Evidence Synthesis Program

Endoscopic Bariatric Interventions versus Lifestyle Interventions or Surgery for Weight Loss in Patients with Obesity: A Systematic Review and Meta-analysis

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, interface with stakeholders, and address urgent evidence needs. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee composed of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

The present report was developed in response to a request from the National Gastroenterology and Hepatology Program Office. The scope was further developed with input from Operational Partners (below), the ESP Coordinating Center, the review team, and the technical expert panel (TEP). The ESP consulted several technical and content experts in designing the research questions and review methodology. In seeking broad expertise and perspectives, divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Ultimately, however, research questions, design, methodologic approaches, and/or conclusions of the review may not necessarily represent the views of individual technical and content experts.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Jason A. Dominitz, MD, MHS
National Program Director
National Gastroenterology and Hepatology Program Office
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Technical Expert Panel

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence (see Appendix B for disposition of comments). Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center works to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

ABBREVIATIONS TABLE

Abbreviation	Name
AGB	Adjustable Gastric Band
ASMBS	American Society of Metabolic and Bariatric Surgery
BMI	Body Mass Index
DM	Diabetes Mellitus
EBW	Excess Body Weight
EBWL	Excess Body Weight Loss
ESG	Endoscopic Sleeve Gastroplasty
FDA	US Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation working group
GERD	Gastroesophageal Reflux Disease
HTN	Hypertension
IGB	Intragastric Balloon
LAGB	Laparoscopic Adjustable Gastric Banding
LSG	Laparoscopic Sleeve Gastrectomy
LOS	Length of Stay
NAFLD	Nonalcoholic fatty liver disease
NH	Non-Hispanic
POSE	Primary Obesity Surgery Endolumina
RCTs	Randomized controlled trials
ROBINS-I	Cochrane Risk of Bias In Non-randomized Studies – of Interventions
RYGB	Roux-en-Y Gastric Bypass
TBWL	Total Body Weight Loss
QOL	Quality of Life

EXECUTIVE SUMMARY

INTRODUCTION

According to the World Health Organization (WHO), over 500 million adults are obese. Obesity contributes to a range of harmful comorbidities and its economic burden approximates $150 billion dollars per year. Bariatric surgery remains a gold-standard treatment of morbid obesity and is effective at reducing weight, along with obesity-related conditions. Despite the prevalence of obesity and the proven efficacy of surgery, few who qualify ultimately receive this intervention, and surgery has associated risks. Endoscopic bariatric therapy is an alternative offering a less invasive, possibly cost-effective approach for patients who otherwise would not qualify for, or who are hesitant about or do not have access to, surgical bariatric therapy. An estimated 78% of Veterans are overweight or obese, however Veterans Affairs (VA) medical centers perform only 500 bariatric surgeries annually. If endoscopic bariatric interventions are to be increasingly utilized, it is important for the VA to understand the evidence of how they compare to surgical and pharmacologic therapies. In this review, we assess the impact of endoscopic bariatric therapies on weight loss, morbidity, mortality, and resolution of comorbid conditions compared to surgery and lifestyle modification.

METHODS

Data Sources and Searches

We conducted broad searches using terms relating to "gastric balloon" or "bariatric surgical procedure" or "endoscopic gastroplasty." We searched PubMed (1/1/2014-7/2/2021), Embase (1/1/2014-7/2/2021), and Cochrane (1/1/2014-7/2/2021). We limited the search to 2014 onwards, as these therapies were being approved by FDA in 2015-2017. Studies published prior to 2014 would have been based on data from procedures done in 2012 or earlier, and we did not consider evidence from this period to be relevant to current practice.

Study Selection

Two team members working independently screened the titles and abstracts; full-text review was conducted in duplicate. Disagreements were resolved through group discussion.

Studies were included if they were randomized controlled trials (RCTs) or observational studies comparing a bariatric endoscopic procedure to alternate bariatric therapies (pharmaceutical, endoscopic, or surgical) or lifestyle management. We included all RCTs regardless of outcomes studied or sample size. Observational studies were subjected to additional selection criteria. Studies with a comparative arm (regardless of sample size) were included. All cases series (*eg*, studies with no comparison treatment arm) were excluded. We excluded studies where similar endoscopic mechanisms were compared to each other (*eg*, intragastric balloon [IGB] vs IGB, primary obesity surgery endoluminal (POSE) vs endoscopic sleeve gastroplasty (ESG), *etc*), as well as investigational procedures (*ie*, duodenal-jejunal bypass liner, Endomina, botulinum injection, duodenal mucosal resurfacing).

Data Abstraction and Assessment

Data extraction was completed in duplicate. All discrepancies were resolved with full group discussion. We abstracted data on study design, sample size, perioperative outcomes (weight

loss, reoperations/revisions, 30-day readmissions, adverse events, effects on obesity-related comorbid conditions, mortality), and some outcomes that were procedure specific. We also abstracted data needed for the Cochrane Risk of Bias tool or Cochrane Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I). We reported outcomes for weight loss at 6 months, 12 months, 24 months, 36 months, 48 months, and last follow up if longer than 48 months, or the time closest to these follow-up periods.

