INTRODUCTION

Obesity-associated metabolic conditions such as hypertension, type 2 diabetes, and dyslipidemia are significant health problems worldwide, and their prevalence rates are increasing. The most effective method for controlling obesity is bariatric surgery, which is more effective than diet and exercise or pharmacologic approaches. Laparoscopic sleeve gastrectomy (LSG), a kind of bariatric surgery, involves resection of the greater curvature and fundus of the stomach under vertically oriented partial gastrectomy, resulting in reduction of the gastric volume by 75%–80% (Fig. 1A).

Although LSG is usually associated with a high rate of weight loss, less than 1% of those who qualify for bariatric surgery actually undergo it because of the high cost and procedure-related complications. The endoscopic approach is a promising alternative modality for the treatment of obesity given its low financial burden and ease of accessibility requiring no incision. Currently, endoscopic methods and techniques are categorized into six classes: (1) space-occupying devices such as intragastric balloons, (2) restrictive procedures such as endoscopic gastroplasty, (3) bypass liners, (4) electrical stimulation, (5) aspiration therapy, and (6) other therapies such as botulinum toxin A injection or duodenal mucosal resurfacing. Of these, restrictive procedures have been proven to be the most effective method for weight loss at 12 months.

Endoscopic sleeve gastroplasty (ESG) is a therapeutic endoscopic technique for reducing the size of the gastric reservoir in obese patients, using a full-thickness endoscopic suturing device. The effectiveness of ESG in weight loss is significantly greater than that of high-intensity diet and lifestyle therapy and lower than that of laparoscopic sleeve gastrectomy (LSG). The efficacy at 12 months after ESG in terms of percentage of total body weight loss and excess body weight loss was approximately 16% and 60%, respectively. The well-known predictive factors for increased weight loss by ESG are good compliance with regular monitoring and post-procedure care involving a multidisciplinary team approach. Although the underlying mechanism of weight loss induced by ESG is debatable, delayed gastric emptying and early satiation are some of the proposed mechanisms. The pooled rate of adverse events after ESG reported in several meta-analysis studies ranged from 1.5% to 2.3% and the incidence of new-onset gastroesophageal reflux disease after ESG was negligible, indicating that ESG has a superior safety profile to LSG. Moreover, ESG reduced the risk of obesity-related metabolic comorbidities, evidenced by the reduction in HbA1c level, systolic blood pressure, triglyceride level, and risk of hepatic steatosis and fibrosis; it even improved the quality of life. ESG could be considered safe and qualify as an alternative treatment to LSG.
procedure, is a novel therapeutic endoscopic technique first introduced by Abu Dayyeh et al. in 2013 (Fig. 1B). It is a minimally invasive technique that reduces the size of the gastric reservoir by using a full-thickness endoscopic suturing device, such as OverStitch™ (Apollo Endosurgery, Austin, TX, USA). The anterior and posterior walls of the stomach are stitched together to achieve a tubular structure, similar to the structure achieved by LSG (Fig. 2). In this review article, we aimed to determine the effectiveness and safety profile of ESG and its usefulness as an alternative treatment for LSG.
EFFECTIVENESS OF ENDOSCOPIC SLEEVE GASTROPLASTY

Cheskin et al. conducted a case-matched study that directly compared ESG with a combination of low-calorie diet, increased physical activity, and behavioral therapy, namely high-intensity diet and lifestyle therapy (HIDLT) as the first-line treatment for obesity. They examined 105 patients who underwent ESG and 281 patients who underwent HIDLT for comparing the efficacy of the interventions between the two groups. The ESG group had a significantly greater mean percentage of total body weight loss (%TBWL) than the HIDLT group at 3 months (14.0% vs. 11.3%, respectively) and at 12 months follow-up (20.6% vs. 14.3%, respectively). Thus, ESG is a valuable alternative for patients with poor compliance to HIDLT.

