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Safety and Efficacy of Endoscopic Sleeve Gastroplasty Worldwide for Treatment of Obesity: A Systematic Review and Meta-analysis.

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Abstract

Introduction—Endoscopic Sleeve Gastroplasty (ESG) has gained momentum as a promising minimally invasive bariatric therapy worldwide.

Objective—We performed the first comprehensive systematic review and meta-analysis of studies to evaluate the efficacy, safety, and procedural technique of ESG.

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Disclosures

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Methods—Bibliographic databases were systematically searched for studies assessing patients who underwent ESG for the treatment of Obesity. Studies were included if they reported percent total weight loss (%TWL) or percent excess weight loss (%EWL) and the incidence of serious adverse events (SAE). Studies with < 15 patients, follow -up period < 6 months and overlapping patients were excluded.

Results—Eight observational studies with 1859 patients were included. Pooled mean %TWL at 6, 12, and 24 months was 14.86 (95% CI: 13.83-15.90), 16.43 (95% CI: 15.23-17.63) and 20.01 (95% CI: 16.92-23.11), respectively. Pooled mean %EWL at 6, 12, and 24 months was 55.75 (95% CI: 50.61-60.89), 61.84 (95% CI: 54.75-68.93), and 60.40 (95% CI: 48.88-71.92), respectively. The pooled incidence of SAE was 2.26% (95% CI 1.25-4.03), and no mortality was reported. Gastrointestinal bleeding and peri-gastric fluid collection were the most common reported SAE; however, the pooled incidence of both was less than 1%. Variations in procedural technique were seen, but the full-thickness nature of suturing was reported in all studies. A layer of reinforcement sutures was performed in the majority of studies (n=6). Limitations include the lack of controlled studies, long term follow-up data, and standardization of technique.

Conclusion—ESG, a minimally invasive bariatric therapy, is reproducible among centers worldwide with effective weight loss and favorable safety profile outcomes. Controlled studies would be valuable to further corroborate these findings.

Keywords

Obesity; endoscopic sleeve gastropasty; ESG; endoscopic suturing; Gastropasty; Endoscopic Bariatric Therapy; EBT; Bariatric Endoscopy; Obesity Endolumenal Surgery; Overstitch; Sleeve Gastrectomy

INTRODUCTION

Obesity has become an epidemic worldwide and is associated with significant morbidity and mortality. Worldwide prevalence of obesity has nearly tripled between 1975 and 2016. According to World Health Organizations (WHO) estimates, in 2016, nearly 2 billion adults (39% of adults) were overweight, and over 650 million were obese ⁽¹⁾. Most patients fail to achieve sustained weight loss with lifestyle modification and pharmacotherapy. Bariatric surgery is an effective long-term solution for weight loss in patients with class III and class II with obesity-related comorbidities. The benefits of bariatric surgery outweigh the risk; however, it is irreversible and carries the risk of complications ⁽²⁾. Moreover, only less than 1-2 % of eligible patients eventually undergo surgery ⁽³⁾.

Endoscopic bariatric and metabolic therapies (EBMTs) have emerged over the years, intending to fill the gap between medical and surgical therapies to combat the obesity epidemic ⁽⁴⁾. Endoscopic Sleeve Gastropasty (ESG) is a minimally invasive technique that utilizes an endoscopic suturing device (OverStitch, Apollo Endosurgery, Austin, TX) to apply full-thickness sutures in the stomach, to reduce gastric capacity and alter gastric motility ^(5, 6). ESG was first performed using the current full-thickness suturing device in 2012 by Thompson and Hawes ^(6, 7). Since then, there has been growing interest in ESG, and many studies have demonstrated safety, and efficacy of this procedure.

Despite growing interest, most studies evaluating the role of ESG are single-center with an overlapping enrollment time. ESG procedure continues to gain popularity and is now being performed worldwide. Previously published systemic review and meta-analyses have included a small number of patients and lack the comprehensive global data reported in recent studies. A recent systematic review by Cohen et al. ⁽⁸⁾ concluded that endoscopic gastroplasty does not have enough quality scientific evidence regarding long-term weight loss and the procedure's safety to recommend the use in current clinical practice. This systemic review had methodical drawbacks and combined ESG with other endoscopic gastroplasty (EG) techniques, including plication of the fundus, that utilize different devices and attempt to exploit different mechanisms of action ^(9,10). Several eligible studies were also not included. Another meta-analysis of EBMT included ESG, AspireAssist, and primary obesity surgery endolumenal (POSE) in a limited number of patients ⁽¹¹⁾.