Synthesis

Pooled Data

For comparisons with at least 3 studies of the same intervention and similar patient populations and the same outcome, we performed random-effects meta-analyses. We conducted a meta-analysis of 6-month weight loss outcomes (mean percent total body weight loss [%TBWL] and mean percent excess body weight loss [%EBWL]) for RCTs and observational studies of IGB vs lifestyle, and for observational studies of ESG versus laparoscopic sleeve gastrectomy (LSG). Pooled estimates of effect are reported as mean difference (MD) with their 95% confidence intervals (CI). Random-effects meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method. The presence of publication bias was evaluated using Begg rank correlation and Egger regression tests. p-values < .05 were considered statistically significant.

Non-pooled Data

A narrative analysis was performed for the remainder of our outcomes. Continuous outcomes were analyzed using the mean or median along with a measure of dispersion (*ie,* standard deviation or inter-quartile range) to calculate the difference and 95% CI between arms. For binary outcomes, the number of subjects with the outcome was collected and a risk difference was derived with its 95% CI.

We created figures for adverse events with 3 or more studies and report these data in Appendix H. Graphical representations of the outcomes' risk and mean differences and 95% CI were plotted when available or able to be estimated using counts and sample sizes. We noted where significance differed between the study-reported p-value and calculated risk or mean differences and 95% CI. For rare outcome events, risk differences were preferentially used during analysis.

RESULTS

Results of Literature Search

The literature search identified 3,541 potentially relevant citations (including 1 recommended by a subject matter expert), 500 of which were included at the abstract screening level. From these, a total of 385 abstracts were excluded, leaving 115 publications for full-text review. On detailed review of the full text of these 115, 79 publications were excluded, leaving 36 publications meeting eligibility criteria. Among these there were 4 RCTs and 2 observational studies comparing intragastric balloon therapy to lifestyle therapy; 1 RCT and 8 observational studies comparing ESG to various other treatments, including lifestyle therapy, adjustable gastric band, and LSG; and 2 RCTs and 1 observational study comparing the device AspireAssist to lifestyle therapy or to gastric bypass surgery.

Summary of Results for Key Questions

Key Question 1: What is the comparative effectiveness of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

Treatment with IGBs was associated with significantly more weight loss compared to lifestyle therapy at multiple short- and intermediate-term follow-up time points (6 and 12 months). These results were consistent across RCTs and observational studies. Treatment with ESG was associated with significantly more weight loss compared to lifestyle therapy, again at 6- and 12-months follow-up. Treatment with ESG was associated with less weight loss than LSG; this conclusion is based solely on observational studies, although results are consistent. Treatment with the AspireAssist was associated with more weight loss than lifestyle therapy in 1 RCT. There was insufficient evidence on associations between treatments and quality of life or HbA1C measures to reach conclusions. Studies describing long-term durability of weight loss after endoscopic therapies have not yet been published.

Results for the most measured outcome, total body weight loss (reported by 14 of the 36 studies), are presented in Figure ES1.

Key Question 2: What are the comparative harms of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

All studies comparing endoscopic bariatric therapy to lifestyle reported more total complications and 30-day readmission or re-intervention rates, which is expected given these patients underwent invasive interventions. There were no or borderline significant differences in total complications between patients treated with LSG compared to ESG, although all studies reported more complications with LSG.

Key Question 3: Do the comparative effectiveness and/or harms vary by patient or intervention characteristics (ie, age, BMI, type of procedure [intragastric balloon, endoscopic gastric reduction, etc])?

