

Endoscopic Bariatric Therapies: Current Status and Future Perspectives

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Abstract

Obesity is a chronic, multifactorial disease associated with multiple cardiometabolic conditions. The successful management of this condition includes a multidisciplinary approach with interventions focused on lifestyle modification, pharmaceutical therapies, and bariatric surgery.

Endoscopic Bariatric Therapies (EBT) has been proposed as a way to bridge the gap between medical management and bariatric surgery. The Association for Bariatric Endoscopy (ABE) in conjunction with the American Society for Gastrointestinal Endoscopy (ASGE) published the position statement approving and integrating EBT into practice. The aim of this article is to review the most common EBT's, their indications, outcomes and complications.

Keywords: Endoscopic bariatric therapies • Obesity • Bariatric surgery • Diabetes • Endoscopy

Introduction

Obesity is a chronic, multifactorial disease associated with multiple cardio metabolic conditions. Obesity affects more than 650 million adults worldwide and it causes an immense strain on the healthcare system [1]. The successful management of this condition includes a multidisciplinary approach with interventions focused on lifestyle modification, pharmaceutical therapies, and bariatric surgery. Despite having proven evidence of the efficacy of bariatric surgery, only 1% of eligible obese patients receive this treatment [2]. This may be due to; high costs, lack of access to healthcare systems, limited insurance coverage, and poor perception of the treatment by referring providers. In the last decade, the concept of Endoscopic Bariatric Therapies (EBT) has been evolving. It comprises of a spectrum of minimally invasive techniques and/or devices using a flexible endoscope access, mainly to manage weight loss as well as the resolution of associated comorbidities. EBT's have been proposed as a way to bridge the gap between medical management and bariatric surgery; especially for the moderately obese patient with Body Mass Index (BMI) between 30 and 35 kg/m², or the severely obese patient (BMI >40 kg/m²) who do not wish to pursue traditional bariatric surgery procedures. The first reported EBT was the Garren Edwards Bubble which was developed in 1985. It was discontinued 3 years later due to high complications rates and low efficacy; however this in turn prompted the development of the current intragastric balloon designs [3]. In 2015, the American Society for Gastrointestinal Endoscopy (ASGE) and the American Society for Metabolic and Bariatric Surgery (ASMBS) defined acceptable thresholds of safety and efficacy for primary EBT as $\geq 25\%$ Excess Weight Loss (EWL) at 12 months and a complications rate of $\leq 5\%$ [4-13]. Later in 2019, the Association for Bariatric Endoscopy (ABE) in conjunction with ASGE published the position statement on EBT. They concluded

that EBT are approved and integrated into practice. These societies are committed to ensure the safety and quality in the delivery of EBT as well as to develop educational and training programs to support the diversification process of these procedures. EBT offers many advantages that make it a desirable option for patients; mainly as a non-invasive, safe and effective option in treating obesity and its associated comorbidities. Based on the current scientific evidence, we summarize the main clinical outcomes and complications of the most common EBTs utilized in clinical practice [14].

Literature Review

Traditional bariatric surgery including Laparoscopic Sleeve Gastrectomy (LSG), and Laparoscopic Roux-En-Y Gastric Bypass (LRYGB) have been evaluated, and their roles have been well-established in treating morbid obesity and its co-morbidities, which is much more effective than intensive medical management [15]. The SLEEVEPASS trial studied 240 patients randomized to LSG vs. LRYGB and showed 49 %EWL after sleeve gastrectomy at 5 years, and 57% EWL after gastric bypass [16-18]. Overall, it concluded that though LRYGB had a greater percentage weight loss, in the long-term excess weight loss difference was not significant. It demonstrated effective remission of type 2 diabetes at 5 years in 37% after sleeve gastrectomy and in 45% of patients after gastric bypass. In addition, there was no statistically significant difference in quality of life between the two groups [19]. Unfortunately, EBT's long-term data is very limited, with most studies only having a one to two-year follow-up which leaves a large gap of evidence to support the durability of their results. The Orbera is the most evaluated Intra-Gastric Balloon (IGB) up to date. It is the only intra-gastric device that has satisfied the PIVI (Preservation and Incorporation of Valuable endoscopic Innovations) standards set by the ASGE. A meta-analysis of 55 studies demonstrated a pooled estimate of 13.2% TBWL at six months and 11.3% at 12 months [20-22]. Similar studies have reported that IGB's have a role in ameliorating obesity-related conditions. A case series of 143 patients who underwent IGB insertion (Bioenteric Intra-gastric Balloon (BIB)[®] Inamed Health, Santa Barbara, CA, USA) had a decreased incidence of metabolic syndromes from 34.8% to 14.5% at six months, in particular, the incidence of diabetes decreased from 32.6% to 20.9%, as well as a 14.1% \pm 5.7% TBWL [23]. In addition, this effect is predicted to be sustainable; with a high TBWL (11.2% \pm 4.6%), and a low incidence of metabolic syndrome and diabetes (11.6% and 21.3% respectively) at one-year post removal of IGB (923). The