Hence, we aimed to conduct a systematic review and meta-analysis of available literature in an attempt to evaluate the outcomes specifically for ESG in the treatment of obesity.

METHODS

Literature search strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines ⁽¹²⁾. Electronic searches were performed by an experienced librarian using Medline (PubMed), Scopus, Cochrane Register of Controlled Trials and Web of Science databases from their dates of inception to June 2019. There was no language restriction; however, we restricted our search query to observational and randomized controlled trials (RCT). In addition to original articles, we searched for abstracts and presentation related to bariatric endoscopy presented at major scientific meetings.

The terms used for data search included “Endoscopic sleeve gastroplasty,” “ESG,” “Gastroplasty,” “Endoscopic Bariatric Therapy,” “EBT,” “Bariatric Endoscopy,” “Obesity Endolumenal Surgery,” “Overstitch,” “Apollo method,” “Endoscopic suturing.” Besides, we reviewed the list of references from retrieved articles for identification of potentially relevant studies. All data were extracted from article texts, tables, and figures with any estimates made based on the presented data and figures. Three investigators (S.S, M.B, and A.K) independently reviewed each included article, and its eligibility was determined based on predetermined inclusion and exclusion criteria. Any discrepancy resolved by discussion and re-evaluation by senior authors (C.C.T and D.T.H.M).

Selection criteria

All RCTs and observational studies published or presented as original research or abstracts in a major international meeting in which human subjects underwent ESG for obesity treatment were included. Studies were excluded if, endoscopic gastroplasty techniques using devices other than the OverStitch endoscopic suturing system were used. Studies were also excluded if percent total weight loss (%TWL) or percent excess weight loss (%EWL) were not clearly defined and reported, serious adverse events (SAE) were not reported, follow up

period was < 6 months, the study had < 15 patients because of the bias associated with case reports/small case series and the learning curve associated with the ESG procedure, patient in the study have undergone a prior endoscopic gastroplasty procedure or bariatric surgery or revision endoscopic procedures after bariatric surgery and overlapping patient cohorts.

Exclusion of duplicate data:

Duplication of studies involving the same patient cohort by the same institution with an accumulated number of patients or extended follow up or report of different outcomes was avoided. Studies were separated based on the author/operator or the institution and the study enrollment period. Studies with the same or overlapping cohort of patients were identified. The most complete and updated studies were selected for each institution/operator for quantitative synthesis. In multicenter studies data for each operator/institution was separated and if updated data was available as a part of another study then that institution's data from the multicenter study was excluded, and the updated data was extracted.

Data extraction and Quality assessment

Three investigators used a standardized data collection form to extract the following information: Study design, sample size, patient demographics, Body mass index (BMI), comorbidities, procedure time, suturing patterns, number of sutures, post-procedure complaints, adverse events, mortality, reversal of ESG, weight loss outcomes at follow up and remission of co-morbidities.

Primary outcomes of interest were %TWL or %EWL at follow up periods 6, 12, 18, or 24 months and incidence of SAE. Secondary outcomes included mild and moderate adverse events, remission of patient comorbidities, and procedure technique. Any missing data in the included studies were supplemented from the previously published studies involving the same cohort of patients. In case of missing data, the authors of the primary studies were contacted.

The quality assessment of the studies was done by two independent authors (A.K and S.S) using the Newcastle-Ottawa scale (NOS) for quality assessment and bias assessment of cohort studies. The NOS is a validated tool to assess reporting bias and accounts the quality of study in three areas, selection, comparability, and exposure/outcome. A score >6 was considered as a good quality score. A disagreement on the score was discussed with a third reviewer (D.T.H.M) and was resolved by consensus.