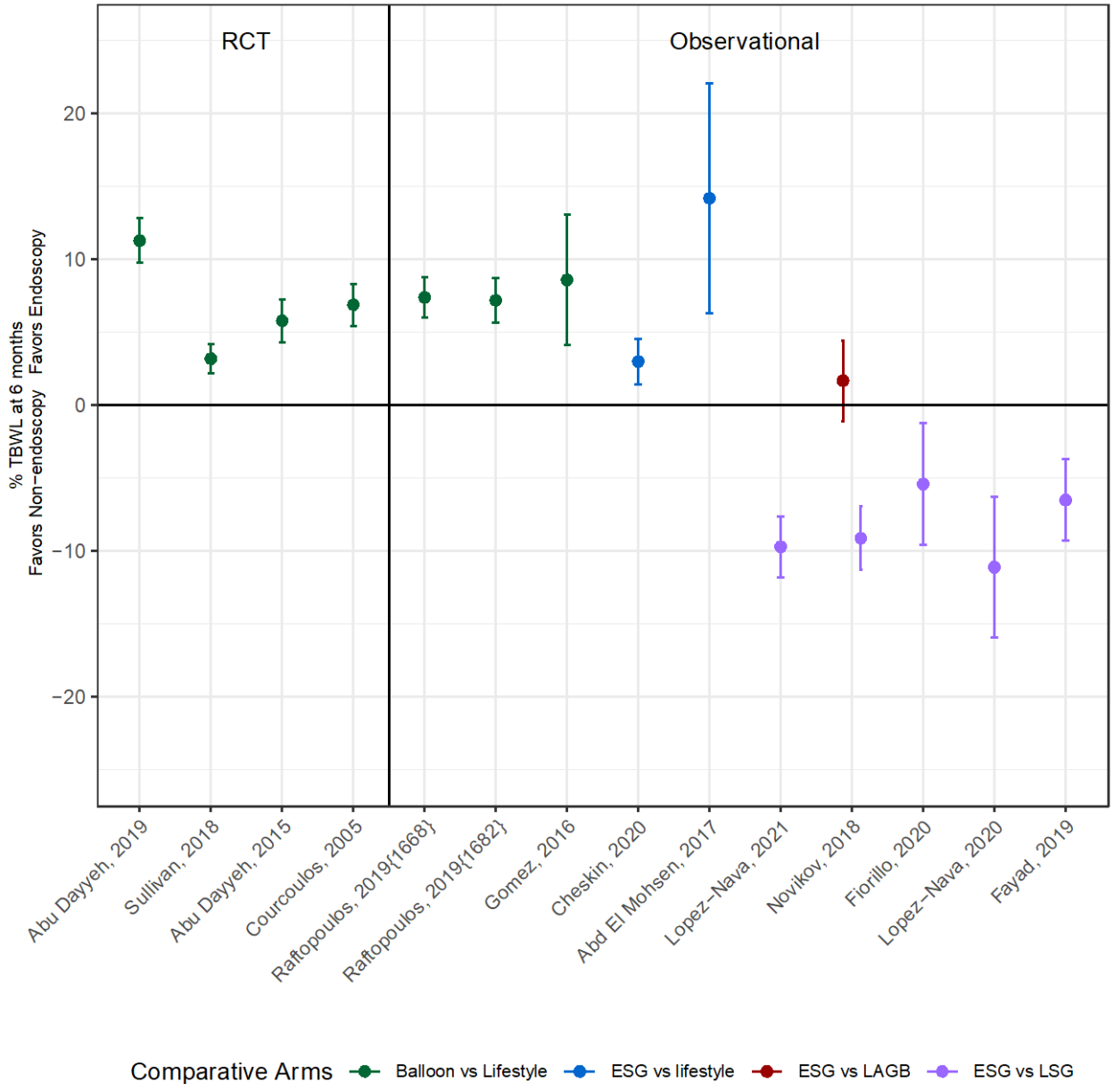
Evidence is insufficient to answer this question.

DISCUSSION

Key Findings and Strength of Evidence

We judged 7 conclusions as being high certainty of evidence, and all were in comparisons between endoscopic interventions and lifestyle therapies. These include: 1) IGB therapy achieves greater %TBWL than lifestyle therapy at 6 and 12 months; 2) IGB therapy achieves more %EBWL than lifestyle therapy at 6 months; 3) ESG achieves more %TBWL than lifestyle therapy at 6 months; and 4) AspireAssist, IGB therapy, and ESG therapy each have greater total complications than lifestyle therapy. Other conclusions were judged to be of moderate or low certainty of evidence due to limitations of the original studies or the presence of only a single study reporting the outcome.

Figure ES1. Total Body Weight Loss at 6 Months for Bariatric Endoscopic Procedures Compared to Lifestyle or Surgery



Abbreviations. %TBWL=mean percent total body weight loss; ESG=endoscopic sleeve gastroplasty; LAGB=laparoscopic adjustable gastric banding; LSG=laparoscopic sleeve gastrectomy.

Applicability

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied in the trials to VA patients as well as the experience of the gastroenterologists performing endoscopic bariatric therapies in the examined studies compared to VA team experience.

Future Research

The history of weight loss interventions is one of innovation and dissemination prior to evaluation. Vertical banded gastroplasty, a prior version of the gastric balloon, and the combination medication of fenfluramine and phentermine ("Fen-Phen") are all examples of interventions developed and widely used before sufficient studies had been done to establish their risk-benefit profile. These interventions have since been removed following research showing the benefit not to be worth the risk. It would behoove the VA to not repeat this history, and to adequately assess new interventions before they are made widely available. Several specific research gaps are noted in the main text of the report.

Conclusions

In conclusion, the endoscopic therapies IGB, ESG, and AspireAssist are associated with greater short- and intermediate-term weight loss in patients with obesity compared to lifestyle management alone. However, various complications are also more likely in patients treated with endoscopic therapies compared with lifestyle management. No long-term studies of weight loss have been published. The degree of weight loss with endoscopic therapies is probably less than their surgical counterparts. As the field continues to grow, future research should include more robust RCTs or well-designed prospective matches studies with adequate power and follow-up to assess long-term weight loss and the effects on obesity-related comorbid conditions.