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Aspire Assist system is even more effective than an IGB. It appears to function through long-term behavior modifications as well as aspiration of approximately 30% of gastric contents. The PATHWAY study, a one year multicenter, Randomized Controlled Trial (RCT), demonstrated a $14.2\% \pm 9.8\%$ TBWL at 12 months (104). However, to date, there is no data regarding sustainability after the device was removed. Though it is not powered to detect changes in cardiometabolic risk factors; the glycated hemoglobin (HbA1c) was decreased significantly in the Aspire Assist group than in the control group. The Duodenal Jejunal Bypass Sleeve (DJBS, Endobarrier) which was designed to simulate the effects of a Roux-en-Y gastric bypass, has been very successful in achieving effective weight loss and decreasing HbA1c. A meta-analysis of three studies, evaluating 105 patients, demonstrated a %EWL of 35.3% at 12 months (52), along with significant improvements in HbA1c, represented with an additional-1% decrease in comparison with the control (52). Unfortunately, neither the DJBS nor its longer counterpart, the Gastro-duodenal jejunal bypass sleeve (Endoluminal Bypass) is currently Food and Drug Administration (FDA) approved in the US. The Incisionless Magnetic Anastomosis System (IAS) is another alternative, it was designed to mimic the duodenal switch and ileal transposition procedure, and however data is scarce. The pilot study included only 10 patients but was able to show a 14.6 %TWL (40.2% EWL at one year). In addition, a significant reduction in HbA1c was observed in all diabetic (1.9%) and prediabetic (1.0%) patients, while reducing or eliminating the use of diabetic medications.

The Endoscopic Sleeve Gastrectomy (ESG) and Primary Obesity Surgery Endoluminal (POSE) were developed as the endoscopic counterparts to the classic LSG. Despite the similarities, and benefits of non-invasiveness, neither procedure has shown to be as effective as the LSG. The largest prospective study, which included 1000 patients who underwent ESG, demonstrated a mean %TWL of $15.0\% \pm 7.7\%$ at 12 months and $14.8\% \pm 8.5\%$ at 18 months (127). In contrast, the POSE procedure has had inconsistent data regarding weight loss, with a mean of %TBWL ranging from 4.9% – 15.1% (138, 1417, 158). The ESSENTIAL trial, a US multicenter, blinded randomized clinical trial evaluating 221 patients, had the lowest %TBWL of $4.94\% \pm 7\%$ at one year. (138). This variation could be explained by the fact that it was the only double-blinded study, and it had less frequent lifestyle and dietary sessions than the other two studies. (138, 147, 158) An unmatched cohort study published by Novikov et al. comparing outcomes of ESG versus LSG, showed that LSG achieved greater deduction in BMI and %TBWL than ESG at 12-months follow-up (29.28% vs. 17.57%, $p < 0.001$), though ESG had a lower complication rate (2.20% vs. 9.17%, $p < 0.05$), and a shorter post-procedure hospital stay ($0.34 \text{ d} \pm 0.73 \text{ d}$ vs. $3.09 \text{ d} \pm 1.47 \text{ d}$, $P < 0.01$) (164). ESG patients generally feel better than LSG patients in post-procedural gastrointestinal symptoms. A recent questionnaire-based, case-matched retrospective study evaluated six-month quality of life after the initial procedure between 23 pairs of ESG and LSG patients. It reported significantly better results for the ESG cohort in the gastrointestinal symptoms subdomain than the LSG cohort ($P = 0.001$) (175).