Statistical analysis

All statistical analysis was conducted using Comprehensive Meta-Analysis Software Version 3 (Biostat; Englewood, NJ, USA). Mean values for %TWL and %EWL were pooled as weighted means. Incidence of SAE was combined and expressed as pooled incidence. Meta-analyses for all outcomes were presented as forest plots with summary statistical estimates, 95% confidence intervals, and relative weights. The analysis was performed using the Dersimonian-Laird random effects model. A p-value of less than 0.05 was considered statistically significant. The I^2 statistic was used to estimate heterogeneity across studies,

where values of 25, 50, and 75% correspond to cut-off points for low, moderate, and high degrees of heterogeneity.

RESULTS

Study selection

The electronic literature search identified a total of 2587 studies with 37 additional records identified through other sources. Figure 1 shows the PRISMA flow diagram detailing the process of study selection. Eight studies were included in the final analysis^(13–20). Phase II and phase III study by Kumar et al.⁽²⁰⁾ were included while phase I study performed to evaluate the safety and technical feasibility was excluded. A three-center observational study by Lopez-Nava et al.⁽²¹⁾ was excluded because updated studies were included from these centers^(14,15,16). Similarly, many single-center studies were excluded^(5, 21–28). Sartoretto et al.⁽¹⁹⁾ included data from three centers; other studies from these centers were excluded^(29,30). Data for outcomes of co-morbidities for Saumoy et al.⁽¹⁴⁾ was supplemented from the study by Sharaiha et al.⁽²⁵⁾ involving the same cohort of patients since it was missing from the included study.

Risk of Bias

The risk of bias between studies was evaluated with Modified New Castle Ottawa, as shown in appendix 1. All articles were considered adequate for analysis in our study given scores of 5.

Study and Population Characteristics

No controlled or randomized studies were identified. All 8 included studies were observational studies^(13–20). Three studies were multi-center while the other five studies were single-center experiences. Majority of the centers were from the United States (n = 5), while the remaining population was from Spain (n = 3), Saudi Arabia (n=1), Brazil (n=1), Australia (n=1) and Dominican Republic (n=1).

The total number of patients in all studies was 1859. The weighted mean age was 42 years (95% CI: 39.64 - 44.39), and 17.8% (332) were males. Weighted mean BMI before ESG was 35.8 kg/m² (95% CI 34.78-36.98). Tables 1 and 2 summarize the individual study designs and population characteristics of the included studies.

Primary Outcomes

Weight loss

%TWL: Weight loss outcomes for individual studies are summarized in Table 2. Seven studies reported % TWL with various lengths of follow-up. Pooled mean % TWL at 6, 12, 18 and 24 months was 14.86 (95% CI 13.83-15.90, $I^2 = 93\%$, 7 studies), 16.43 (95% CI 15.23-17.63, $I^2 = 88\%$, 6 studies), 16.81 (95% CI =13.02-20.59, $I^2 = 86\%$, 2 studies) and 20.01 (95% CI =16.92-23.11, $I^2 = 0\%$, 2 studies), respectively (Table 3 and Figure 2a).

%EWL: Six studies reported %EWL with various lengths of follow-up. Pooled mean %EWL at 6, 12, 18 and 24 months was 55.75 (95% CI 50.61-60.89, $I^2 = 82\%$, 6 studies),

61.84 (95% CI 54.75-68.93, $I^2 = 69\%$, 5 studies), 66.87 (95% CI 50.14-83.60, $I^2 = 69\%$, 3 studies) and 60.40 (95% CI 48.88-71.92, $I^2 = 0\%$), respectively (Table 3 and Figure 2b).