Given the accumulated knowledge on the effectiveness of ESG in current studies, several systematic reviews and meta-analyses have been published; five recent systematic reviews and meta-analyses evaluated the effectiveness and safety of ESG for the treatment of obesity in the same year. First, Hedjoudj et al. included 1,772 patients from eight studies published between 2016 and 2019 and reported a 6-month mean %TBWL of 15.1%, mean percentage of excess body weight loss (%EBWL) of 57.7%, and mean reduction in body mass index (BMI) of 5.65 kg/m$^2$. Weight loss was sustained at 1 year and at 18–24 months with %TBWL of 16.5% and 17.2%, respectively. Second, in a meta-analysis of 2,170 patients from 11 studies published before October 2019, the pooled mean %TBWL values observed at 6, 12, and 18 months were 15.3%, 16.1%, and 16.8%, respectively. The pooled mean %EBWL values at 6, 12, and 18 months were 55.8%, 60%, and 73%, respectively. Third, Li et al. enrolled a total of 1,542 patients from nine studies published up to February 2019 and reported the pooled %TBWL values of 8.8%, 11.9%, 14.5%, and 16.1%, respectively, at 1, 3, 6, and 12 months. The pooled %EBWL values at 1, 3, 6, and 12 months were 31.2%, 43.6%, 53.1%, and 59.1%, respectively. Fourth, in a meta-analysis by Singh et al. with 1,859 patients from eight studies published before June 2019, the pooled mean %TBWL values at 6, 12, and 24 months were 14.9%, 16.4%, and 20.0%, respectively. Lastly, Due-Petersson et al. included a total of 2,142 patients from 23 studies regardless of publication date and reported a %TBWL of 16.3% at 12 months. In addition, ESG led to a significantly greater %TBWL than intragastric balloon insertion (20.6% vs. 13.9%) and HIDLT (20.6% vs. 14.3%), but significantly lower %TBWL than LSG (17.1% vs. 23.6%).

Comparisons of endoscopic sleeve gastroplasty and laparoscopic sleeve gastrectomy

Three observational studies and two meta-analyses directly compared the effectiveness of ESG and LSG. An unmatched cohort study by Novikov et al. in 2018 reported that the %TBWL with LSG was significantly superior at 12 months than that with ESG (29.3% vs. 17.6%, p < 0.001). This difference remained significant in patients with BMI > 40 kg/m$^2$, but not in those with BMI < 40 kg/m$^2$. In a case-matched study conducted by Fayad et al. in 2019, there was a significantly greater %TBWL in the ESG group than in the LSG group at the 1-month follow-up (9.8% vs. 6.6%, p < 0.001), whereas it was lower in the ESG group than in the LSG group at 6 months (17.1% vs. 23.6%, p < 0.001). Similar to an earlier meta-analyses demonstrated that ESG was effective for weight loss in obese patients, with relatively narrow spectrum of weight loss ranging from 16.1% to 16.9% %TBWL and 59.1% to 61.8% EBWL at 12 months of follow-up. This finding indicates that ESG is reproducible worldwide with effective weight loss outcomes. However, because none of the included studies were randomized controlled studies and most did not clarify adjuvant treatments such as nutritional care or pharmacotherapy during follow-up, these systematic reviews and meta-analyses did not show high-level evidence.

Neto et al. prospectively enrolled only patients with moderate obesity (Class I and II; BMI, 30–40 kg/m$^2$) excluding those with severe obesity (BMI > 40 kg/m$^2$). The %TBWL was 17.1% at 6 months and 19.7% at 12 months. Interestingly, the mean percentage of excess BMI loss was significantly greater among patients with Class I obesity than among those with Class II obesity at 6 (51.1% vs. 43.9%) and 12 months (60.2% vs. 49.2%). These results suggest that ESG is a safe and effective option for patients with mild to moderate obesity as well as those with severe.

Most previous studies have reported clinical outcomes of ESG for up to 2 years after the procedure. Long-term studies on its effectiveness are lacking. Recently, Sharaiha et al. conducted a 5-year analysis of a prospectively maintained cohort. At 1, 3, and 5 years, the mean %TBWL values were 15.6%, 14.9%, and 15.9%, respectively. Further, 5% and 10% TBWL was maintained by 89% and 77% of the patients at 1 year, 85% and 63%, at 3 years, and 90% and 61%, at 5 years, respectively. These results suggest that ESG is effective for up to 5 years after the procedure, and its long-term durability is good for maintaining weight loss.
study, %TBWL remained significantly low in the ESG group in patients with BMI >40 kg/m², with a borderline significant difference in those with BMI <40 kg/m². Both studies showed that weight loss with the endoscopic and surgical approaches was equivalent in patients with BMI <40 kg/m². However, as the BMI increases, bariatric surgery is likely to be more effective than ESG. These findings indicate that the endoscopic approach could be preferentially considered in patients with BMI between 30 and 40 kg/m², although those with BMI >40 kg/m² should be assessed for bariatric surgery, considering the extensive data supporting weight loss with the surgical option. A recent study compared ESG and LSG with 135 ESG and 43 LSG patients followed for 1 year and 46 ESG and 34 LSG patients followed for 2 years; this study showed that the mean %TBWL values at 2 years for ESG and LSG were 18.5% and 28.3%, respectively (p < 0.001). Both procedures achieved maximum weight loss in the 18 months, with gradual regression starting from 12 months.

