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ORIGINAL CONTRIBUTIONS

Efficacy of Endoscopic Interventions for the Management of Obesity: a Meta-analysis to Compare Endoscopic Sleeve Gastroplasty, AspireAssist, and Primary Obesity Surgery Endolumenal

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Abstract

Background and Aims Novel endoscopic procedures (endoscopic sleeve gastroplasty (ESG), AspireAssist (AA), and primary obesity surgery endolumenal (POSE)) have been developed for treatment of obesity. We aimed to conduct a systematic review and meta-analysis to evaluate and compare the efficacy of these three endoscopic procedures.

Methods Main outcomes of interest were percent excess weight loss (%EWL) and percent total body weight loss (%TBWL). Weighted pooled means (WPMs) were calculated and analyzed using random effects model. Mean differences (MDs) were calculated to compare these procedures.

Results Twelve studies with 1149 patients were included. WPMs for %EWL at 6 and 12 months with ESG were 49.67 (45.67, 53.66) and 52.75 (43.52, 61.98), respectively, while %TBWLs at 6 and 12 months with ESG were 16.01 (15.10, 16.92) and 17.41 (17.08, 17.74), respectively. WPMs for %EWL at 6 and 12 months with POSE were 43.79 (40.17, 47.42) and 44.91 (40.90, 48.92), respectively. WPM for %EWL at 12 months with AA was 50.85 (46.03, 55.68). While comparing ESG and POSE, at 6 months and 12 months, MD for %EWL was 6.17 (1.07, 11.26; $P = 0.01$) and 7.84 (− 2.05, 17.71; $P = 0.06$) in favor of ESG. No difference in %EWL was observed while comparing ESG with AA ($P = 0.29$). Likewise, MD for %EWL to compare AA and POSE was not significant ($P = 0.68$).

Conclusions During a follow-up of 6–12 months, both AA and ESG had excellent efficacy in achieving significant and sustained weight loss; however, ESG was found to be superior in terms of weight loss when compared with POSE.

Keywords Bariatric endoscopy · Obesity · Sleeve gastroplasty · POSE · AspireAssist

Introduction

Obesity continues to be a major global health burden of the twenty-first century. In 2014, the World Health Organization estimated that nearly 600 million people were obese and 1.9 billion people were overweight [1]. Age-adjusted prevalence of obesity among adults in the USA was 35% of men and 40% of women and continues to rise [2]. Comorbid illnesses like cardiovascular disease, diabetes, obstructive sleep apnea, osteoarthritis, and gastroesophageal reflux disease are common in patients with obesity, leading to decreased longevity and constituting a significant socioeconomic burden on the US healthcare system [3, 4].

Noninvasive treatment options include lifestyle modification and pharmacotherapy. However, for patients with obesity, sustained modest weight loss is difficult to achieve with these noninvasive interventions. Bariatric surgery has been more effective for not only achieving but also sustaining greater weight loss over a prolonged period of time, as well as significant improvement in comorbidities [5, 6]. However, these surgical procedures carry a low rate of perioperative mortality and multiple long-term adverse events [7, 8]. Bariatric surgery is recommended for patients with class III obesity or those with class II obesity and significant obesity-related comorbidities

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[9]. Furthermore, only 1% of qualified patients undergo surgery because of patient preference, fear of risks, limited access, and costs of surgery [10]. Therefore, a vast majority of patients do not get sufficient treatment for obesity. Endoscopic bariatric and metabolic therapies (EMBTs) have been developed to fill this treatment gap.

Endoscopic sleeve gastroplasty (ESG) and primary obesity surgery endolumenal (POSE) are two plication procedures for the management of obesity. ESG utilizes a full-thickness endoscopic suturing system to reduce the length and width of the stomach causing restriction. POSE involves the endoluminal placement of durable, full-thickness tissue plications in the fundus and distal body of the stomach, leading to some restriction but mainly reducing accommodation of the fundus. The AspireAssist (AA) system is an alternative method for decreasing caloric intake. It consists of an endoscopically placed percutaneous gastrostomy tube, a skin port, and an accessory device. This allows for instillation of water in the stomach after meals along with partial aspiration of ingested contents. Observational studies and a few randomized trials have evaluated the efficacy of the aforementioned three endoscopic procedures and have shown varying degree of success. Therefore, in this meta-analysis, we aim to individually evaluate and compare the clinical outcomes among the three procedures.

Methods

Identification and Retrieval of Primary Studies

This systematic review and meta-analysis was carried out in accordance with the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) [11] and meta-analysis of observational studies in epidemiology (MOOSE) [12]. Systematic search of the literature was conducted by an experienced medical librarian. Ovid Medline was used to develop search strategies that were further translated to match subject headings and keywords for Ovid EMBASE, Cochrane database, and Scopus from inception through November 10, 2017. The search terms included, but were not limited to, "sleeve gastroplasty," "sleeve gastrectomy," "primary obesity endolumenal surgery," "POSE," "ESG," "Overstitch," "obesity endoluminal surgery," "gastrostomy tube," "ASPIREASSIST," "bariatric," and "bariatric endoscopy." These terms were used in various combinations accounting for plurals and use of appropriate wildcards. There was no restriction on language. Articles were selected for full-text review based on their title and abstract. A manual search through the bibliographies of the retrieved publications (backward snowballing) was conducted to increase the yield of potentially relevant articles. All results were downloaded into End-Note 7.0 (Thomson ISI ResearchSoft, Philadelphia, PA, USA) and any duplicate citation was identified and removed.