Serious Adverse Events: SAE for individual studies are listed in Table 2. All 8 studies reported the incidence of SAE. The overall pooled incidence of SAE was 2.26% (95% CI 1.25-4.03, $I^2 = 47\%$) (Figure 3). The pooled incidence of gastrointestinal (GI) bleeding was 0.82% (95% CI 0.49- 1.38) and was reported in 4 studies. In all studies, GI bleeding was managed conservatively with observation with or without 1-2 units packed red blood cells transfusion. Emergent esophagogastroduodenoscopy (EGD) was reported in 1 patient with GI bleeding showed linear ulcerations in the proximal body at the suture line⁽¹⁹⁾. Peri-gastric fluid collection was seen in 9 patients (5 studies) with a pooled incidence of 0.68% (95% CI 0.37- 1.24). Out of these, 2 patients were managed with observation without a need for drainage, 5 patients required percutaneous drainage, and 2 patients underwent surgical intervention. Pooled incidence of perforation was 0.54% (95% CI 0.22- 1.34, 2 studies). Perforation was reported in 2 patients, one patient developed pneumoperitoneum and pneumothorax requiring chest tube placement, and the other patient underwent surgical washout. Severe abdominal pain was reported in 8 patients in one study with a pooled incidence of 0.68% (95% CI 0.38- 1.20) ⁽¹³⁾. Post-procedure fever with no sequelae was also reported in one study in 5 patients (pooled incidence 0.48% (95% CI 0.25-0.95) ⁽¹³⁾. Pulmonary embolism was reported in one patient (pooled incidence 0.48%, 95% CI 0.19-1.25) ⁽¹⁵⁾. In one study, only 3 (0.003%) patients required reversal of ESG due to persistent symptoms⁽¹³⁾. No mortality associated with ESG was reported in the included studies. The detailed SAE analysis is summarized in Table 4.

Secondary Outcomes

Mild-moderate post-procedure symptoms—Mild or moderate post-procedure symptoms were not uniformly reported. Majority of the patients in all included studies reported abdominal pain or nausea that was controlled with medications. Barrichello et al. reported mild symptoms of nausea, emesis, and abdominal pain in more than 50% of patients on the first day⁽¹⁸⁾. These symptoms significantly improved between the first and third day and eventually subsided after one week. Saumoy et al. reported that 31.2% of patients had post-procedure nausea, and 24.2% had mild-to-moderate post-procedure abdominal pain, which lasted less than 48 hours and was managed with anti-emetics and liquid acetaminophen⁽¹⁴⁾. Whereas, Alqahtani et al. reported abdominal pain or nausea controlled with medications during the first five days after surgery in 92.4% of patients⁽¹³⁾.

Comorbidities—Most studies did not report the outcomes related to comorbidities; two studies analyzed comorbidities after ESG. One study reported complete remission in T2D by the third month following the procedure in 76.5% (n=13) of the patients, while all the remaining patients showed improvement. All patients with hypertension (n=28) and 56.3 % (n=18) of patients with dyslipidemia were in complete remission at the last follow-up⁽¹³⁾. Other study reported significant reductions in levels of hemoglobin A1c (6.1 ± 1.1 vs 5.5 ± 0.4), systolic blood pressure (129.0 ± 13.4 mm Hg vs 122.2 ± 11.69 mm Hg [$P = .02$]), triglycerides (131.84 ± 83.19 mmol/dL vs 92.36 ± 39.43 mmol/dL [$P = .02$]), and ALT

(U/L) (42.4 vs 22 in men, $P = .05$, and 28 vs 20 in women, $P = .01$) at 12 months after ESG when compared to baseline⁽²⁵⁾.

Procedure Technique, suture pattern, number of sutures and procedure time

—ESG procedure technique was not uniformly reported in all studies. ESG in all included studies was performed under general anesthesia, and an esophageal overtube was used. ESG in all studies was performed using Apollo OverStitch device (Apollo Endosurgery, Austin, TX) mounted on a double-channel gastroscope (GIF2T160 or 180 series, Olympus Optical, Tokyo, Japan) with the use of a tissue helix and carbon dioxide insufflation. Mapping of the stomach anterior, greater curvature, and posterior surfaces for suture placement sites by using argon plasma coagulation were reported in most studies ($n=5$)^(14–16, 19, 20). Full-thickness nature of the suturing was reported in all included studies. Different patterns of suturing were reported as interrupted “Z” pattern in 3 studies^(14, 17, 19), triangular pattern in 4 studies^(13, 15, 16, 19), “U” pattern in 1 study⁽¹⁸⁾ and only interrupted suturing in 1 study⁽²⁰⁾. A layer of reinforcement sutures was also reported in the majority of studies ($n=6$)^(13–16, 19, 20). The number of sutures used was not uniformly reported in all studies. The pooled mean number of sutures used per patient based on 4 studies^(13–15, 19) was 7.87 (95% CI 5.52–10.21). Other studies reported 4⁽¹⁷⁾, 4–6⁽¹⁸⁾, 6–8⁽¹⁶⁾, and 9 sutures per patient⁽²⁰⁾. One study reported a median of 3 (range, 2–9) sutures for the reinforcement layer⁽¹⁴⁾. Three studies reported the mean procedure time^(13–15); pooled mean procedure time was 80.48 minutes (95% CI 51.71–109.262). One other study reported that the majority of the procedures were completed in 45–60 min⁽¹⁷⁾.

