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Review

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Endoscopic gastric remodeling procedures for obesity treatment: a comprehensive review

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Abstract

Obesity has become a global epidemic, posing significant health challenges for individuals and straining healthcare systems worldwide. Endoscopic bariatric and metabolic therapies have emerged as an evolving field, characterized by their minimally invasive, reversible, and organ-preserving nature. This modality offers a promising alternative to traditional bariatric surgery. Various endoscopic therapies targeting the stomach and small bowel have been developed. Among these, endoscopic gastric remodeling interventions have demonstrated superior effectiveness and durability. These procedures utilize endoscopic tissue approximation devices to perform full-thickness suturing or plication of the gastric wall, thereby restricting the stomach volume and altering gastric motility to induce early satiety. This review aims to provide a comprehensive summary of the different endoscopic gastric remodeling interventions and discuss potential future developments in this rapidly evolving field, which holds the promise of offering an alternative therapeutic approach to the management of the global obesity epidemic.

Keywords: Endoscopic gastric remodeling, endoscopic sleeve gastroplasty, primary obesity surgery endoluminal, endomina, obesity, bariatric endoscopy, endoscopic bariatric, metabolic therapy

INTRODUCTION

Obesity is recognized as a chronic, multifactorial disease that often presents as a complex and relapsing condition. It is associated with a myriad of health complications, including but not limited to diabetes, metabolic syndrome, cardiovascular disease, and malignancy. These conditions not only compromise the life expectancy and quality of life (QOL) of affected individuals but also impose a significant burden on the healthcare system globally[1]. The World Health Organization (WHO) had declared obesity an epidemic in 1997, marking a pivotal moment in public health awareness. Ever since then, the prevalence of obesity has continued to escalate on a global scale, with approximately 38% of the global population classified as either overweight or obese[2]. Notably, a rapid increase in obesity rates has been observed among adolescents and in lower-income countries[3,4].

Initial treatment strategies for obesity typically involve diet and lifestyle modifications. However, the efficacy of these interventions in managing obesity remains limited. While pharmacotherapies are available, they frequently lack long-term sustainability. Bariatric surgery has been established as an effective and enduring treatment option for severe obesity, resulting in significant weight reduction and improvements in associated comorbidities[5]. Nonetheless, the high costs, invasiveness, and irreversible nature of bariatric surgery remain major obstacles that hinder its broader adoption, with fewer than 2% of eligible patients opting for surgical intervention[6]. Furthermore, concerns regarding potential long-term complications, as well as nutritional deficiencies, persist[7]. Some patients who undergo surgery may experience suboptimal weight reduction or weight recurrence. However, revisional operation is more technically challenging and associated with increased morbidity and mortality[8].

The increasing demand for less invasive alternatives to conventional bariatric surgery has fostered the rapid advancement of endoscopic bariatric and metabolic therapies (EBMTs) in recent years. These interventions offer safe and effective options for patients who do not qualify for surgery or prefer less invasive, reversible, and organ-preserving procedures with lower risks. Recently, the joint guideline from American Society for Gastrointestinal Endoscopy (ASGE) and European Society of Gastrointestinal Endoscopy (ESGE) suggests the use of EBMT plus lifestyle modification for obese patients with a BMI ≥ 30 kg/m^2, or in overweight patients (BMI of 27 to 29.9 kg/m^2) with at least one obesity-related comorbidity[9]. Among these EBMTs, gastric remodeling interventions have demonstrated superior efficacy as primary endoscopic therapies for achieving weight loss at the 12-month mark[10]. These endoscopic procedures utilize suturing or plication techniques to effectively reduce stomach volume and modify gastric motility to promote feelings of satiety. These techniques can also be performed as a revisional intervention for patients who have undergone prior bariatric surgery.

This review offers a thorough overview of the different endoscopic gastric remodeling (EGR) interventions and explores potential future developments in this rapidly evolving field. The goal is to enhance our understanding and application of these cutting-edge approaches in combating the global obesity crisis and promoting metabolic health.

DEVELOPMENT OF GASTRIC REMODELING TECHNIQUE

A critical aspect in the advancement of EBMTs lies in comprehending the mechanisms underlying weight loss following bariatric surgery. It is now established that the surgical modification of the gastrointestinal (GI) tract anatomy, particularly targeted at the stomach or small bowel, elicits a complex cascade of changes in GI motility, enteric neuroendocrine signaling, and gut microbiota[11]. This paradigm shift in understanding has instigated the development of endoscopic technologies, moving beyond the simplistic concepts of restriction or malabsorption toward the goal of remodeling the foregut. The ultimate objective is to achieve outcomes in line with the durable effectiveness of bariatric surgery.

Restricting gastric volume is central to inducing weight loss. Virtually all bariatric surgical procedures involve reducing the size of the stomach through resection or exclusion. This not only precipitates early satiety, but also instigates changes in appetite-regulating hormones and gastric emptying[12,13]. The accessibility via flexible endoscopy and ample space for manipulation have spurred the development of multiple EBMTs focusing on the stomach. Techniques employing endoscopic suturing devices, plication baskets, and staples have been devised to effectively remodel and reduce the volume of the stomach[14].

Pioneering efforts in EGR focused on the creation of a gastric partition akin to vertical banded gastroplasty. Innovations such as the EndoCinch and TOGA systems were introduced and initially trialed in human subjects in 2008. The EndoCinch endoscopic plicating system (CR Bard, Murray Hill, NJ) utilized suction to draw the gastric wall into the device, forming partial-thickness plications, while the TOGA sleeve stapler (Satiety Inc., Palo Alto, CA) facilitated transoral gastroplasty along the mid-proximal gastric body. Nonetheless, outcomes from these techniques proved largely underwhelming, with early suture breakage and insufficient physiological changes in the remodeled stomach[15,16] [Figures 1 and 2].

Later on, with the increased popularity of sleeve gastrectomy, the focus was changed to remodel the greater curvature of the stomach to emulate the surgical outcome. Physiological studies have confirmed that remodeling the greater curvature of the stomach to create a narrow, shortened sleeve configuration not only causes mechanical restriction but also delays gastric emptying, enhances satiation, and potentially improves insulin sensitivity[19,20]. At the same time, preclinical works on the optimal endoscopic suturing techniques and materials and the histopathological correlation were carried out. The findings showed that full-thickness suturing (serosa-to-serosa apposition), in contrast to superficial (mucosa-to-mucosa) plications, could produce serosal fusion and durable plication folds[21,22].

Subsequently, with the rise in popularity of sleeve gastrectomy, the focus shifted toward remodeling the greater curvature of the stomach to emulate surgical outcomes. Physiological studies have confirmed that remodeling the greater curvature of the stomach to create a narrow, shortened sleeve configuration not only causes mechanical restriction but also delays gastric emptying, enhances satiation, and potentially improves insulin sensitivity[21,22]. At the same time, preclinical works delved into optimal endoscopic suturing techniques, materials, and their histopathological correlations. Results indicated that full-thickness suturing, as opposed to mucosal suturing, could lead to serosal fusion and more durable plication folds[19,20]. Various full-thickness suturing or plication endoscopic devices have been developed for tissue approximation and gastric remodeling. Currently, EGR can be performed using three approaches, namely endoscopic sleeve gastroplasty (Apollo Overstitch), primary obesity surgery endoluminal [USGI Incisionless operating platform (IOP)], and Endomina gastric plication (Endomina plication system).

ENDOSCOPIC SLEEVE GASTROPLASTY

Device and technique

Endoscopic sleeve gastroplasty (ESG) was first described in 2013, utilizing the Overstitch (Apollo Endosurgery, Austin, TX, USA) endoscopic suturing device to create a tubular stomach that mimics the results of a sleeve gastrectomy through multiple full-thickness sutures.

