Intragastric Occupying Space Devices

Alfredo Genco, Ilaria Ernesti, and Loredana Gualtieri

Contents

Abstract

In 2016, 39% of adults were overweight, and about 13% of the world's adult population were obese. Obesity represents a growing global public health despite the availability of diet and lifestyle counseling, pharmacologic therapy, and bariatric surgery. Endoscopic bariatric therapies (EBTs) encompass a wide range of devices requiring flexible endoscopy for placement or removal and procedures performed via flexible endoscopy for the treatment of obesity. Current primary EBTs can be classified as space-occupying or non-space-occupying devices (restrictive, bypass, or aspiration therapy).

Intragastric balloons (IBG) act as space-occupying devices, reducing stomach capacity and inducing satiety by several mechanisms. To date, ORBERA® Intragastric Balloon System, RESHAPE DUO Intragastric Balloon, and OBALON Balloon System are approved by the US Food and Drug Administration (FDA) based on demonstrated safety and efficacy in randomized controlled trials (RCTs). Two other balloons are currently under FDA investigation: the

A. Genco (✉) · L. Gualtieri
Department of Surgical Sciences, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy
e-mail: alfredo.genco@uniroma1.it

I. Ernesti
Department of Experimental Medicine, RU of Food Science and Human Nutrition, Sapienza University of Rome, Rome, Italy
e-mail: ilaria.ernesti@uniroma1.it

P. A. Testoni et al. (eds.), *Gastrointestinal and Pancreatico-Biliary Diseases: Advanced Diagnostic and Therapeutic Endoscopy*,
https://doi.org/10.1007/978-3-030-29964-4_43-2

Spatz Adjustable (Spatz Medical, Great Neck, NY) and the Elipse Balloon (Allurion, Natick, MA).

TransPyloric Shuttle consists of two bulbs connected by a flexible silicone tether which facilitates partial gastric obstruction resulting in delayed gastric emptying and early satiety.

Space-occupying devices represent a good therapeutic option in the treatment of morbid patients, above all if used as obesity prevention tool. Some of those devices need to demonstrate greater reliability in terms of safety.

Keywords

Intragastric balloons · TransPyloric Shuttle · Weight loss

Introduction

Obesity represents a growing global public health threat. A recent report by the World Health Organization (WHO) estimated that more than 1.9 billion adults were overweight, and, among these, over 650 million adults were obese [49]. In 2016, 39% of adults were overweight, and about 13% of the world's adult population were obese. The worldwide prevalence of obesity nearly tripled between 1975 and 2016 [21].

The first options to lose weight for obese patients include lifestyle modification and pharmacological therapy, but these treatments are only modestly effective with an expected percent total body weight loss (%TBWL) <3% [29]. On the other hand, bariatric surgery has been extensively shown to be effective in the long term on weight loss outcomes, but it is not exempt from complications, and only a small number of eligible patients undergo such invasive procedures [9] (Fig. 1).

Endoscopic bariatric therapies (EBTs) encompass a wide range of devices requiring flexible endoscopy for placement or removal and procedures performed via flexible endoscopy for the treatment of obesity [45].

EBTs can achieve greater than 10% TBWL in most patients, with excellent safety rates and lower costs than bariatric surgery. Furthermore, they are anatomy preserving and reversible. Current primary EBTs can be classified as **space-occupying** or **non-space-occupying** devices (restrictive, bypass, or aspiration therapy) [27] (Fig. 2).

In this chapter we present the descriptive characteristics of a number of intragastric space-occupying devices, including most worldwide used intragastric balloons and TransPyloric Shuttle, a non-balloon space-occupying device.

Intragastric Balloons

The intragastric balloon (IGB) owes its pathophysiological concept to the original observation that patients affected by bezoar, an intragastric agglomeration of