DISCUSSION

In this study, we performed the first comprehensive systematic review and meta-analysis of all available literature worldwide to assess the effectiveness and safety of ESG in over 1800 patients. Our analysis shows that ESG is safe and effective in the treatment of Obesity.

We found that the pooled mean %TWL at 6, 12, and 24 months was 14.86, 16.43, and 20.01, respectively. Similarly, %EWL at 6, 12, and 24 months was 55.75, 61.84, and 60.40. The pooled incidence of serious adverse events was 2.26%, and no mortality associated with ESG was reported.

A joint task force organized by the American Society for Gastrointestinal Endoscopy (ASGE) and American Society for Metabolic & Bariatric Surgery (ASMBS) has previously defined thresholds regarding safety and efficacy for EBMT⁽³¹⁾. The task force recommended a minimum of 25 %EWL at 12 months for primary obesity therapies and SAE < 5% for all EBT. The outcomes for ESG surpasses these thresholds and meets these criteria to be incorporated into clinical practice after adequate training as per the task force recommendations. Although the majority of studies were from centers in the USA and Spain, studies from centers across the world from Saudi Arabia, Brazil, Australia, and the Dominican Republic were also included. Most studies included patients with a BMI > 30 kg/m², and the weighted mean BMI before the procedure was 35.8. Effective weight loss outcomes were seen in all studies from centers worldwide in this lower BMI obesity group (30–40).

SAE profile was very favorable; the overall incidence of SAE was only 2.26%. GI bleeding and peri-gastric fluid collection were the most commonly reported SAE, but the incidence of both was less than 1%. GI bleeding in all cases was managed conservatively with or without blood transfusions. Peri-gastric fluid collections were successfully managed with a percutaneous drain in most cases. In the largest included study, only 0.003% of patients required reversal of ESG due to persistent symptoms⁽¹³⁾. Included studies reported these events as SAE, but a standardized nomenclature and definitions for SAE were lacking. According to ASGE Quality Task Force recommendations, most of these reported SAEs can be classified as mild to moderate adverse events⁽³²⁾.

According to the ASMBS, laparoscopic sleeve gastrectomy (LSG) is the most common bariatric surgical procedure performed⁽³³⁾. ESG technique similarly focuses on the greater curvature of the stomach, however, there are several differences⁽³⁰⁾. In contrast to LSG, ESG requires no abdominal incisions, does not require an operating room, and is reversible in some cases. ESG produces remodeling, but the stomach remains intact with its innervation, and blood supply with potential for repeatability, and conversion to bariatric surgery if necessary⁽³⁴⁾. LSG and other bariatric surgeries are associated with substantial and durable weight loss^(29, 35); meanwhile, long-term data with ESG is still not available in the published literature. In a short term follow up study of matched cohorts, ESG achieved lower weight loss (17.1 %TWL) than LSG (23.6 %TWL) at 6 months, but the ESG patients had significantly lower adverse events⁽²⁹⁾. Gastroesophageal reflux disease (GERD) is also a common and distressing problem reported in patients after LSG with a frequency as high as 47%⁽³⁶⁾. There is considerable overlap in patients eligible for ESG and bariatric surgery. ESG studies included patients who do not otherwise qualify for bariatric surgery or are non-surgical candidates, thus bridging the gap.