Among two meta-analysis comparing ESG with LSG, one included 1,451 ESG and 203 LSG patients from five studies and found pooled %TBWL values of 14.2%, 15.2%, 14.8%, and 18.6% at 6, 12, 18, and 24 months, respectively, with ESG. Meanwhile, LSG showed high pooled %TBWL values of 23.5% at 6 months and 29.3% at 12 months. A meta-analysis of two studies directly comparing LSG and ESG showed significant differences in the mean %TBWL (8.52; 95% CI, 6.35–10.69; p < 0.0001) at 6 months, favoring LSG over ESG. In another meta-analysis of eight studies with 1,815 ESG patients and seven studies with 2,179 LSG patients, the pooled rates of %TBWL with LSG were statistically superior at 12 months to the rates with ESG (30.5% vs. 17.1%, p = 0.001). Current evidence indicates that ESG offers satisfactory efficacy in patients with mild-to moderate and inferior efficacy to LSG in those with severe obesity; it is better than other endoscopic procedures like intra-gastric balloon.

**MECHANISMS OF WEIGHT LOSS INDUCED BY ENDOSCOPIC SLEEVE GASTROPLASTY**

The changes in anatomical configuration induced by ESG might be an essential element of weight loss, but the exact mechanism of weight loss after the procedure is debatable. The proposed mechanisms include delayed gastric emptying, increased early satiation, and possibly alteration of the gut and metabolic hormones.

Although ESG is structurally analogous to LSG, the mechanisms of weight loss are different between these procedures.
in terms of gut and metabolic hormones. Lopez-Nava et al. found that in patients after ESG, leptin and insulin levels decreased with improvement in insulin secretion patterns and no changes in fasting ghrelin, glucagon-like peptide (GLP-1), and peptide-YY (PYY) levels at 6 months.\textsuperscript{33} Meanwhile, after LSG, patients showed a significant increase in GLP-1, PYY, and adiponectin levels and a decrease in ghrelin and leptin levels at 6 months. The observed differences in these hormone changes are likely associated with the anatomical differences between the two procedures. In ESG, the gastric fundus, which acts as a reservoir to store food, and neuronal innervation are left intact, and consequently stasis and delayed transit of food stimulates early satiety through the signals origination from the stomach to the brain.\textsuperscript{34} On the other hand, in LSG, the excised gastric fundus and up to 80% reduction of gastric volume with disconnection of the gastric nerves promote early emptying of food contents into the small bowel, and consequently, various gut and metabolic hormones undergo unusual alterations.\textsuperscript{31}

These explanations were supported by several studies that measured emptying time. Vargas et al. showed that LSG reduced gastric emptying T½ by 29.2 minutes and accelerated emptying of solid gastric contents in particular.\textsuperscript{35} In contrast, ESG increased gastric emptying T½ by 90 minutes and delayed gastric emptying for solids.\textsuperscript{36} The retention of food after ESG led to early meal termination in 11 minutes and reduced food intake.\textsuperscript{32} Thus, gut hormone changes play a minor role in weight loss after ESG and changes in gastric emptying and time to satiation are some of the plausible mechanisms that lead to beneficial effects of ESG.

### SAFETY OF ENDOSCOPIC SLEEVE GASTROPLASTY

We speculated that the minimally invasive ESG procedure is relatively safe, as per current evidence. Mild adverse events (AEs) such as abdominal pain, nausea, and vomiting occurred immediately after the procedure, but almost all of the symptoms improved after a few days with conservative management or spontaneously regressed.\textsuperscript{13}

There is a risk of ESG-related infection. The full-thickness sutures performed during ESG may lead to intraperitoneal contamination by gastric contents and bacterial translocation. Thus, antibiotic prophylaxis with cefazolin (1 to 2 g) is recommended an hour before the procedure.\textsuperscript{37} Tissue tearing around the suture site by excessive tension can cause large perforations as well as microperforations, resulting in perigastric fluid collection or abscess formation. Most of the fluid collections identified on computed tomography were resolved by antibiotic administration alone, with occasional radiologic intervention, and rarely required surgical procedure. AEs associated with gastric leak were reported in < 1% of cases.\textsuperscript{10}