Study Selection and Data Extraction

Eligibility criteria were determined a priori by two study authors (R. Z. S and M. A. K) and included studies with patients who had undergone one of the three endoscopic procedures: ESG, POSE, and AA. Studies were included if they reported either percent excess weight loss (%EWL) or percent total body weight loss (%TBWL) with a follow-up of at least 6 months. Only studies with 10 or more patients were included to minimize bias associated with individual case reports and small case series. Also, studies were excluded if overlap of patients was suspected based on inclusion dates mentioned in the individual study methods section. Upon any doubt about overlap, corresponding authors of the studies were contacted to ensure the patient cohort was not duplicated. Two reviewers (M. A. K and Z. K.) screened citations and abstracts and retrieved full-text publications of all potentially eligible articles. Study eligibility was assessed by both reviewers independently based on the inclusion criteria, and any disagreement between reviewers was discussed with a third reviewer (R. Z. S). Once studies matching the eligibility criteria were identified, two reviewers (Z. K. and M. A. K) independently extracted data using predefined data spreadsheets. Extracted data included study design, country and year of publication, demographic characteristics of patients including age, gender, and body mass index (BMI) at baseline, and, where available, changes in hemoglobin A1c and adverse events. Once data extraction was completed, data sheets were compared. Any discrepancies between the two reviewers were discussed with the third reviewer (R. Z. S) and agreement was reached by consensus.

Quality Assessment, Data Synthesis, and Statistical Analysis

Quality assessment of randomized controlled trials (RCTs) was done using the Cochrane tool for assessing risk of bias. This tool assesses presence of selection bias by evaluating methods of randomization and allocation concealment; performance and detection of bias by checking for blinding of personnel and outcome assessment; and attrition and reporting bias by evaluating for incomplete and selective data reporting [13]. For quality assessment of observational studies, the National Institutes of Health (NIH) quality assessment tool was used for before–after studies with no control group [14]. Quality assessment was independently performed by two reviewers (M. A. K and R. Z. S.), and any disagreement was resolved with consensus.

Our main outcomes of interest were %EWL and %TBWL. These were pooled as weighted means and analyzed using Der Simonian and Laird random effects model [15]. Outcomes were evaluated at 6, 12, and 24 months. Weighted mean difference (WMD) of %EWL and %TBWL was calculated to compare all three procedures. Cochrane X^2 and I^2 statistics

were used to estimate statistical heterogeneity. Presence of heterogeneity was defined as a P value of < 0.1 with $I^2 > 50\%$ consistent with substantial heterogeneity. We conducted predetermined subgroup analysis based on months of follow-up. All analyses were carried out using Comprehensive Meta-analysis software (version 3.0; Biostat; Englewood, NJ, USA).

Results

Search Strategy Yield, Study Characteristics, and Quality Assessment

Our search strategy identified 1142 citations of which 849 remained after deduplication. Further, 785 citations were removed after title and abstract review. Bibliographic search of the remaining 64 articles revealed two more studies in abstract forms, and thereby, a total of 66 were reviewed of which 54 articles were excluded as they did not match our inclusion criteria or had duplicate data. Finally, 12 studies [16–27] with 1149 patients were included in this systematic review and meta-analysis. The study selection process is outlined in Fig. 1. Four studies each evaluated AA [16–19], ESG [20–23], and POSE [24–27]. Four studies were randomized controlled trials (RCTs) [16, 18, 24, 25] while the remaining 8 were observational studies [17, 19–23, 26, 27]. One study [23] included two prospective phases during which ESG was performed. A multicenter observational study [28] on ESG was not included in the analysis as it had overlapping data with three studies [20–22]. Therefore, we only included the latter three studies which provided all data from these three different centers. Likewise, four single-center studies [29–32] were excluded as their data were incorporated into the latest study by Lopez-Nava et al. describing a 2-year follow-up [21]. Further, we excluded several abstracts [33–39] as these were either published as fully peer-reviewed journal articles later or their data were incorporated in studies published subsequently (in which case fully published studies in journals were included). All RCTs [16, 18, 24, 25] had low risk of selection, attrition, and reporting biases based on the Cochrane tool for assessing risk of bias. Three RCTs [16, 18, 25] had high risks of performance and detection biases as blinding of endoscopists and patients was not possible and likewise, patient outcome assessment could not be blinded. However, one RCT [24] which compared POSE with a sham procedure had only high risk of performance bias, while the risk of detection bias was low as the patients and outcome assessors could not differentiate the two groups. Among observational studies, 7 [17, 20–23, 26, 27] were of good quality and 1 [19] was of fair quality as per NIH quality assessment tool for before–after studies without control group. Quality assessment is highlighted in Appendix. A total of 333 patients underwent AA placement, 369 underwent ESG, and the remaining 447 patients underwent POSE. Eighty percent of our cohort consisted of female patients. Study characteristics and patient demographics are highlighted in Table 1.

Meta-analysis

Four studies evaluated the performance of ESG in patients with obesity. The %EWL was reported in 158, 77, and 28 patients over 6, 12, and 24 months, respectively. Pooled mean %EWL at 6 months was 49.67 (95% CI 45.67, 53.66; Cochran's Q test $P = 0.22$; $I^2 = 22\%$). Likewise, pooled mean %EWL at 12 and 24 months was 52.75 (43.52, 61.98; $I^2 = 0\%$) and 60.40 (48.88, 71.91; $I^2 = 0\%$), respectively. The %TBWL was reported in 305, 183, and 36 patients during 6, 12, and 24 months of follow-up, respectively. Pooled mean %TBWL at 6 months was 16.01 (15.10, 16.92; Cochran's Q test $P < 0.001$; $I^2 = 78\%$). At 12 and 24 months, pooled mean %TBWL was 17.41 (17.08, 17.74; $I^2 = 0\%$) and 19.61 (16.32, 22.90; $I^2 = 0\%$) (Fig. 2).