Intragastric balloons (IGB) a space-occupying device is the most common and well-established EBMT. A systematic review and meta-analysis reported 13.2% TWL with IGB at 6 months⁽³⁷⁾, while a recent review reported 9.7% TWL at 6 months⁽³⁸⁾. One of the limitations of IGB therapy is the weight recidivism after removal of the balloon at the end of 6 months^(38–40). In our analysis of ESG studies, %TWL of 14.9 at 6 months was comparable to IGB, but ESG patients did not regain weight at 12 months (%TWL 16.8) or 24 months (%TWL 20.0). In one recent report, the incidence of SAE associated with IGB was higher than the SAE for ESG in our analysis⁽⁴⁰⁾. ESG seems to provide durable weight loss with less adverse events compared with an IGB up to a follow up of 2 years.

Studies in our analysis demonstrated effective but small variability in weight loss outcomes, ranging from 15.0 to 18.2 %TWL and 52.6 to 75.4 % EWL at 12 months follow up. The reason for the small variability is perhaps related to the difference in patient characteristics, post-procedure diet, concomitant weight loss medication, the intensity of lifestyle modification, and procedure technique. Full-thickness suturing of the gastric greater curvature was reported in all studies, but there were variations in procedure technique. The different patterns of suturing were reported as “Z,” “U,” and triangular patterns. The number of sutures used was highly variable, but the layer of reinforcement sutures was reported in the majority of studies. Currently, there is not enough evidence regarding the optimal number of sutures or the suture pattern. Use of a few sutures is cost-effective and reduces

procedure time but can limit the efficacy of the procedure. We believe full-thickness suture bites and a layer of reinforcement sutures are likely associated with better efficacy, but further studies are needed.

As more physicians gain proficiency with the procedure, we expect a widespread expansion of ESG; however, several areas need to be addressed⁽⁴¹⁾. Training in this subspecialized area is sparse, standardized training and credentialing methods are required. Identifying the right patient phenotype and physiology will be essential for optimizing outcomes. Further research and development in device design and technology are underway to simplify the procedure for broader dissemination. Concomitant pharmacotherapy with ESG will need to be evaluated to promote durable weight loss. ESG combined with other EBMT, especially small bowel endoscopic procedures either applied simultaneously or sequentially, has the potential to produce the same efficacy as bariatric surgery with beneficial adverse event profile. Finally, ESG is mostly a self-pay procedure in the United States, with coding and insurance coverage remaining significant barriers to widespread adoption.

Ours is the first comprehensive systematic review and meta-analysis to evaluate the cumulative efficacy, safety and procedural technique, specifically for ESG and from an international perspective. In contrast to prior studies, this analysis follows the PRISMA guidelines to better define outcomes following ESG. Updated studies from many centers with an overall large number of patients were included. A recently published meta-analysis by Li et al.⁽⁴²⁾ included overlapping patient from a single operator in two studies^(19, 29). We meticulously examined all studies and avoided overlapping of patients cohorts and duplication of data. A recent multicenter study by Barrichello et al.⁽¹⁸⁾ included in our analysis has not been included in any previous analysis.

Despite our rigorous inclusion criteria, our study has several limitations. The quality of the included studies limits the quality of our systematic review and meta-analysis. None of the included studies were RCTs; all were observational studies of variable sample size. Length of follow-up, outcome measures, and procedural techniques all slightly varied between studies and considerable heterogeneity was seen in a few of our estimates. Most of the included studies did not clarify about concomitant weight-loss medications during follow-up. Although the overall number of patients was relatively large (1859), but for each outcome, the number of patients available for analysis was less. There is a paucity of controlled data and evidence regarding the impact of ESG on obesity-related comorbidities. Lack of standardized definition for SAE in included studies also affects the comparison. ESG has only recently gained momentum as a promising technique that naturally limits the availability of long-term follow-up data.

In conclusion, ESG is a minimally invasive bariatric therapy that is reproducible among centers worldwide with effective weight loss outcomes and a favorable safety profile in light of the ASGE/ASMBS threshold.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

Endoscopic Sleeve Gastroplasty has gained momentum as a promising minimally invasive endoscopic bariatric therapy worldwide.

Our meta-analysis shows that Endoscopic Sleeve Gastroplasty has effective weight loss outcomes and favorable safety profile.

Variations in the technique of Endoscopic Sleeve Gastroplasty exist, but the full-thickness nature of suturing in all studies and layer of reinforcement sutures was performed in the majority of studies.