The Apollo Overstitch system is a single-use, single-operator endoscopic suturing device developed in 2009, which has demonstrated its feasibility for performing full-thickness suturing[23,24]. It consists of four components: a needle driver mounted externally at the tip of the endoscope, which connects to a handle that controls the arc-like movements of the needle; an anchor exchange catheter with a suture; a corkscrew-like tissue helix that helps draw tissue into the needle jaws for full-thickness suturing; and a suture cinch

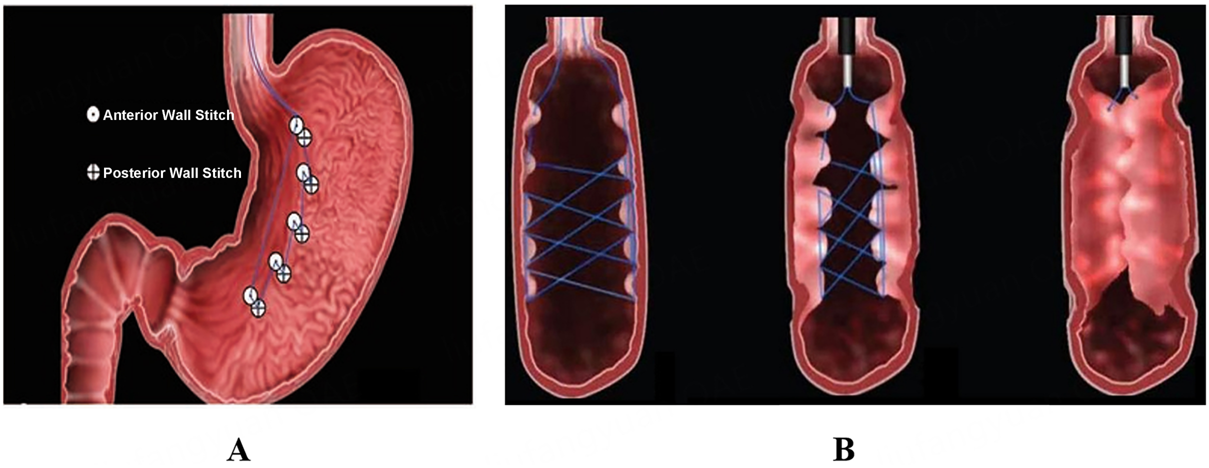

Figure 1. Endoscopic vertical gastroplasty using the EndoCinch endoscopic suturing device: (A) endoscopic suturing pattern for the creation of a vertical gastroplasty; (B) vertical partial-thickness plication is formed as the suture is pulled tight. This figure is quoted with permission from Elsevier[17].

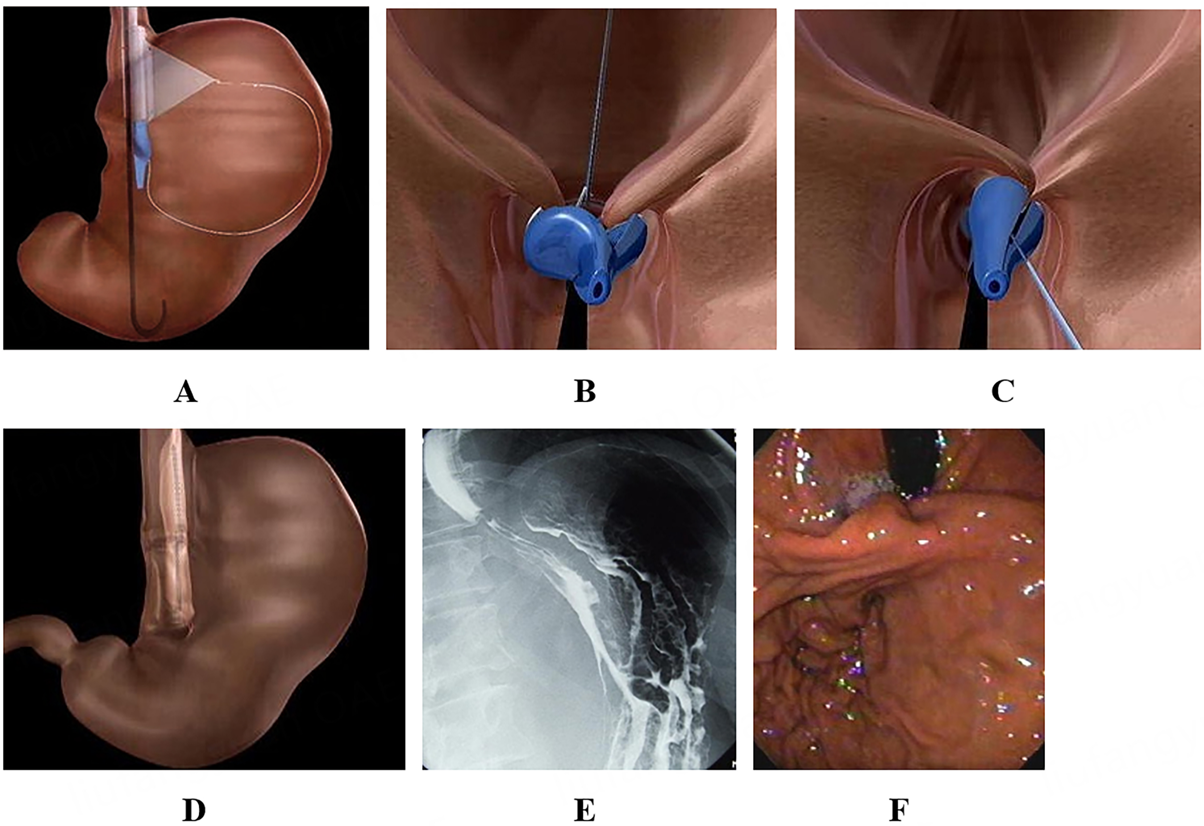

Figure 2. Transoral gastroplasty using TOGA Sleeve Stapler. (A) TOGA Sleeve Stapler with retraction wire deployed, orienting tissue for capture by suction; (B-D) After suction was applied, collecting tissue from anterior and posterior walls of the stomach, the stapler was clamped and fired, creating a sleeve from the angle of His parallel to the lesser curve; (E) barium swallow at 3 months; (F) sleeve outlet and staple line at 6 months. This figure is quoted with permission from Springer Nature[18].

that secures and cuts the suture [Figure 3]. The first generation of the Overstitch device requires a double-channel therapeutic endoscope, while the second generation, the Overstitch SX, is compatible with any