Four studies reported the results of POSE %EWL were reported in 177 and 150 patients at 6 and 12 months, respectively. Pooled mean %EWL at 6 and 12 months was 43.79 (40.17, 47.42; $I^2 = 0\%$) and 44.91 (40.90, 48.92; $I^2 = 0\%$). The %TBWL was reported in 192 and 165 patients at 6 and 12 months, respectively. Pooled mean %TBWL at 6 months was 13.82 (12.51, 15.13; Cochran's Q test $P = 0.12$; $I^2 = 38\%$). At 12 months, pooled mean %TBWL was 10.98 (3.48, 18.48; Cochran's Q test $P < 0.001$; $I^2 = 90\%$). Sullivan et al [24] appeared to be the outlier in the estimate and accounted for most of statistical heterogeneity. We conducted a sensitivity analysis; after excluding this RCT, pooled mean %TBWL was 14.37 (12.42, 16.33; Cochran Q test $P = 0.19$; $I^2 = 39\%$). Eighteen patients were lost to follow-up in the intervention arm of RCTs. Non-responder rate for RCTs was defined as at least > 5% TBWL at 12 months. Miller et al. [25] had a non-responder rate of 10% while Sullivan et al. [24] had a non-responder rate of 58% (Fig. 3).

Finally, four studies evaluated the AA device in patients with obesity. The %EWL was reported in 258 and 100 patients at 12 and 24 months, respectively. Pooled mean %EWL at 6 and 12 months was 43.25 (33.87, 52.63; $I^2 = 80\%$) and 50.85 (46.03, 55.68; $I^2 = 0\%$), respectively. Pooled mean %TBWL at 12 months was 15.37 (9.00, 21.74; $I^2 = 80\%$), while at 24 months was 20.10 (17.50, 22.69). In RCTs, 29 patients were lost to follow-up in the intervention arm and non-responder rate was 31% (Fig. 4).

When comparing ESG with POSE at 6 months, WMD for %EWL was 6.17 (1.07, 11.26; $P = 0.01$) in favor of ESG. Therefore at 6 months, significantly greater weight loss was achieved with ESG as compared with POSE. The WMD for %EWL at 12 months was 7.84 (− 2.05, 17.71; $P = 0.06$), suggesting that at 12 months, ESG showed a trend towards greater weight loss in comparison with POSE. Likewise, WMD for