A meta-analysis of 1,772 patients reported a pooled rate of severe AEs of 2.2% after ESG.\textsuperscript{10} The reported AEs were pain or nausea requiring hospitalization in 18 cases (1.08%), upper gastrointestinal (GI) bleeding in nine cases (0.56%), perigastric leak or collection in eight cases (0.48%), pulmonary embolism in one case (0.06%), and pneumoperitoneum in one case (0.06%).\textsuperscript{10} Another recent systematic review and meta-analysis including 2,170 patients from 11 studies observed an overall rate of AEs of 2.3%, consisting of 1.5% of mild, 1.7% of moderate, and 0.8% of severe AEs\textsuperscript{11}; this study reported a total of 38 AEs including 13 cases of GI bleeding, 10 cases of perigastric fluid collection, eight cases of severe abdominal pain, five cases of fever, one case of deep vein thrombosis treated with full anticoagulation, and one case of pneumothorax requiring thoracic drainage.\textsuperscript{11} Most of major AEs were managed conservatively, except two cases of GI bleeding requiring sclerotherapy and three cases of perigastric fluid collection requiring surgical drainage and closure. A study by Li et al. reported that the pooled rate of mild AEs such as self-limited abdominal pain and nausea was 72%, and that of severe adverse events (SAEs) such as perigastric fluid collection, GI bleeding, pulmonary embolism, pneumoperitoneum, and pneumothorax was only 1%.\textsuperscript{13} The pooled incidence of SAEs was 2.3% in the meta-analysis by Singh et al. and 1.5% the study by Due-Peterson et al.\textsuperscript{12,14} No procedure-related mortality was reported in any of the included studies. Several recent meta-analyses confirmed that ESG could be introduced as a safe clinical practice.

ESG is generally associated with significantly lower AEs than LSG. Three observational studies showed significant differences in the AEs between ESG and LSG, i.e., 5.2% vs. 16.9% in the study by Fayad et al., 2.2% vs. 9.2% in the study by Novikov et al., and 0.5% vs. 4.9% in the study by Lopez-Nava et al.\textsuperscript{17-19} In a meta-analysis study, the pooled rate of all AEs with ESG was 2.9% and with LSG was 11.8% (p = 0.001).\textsuperscript{21} ESG had a significantly lower incidence of bleeding events (1.1% vs. 2.6%, p = 0.005) and gastroesophageal reflux disease (GERD) (0.4% vs. 5.8%, p = 0.001) than LSG.\textsuperscript{21} Several recent meta-analyses demonstrated that ESG has a better safety profile than LSG.

GERD is known to be a considerable sequela to LSG. The development of GERD after LSG can be explained by the low resting esophageal sphincter pressure and low maximal distal contraction integral.\textsuperscript{18} The incidence rate of new-onset GERD after LSG was up to 34%, as reported in a systematic review and up to 60% during a mean follow-up of 5.5 years after
Fayad et al. found that the incidence of new-onset GERD was significantly lower after ESG than after LSG (1.9% vs. 14.5%). This lower rate of GERD after ESG was explained by the fact that the fundus of the stomach is left intact and the neuronal innervation of the stomach is maintained. In a recent meta-analysis study of 1,772 patients from eight studies between 2016 and 2019, GERD was not listed as a SAE in any study. Therefore, the rate of new-onset GERD after ESG is negligible and may cause patients to see ESG as a more favorable treatment option than LSG. In addition to the safety profile, the mean procedure time is shorter for ES than for LSG (45–80 min vs. 60–120 min, respectively) so is the mean hospital length of stay (1–2 days vs. 5–9 days, respectively). It was noted that same-day discharge after LSG was associated with increased overall rates of morbidity, readmission, and reoperation. In contrast, no AEs have been during the initial in-hospital recovery period after ESG and all patients can be discharged on the same day.

ADJUVANT TREATMENT AFTER ENDO SCOPIC SLEEVE GASTROPLASTY

A recent study on the effect of adjunct pharmacotherapy in patients undergoing ESG found that the combination of ESG and liraglutide was more effective than ESG alone. Liraglutide is a GLP-1 agonist that amplifies glucose-stimulated insulin secretion, delays gastric emptying, and increases satiety via the central effects on the hypothalamus. Pharmacotherapy with only liraglutide also showed favorable results of TBWL of 10%–15%. The combination group had significantly higher mean %TBWL than the ESG alone group at 7 months (24.7 ± 2.1% vs. 20.5 ± 1.7%, p < 0.001) and also greater reduction in percent body fat at 12 months (7.9 ± 1.3 vs. 10.5 ± 1.9, p < 0.001). On the contrary, a study with 5-year long-term outcomes of ESG revealed that post-procedural adjunct pharmacotherapy might not induce noticeably further weight loss but prevent further weight gain in patients. Clinicians should support that patients with obesity recognize the importance of multidisciplinary and comprehensive post-procedural care plans with respect to nutritional planning, endocrinology consultation, physical training, and even psychiatric care.