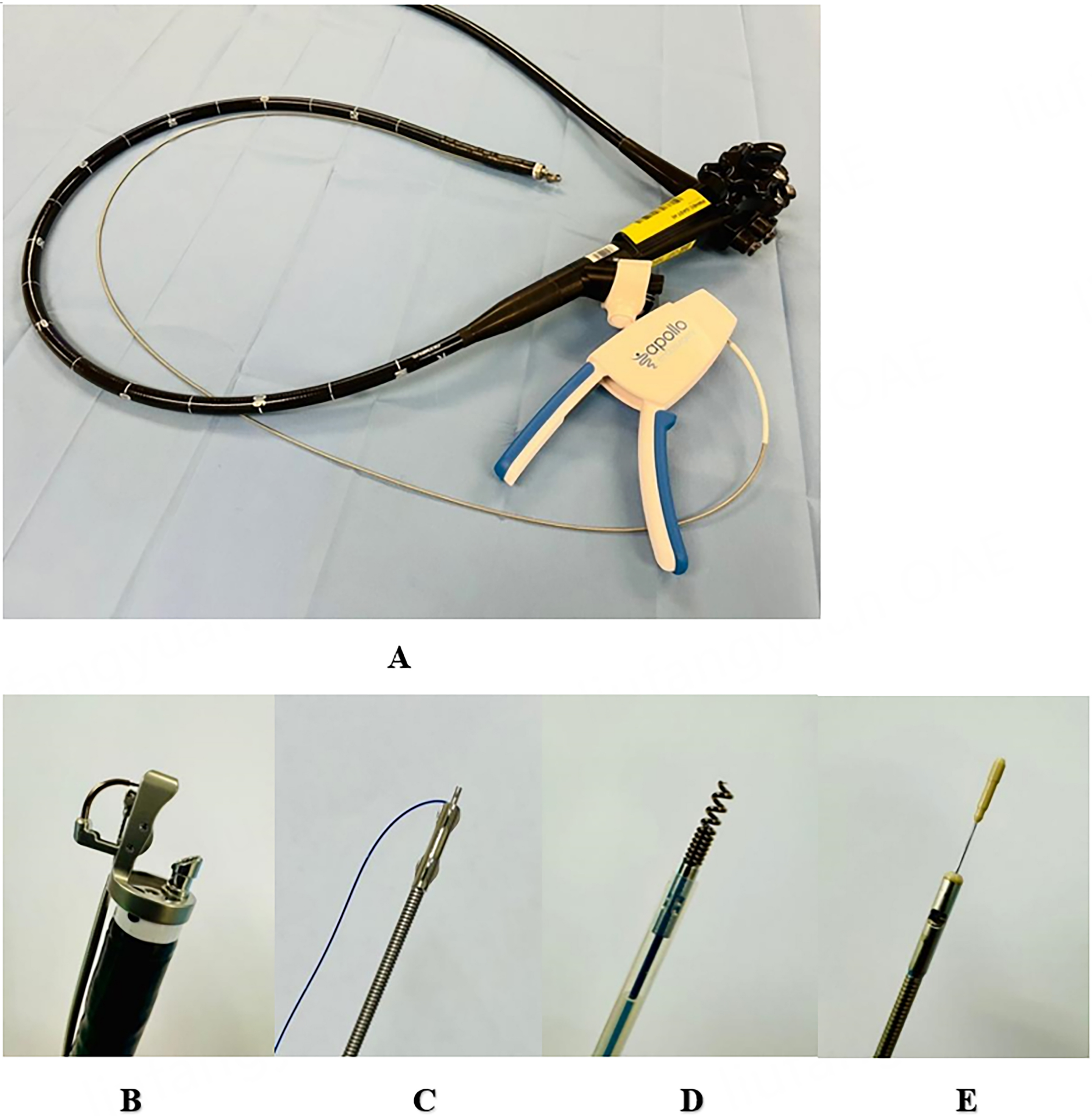

Figure 3. The Apollo Overstitch system. (A) The device after mounted on a double-channel gastroscope; (B) Close view of the needle driver; (C) Anchor exchange catheter with suture mounted; (D) Tissue helix; (E) Suture cinch.

single-channel gastroscope with a diameter of 8.8 to 9.8 mm. Recently, a new single-channel model, the Overstitch NXT, has been released. It features an operator-controlled helix for tissue acquisition and enables advanced retroflexion of the scope. The Overstitch suturing device has a wide range of clinical applications, including defect closure, stent anchoring, and bariatric endoscopy[25]. It is currently the only EGR device that has CE mark and The Food and Drug Administration (FDA) marketing authorization for the treatment of obesity.

In general, the ESG procedure is carried out under general anesthesia using a flexible gastroscope with CO_2 insufflation. The patient is positioned in a left semi-lateral or lateral position, and prophylactic broadspectrum antibiotics are administered. A diagnostic upper endoscopy is initially performed to assess the anatomy and rule out any contraindications, such as large hiatal hernias, active gastric ulcers, or malignancy. Although extensive gastric intestinal metaplasia or a strong family history of gastric cancer are not absolute contraindications for ESG, patients should be made aware of the risks, as subsequent surveillance of the plication folds may not be feasible. Suturing sites can be pre-marked using Argon plasma coagulation (APC) along the anterior and posterior walls of the stomach. The Overstitch system is then assembled onto the gastroscope and introduced into the stomach. An esophageal overtube is optional if gentle manipulation of the scope is employed.

The basic suturing technique involves placing sets of full-thickness running sutures along the greater curvature of the gastric body, starting 1 cm from the angular incisura and moving from distal to proximal. To achieve a full-thickness bite, the tissue helix is positioned on the targeted mucosa and turned clockwise, typically three times, to penetrate the muscularis propria of the stomach. It is then pulled back to capture the tissue, aligning it perpendicularly to the needle driver, with suction applied before closing and driving the curved needle through the tissue.

At present, there is no consensus on the optimal suturing pattern, the number and orientation of bites for each running stitch, or the spacing and quantity of sutures used. Various suturing patterns, including "M", "Z", and "U", have been described[26-28]. Research suggests that the suture pattern does not significantly impact weight loss outcomes, as long as the primary goal of shortening and narrowing the stomach through full-thickness suturing is achieved[29].

The gastric fundus is intentionally left intact, creating a small fundal pouch proximal to the sleeve. This pouch acts as a food reservoir, promoting satiety and delaying gastric emptying. Notably, the wall of the gastric fundus is particularly thin, and suturing in this area may lead to serious complications such as leaks or splenic injury [Figure 4].

Efficacy on weight loss and comorbidities

In 2011, a joint task force was established by the ASGE and the American Society for Metabolic and Bariatric Surgery (ASMBS) to evaluate and define safety and efficacy standards for EBMT. It stated that a primary EBMT must achieve an efficacy threshold of at least 25% excess weight loss (EWL) at 12 months, with a statistically significant mean EWL difference of at least 15% compared to a control group. Additionally, the rate of serious adverse events (AEs) associated with the EBMT must be 5% or lower[30]. Any primary EBMT that meets these criteria would be deemed appropriate for integration into clinical practice following adequate training.

The largest cohort to date involved 1,000 patients who underwent ESG, achieving a mean EWL of 64.3% at 6 months, 67.5% at 12 months, and 64.7% at 18 months[31]. A multicenter study in Australia and the United States with 112 obese patients reported a mean EWL of 50.3% at 6 months, with 86.5% of participants reaching over 25% EWL[32]. Another large international study with 248 patients showed similar results, with a total weight loss (TWL) of 15.2% at 6 months and 18.6% at 24 months. At 24 months, 84.2% of patients had a TWL of 10% or more. Notably, weight loss at 6 months was found to predict weight maintenance at 24 months. The authors suggested that patients losing less than 10% of their weight by 6 months may benefit from additional therapies to enhance weight loss[33]. Furthermore, a meta-analysis of 2,170 patients from 11 studies found a pooled mean TWL of 15.3%, 16.1%, and 16.8%, and a pooled mean EWL of 55.8%, 60%, and 73% at 6, 12, and 18 months post-ESG, respectively[34]. These findings indicate that ESG is effective and reproducible.