Discussion

Traditional bariatric surgery approaches are proven to be safe with a low complication rate, however when complications occur, they can be devastating and life-altering. The overall morbidity and mortality rate for LSG is low and ranges from ranges from (I would only include risk of serious complications which are significantly lower than the 17% you are quoting), 0%-17.5% and 0%-1.2% respectively (1821). Early postoperative complications include; include leaks (0.1%), strictures (0.1%), and bleeding not requiring re intervention (3%). Long-term complications include; strictures (0.49%) and gastroesophageal reflux disease (6%) (19). LRYGB has had a higher complication rate than LSG, with a 0.09% to 0.12% 30-day and 0.5% 30-day mortality rate

(20). The most serious complication is a gastrointestinal leak, which occurs in up to 2% of all patients which has an incidence rate ranging from 0%-5% (212). On the contrary, EBT's are the ideal choice for patients who desire for a safer option a safer therapeutic alternative. Recent reports suggest that IGB's are safe but can be uncomfortable to patients. Gastrointestinal discomfort and nausea are common symptoms, and in some cases may persist beyond to the first week. A meta-analysis of 68 studies estimated that the early removal rate for the Orbera IGB was approximately 7% (5). Serious complications were rare, with an incidence of migration and gastric perforation of 1.4% and 0.1%, respectively (52). It is important to note, that four out of the eight cases of gastric perforations occurred in patients who had undergone previous gastric surgeries (a relative contraindication). Since the Aspire Assist is basically a modified Percutaneous Endoscopic Gastrostomy (PEG) device, the most common minor complications include stoma granulation tissue (40.5%), followed by stoma infection (14.4%) (10). Severe complications are rare, the PATHWAY study reported a 3.6% rate which included one case of mild peritonitis managed with antibiotics and one case of gastric ulcer (104). The early removal rate in Endobarrier is similar to the Orbera device; approximately 18.37%. The safety profile is acceptable, with serious complications including; migration (4.9%), gastrointestinal bleeding (3.86%), sleeve obstruction (3.4%), liver abscess (0.126%), cholangitis (0.126%), acute cholecystitis (0.126%), and an esophageal perforation (0.126%) secondary to trauma from an uncovered barb at withdrawal (52). It is important to note that other studies have found higher rates of liver abscess; a US multicenter RCT was discontinued early due to a 3.5% incidence of hepatic abscess. The exact cause is uncertain, but all patients recovered with IV antibiotics +/- percutaneous drainage (2216). The 10-patient pilot study assessing outcomes on IAS showed low complication rates, mainly related to post-procedural diarrhea which resolved spontaneously in 60% of cases (116). There was only one serious complication related to a trocar site serosal injury in the concomitant laparoscopy.

When comparing ESG to LSG, there was no mortality or significant morbidity in the 1000 ESG patient RCT; however complications included bleeding (0.7%) and intra-abdominal collection (0.4%). Interestingly, in the same study, 23 patients (10.6%) experienced %TWL less than 5%. Of those, 13 patients underwent revision to LSG or redo-ESG (127). The ESSENTIAL trial showed a slightly higher risk rate for the POSE procedure (though still acceptable for the PIVI 5% cutoff), with a rate of serious adverse events of 4.7%; including extra-gastric bleeding (0.4%) and hepatic abscess (0.4%).

Conclusion

The ASGE and ABE position statement emphasizes the importance of a multidisciplinary approach when treating obesity. This principle includes endoscopic bariatric therapies, (9) which should only be offered in conjunction with lifestyle modification and with nutritional guidance (23). However, due to a wide range of available therapies, most of which are not FDA approved, there is a lack of a standardized therapeutic approach, and a lack of training programs that have limitations to their spread and usage. Another factor that limits the application of upcoming EBTs relates to the financial burden to the patient. Multiple international societies have made significant progress towards including metabolic surgery as an accepted treatment for patients with obesity across the world however no advancement has been made to include EBT as part of this list. We hope that as more data becomes available, and technological progress is made, these interventions will become part of the recognized treatment options for this devastating disease. EBT's require a formal training process for endoscopists and bariatric surgeons to obtain the endoscopic skills needed before performing these procedures. In addition, advanced endoscopy is now becoming a core feature of minimally invasive fellowships, providing surgeons with formal training to take on the role of bariatric endoscopists.

With further technological developments, and increased widespread awareness of EBT; advanced endoscopy is a priority for surgeons and gastroenterologists. Moreover, longer follow-up and larger trials are needed to validate current evidence, in order to enhance the process of standardization of these techniques. In conclusion, EBT's have the potential to be a cornerstone in the management of obesity, which prompts the modern surgeon to acquire advanced endoscopy skills.

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