Furthermore, ESG is increasingly being used in salvage management for weight regain after LSG. In a study conducted by de Moura et al. with 34 patients who underwent ESG for weight regain after sleeve gastrectomy, the technical success rate was 100% with no SAEs and ≥25% EBWL in all patients, with a mean %TBWL of 18.3% at 12 months. One case report on conversion to surgical treatment in patients with failed weight loss after ESG demonstrated to be feasible to remove suture and hardware relating to ESG and then perform safe stapling and pouch formation during bariatric surgery. The clinical outcomes and safety profile of revisional bariatric surgery require further examination.

EFFECT OF ENDO SCOPIC SLEEVE GASTROPLASTY ON METABOLIC COMORBIDITY

Achieving at least 10% TBWL after obesity treatment improves obesity-related metabolic diseases. The mean %TBWL of ESG has been reported to be more than 16%, and it is considered beneficial in light of the threshold value. Several studies have demonstrated that endoscopic bariatric procedures such as ESG can reduce obesity-associated comorbidities. A study reported by Shariha et al. demonstrated that ESG significantly reduced HbA1c levels from 6.1% to 5.5%, systolic blood pressure from 129 mm Hg to 122 mm Hg, and triglyceride levels from 131.8 mmol/dL to 92.4 mmol/dL at 12 months. Alqahtani et al. reported complete remission of diabetes in 76.5% of the patients at 3 months and that of hypertension and dyslipidemia in 100% and 56.3% at 12 months, respectively. A recent study showed a significant decrease in the homeostatic model assessment of insulin resistance (HOMA-IR) and leptin level at 6 months. Several studies have shown the benefits of ESG in terms of hepatic problem. There was a reduction in serum alanine aminotransferase (ALT) level at 12 months from 42 IU/L to 22 IU/L in men and from 28 IU/L to 20 IU/L in women. ESG has been proven to be effective in patients with both obesity and non-alcoholic fatty liver disease (NAFLD) in terms of the risk of hepatic steatosis (NAFLD-fibrosis score), insulin resistance (HOMA-IR), and insulin and triglyceride levels at 12 months. These ameliorating effects of ESG on insulin resistance and changes in hepatic steatosis and fibrosis lasted for 2 years after the procedure.

Obese patients have lower quality of life (QOL) than the healthy general population. ESG leads to not only significant weight loss but also improvement in health-related QOL and physical activity and is particularly beneficial for patients with high initial BMI and physical inactivity at baseline. In a study evaluating QOL measured by the Gastrointestinal Quality of Life Index with propensity-matching score analysis between ESG and LSG, it was worth noting that the ESG group, despite having significant low %EBWL (39.9% vs. 54.9%, p = 0.01) and %TBWL (13.4% vs. 18.8%, p = 0.03) presented improved QOL with clear benefits in the GI symptom subdomain, while the LSG group showed a worsening of GERD symptoms (30.7%
vs. 0%) and increased use of PPI therapy. While the overall weight loss after ESG is lower than that after LSG, ESG seems to be a good modality for preserving weight reduction and even improving QOL.

CONCLUSIONS

According to the minimal thresholds of 25% EBWL and <5% SAE recommended by the American Society for Gastrointestinal Endoscopy and the American Society for Metabolic and Bariatric Surgery joint task force for proving effective bariatric treatment, ESG with a reported mean SAE rate of 1.5%–2.3% and %EBWL of 59.1%–61.8% could qualify as a safe and primary endoscopic bariatric intervention.

Considering the increasing evidence supporting the efficacy and safety of ESG, it appears to be more cost-effective and have a better safety profile than LSG. Hence, ESG can be considered as an option for the obese population, especially those with mild-to-moderate obesity. Thus, endoscopists are positioned to play a pivotal role in the future treatment of obesity. Unfortunately, in Korea, appropriate government-certified procedures covered by insurance are lacking, and this remains a significant barrier to the widespread use of endobariatric techniques. It is difficult to adequately compare the cost-effectiveness of ESG and LSG because LSG is covered by insurance for the eligible obese population, while ESG is mostly a self-pay procedure in Korea. In addition, the relatively high prevalence of gastric cancer in Korea makes endoscopists to hesitate performance of ESG inevitably remaining blind gastric mucosa.

In conclusion, ESG appears to be an effective alternative to LSG for obese patients who are not suitable for or unwilling to undergo a surgical procedure. Although LSG resulted in greater weight loss than ESG at 12 months, ESG has a better safety profile and shorter procedure time and length of hospital stay than LSG and is even reversible. Future studies and randomized controlled trials are needed to identify the long-term safety and efficacy of ESG and compare the advantages and cost-effectiveness against between ESG and LSG.

Conflicts of Interest

The authors have no potential conflicts of interest.

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Author Contributions

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