Current status of endoscopic sleeve gastroplasty: An opinion review

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Abstract
Bariatric surgeries have been demonstrated to be safe and effective treatment options for morbid obesity patients, but operative risks and high health care costs limit their clinical application. Endoscopic bariatric therapies are emerging as valuable alternatives for patients with doubts about bariatric surgery or ineligible for it. Endoscopic sleeve gastroplasty (ESG), a relatively novel technique of endoscopic bariatric therapies, has gained standing in the past few years. The safety, feasibility, repeatability, and potential for reversibility of ESG have been proven by multicenter studies. Compared to other weight loss strategies, current evidence demonstrates that ESG offers satisfactory efficacy in weight loss. Even though it is inferior to laparoscopic sleeve gastrectomy, it has lower risks of adverse events than surgical interventions and intragastric balloon within one-year follow-up. Furthermore, ESG may be the ideal weight control strategy for patients who have poor adherence to behavioral interventions. Even so, trends in decreased weight loss effect over time, post-procedure weight regain, post-procedure gut hormone alteration, and possible effects of race and ethnicity on ESG still remain undetermined due to very limited reports and very short follow-up.
INTRODUCTION
Growing prevalence of obesity has become a current worldwide public health epidemic in adults, children, and adolescents. The increasing trend in obesity is also of concern owing to the high comorbidity and mortality in obesity patients and the expanding economic burden for society[1,2]. Bariatric surgeries have been demonstrated to be safe and effective treatment options for morbid obesity patients, but low patient acceptance due to fear of operative risks and high health care costs limit its clinical application[3]. In this situation, endoscopic bariatric therapies (EBTs), with their characteristics of minimally invasive nature, reversibility, and high applicability, are emerging as valuable alternatives for patients with doubts about bariatric surgery or ineligible for it[4]. Endoscopic sleeve gastroplasty (ESG), a relatively novel technique of EBTs, was first published by the Mayo Clinic in the USA in 2013 and has gained standing in the past few years[5]. ESG is an incisionless transoral endoscopic procedure that uses a full-thickness endoscopic suturing system to reduce stomach volume into a tubular gastric cavity[6]. The safety, feasibility, repeatability, and potential for reversibility of ESG have been shown by several multicenter studies[7,8]. Furthermore, there are many studies making a direct comparison between ESG and other weight loss strategies[9-12], which are separately discussed in the following sections.

ESG VS LAPAROSCOPIC SLEEVE GASTRECTOMY
Laparoscopic sleeve gastrectomy (LSG) is the most popular restrictive bariatric surgical procedure because of its high efficiency in weight loss, reduction in obesity-related morbidities, and simple surgical technique[13]. Novikov et al[9] conducted an unmatched cohort study to compare the outcomes of ESG with surgical interventions. The study showed that LSG achieved greater body mass index (BMI) decrease and percent total body weight loss (%TBWL) than ESG at 12-mo follow-up (29.28% vs 17.57%, P < 0.001). Furthermore, and there were no significant differences (P = 0.21) in %TBWL between the two procedures in the subgroup of patients with BMI < 40 kg/m² after multivariable adjustment. Significantly lower post-procedure length of stay (0.34 d ± 0.73 d vs 3.09 d ± 1.47 d, P < 0.01) and adverse event rate (2.20% vs 9.17%, P < 0.05) were both observed in ESG compared with those in LSG. The other case-match study by Fayad et al[10] enrolled 54 ESG and 83 LSG patients. ESG initially presented more %TBWL and BMI decrease than LSG at 30 d (9.8% vs 6.6%, P < 0.001; 9.4% vs 6.7%, P < 0.001, respectively), but reverse outcomes in both %TBWL and BMI decrease for ESG and LSG (17.1% vs 23.6%, P < 0.001; 17.2% vs 23.7%, P < 0.001, respectively) were shown at 6-mo follow-up. Moreover, a significantly lower rate of adverse events was observed in ESG than in LSG (5.2 vs 16.9%, P < 0.05), especially in new onset gastroesophageal reflux disease (1.9% vs 14.5%, P < 0.05). Both comparison......
studies both demonstrated the superior weight loss effects of LSG and increased safety of ESG at 6-mo and 12-mo follow-up. In addition, the recent case-match retrospective study evaluated 6-mo quality of life after operation between 23 pairs of ESG and LSG patients with questionnaire[14]. ESG cohort reported significantly better results in gastrointestinal symptoms subdomain than LSG cohort ($P = 0.001$). No ESG patients but 7 LSG patients developed postoperative gastroesophageal reflux disease and required daily proton-pump inhibitors use ($P = 0.004$). Nevertheless, the current results are limited due to the retrospective nature of the studies and short-term follow-up, and they should be validated in future randomized controlled trials with longer follow-up.