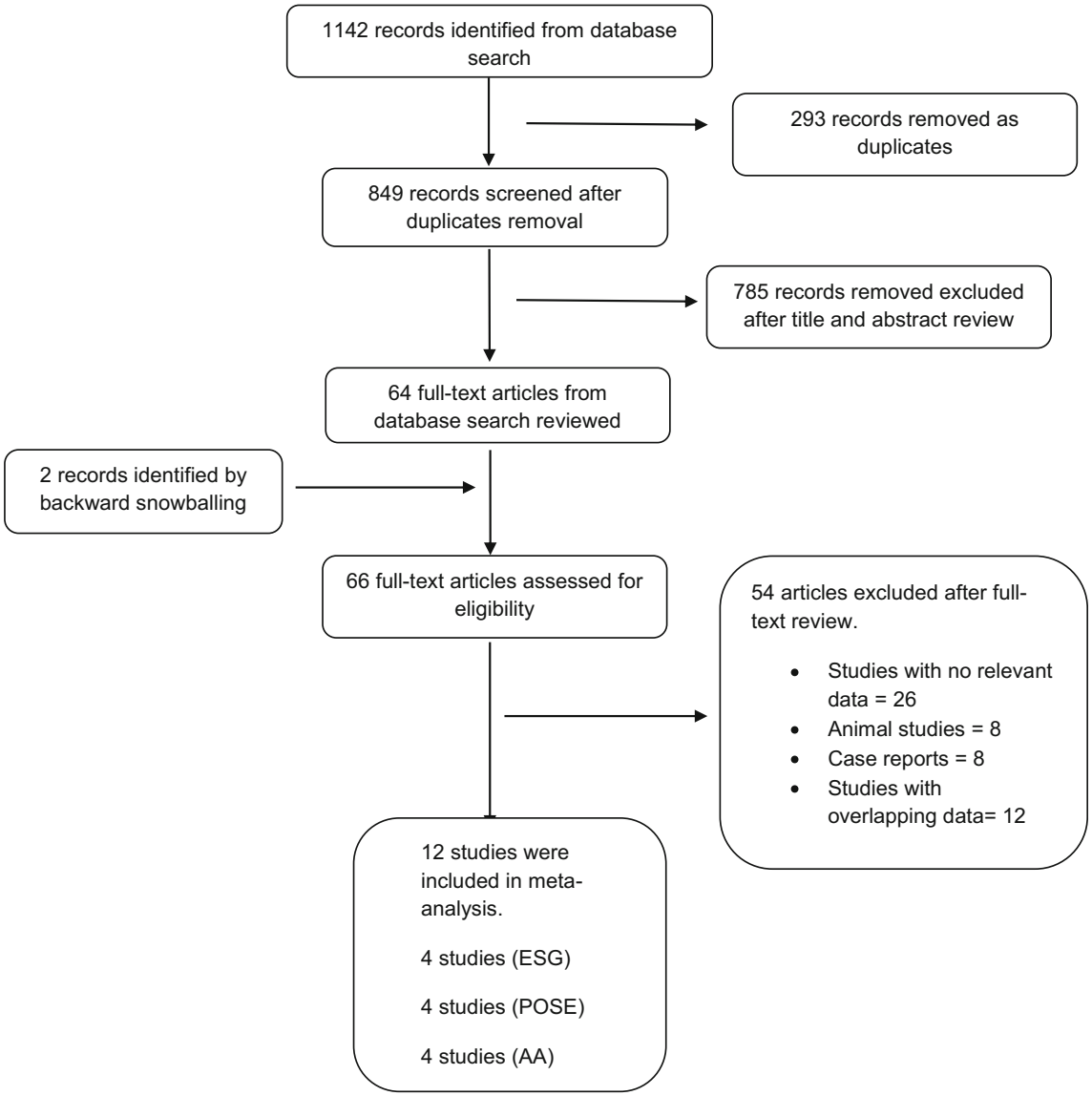

Fig. 1 PRISMA flowchart for study selection

%TBWL at 6 months was 2.19 (0.62, 3.77; $P = 0.005$) in favor of ESG, and WMD for %TBWL at 12 months was 6.43 (− 1.02, 13.88; $P = 0.09$). Similarly, based on %TBWL, ESG demonstrated superior weight loss to POSE at 6 months and showed a trend towards greater weight loss at 12 months.

While comparing ESG with AA, we found no difference in weight loss based on %EWL or %TBWL at 12 and 24 months. The WMD for %EWL at 12 months was 9.50 (− 3.50, 22.52; $P = 0.29$), and at 24 months was 9.55 (− 2.40, 21.54; $P = 0.10$). The WMD for %TBWL at 12 months was 2.04 (− 4.27, 8.35; $P = 0.43$). Finally, when comparing AA with POSE, we found no difference in weight loss based on %EWL and %TBWL at 12 months. The WMD for %EWL was 2.53 (− 6.84, 11.90; $P = 0.68$) and %TBWL was 4.39 (− 5.36, 14.44; $P = 0.40$) (Figs. 5 and 6).

Adverse events were not uniformly described by all studies and therefore were not incorporated in this meta-analysis. Crude percentages were calculated for the most common adverse events such as abdominal pain, nausea, and vomiting, and specifically for AA, peristomal infections, and granulation tissue formation. Abdominal pain post-procedure requiring pharmacotherapy was encountered in 25% and 22% of patients undergoing AA and ESG, respectively. Likewise, nausea and vomiting were reported in 13% of patients with ESG and 14% with AA. Further, 27% of patients undergoing AA developed peristomal complications including infection, irritation, and granulation tissue. Only Sullivan et al. [24] described adverse events that occurred after POSE. The authors reported that 45% of patients had post-procedure abdominal pain requiring

Table 1 Characteristics of included studies

Study, year, and country	Design	Intervention	Inclusion criteria	Exclusion criteria	N	Males	Age	%TBWL	%EWL	Adverse events
Sullivan (2013), USA	RCT	AspireAssist	BMI 40–50 or 35–39.9 with comorbidities	Eating disorder, major depression, history of GI disease or surgery, uncontrolled HTN, sleep apnea, pregnancy, lactation	11	0	38.7	18.6 at 12 months 20.1 at 24 months	49.0 at 12 months 54.6 at 24 months	Abdominal pain (11) Peristomal skin irritation (6) Peristomal bleeding (5) Peristomal infection (3) Nausea and/or vomiting (7) Constipation (8)
Noren, (2016), Sweden	Observational study	AspireAssist	BMI ≥ 35.0 Age 25 to 65 years	Myocardial infarction during the last 3 months, known malignancy, chronic liver, or kidney disease, prior to major surgery in the upper gastrointestinal tract, psychiatric disease including substance abuse, eating disorder, mental retardation, or other intellectual disability	25	2	48	NR	44.5 at 12 months 44.9 at 24 months	Abdominal pain (16) Stoma site complications (3)
Thompson (2017), USA	RCT	AspireAssist	BMI 35–55 Age 21–65 years	History of GI disease or abdominal surgery, previous bariatric surgery, chronic abdominal pain, CAD, use of medications that cause clinically significant weight gain or loss, or a history of major depressive or other severe psychiatric disorders, history of an eating disorder.	111	15	42.2	12.1 at 12 months	31.5 at 12 months	Peristomal granulation tissue (45) Abdominal pain (51) Nausea and/or vomiting (19)
Machytka, (2017), International	Observational study	AspireAssist	BMI > 35	NR	160	NR	NR	NR	48.3 at 12 months 50.0 at 12 months	Abdominal pain (6) Buried bumpers (3)
Abu Dayyeh (2017), USA	Observational study	ESG	BMI between 30 and 40, stable weight for 3 months before the procedure	Anticoagulation, previous gastric surgery, gastric ulceration, hiatal hernia 5 cm or pregnancy	25	4	47.6	NR	53.0 at 6 months 54.0 at 12 months	Post ESG-pain and nausea (25) Perigastric fluid collection (1) Pulmonary embolism (1) Pneumoperitoneum (1)
Lopez, (2017), Spain	Observational study	ESG	BMI > 30	Acute, potentially bleeding gastric mucosal lesions (ulcers, acute gastritis), neoplastic lesions, hiatus hernia >3 cm, coagulopathy, and psychiatric disorders	154	46	44.9	15.8 at 6 months 18.2 at 12 months 19.1 at 24 months	47.8 at 6 months 52.6 at 12 months 60.4 at 24 months	NR
Sharaiha, (2017), USA	Observational study	ESG	BMI > 30 and previous failed attempts at noninvasive weight loss measures. BMI > 40 who refused surgery or were deemed not to be surgical candidates	Gastric lesions, neoplastic findings, or family history of gastric cancer. Mental health disorders, significant medical comorbidities precluding sedation, or coagulopathies	91	29	43.66	14.4 at 6 months 17.6 at 12 months 20.9 at 24 months	NR	Nausea (35) Abdominal pain (25) Perigastric leak (1)
		ESG			22	2	39.2	17.3 at 6 months	NR	NR