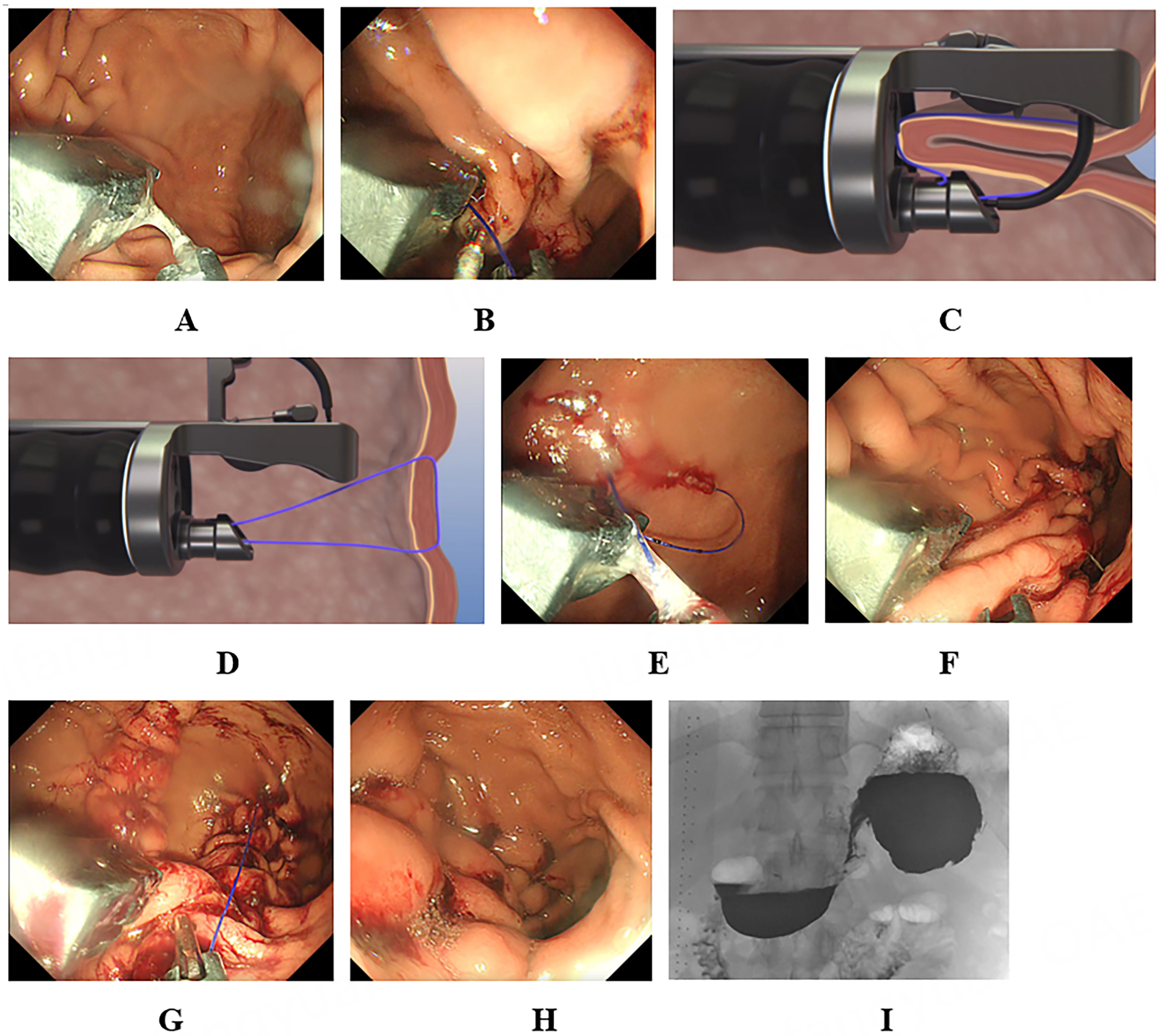

Figure 4. Endoscopic sleeve gastroplasty using the Overstitch NXT. (A) The device under endoscopic view; (B) Endoscopic suturing starts from the level of the gastric incisura. Tissue helix is used to draw the gastric wall into the suturing device to perform a full-thickness bite; (C-E) Needle drive through the gastric wall to achieve full-thickness suturing; (F) A neo-pylorus is created after the first row of plication; (G) Further plications made at greater curvature in a U suturing pattern; (H) Final endoscopic appearance after completion of ESG showing the sleeve-like stomach; (I) The barium meal study conducted one year after ESG shows a narrow, sleeve-like gastric body with delayed emptying and retained contrast in the fundal pouch. ESG: Endoscopic sleeve gastroplasty.

Cheskin *et al*. conducted a case-matched study comparing weight loss between ESG and high-intensity diet and lifestyle therapy (HIDLT). The ESG group showed significantly higher TWL than the HIDLT group at 6 months (14.0% *vs*. 11.3%) and 12 months (20.6% *vs*. 14.3%)[35]. Recently, the MERIT trial, published in *The Lancet*, further explored this topic. This prospective, multicenter randomized controlled trial compared ESG with lifestyle modification alone in class 1 and class 2 obese patients (BMI 30-40 kg/m^2). The results showed that at 52 weeks, the ESG group had significantly higher mean EWL (49.2% *vs*. 3.2%) and TWL (13.6% *vs*. 0.8%) compared to the lifestyle-only group (P < 0.0001). Additionally, 77% of patients in the ESG group achieved 25% or more EWL, compared to just 12% in the control group (P < 0.0001). In the crossover ESG group, there was an improvement in EWL of 44.1%. At 104 weeks, the mean EWL for all ESG patients was 46.7%, with 68% of those in the primary ESG group maintaining at least 25% EWL[36]. These findings confirm that ESG, combined with lifestyle modifications, is an effective treatment option for class 1 and class 2 obesity patients.

It is well known that achieving at least 10% TWL can improve obesity-related metabolic diseases[37,38]. As discussed earlier, ESG can lead to more than 10% TWL, and several studies have shown associated metabolic improvements. Sharaiha *et al*. reported significant improvements in metabolic markers, including hemoglobin A1c (HbA1c), liver enzymes, serum triglycerides, and systolic blood pressure[39]. Another study found a notable decrease in leptin levels and insulin resistance (HOMA-IR) after six months[40]. In a study by Algahtani *et al*. involving 1,000 individuals, complete remission rates for type 2 diabetes (T2DM), hypertension, and dyslipidemia were reported at 76.5%, 100%, and 56.3%, respectively[31]. Furthermore, clinical evidence suggests that ESG can improve conditions such as non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) in obese patients. A recent meta-analysis of 175 patients from four cohort studies found a significant reduction in the hepatic steatosis index (-4.85) and the NAFLD fibrosis score (-0.5) at 12 months[41]. Improvements in liver fat and fibrosis were sustained for up to two years after ESG[42]. The MERIT trial also highlighted the benefits of ESG for metabolic diseases, showing that 80% of participants in the ESG group experienced improvements in one or more metabolic comorbidities at 52 weeks, compared to 45% in the control group. Additionally, 93% and 83% of ESG participants saw improvements in T2DM and metabolic syndrome, respectively, along with significant enhancements in liver enzymes and the hepatic steatosis index[36].

Recent data show that ESG can effectively maintain weight loss and improve comorbidities in the long term. A large single-center study in India involving 612 patients with a four-year follow-up reported a TWL of 18.19%. In this cohort, 90% of patients maintained 5% TWL, and 70% achieved at least 25% EWL. Additionally, many patients experienced remission or improvement in various comorbid conditions: 51.2% for T2DM, 65.8% for hypertension, 73.6% for dyslipidemia, and 89.9% for obstructive sleep apnoea[43]. Another study found a mean TWL of 15.9% five years after ESG, with 90% and 60% of patients maintaining a 5% and 10% TWL, respectively[44]. Jirapinyo *et al*. recently reported ten-year outcomes for three patients who underwent ESG, showing a mean TWL of 12.9%[45]. Further research and longer-term follow-up studies are necessary to confirm the durability of ESG.

Moreover, studies have explored the potential of ESG in addressing overweight issues. A multicenter international study involving 189 overweight patients (mean BMI of 27.79 kg/m^2) found a mean TWL of 15.03% at 12 months and 14.91% at 36 months, with 86% achieving a normal BMI by 24 months[46]. Another large cohort study in Saudi Arabia with 656 patients (BMI 27-30 kg/m^2) reported promising results as well, with mean TWL of 11.0%, 15.5%, 15.1%, and 13.3% at 6, 12, 24, and 36 months, respectively. Additionally, 36% and 18% of patients experienced complete remission of diabetes and hypertension, respectively, while 82% reported improved QOL after ESG[47]. These results suggest that ESG could be an effective early intervention for obesity.