### ESG VS INTRAGASTRIC BALLOON INSERTION

EBTs have several promising applications in metabolic obesity disease, and one of them is intragastric balloon (IGB), whose efficacy in body weight loss and safety were demonstrated by a systematic review and meta-analysis[15]. IGB was introduced 30 years ago and underwent several upgraded product developments but, so far, weight regain remains the major limitation because of necessary removal of the balloon at 6 mo[16]. Likewise, ESG, a new emerging EBT, presented satisfactory effects against obesity disease. One recent retrospective study reported by Fayad and his colleague compared the two EBTs (ESG and IGB)[11]. All 58 ESG and 47 IGB patients achieved meaningful body weight loss. The ESG group showed significant higher mean %TBWL than the IGB group over 12 mo post-procedure (at 12-mo follow-up, 21.3% vs 13.9%, $P = 0.005$, respectively). Notably, a decreasing trend in %TBWL was seen in the ESG group and decreasing %TBWL presented after 6 mo for the IGB group, which can be explained by balloon removal at 6 mo. There was a significantly lower rate of adverse events in the ESG group than in the IGB group (5.2% vs 17.0%, $P = 0.048$, respectively). Up to 17% of IGB patients had adverse events requiring balloon removal, and these events completely subsided after balloon removal. In contrast, ESG-associated adverse events are more likely to require medical treatment. This study provided evidence that ESG may be a more appropriate EBT than IGB in clinical practice even with limitation of selection bias.

### ESG VS BEHAVIORAL INTERVENTIONS

The United States Department of Health and Human Services has proposed lifestyle interventions, such as dietary therapy and physical activity, as first-line treatment for weight loss and maintenance since 1998[17]. One systemic review and meta-analysis revealed that behavioral interventions bring about small but significant benefits for weight loss and maintenance[18]. Certain obese patients prefer these non-surgical interventions over invasive therapies. Cheskin et al[12] conducted a case-matched study of 105 patients who underwent ESG and 281 patients who underwent high-intensity diet and lifestyle therapy (HIDLT) to compare weight loss between the two groups. The ESG group had a significantly greater mean %TBWL than the HIDLT group throughout the 12-mo follow-up (20.6% vs 14.3%, respectively). It is worth noting that ESG had no superiority in weight loss over 6 mo post-procedure compared with HIDLT in BMI $> 40$ kg/m$^2$ patients. In addition, a low proportion of patients (4.8%) experienced moderate-to-severe adverse events in the ESG group, and no subjects suffered from any adverse event in the HIDLT group. Consequently, ESG is likely a valuable alternative for patients who do not comply with HIDLT.

### CONCLUSION

Current evidence, summarized in Table 1, indicates that ESG offers satisfactory efficacy in weight loss even if inferior to LSG, and has lower risks of adverse events compared to surgical interventions and IGB within one-year follow-up. Moreover, ESG may be the ideal weight control strategy for patients who have poor adherence to behavioral interventions. Even so, the reasons for the trends in decreased weight loss effect with time and post-procedure weight regain in ESG still remain undetermined. As gut hormones[19,20], cytokines[21], adipokines[22], hepatokines[23], and bile acids[24] play important roles in promoting weight loss, ameliorating type 2 diabetes mellitus and improving fatty liver disease, basic mechanistic insights into EBT, including ESG, are required. Since the Y-Y paradox exists between Caucasians and Asians[25], direct extrapolation of the results obtained from Western countries may not be proper in
Eastern countries. Thus, analyses of the possible effects of race, ethnicity, and comorbidities on weight loss outcomes in each cohort become more and more imperative. With very limited reports and very short follow-ups, this novel endoscopic technique for obesity treatment, ESG, will require more large-scale randomized controlled trials in order to validate its clinical efficacy and safety in long-term follow-up.
Table 1  Summary of comparison studies for weight control strategies

| Ref. | Type of study | Comparison | Subject numbers | Length of follow-up (mo) | Weight loss efficacy (%TBWL) | Adverse event rate |
|------|---------------|------------|----------------|--------------------------|-------------------------------|--------------------|
| Novikov et al[8] 2018 | Retrospective cohort study, case-unmatched | ESG vs LSG vs LAGB | 91 ESG/120 LSG/67 LAGB | 12 | LSG (29.28%) > ESG (17.57%) > LAGB (13.30%), P < 0.001 | LSG (9.17%) > LAGB (8.96%) > ESG (2.20%), P < 0.05 |
| Fayad et al[9][10][11] 2019 | Retrospective cohort study, case-matched | ESG vs LSG | 54 ESG/83 LSG | 6 | LSG (23.6%) > ESG (17.1%), P < 0.001 | LSG (16.9%) > ESG (5.2%), P < 0.05 |
| Fiorillo et al[12][13][14] 2020 | Retrospective cohort study, case-matched | ESG vs LSG | 23 ESG/23 LSG | 6 | LSG (18.8%) > ESG (13.4%), P = 0.03 | GERD symptoms LSG (50.7%) > ESG (9%), P = 0.004 |
| Fayad et al[15] 2019 | Retrospective cohort study, case-matched | ESG vs IGB | 58 ESG/47 IGB | 12 | ESG (21.3%) > IGB (15.9%), P = 0.005 | IGB (17.0%) > ESG (5.2%), P = 0.048 |
| Cheskin et al[16][17] 2019 | Retrospective cohort study, case-unmatched | ESG vs HIDLT | 105 ESG/281 HIDLT | 12 | ESG (20.6%) > HIDLT (14.3%), P < 0.001 | ESG (4.8%) > HIDLT (0.0%) |

ESG: Endoscopic sleeve gastoplasty; GERD: Gastroesophageal reflux disease; HIDLT: High-intensity diet and lifestyle therapy; IGB: Intragastric balloon; LAGB: Laparoscopic adjustable gastric band; LSG: Laparoscopic sleeve gastrectomy; %TBWL: Percent total body weight loss.

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