Table 1 (continued)

Study, year, and country	Design	Intervention	Inclusion criteria	Exclusion criteria	N	Males	Age	%TBWL	%EWL	Adverse events
Kumar (2017), International	Observational study Phase II Observational study Phase III	ESG	BMI > 30 and failed diet and lifestyle modifications same as above	Bleeding disorders, Gastrointestinal disease, prior gastric surgery, Active use of weight loss medication, eating disorders, or uncontrolled or severe psychiatric disease. Same as above	77	18	41.3	17.3 at 12 months 16.0 at 6 months 17.4 at 12 months	NR	NR
Sullivan, (2017), USA	RCT	POSE	Age 22–60 years BMI 30–35 with any one obesity-related comorbid illness BMI 35–40 with or without obesity-related comorbid illness	History of prior bariatric, gastric, or esophageal surgery, severe systemic disease, esophageal stricture or other condition that would limit passage of endoluminal instruments, severe gastroesophageal reflux disease, hiatal hernia >3 cm, inflammatory disease of the gastrointestinal tract. Known genetic cause of obesity	221	26	44.2	4.95 at 12 months	NR	Abdominal pain (100) Nausea vomiting (87)
Miller, (2017), International	RCT	POSE	Age 20–60 years BMI 30–40 with failed diet and lifestyle interventions, ASA score 2 or less, not taking any weight modifying medications	History of bariatric, gastric, or esophageal surgery, stricture, or condition that could preclude passage of endoluminal instruments, GERD, hiatal hernia >3 cm, pancreatic insufficiency/disease; active peptic ulcer; pregnancy or plans of pregnancy within 12 months; steroid use; inflammatory gastrointestinal disease; coagulation disorders; chronic liver disease; uncontrolled diabetes	34	9	38.3	12.7 at 6 months 13.0 at 12 months	45.5 at 6 months 45.0 at 12 months	NR
Lopez, (2014), Spain	Observational study	POSE	Class I or II obesity with or without co-morbid conditions such as diabetes, hypertension, and hyperlipidemia	Any physiologic or psychological conditions that would create a risk or hamper their ability to comply with the diet and exercise guidelines necessary to lose weight	147	45	43.8	13.6 at 6 months 15.1 at 12 months	42.1 at 6 months 44.9 at 12 months	NR
Espinos (2013), Spain	Observational study	POSE	BMI in the class I or II obesity range. BMI in class III range but be unwilling to undergo a surgical procedure	Non-ambulatory or significant mobility impairment; known and untreated hormonal or genetic cause for obesity	45	11	43.4	15.5 at 6 months	49.4 at 6 months	NR

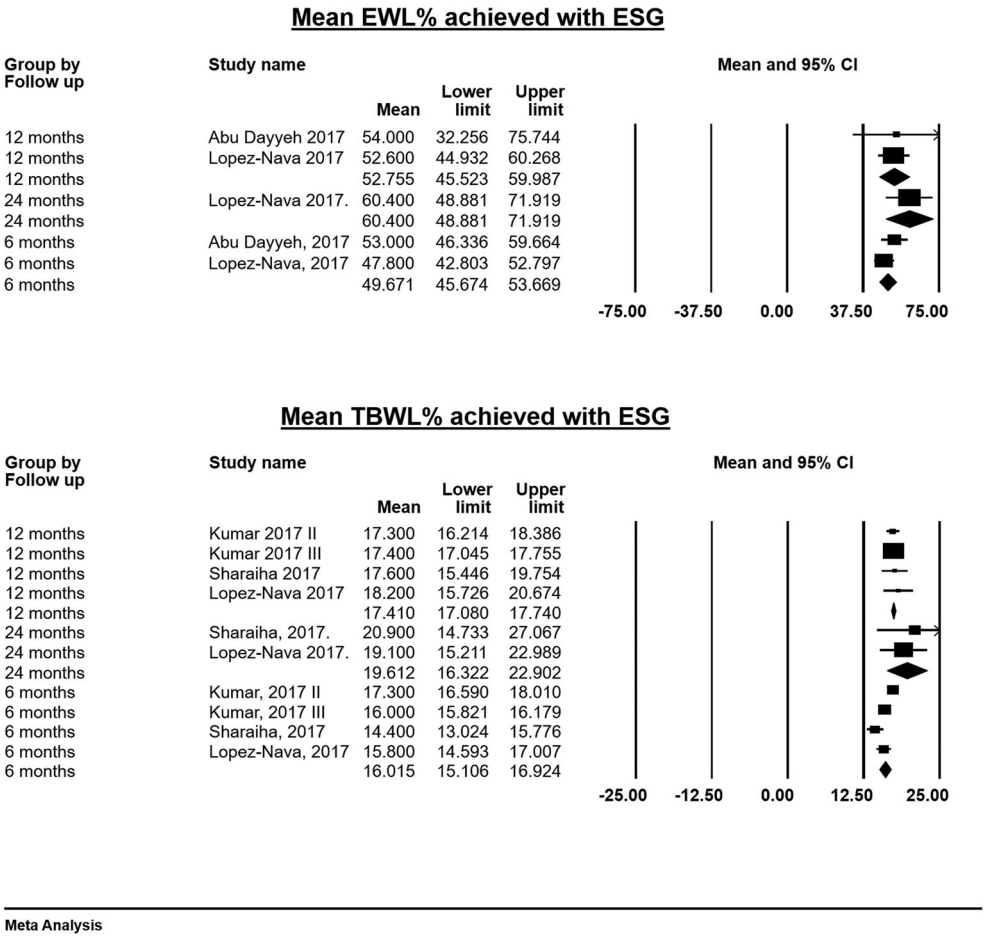

Fig. 2 Forest plot evaluating %EWL and %TBWL achieved with ESG

pharmacotherapy, and 40% reported nausea and vomiting. Among patients undergoing ESG, pulmonary embolism, pneumoperitoneum, and perigastric fluid collection were seen in one patient each.