Currently, the FDA approves ESG devices only for adult patients with a BMI of up to 50 kg/m^2. Therefore, ongoing clinical research aims to expand the application of gastric remodeling procedures. One study evaluated the efficacy and safety of ESG in high-risk, extremely obese patients (BMI > 50 kg/m^2) who are contraindicated for abdominal surgery. ESG was successfully performed on all 24 patients, with a 12-month TWL of 12.2% ± 8.9%. Notably, there were significant improvements in comorbidities, with remission rates of 62.9% for hypertension, 87.5% for T2DM, 25% for dyslipidemia, and 100% for gastroesophageal reflux disease (GERD). Only one patient experienced a post-procedure adverse effect, gastric mucosal bleeding, which was managed endoscopically[48].

Additionally, a study explored the role of ESG in children and adolescents, finding results comparable to those in adults. In this cohort, 109 pediatric patients with a mean BMI of 33.0 kg/m^2 and an average age of 17.6 years underwent ESG, achieving mean TWL of 14.4%, 16.2%, and 13.7% at 6, 12, and 24 months, respectively[49]. These findings highlight the potential for broader applications of EGR, benefiting a wider range of patients.

Safety profile

Most AEs related to ESG are mild to moderate. Common post-procedure complaints include nausea, epigastric pain, tightness, sore throat, and shoulder discomfort, which typically resolve on their own within a few days. A meta-analysis of 1,772 patients reported an overall AE rate of 2.2% (95%CI: 1.6-3.1), including severe pain or nausea requiring hospitalization (1.08%), GI bleeding (0.56%), and peri-gastric leaks or fluid collections (0.48%)[50]. Another meta-analysis found a similar overall AE rate of 2.3%, with 1.5% classified as mild, 1.7% as moderate, and 0.8% as serious AEs[34]. Importantly, no procedure-related deaths were reported in any of the studies. Most major AEs were managed conservatively, with only two cases of GI bleeding requiring sclerotherapy and three cases of perigastric fluid collections needing surgical drainage. In a series assessing ESG in children and adolescents, there were no instances of blood transfusion, emergency admissions, or severe AEs[49]. Additionally, a study also examined whether ESG could lead to nutritional deficiencies. Despite significant weight loss and changes in body composition, no deficiencies in micro- or macronutrients were found in the short term[51].

Overall, ESG is considered safe, within the ASGE and ASMBS threshold of ≤ 5% for severe AEs. Additionally, if a surgical conversion from ESG to sleeve gastrectomy or Roux-en-Y gastric bypass (RYGB) is necessary, recent studies suggest that such conversions are feasible and safe, with no AEs reported[52-54].

PRIMARY OBESITY SURGERY ENDOLUMINAL

Device and technique

Primary obesity surgery endoluminal (POSE) is another EGR technique that reduces the stomach size using an IOP (USGI Medical, San Clemente, CA, USG).

The IOP features a large 54-Fr transport with four working channels, allowing for the use of a slim endoscope and three specialized instruments: the g-Prox EZ Endoscopic Grasper, which is a flexible shaft with a jawed gripper for creating and approximating full-thickness (serosa-to-serosa) tissue folds; the g-Lix Tissue Grasper, a flexible probe with a distal helical tip that helps the g-Prox capture target tissue for a full-thickness mini-plication; and the g-Cath EZ Suture Anchor Delivery Catheter, which has a needle at its distal tip that, after being advanced through the g-Prox, penetrates the mobilized target tissue to install preloaded paired tissue anchors connected by suture material, holding the plication in place until serosal fusion occurs [Figure 5]. Unlike the Overstitch suturing system, the IOP uses polypropylene anchors with cinched baskets on both ends of the tissue folds, designed for permanent remodeling. It has received CE mark and FDA approval for tissue apposition.

The POSE procedure is performed under general anesthesia by two endoscopists working simultaneously: one controls the IOP, while the other manages the slim gastroscope. Before the procedure, the transport and all working channels must be well lubricated. A laparoscopic CO2 insufflator is typically connected to the IOP and set to 8-10 mmHg to maintain gastric distension. The transport is gently advanced into the stomach, and the target site is captured using the g-Lix, pulling tissue into the jaws of the g-Prox, which is preloaded with a g-Cath snowshoe anchor delivery catheter. The jaws are closed, the needle is advanced, and the distal snowshoe anchor is released. After retracting the needle and g-Lix, the jaws are opened, and

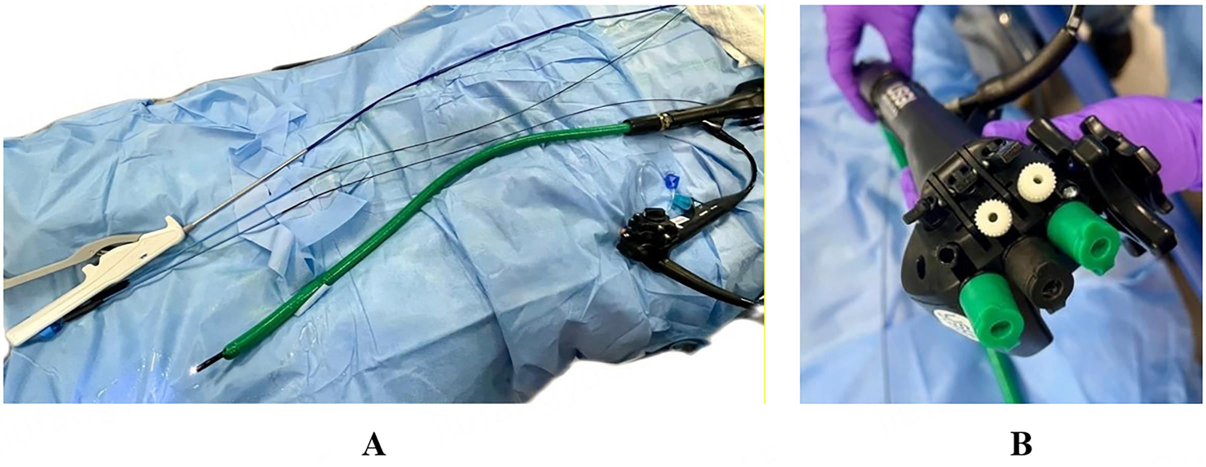

Figure 5. USGI IOP in Figure 5. (A) The IOP device, equipped with the slim scope, is displayed alongside other necessary accessories; (B) Close view of the working channels of the IOP transport. IOP: Incisionless operating platform.

the proximal shoe is released and cinched to bring the anchors together, creating a full-thickness plication. A new g-Cath is then loaded to perform the next plication [Figure 6].

Initially, POSE targeted the gastric fundus and proximal stomach to impair fundal accommodation; however, results from a multicenter trial indicated suboptimal weight loss outcomes[55]. As a result, a modified version called POSE 2.0 was developed. This approach involves creating multiple suture plications along the gastric body while sparing the fundus, resembling the suturing pattern used in ESG. The procedure starts at the level of the incisura, where horizontal plications form a "neo-pylorus" to delay gastric emptying[56]. Recently, a "belt-and-suspender" pattern has been introduced, which combines vertical and horizontal plications along the greater curvature of the stomach, effectively reducing both the anteroposterior diameter and the vertical length of the stomach[57].

Efficacy on weight loss and comorbidities

The initial result of the POSE 2.0 procedure with 73 obese patients showed a TWL of 15.7% at 6 months[56]. Following this, the same group conducted a multicenter study with 44 patients across three centers. This study reported 100% technical success, with a mean TWL of 15.7% ± 6.8% at 12 months. At that time, 98% of patients achieved more than 5% TWL, 86% exceeded 10%, and 58% surpassed 15%. Importantly, 26 patients who had repeat endoscopy at 24 months showed all plications were intact, confirming the durability of the snowshoe suture anchors and indicating potential for meaningful long-term results[58]. An international multicenter randomized controlled study (INSPIRO trial) has recently been approved by the FDA and will further validate the safety, durability, and effectiveness of the POSE 2.0 procedure in treating primary obesity.

