC, et al. Partial jejunal diversion using an incisionless magnetic anastomosis system: 1-year interim results in patients with obesity and diabetes. Gastrointestinal Endoscopy. 2017;**86**(5):904-912

[38] Vargas EJ, Rizk M, Bazerbachi F, Abu Dayyeh BK. Medical devices for obesity treatment: Endoscopic bariatric therapies. The Medical Clinics of North America. 2018;**102**(1):149-163

[39] Marinos G, Eliades C, Raman Muthusamy V, Greenway F. Weight loss and improved quality of life with a nonsurgical endoscopic treatment for obesity: Clinical results from a 3- and 6-month study. Surgery for Obesity and Related Diseases. 2014;**10**(5):929-934

[40] Sullivan S, Edmundowicz SA, Thompson CC. Endoscopic bariatric and metabolic therapies: New and emerging technologies. Gastroenterology. 2017;**152**(7):1791-1801

[41] Smith DK, Sarfeh J, Howard L. Truncal vagotomy in hypothalamic obesity. The Lancet. 1983;**1**(8337): 1330-1331

[42] Kral JG. Vagotomy as a treatment for morbid obesity. The Surgical Clinics of North America. 1979;**59**(6):1131-1138

[43] Hwang SS, Takata MC, Fujioka K, Fuller W. Update on bariatric surgical procedures and an introduction to the implantable weight loss device: The maestro rechargeable system. Medical Devices. 2016;**9**:291-299

[44] Stimac D, Klobucar Majanovic S, Licina M. Recent trends in endoscopic

management of obesity. Surgical Innovation. 2016;**23**(5):525-537

[45] Camilleri M, Toouli J, Herrera MF, Kulseng B, Kow L, Pantoja JP, et al. Intra-abdominal vagal blocking (VBLOC therapy): Clinical results with a new implantable medical device. Surgery. 2008;**143**(6):723-731

[46] Sarr MG, Billington CJ, Brancatisano R, Brancatisano A, Toouli J, Kow L, et al. The EMPOWER study: Randomized, prospective, double-blind, multicenter trial of vagal blockade to induce weight loss in morbid obesity. Obesity Surgery. 2012;**22**(11):1771-1782

[47] Ikramuddin S, Blackstone RP, Brancatisano A, Toouli J, Shah SN, Wolfe BM, et al. Effect of reversible intermittent intra-abdominal vagal nerve blockade on morbid obesity: The ReCharge randomized clinical trial. Journal of the American Medical Association. 2014;**312**(9):915-922

[48] Apovian CM, Shah SN, Wolfe BM, Ikramuddin S, Miller CJ, Tweden KS, et al. Two-year outcomes of vagal nerve blocking (vBloc) for the treatment of obesity in the ReCharge trial. Obesity Surgery. 2017;**27**(1):169-176

[49] Greenway F, Zheng J. Electrical stimulation as treatment for obesity and diabetes. Journal of Diabetes Science and Technology. 2007;**1**(2):251-259

[50] Cha R, Marescaux J, Diana M. Updates on gastric electrical stimulation to treat obesity: Systematic review and future perspectives. World Journal of Gastrointestinal Endoscopy. 2014;**6**(9):419-431

[51] Cigaina VV, Pinato G, Rigo VV, Bevilacqua M, Ferraro F, Ischia S, et al. Gastric peristalsis control by mono situ electrical stimulation: A preliminary study. Obesity Surgery. 1996;**6**(3):247-249

[52] Chen J. Mechanisms of action of the implantable gastric stimulator for obesity. Obesity Surgery. 2004;**14** (Suppl 1):S28-S32

[53] D'Argent J. Gastric electrical stimulation as therapy of morbid obesity: Preliminary results from the French study. Obesity Surgery. 2002;**12**(Suppl 1):21s-25s

[54] Favretti F, De Luca M, Segato G, Busetto L, Ceoloni A, Magon A, et al. Treatment of morbid obesity with the transcend implantable gastric stimulator (IGS): A prospective survey. Obesity Surgery. 2004;**14**(5):666-670

[55] Shikora SA, Bergenstal R, Bessler M, Brody F, Foster G, Frank A, et al. Implantable gastric stimulation for the treatment of clinically severe obesity: Results of the SHAPE trial. Surgery for Obesity and Related Diseases. 2009;**5**(1):31-37

[56] Korner J, Nandi A, Wright SM, Waitman J, McMahon DJ, Bessler M, et al. Implantable gastric stimulator does not prevent the increase in plasma ghrelin levels that occurs with weight loss. Obesity. 2011;**19**(10):1935-1939

[57] Bohdjalian A, Prager G, Aviv R, Policker S, Schindler K, Kretschmer S, et al. One-year experience with Tantalus: A new surgical approach to treat morbid obesity. Obesity Surgery. 2006;**16**(5):627-634

[58] Policker S, Lu H, Haddad W, Aviv R, Kliger A, Glasberg O, et al. Electrical stimulation of the gut for the treatment of type 2 diabetes: The role of automatic eating detection. Journal of Diabetes Science and Technology. 2008;**2**(5):906-912

[59] Policker S, Haddad W, Yaniv I. Treatment of type 2 diabetes using meal-triggered gastric electrical stimulation. The Israel Medical Association Journal. 2009;**11**(4):206-208

[60] Sanmiguel CP, Conklin JL, Cunneen SA, Barnett P, Phillips EH, Kipnes M, et al. Gastric electrical stimulation with the TANTALUS system in obese type 2 diabetes patients: Effect on weight and glycemic control. Journal of Diabetes Science and Technology. 2009;**3**(4):964-970