Figure 1:
PRISMA flow diagram of the search strategy and study selection.

Mean % TWL

Meta Analysis

Mean %EWL

Meta Analysis

Figure 2.

- a: Forest plots showing Percent Total Weight Loss (%TWL) achieved with Endoscopic Sleeve Gastroplasty (ESG).
- b: Forest plots showing Percent Excess Weight Loss (%EWL) achieved with Endoscopic Sleeve Gastroplasty (ESG).

Figure 3:

Forest plot evaluating the pooled incidence of serious adverse events.

Table 1:

Study designs, inclusion, and exclusion criteria of the included studies.

Study (Year published)	Design	Setting	Country	N	Inclusion Criteria	Exclusion Criteria
Saumoy (2018)	Observational	Single-Center	USA	128	BMI>30 Kg/m ² with failed noninvasive weight loss measures OR BMI >40 Kg/m ² AND nonsurgical candidates or declined surgery.	History of gastric lesions, neoplastic changes or gastric cancer, Contraindications or at high risk to undergo general anesthesia.
Alqahtani (2019)	Observational	Single-Center	Saudi Arabia	1000	BMI> 40 Kg/m ² or 35 Kg/m ² with comorbidities.	Bleeding disorders, large hiatal hernia, and active peptic ulcer disease.
Abu Dayyeh (2017)	Observational	Single-Center	USA	25	BMI between 30 to 40 Kg/m ² with stable weight for 3 months.	Anticoagulation, previous gastric surgery, gastric ulceration, hiatal hernia > 5 cm, or pregnancy.
Lopez-Nava (2017)	Observational	Single-Center	Spain	154	BMI>30 Kg/m ² who committed for 1 year multidisciplinary follow-up.	Acute, potentially bleeding gastric mucosal lesions (ulcers, acute gastritis), neoplastic lesions, hiatal hernia >3 cm, coagulopathy, and psychiatric disorders.
Morales (2018)	Observational	Single-Center	Spain	148	BMI > 30 Kg/m ² to >40 Kg/m ²	Potentially bleeding lesions, such as ulcers or erosive duodenitis, and preneoplastic or neoplastic findings, Contraindications or at high risk to undergo general anesthesia.
Barrichello (2019)	Observational	Multi-center	Brazil (6 centers, USA (1 center)	193	Overweight or obese patients who failed diet and lifestyle modifications.	Previous gastric surgery, anticoagulation, acute gastric ulceration, cancer, hiatal hernia >5 cm, gastroesophageal motility disorder, and pregnancy.
Sartoretto (2018)	Observational	Multi-center	Australia	51	BMI > 27 Kg/m ² and failed multiple diet and lifestyle modifications.	Personal or family history of gastric cancer, active gastric ulcers, presence of any gastric condition which required endoscopic surveillance (e.g., known gastric intestinal metaplasia), known vascular abnormalities, decompensated organ failure, obligate therapeutic anticoagulation, pregnancy/lactation.
			USA center 1	42		
			USA center 2	19		
Kumar (2017)	Observational	Multi-center	Phase II Dominican Republic, USA	22	BMI > 30 Kg/m ² with unsuccessful diet and lifestyle modifications.	Bleeding disorders, gastrointestinal disease, prior gastric surgery, active use of weight loss medication, eating disorders, or uncontrolled or severe psychiatric disease.
			Phase III Dominican Republic, Spain, USA	77		

* Body Mass Index (BMI)

Table 2:

Population characteristics and outcomes of the included studies.