The impact of POSE on obesity-related diseases was studied in the ESSENTIAL trial. Although the TWL at 12 months was only 4.95%, patients in the POSE group experienced significant improvements in T2DM, with reductions in diabetes medication and fasting glucose levels. Additionally, 35.1% and 19.39% of patients showed improvements in dyslipidemia and hypertension, respectively[55]. In the multicenter POSE 2.0 study, improvements in obesity-related comorbidities, such as lipid profiles, liver biochemistry, and hepatic steatosis, were observed at 6 months. QOL also improved following the procedure[58].

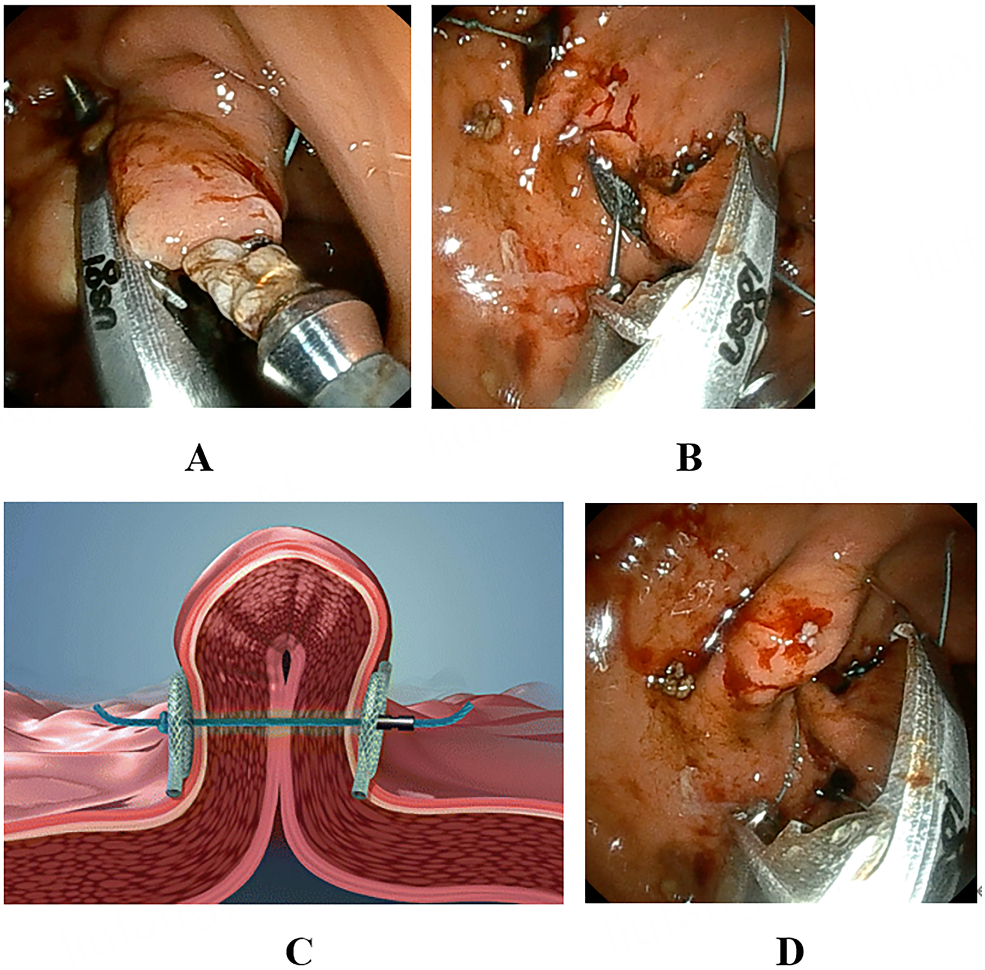

Figure 6. POSE in Figure 6. (A) the gastric wall is targeted and pulled back to enable capture by g-Prox EZ, then the g-Cath EZ is advanced through the g-Prox to penetrate the gastric wall; (B-D) The paired snowshoe suture anchors secure the full-thickness plication in place after tightening the suture. POSE: Primary obesity surgery endoluminal.

Studies have also explored POSE 2.0 as a treatment for NAFLD. AIKhatry *et al*. compared 20 patients who underwent POSE 2.0 with 22 patients who made lifestyle modifications. They found that POSE 2.0 significantly improved the controlled attenuation parameter, hepatic steatosis index, and liver enzymes at 12 months, which was not observed in the lifestyle modification group. Additionally, 52.6% of patients who had POSE 2.0 achieved resolution of steatosis at 12 months, with no cases of progression in steatosis during the study[59]. Another study involving 42 obese patients with NAFLD reported similar positive effects from POSE 2.0. Significant reductions were noted in liver enzymes, composite fibrosis scores, and imaging-based markers of fibrosis at 6-12 months. There were also notable reductions in the controlled attenuation parameter, HOMA-IR, and HbA1c[60]. Further research is needed to clarify the effectiveness of POSE 2.0 for patients with NASH, understand the physiological mechanisms behind NAFLD improvement, and assess its safety and efficacy in individuals with advanced fibrosis.

Safety profile

POSE is generally safe, with a pooled serious AE rate of 2.84%[61]. Common AEs include post-procedural abdominal pain, nausea, vomiting, and sore throat. Serious AEs, such as GI bleeding, intra-abdominal bleeding, liver abscesses, and perforations, are rare and can typically be managed conservatively.

ENDOMINA GASTRIC PLICATION

Device and technique

The Endomina triangulation platform (Endo Tools, Gosselies, Belgium) is a single-use, over-the-scope plication device specifically designed for EGR. It features a 5-Fr needle that facilitates the passage of sutures, known as Transmural Antero-Posterior Endoscopic Suture (TAPES), through full-thickness gastric folds to achieve transmural serosa-to-serosa apposition. This device has received FDA approval for tissue-to-tissue apposition.

First, the Endomina system is advanced along two stiff guidewires into the stomach. A flexible endoscope is then inserted through the device's channel. Once inside the stomach, the device is opened and assembled with the endoscope centered within its aperture. The TAPES is advanced into the flexible arm of the platform and bent perpendicularly. Endoscopic forceps is used to grasp the stomach wall and pull it between the arms of the platform. A needle is then advanced through two layers of the gastric wall, and a pre-tied knot is released to create the first plication [Figure 7]. After retracting the needle and opening the forceps to release the gastric tissue, the process is repeated to create a second plication on the opposite wall of the stomach, moving from distal to proximal. A recent study comparing three different plication patterns using the Endomina system found no significant differences between the groups, with all patterns resulting in effective weight loss outcomes[62].

Efficacy on weight loss and safety profile

An initial multicenter prospective study involved 51 patients with a mean BMI of 35.1 kg/m^2 who underwent Endomina gastric plication. After one year, the participants achieved a TWL of 7.4% and an EWL of 29%. Importantly, no serious AEs were reported. Additionally, 88% of the plications remained intact in 30 patients who underwent repeat endoscopy at the one-year mark[63].

Following this, the same research group conducted a randomized controlled trial with 71 patients classified as having class 1 or class 2 obesity. These patients received either lifestyle modification alone or lifestyle modification combined with Endomina gastric plication. At six months, the group receiving Endomina gastric plication along with lifestyle modification displayed significantly greater mean EWL (38.6% *vs.* 13.4%, $P < 0.001$) and improved QOL scores (52.8% *vs.* 45.1%, $P < 0.05$) compared to the lifestyle modification alone group. Follow-up at nine and twelve months for the combined group indicated EWL of 51% and 41.3%, respectively[64]. Further studies are underway to assess the efficacy of this intervention on weight loss in the longer term and associated comorbidities.