Discussion

This systematic review and meta-analysis suggests that these three endoscopic interventions for management of obesity have excellent cumulative efficacy. Mean %EWL at 1 year with ESG, POSE, and AA was 52.75, 44.91, and 50.85, respectively. Likewise, mean %TBWL at 1 year with ESG, POSE, and AA was 17.41, 10.98, and 15.37, respectively. These results surpass the mean minimum threshold of %EWL = 25 as recommended by American Society for Gastrointestinal Endoscopy/American Society for Metabolic and Bariatric Surgery Task Force on Endoscopic Bariatric Therapy [40]. Obesity has been labeled as an epidemic, with a majority of patients unable to achieve sufficient weight loss from noninvasive measures like diet and exercise and pharmacotherapy. Many patients either do not qualify or are unwilling to undergo surgical procedure; minimally invasive endoscopic procedures can fill this treatment gap and even provide a bridge to surgery.

Observational studies have reported impressive weight loss results after ESG. In our analysis, ESG achieved a mean %EWL of 52.75 and mean %TBWL of 17.41. This is similar to %EWL achieved by laparoscopic gastric banding but less than that achieved by gastric bypass surgery (i.e., Roux-en-Y gastric bypass), which can produce a %EWL between 60 and 90 [41]. An ESG restricts the greater curvature, somewhat mimicking a gastric sleeve to decrease total gastric capacity. Additionally, Abu Dayyeh et al. [20] reported that after 3 months, ESG significantly delays gastric emptying as well as increases satiation by early termination of meals resulting in a 59% decrease in caloric intake to reach maximum fullness. Further, ESG has demonstrated improvement in patient's metabolic profile. Sharaiha et al. [22] reported significant reduction at 1 year in mean hemoglobin A1c values, mean systolic blood pressure, mean triglycerides, and ALT levels. Although not pooled in this meta-analysis (as these were not uniformly reported by all studies), reduction in comorbidities constitutes a very promising future for this intervention. The multicenter ESG Trial (MERIT) is the first randomized trial which is underway to substantiate these findings of ESG efficacy in obese patients [42].

The POSE procedure demonstrated a mean %EWL of 44.91. However, based on %TBWL, the weight loss achieved at 6 months (13.82) could not be sustained at 12 months