Study (Year published)	N	Males N (%)	Age yrs Mean (S.D)	BMI Pre-ESG (S.D)	Follow up (Months)	% TWL	% EWL	Serious Adverse Events N (%)
Saumoy (2018)	128	42 (32.8%)	43.6 (11.3)	38.92 (6.95)	6	13.43 (7.4)	NA	2 (1.5%) (1 perigastric leak, 1 perforation)
					12	15.8 (9.5)	NA	
Alqahtani (2019)	1000	103 (10.3%)	34.4 (9.5)	33.3 (4.5)	6	13.7 (6.8)	64.3 (56.2)	24 (2.4%) (8 severe abdominal pain, 7 post-procedure bleeding, 4 perigastric collections with pleural effusion, 5 post-procedure fever with no sequelae)
					12	15.0 (7.7)	67.5 (52.3)	
					18	14.8 (8.5)	64.7 (55.4)	
Abu Dayyeh (2017)	25	4 (16%)	47.6 (10)	35.5 (2.6)	6	NA	54 (40)	3 (12%) (1 peri-gastric fluid collection, 1 pulmonary embolism, 1 pneumoperitoneum/pneumothorax)
					12	NA	54 (40)	
					20	NA	45 (41)	
Lopez-Nava (2017)	154	46 (30%)	44.9 (9.5)	38.3 (5.5)	6	15.8 (7.1)	47.8 (29.4)	0 (No SAE)
					12	18.2 (10.1)	52.6 (31.3)	
					24	19.5 (10.5)	60.4 (31.1)	
Morales (2018)	148	27 (18.2%)	41.53 (10)	35.11 (5.5)	6	15.45 (5.9)	64.93 (51)	1 (0.67%) Mild GI bleeding
					12	17.53 (7.57)	75.4 (85.0)	
					18	18.66 (7.3)	79.25 (43)	
Barrichello (2019)	193	45 (23.3%)	42.3 (9.6)	34.11 (2.97)	6	14.25 (5.26)	56.15 (22.93)	4 (2.07) (2 GI bleeding, 2 perigastric fluid collections)
					12	15.06 (5.22)	59.41 (25.69)	
Sartoretto (2018)	51 (Australia)	15 (29.4%)	43 (11.9)	36.7 (4.9)	6	14.0 (5.6)	49.2 (23.2)	3 (2.6%) (2 GI bleeding, 1 perigastric fluid collection)
	42 (US Ctr 1)	17 (40.5%)	49.2 (11.4)	41.2 (8.0)	6	16.3 (7.9)	46.9 (20.3)	
	19 (US Ctr 2)	3 (15.8%)	41.2 (8.0)	33.6 (4.0)	6	17.7 (1.7)	72.1 (9.7)	
Kumar (2017)	22	2 (9.1%)	39.2 (1.6)	34.3 (1.0)	6	17.3 (1.7)	NA	0 (No SAE)
					12	17.3 (2.6)	NA	
	77	18 (23.4%)	41.3 $\pm$ 1.1	36.1 (0.6)	6	16.0 (0.8)	NA	0 (No SAE)
					12	17.4 (1.2)	NA	

* NA data was not available

[†]Percent total weight loss (%TWL); Percent Excess Weight Loss (%EWL); Standard Deviation (S.D.); Serious Adverse Event (SAE)

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Table 3:

Pooled Percent Total Weight Loss (%TWL) and Percent Excess Weight Loss (%EWL).

Follow up	Outcome	Studies	Total patients	% (95% CI)
6 Months	% TWL	7	1074	14.86 (13.83-15.90)
	% EWL	6	926	55.75 (50.61-60.89)
12 Months	% TWL	6	673	16.43 (15.23-17.63)
	% EWL	5	559	61.84 (54.75-68.93)
18 Months	% TWL	2	126	16.81 (13.02-20.59)
	% EWL	3	134	66.87 (50.14-83.60)
24 Months	% TWL	2	36	20.01 (16.92-23.11)
	% EWL	1	28	60.40 (48.88-71.92)

* Percent Total Weight Loss (%TWL); Percent Excess Weight Loss (%EWL); Confidence Interval (CI)

Table 4:

Serious Adverse Events described in included eight studies (N=1859).

Event	No of Occurrence	Occurrence in no of Studies	Pooled incidence (95% CI)
Gastrointestinal Bleeding	12	4	0.82% (0.49- 1.38)
Peri-gastric fluid collection	9	5	0.68% (0.37- 1.24)
Perforation, pneumoperitoneum or pneumothorax	2	2	0.54% (0.22- 1.34)
Severe abdominal pain	8	1	0.68% (0.38- 1.20)
Post procedure fever	5	1	0.48% (0.25-0.95)
Pulmonary Embolism	1	1	0.48% (0.19-1.25)
Overall	37	8	2.26% (1.25-4.03)

* Confidence Interval (CI)