CONTRAINDICATIONS FOR EGR PROCEDURES

The contraindications for EGR procedures are similar to those for bariatric and metabolic surgery. These include active malignancy, untreated psychiatric illness, and pregnancy. Additionally, conditions such as gastric ulcers, gastric neoplasms, congestive gastropathy, gastric polyposis, gastric or esophageal varices, and hiatal hernias larger than 3 cm are also considered contraindications.

Figure 7. Endomina gastric plication. (A) The device and endoscope are assembled inside the stomach; (B) An endoscopic forceps is used to grasp and pull the stomach wall toward the device; (C) The needle is advanced through the gastric wall, and a pre-tied knot is released to form a full-thickness plication.

Although there have been no reported cases of gastric cancer following EGR procedures, the authors do not recommend these procedures for patients with a strong family history of gastric cancer, a personal history of gastric neoplasia, or extensive gastric intestinal metaplasia. This caution is due to the challenges in surveillance and the potential risk of undetected gastric cancer over the long term.

COMPARISONS WITH OTHER WEIGHT LOSS THERAPIES [Table 1]

Intragastric balloons

The intragastric balloon (IGB) is one of the earliest EBMTs developed, and its effectiveness for weight loss has been well established. A meta-analysis by the ASGE Bariatric Endoscopy Task Force, which included 55 studies and 6,645 Orbera balloon insertions, reported a mean TWL of 12.3%, 13.16%, and 11.27% at 3, 6, and 12 months, respectively[65]. However, weight recurrence after balloon removal is common, with only 50% of patients maintaining a 20% EWL one year post-removal and 25% at five years[66].

Several studies have compared ESG with IGB. Fayad *et al*. conducted a retrospective comparison of 58 ESG and 47 IGB patients. Both methods resulted in significant weight loss, but the ESG group had a greater mean TWL at 12 months (21.3% *vs*. 13.9%, $P = 0.005$). Additionally, the rate of AEs was much lower in the ESG group (5.2% *vs*. 17.0%, $P = 0.048$). Common AEs after IGB insertion included nausea, vomiting, abdominal pain, balloon hyperinflation, and balloon migration, all of which led to early balloon removal[67]. A systematic review and meta-analysis of 1,979 ESG patients and 3,025 IGB patients from 28 studies published up to 2019 found that the mean TWL was significantly higher in the ESG group at 12 months (17.51% *vs*. 10.35%, $P = 0.001$). The IGB group showed a significant decrease in TWL at 18-24 months, indicating weight regain, while this was not observed in the ESG group. About 5.92% of IGB patients required early balloon removal due to intolerance[68]. A recent study compared ESG to 6-month and 12-month IGB therapies (Orbera and Orbera365 balloon) and again found higher mean TWL in the ESG group at both 6 months (19.8% *vs*. 15.3%, $P = 0.005$) and 12 months (22.5% *vs*. 14.7%, $P < 0.001$)[69]. Additionally, Gudur *et al*. examined the short-term safety of ESG and IGB using the ASMBS database, comparing 1,998 matched patients in each group. They found that ESG patients had more readmissions within 30 days, while IGB patients needed more outpatient treatments for dehydration, with 3.7% undergoing early balloon removal within 30 days. Both procedures are safe, with a serious adverse event rate of less than 1%[70].

Overall, ESG appears to be more effective, durable, and better tolerated than IGB placement.

Table 1. Comparisons between endoscopic gastric remodeling procedures and other weight loss treatments

Procedure	Mode of anesthesia	Procedural time	Target weight loss (%TWL)	Overall AE rate	Favorable aspects	Unfavorable aspects
Endoscopic sleeve gastroplasty[67,79]	GA	45-80 min	16%-20%	3%-5%	FDA-approved Incisionless Good safety profile Low risk of *de novo* GERD Micronutrient deficiency uncommon	Limited long-term data No standardized technique
POSE 2.0[58,61]	GA	35-50 min	15%	3%	Incisionless Potentially more durable Easier to create full-thickness plication	No RCT Requires two operators simultaneously
Endomina Gastric plication[63,64]	GA	44-146 min	7%-12%	2%	Incisionless Fits all endoscopes Improved maneuverability	Limited data
Intragastric balloon[65-69]	IV sedation or GA	20-30 min	10%-12%	17%	FDA-approved Incisionless No anatomic alteration Easy to perform	Severe nausea and vomiting common during the first few days 5.9% required early balloon removal Weight recurrence common
Sleeve Gastrectomy[75,78,79]	GA	60-120 min	24%-30%	12%	Significant weight loss Metabolic effects Decrease in serum ghrelin	10%-30% *de novo* GERD Risk of leaks and incisional hernia Higher BMI criteria
Anti-obesity medication (GLP-1 RA)[72-74]	N/A	N/A	15%	10%	Non-invasive No anatomic alteration	Discontinuation common due to AE Weight recurrence common Uncertain side effects of long-term use Less cost-effective

POSE: Primary obesity surgery endoluminal; GLP-1 RA: glucagon-like peptide-1 receptor agonist; GA: general anesthesia; IV: intravenous; N/A: not applicable; %TWL: percentage of total weight loss; AE: adverse event; RCT: randomized controlled trial; GERD: gastroesophageal reflux disease.

Anti-obesity medications

Recent advancements in weight-loss medications, especially glucagon-like peptide-1 (GLP-1) receptor agonists, have drawn significant interest. Originally developed for the management of T2DM, GLP-1 agonists not only help regulate blood sugar levels but also promote appetite suppression, enhance satiety, and delay gastric emptying, making them increasingly popular for the treatment of obesity[71].

Among these, semaglutide is one of the most extensively studied GLP-1 agonists for obesity treatment. The Semaglutide Treatment Effect in People With Obesity (STEP 1) study revealed that participants who received semaglutide, along with lifestyle modifications, achieved an average TWL of 14.9% over 68 weeks. This significantly exceeded the 2.4% weight reduction seen in the placebo group, with 86.4% of semaglutide users losing more than 5% of their initial body weight. However, side effects are common, with serious AEs reported in 9.8% of semaglutide cases. Furthermore, 7.0% of participants in the semaglutide group discontinued treatment due to AEs, primarily GI disorders[72]. Additionally, weight regain is almost certain after stopping the medication. The STEP 4 multicenter randomized controlled trial compared continued semaglutide treatment with a switch to placebo for weight maintenance (both paired with lifestyle interventions) in adults with overweight or obesity after 20 weeks on semaglutide. Those who discontinued experienced weight regain compared to those who continued treatment (+6.9% *vs*. -7.9%, mean difference -14.8%)[73].

Currently, there are no direct comparative studies between GLP-1 agonists and EGR. However, a recent study evaluating the cost-effectiveness of ESG versus semaglutide, utilizing data from the STEP 1 and MERIT studies along with other public data sources, indicated that ESG is the more favorable option. Over a five-year time horizon, the incremental cost-effectiveness ratio (ICER) for ESG was calculated at -$595,532 per quality-adjusted life year (QALY), resulting in an additional 0.06 QALYs and a total cost reduction of $33,583 compared to semaglutide. Moreover, ESG led to greater weight loss, with patients experiencing an average TWL of 18% and an average BMI of 31.7 kg/m^2 after five years, down from an initial BMI of 37 kg/m^2. In contrast, semaglutide users achieved an average weight loss of 15% to 16%, resulting in a final average BMI of 33.0 kg/m^2[74].

These findings suggest that ESG may be a more cost-effective option with fewer long-term side effects compared to anti-obesity medications.

Laparoscopic sleeve gastrectomy

Recent laparoscopic sleeve gastrectomy (LSG) has emerged as a highly effective and durable bariatric surgical option for treating severe obesity. This procedure promotes significant weight loss by reducing stomach volume and lowering levels of the appetite-regulating hormone ghrelin, resulting in decreased food intake[75]. Currently, LSG is the most common bariatric surgery, accounting for 60.4% of all procedures performed worldwide[76].