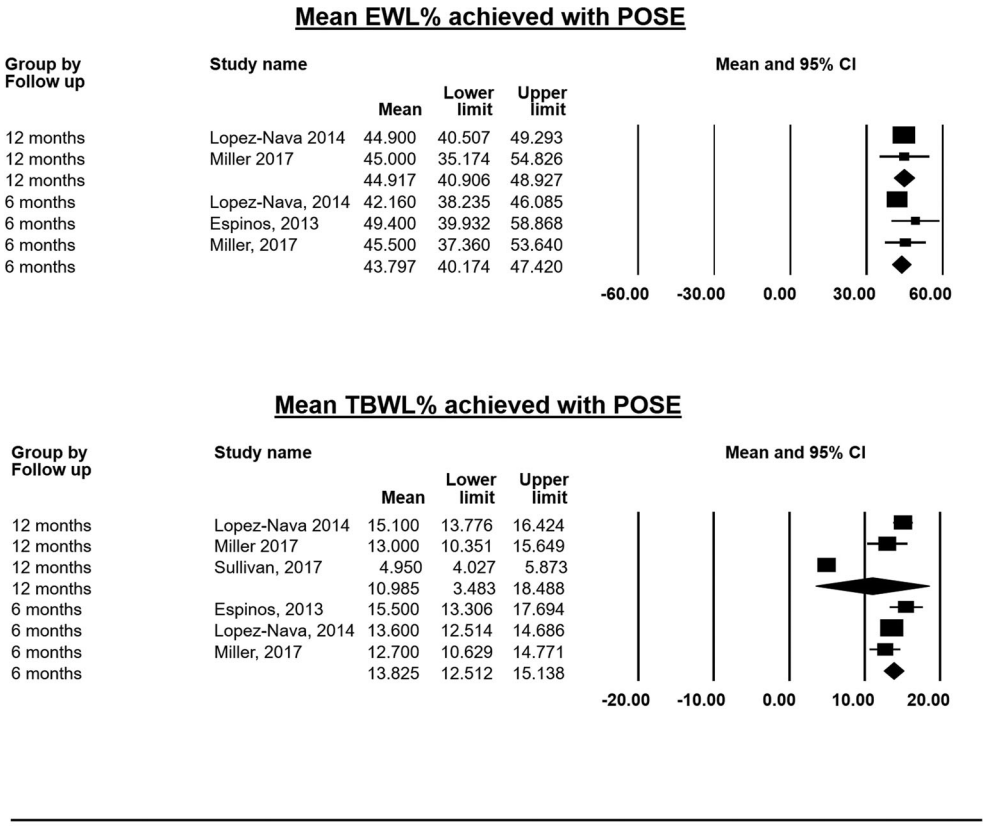

Fig. 3 Forest plot evaluating %EWL and %TBWL achieved with POSE

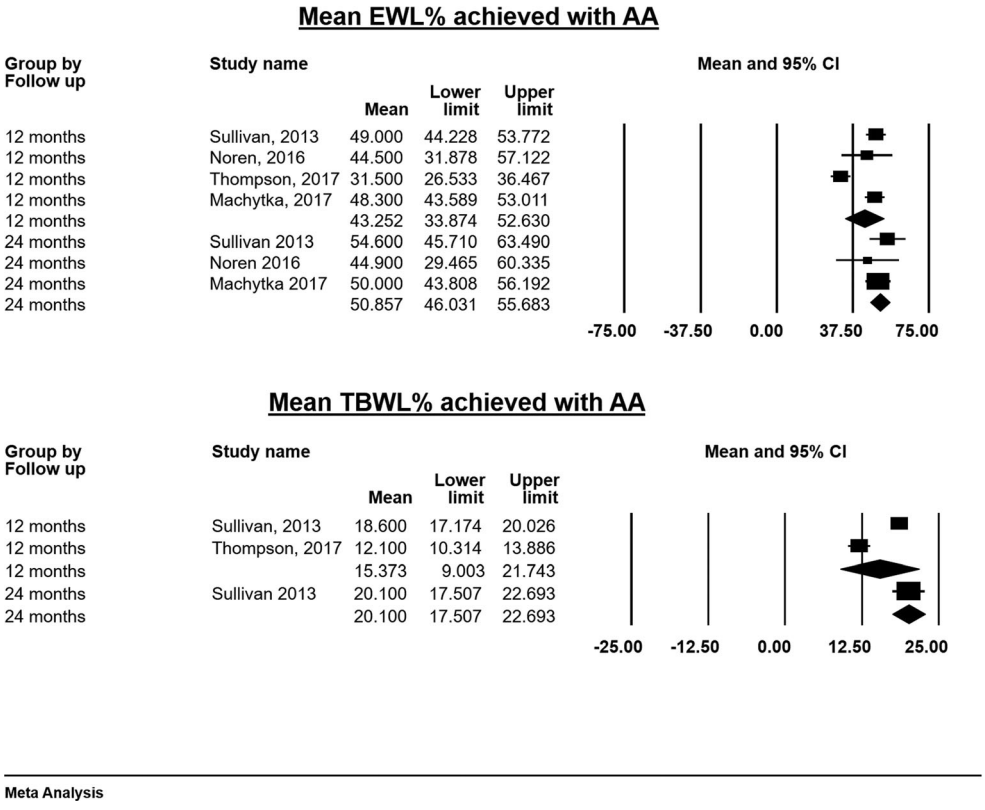

Fig. 4 Forest plot evaluating %EWL and %TBWL achieved with AA

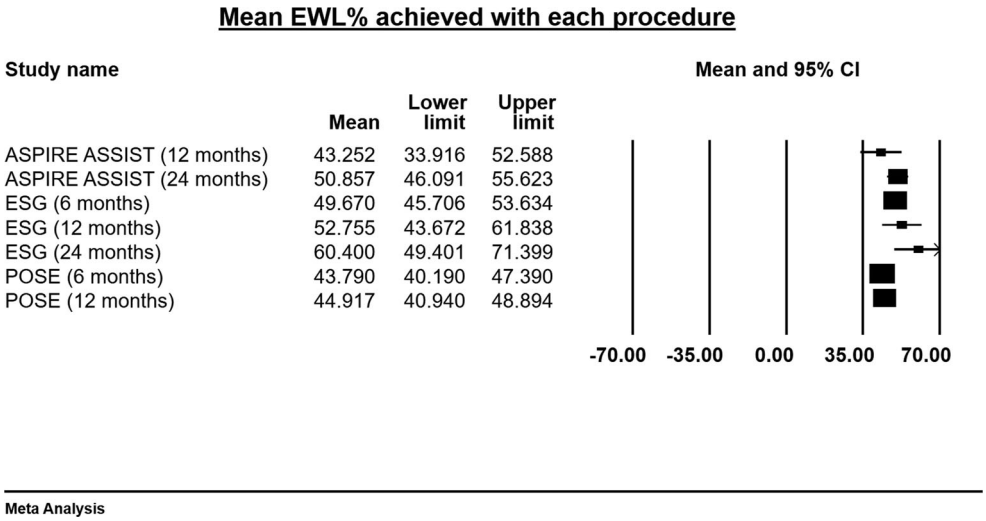

Fig. 5 Forest plot for mean %EWL with each procedure

(10.92). In our analysis, ESG showed significantly greater weight loss than POSE in the first 6 months, both %EWL and %TBWL, and also showed a trend towards greater weight loss at 12 months. This trend may have been because of the relatively low number of ESG patients at 12 months. One observational study [27] evaluated the effects of POSE on obese patients and reported that although gastric emptying was initially delayed during the first 2 months, it normalized by 6 months post-procedure. Patients also reported a similarly statistically significant reduced caloric intake to achieve maximum satiation. However, such results could not be replicated in the subsequent "Multicenter Study of an Incisionless Operating Platform for.

Primary Obesity vs. Diet and Exercise" (MILEPOST) randomized trial [25]. This trial did not find any significant difference in satiety between the treatment and control groups. Finally, the randomized, sham controlled, ESSENTIAL trial found that POSE achieved 3.6 times better %TBWL as compared with placebo [24]. However, a pre-defined primary endpoint that at least 50% of patients in the POSE group should achieve more than 5% TBWL was not achieved.