Several studies have compared the effectiveness of ESG and LSG. An unmatched cohort study involving 91 ESG and 120 LSG patients found that LSG resulted in a significantly higher percentage of TWL at 12 months (29.3% *vs*. 17.6%, $P < 0.001$)[77]. However, this difference was not observed in patients with a BMI under 40 kg/m^2 after multivariable adjustments. In a case-matched study with 54 ESG and 83 LSG patients, the ESG group showed greater TWL at one month (9.8% *vs*. 6.6%, $P < 0.001$) but had lower TWL at six months compared to the LSG group (17.1% *vs*. 23.6%, $P < 0.001$)[78]. A meta-analysis including 1,815 ESG and 2,179 LSG patients confirmed that LSG had significantly higher TWL rates at 12 months (30.5% *vs*. 17.1%, $P = 0.001$)[79]. These findings indicate that while ESG usually results in less weight loss than LSG overall, outcomes may be more comparable for patients with a BMI under 40 kg/m^2. Further research focusing on this specific group could help determine the most effective surgical approach.

ESG also has a better safety profile compared to LSG. A meta-analysis showed that the overall AE rate for ESG was 2.9%, while it was 11.8% for LSG. ESG had lower rates of bleeding (1.1% *vs*. 2.6%, $P = 0.005$) and *de novo* GERD (0.4% *vs*. 5.8%, $P = 0.001$) compared to LSG[79]. A case-matched study indicated that ESG patients reported a better QOL at six months, especially regarding GI symptoms, despite lower %TWL. Notably, no ESG patients developed GERD requiring daily proton-pump inhibitors, while seven LSG patients did[80]. The lower GERD incidence in ESG may be due to the preservation of the stomach's fundus and its neuronal connections. Additionally, ESG typically requires a shorter procedure time (45-80 min *vs*. 60-120 min) and a shorter hospital stay (1-2 days *vs*. 5-9 days) compared to LSG[79].

In summary, while ESG leads to less weight loss than LSG, it is a promising alternative to LSG for treating mild-to-moderate obesity, offering quicker recovery and lower risks, particularly regarding *de novo* GERD. Further research should explore the outcomes of ESG on obesity-related comorbidities, compare it with other EGR techniques such as the POSE procedure, and assess its long-term outcomes relative to LSG.

EGR AS A REVISIONAL PROCEDURE

Weight recurrence after LSG can occur in 14% to 37% of patients over seven or more years[81]. This long-term failure is often linked to sleeve dilation[82], necessitating revisional bariatric surgery for many patients. Surgical options for revision include resizing the gastric sleeve, converting to RYGB, one anastomosis gastric bypass (OAGB), or duodenal switch. While converting to a malabsorptive procedure generally yields better weight loss, it carries risks of serious complications such as anastomotic leaks, bleeding, and stenosis, which can occur in 10%-15% of cases[83-86]. In contrast, resleeve is technically easier and may offer weight loss results comparable to RYGB in mid-term[87].

Given the benefits of endoscopic gastroplasty remodeling as a primary EMBT for weight loss, researchers have begun exploring its use as a revisional procedure for patients experiencing weight regain after LSG. Sharaiha *et al*. were the first to describe revisional ESG (R-ESG) for this purpose, with one patient successfully losing 9 kg[88]. In a multicenter retrospective study involving 34 patients who underwent R-ESG for weight recurrence after LSG, 82.4% achieved at least 10% TWL at 12 months. The median %TWL was 13.2% at six months and 18.3% at 12 months[89]. More recently, a study involving 82 consecutive patients who underwent R-ESG at nine different centres, approximately five years after their initial LSG, reported a mean TWL of 13.2% ± 10.1% at six months and 15.7% ± 7.6% at 12 months. At these intervals, 63.4% and 51.2% of patients maintained their weight loss, respectively. Importantly, 81% of patients achieved over 10% TWL at 12 months, and 52.5% lost more than 15% TWL during the same period. Only one moderate adverse event occurred, which involved a narrowed gastroesophageal junction that was resolved with a single endoscopic dilation[90].

Another innovative approach, the revisional POSE, or better known as the sleeve-in-sleeve procedure, uses a belt-and-suspenders pattern of plications along the greater curvature of the gastric sleeve. This endoscopic technique showed promising results, with one patient reporting a weight loss of 7 kg (8% TWL) at three months post-procedure[91].

Overall, EGR techniques appear to offer a promising revisional solution for managing weight recurrence following LSG. They provide a minimally invasive alternative for patients who are unwilling or at high risk for more invasive surgical revisions.

FUTURE DIRECTIONS

Research is underway to refine techniques for enhancing tissue approximation and the durability of gastric plications. One innovative technique, called Oscillating Circles Gastroplasty (OCG), utilizes endoscopic mucosal resection (EMR) with band ligation to create a submucosal wound before ESG, resulting in enhanced weight loss and better tissue fusion[92]. Another method, APC, offers advantages over EMR by being simpler, quicker, and potentially safer. Itani *et al*. reported 14.5% TWL at six months, with improved tissue fibrosis observed during follow-up endoscopies[93]. Meanwhile, refinements to the plication technique in the POSE procedure are also being explored. One study compared single-helix and double-helix plications, finding that the double-helix method led to greater weight loss and a higher percentage of patients achieving 10% TWL[94]. Another innovative method, POSE2.0et, uses only 6-8 plications, increasing efficiency and cost-effectiveness[95].

On the other hand, the impact of combining ESG with pharmacotherapy or other endoscopic procedures is being investigated. A study from Brazil found that adding liraglutide at five months led to higher total body weight loss (TBWL) at seven months compared to ESG alone[96]. Thompson *et al*. incorporated an endoscopic pyloric-sparing myotomy via submucosal tunnelling into standard ESG, which helps weaken the stomach's antral pump and enhances delayed gastric emptying[97]. Furthermore, an animal study has recently shown the technical feasibility of combining ESG with a fully endoscopic OAGB using a natural orifice transluminal endoscopic surgery (NOTES) approach, which includes duodenal exclusion[98].

Looking ahead, enhancing patient acceptability for obesity treatments is crucial. The shift from bariatric surgery to endobariatrics offers a valuable opportunity for many individuals who may prefer endoscopic bariatric therapy due to its lower risks compared to traditional surgical options. EGR procedure can also serve as a staged procedure before bariatric surgery, enabling patients to achieve initial weight loss and improve their health status prior to more invasive surgical interventions. Alternatively, it can be combined with pharmacological therapies to optimize outcomes for high-risk patients, providing a comprehensive approach to weight management.

By focusing on improving techniques and outcomes, we can substantially increase the durability and efficacy of these endoscopic treatments, potentially achieving the results of conventional surgical procedures. As advancements in technology and technique continue to evolve, we anticipate a significant rise in the number of endobariatric procedures performed. These innovations aim not only to enhance the effectiveness of treatments, but also to offer hope to patients who are not eligible for conventional surgery. Ultimately, this progress is expected to lead to broader acceptance and success of endoscopic procedures, significantly improving the QOL for many individuals facing the challenges of obesity.

CONCLUSION

In conclusion, EGR interventions represent a promising strategy for the treatment of obesity and its related health complications. Evidence indicates their effectiveness in facilitating substantial weight loss, improving associated comorbidities, and enhancing overall QOL. Furthermore, their favorable safety profile and minimal invasiveness render them an attractive alternative to conventional bariatric surgeries. As the field of endo-bariatrics advances, continued research will be imperative to fully unlock the potential of EGR and to enhance the standard of care for individuals grappling with obesity.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception and design of the study, data collection and draft manuscript preparation: Ng SKK

Reviewed and approved the final version of the manuscript: Ng SKK, Chiu PWY

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Both authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

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Not applicable.

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