Among these three procedures, AA is the only procedure which is reversible and is not restrictive in nature. The AA achieved a %EWL of 43.25 and 50.85 at 6 and 12 months, respectively. Therefore, weight loss was consistent and sustained over a year period. We did not find any difference in terms of %EWL and %TBWL when comparing AA with ESG and POSE. The AA induces weight loss by aspiration of chyme during the lag phase in the stomach after eating (i.e., before churned food passes into the duodenum). Thompson et al. [18] reported connector count data which was used as a surrogate for the number of times the device was used during the day. They found that during the first 14 weeks, the device was used on average 2.5 times a day, and during subsequent weeks, it was used at least 2 times a day. The potential concerns with the use of AA were development of eating disorders and electrolyte deficiencies (e.g., potassium) due to removal of stomach acid. However, such problems were not encountered in any of the patients.

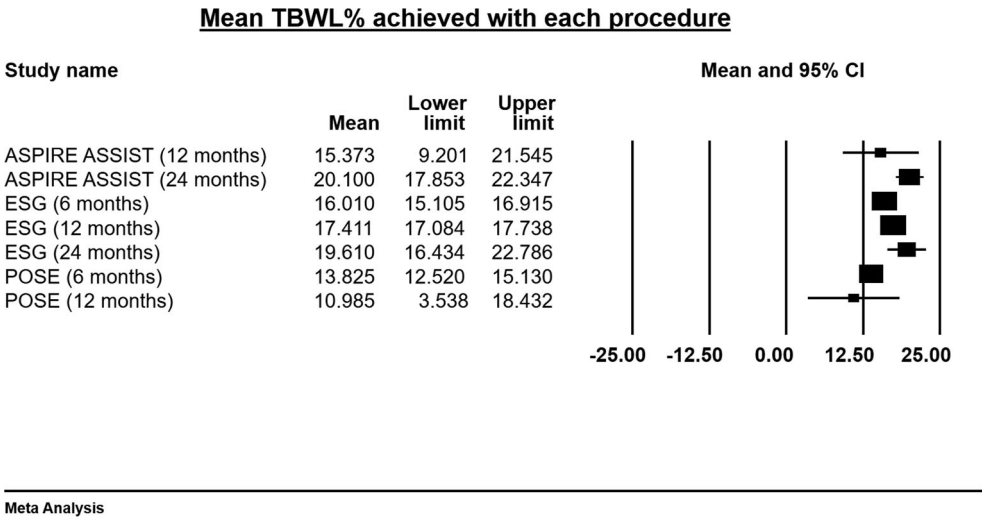

Fig. 6 Forest plot for mean %TBWL with each procedure

This is the first systematic review and meta-analysis to not only evaluate the cumulative efficacy of ESG, AA, and POSE but also compare them in terms of %EWL and %TBWL. We conducted a comprehensive literature search and included a large number of relevant studies. Our analyses may be weakened by inherent limitations of meta-analyses and of the included studies, as majority of the studies were observational in nature. As such, we encountered considerable heterogeneity in few of our estimates, but the %EWL at 12 months did not have any heterogeneity among the three procedures. We also performed an indirect comparison for all three procedures as none of the studies compared them head to head and found that ESG was superior to POSE. Consistent with our results, only ESG and AA have been approved by the US Food and Drug Administration (FDA). We also attempted to rigorously avoid overlap of patients by meticulously examining the study inclusion period and when in doubt, asking corresponding authors and extracting raw data from studies conducted by our group. Unfortunately, we could not analyze adverse events in this meta-analysis as such were not uniformly reported by individual studies. Further, we could not evaluate the effect on comorbidities like diabetes (HbA1C), blood pressure, and lipid profiles due to the paucity of data presented in individual studies as secondary analyses.

In summary, the minimally invasive endoscopic bariatric procedures of ESG, POSE, and AA hold promise of filling the vacuum of treatment options available to obese patients who cannot, or choose not to, undergo bariatric surgery. Based on studies having 6–12 months of follow-up, both AA and ESG have excellent efficacy in achieving significant and sustained weight loss; however, ESG was found to be superior in terms of weight loss when compared with POSE. Future RCTs comparing the overall improvement of medical comorbidities from these procedures would further elucidate the differences between these endobariatric techniques.

Compliance with Ethical Standards

Disclosures and Conflict of Interest Reem Z. Sharaiha is a consultant of BSC and Apollo Endosurgery. All other authors have no financial disclosures or conflicts of interest relevant to this study.

Ethical Approval Systematic review and meta-analysis does not require formal consent.

Informed Consent Informed consent does not apply to this systematic review and meta-analysis.

Appendix. Quality assessment of studies with NIH Quality assessment tool for before–after studies with no control group

Criteria	Noren (2016)	Machytka (2017)	Abu Dayyeh (2017)	Lopez (2017)	Sharaiha (2017)	Kumar (2017)	Lopez (2014)	Espinos (2013)
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes
4. Were all eligible participants that met the prespecified entry criteria enrolled?	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the sample size sufficiently large to provide confidence in the findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	No	No	No	No	No	No	No	No
	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

(continued)

Criteria	Noren (2016)	Machytka (2017)	Abu Dayyeh (2017)	Lopez (2017)	Sharaiha (2017)	Kumar (2017)	Lopez (2014)	Espinos (2013)
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?								
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided *p* values for the pre-to-post changes?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Result	Good	Fair	Good	Good	Good	Good	Good	Good

NIH, National Institutes of Health; *N/A*, not applicable

Quality assessment of randomized controlled trial using Cochrane tool for assessing risk of bias

	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
Sullivan (2017)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Miller (2017)	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Sullivan (2013)	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Thompson (2017)	Low risk	High risk	High risk	Low risk	Low risk	Low risk

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