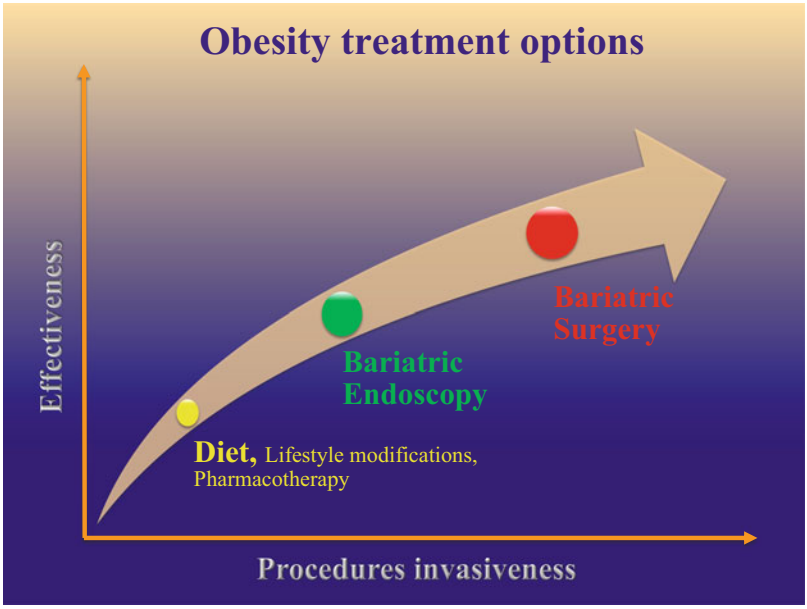

Fig. 1 Obesity therapy options: effectiveness/invasiveness

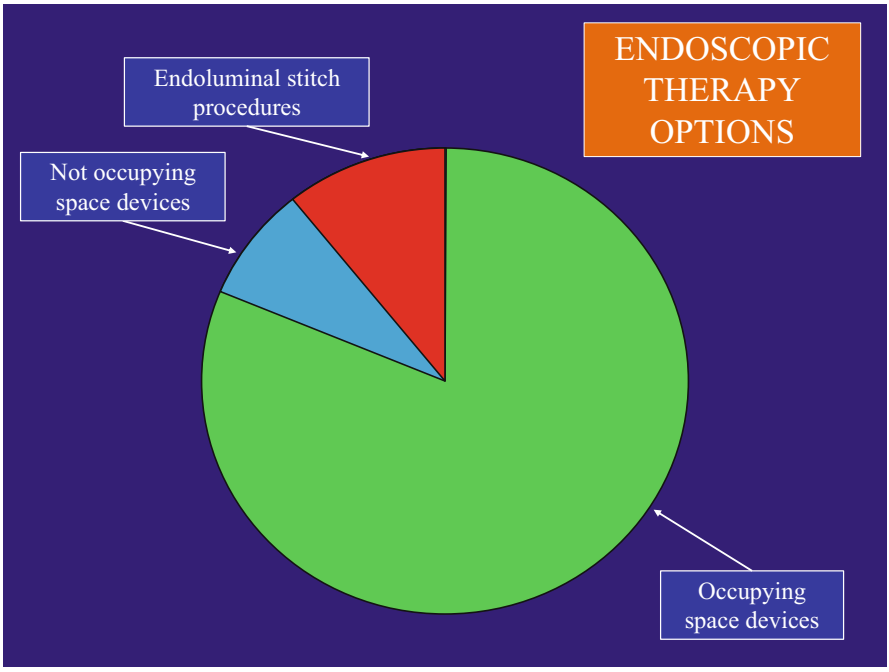

Fig. 2 Endoscopic therapy options

partially digested hairs and vegetable fibers, could experience nausea and vomiting and complain of post-prandial fullness. This has led to the designing of a device which would imitate an intragastric bezoar by partially filling the stomach [39].

The history of IGB began in 1985, when the US Food and Drug Administration (FDA) approved the first intragastric balloon Garren-Edwards Gastric Bubble (GEB, American Edwards Company, Santa Ana, Calif), as a weight loss temporary device.

However, in 1992, GEB was voluntarily pulled from the market due to its adverse events and complications such as gastric ulceration, bowel obstruction, and not achieving the weight loss shown in several sham-controlled trials.

In 1987, an international conference in Florida defined the ideal intragastric balloon: effective at promoting weight loss, filled with liquid (not air), with a spherical shape and soft surface in order to reduce ulcerogenic and obstructive potential, containing a radiopaque marker for easy visualization once in the stomach [43]. According to these indications, over the last decades, several IGBs were subsequently developed, showing > high safety and efficacy profiles.

Recently, a Brazilian consensus gathered experience from more than 40,000 IGB placements. It standardized numerous particularities of the procedure, such as anesthesia, pre-procedural fasting time, indications, and contraindications, among others [38]. Previously, the American Society for Metabolic and Bariatric Surgery published a position statement on intragastric balloon therapy [3]. The main points are referred below:

IGB: Action Mechanisms

IGB works through a not fully comprehended pathway. Several action-based mechanisms are:

- The balloon weight (gas or liquid filled) stimulates the baroreceptors/stretch receptor by activating the brain-gut axis and stimulating the satiety center placed in hypothalamic side.
- The space occupied by IGB induces a reduction in gastric volume (about 700 ccs) and consequently a reduction of food intake.
- Delayed gastric emptying, the most important mechanism, may be due to gastric musculature stretching or could be related to changes in circulating levels of leptin, ghrelin, and cholecystokinin (Martinez-Brocca et al. 2014).

IGB: Indications for Treatment

IGBs are indicated in overweight or obese patient with a history of numerous dietary treatment failures. Current indications suggest IGB treatment in:

- *Patients with BMI > 27 kg/m^2 with obesity-related comorbidities* or *patients with BMI* 30–40 *kg/m^2* according to US indications. Otherwise, Brazilian authors reported that the minimum BMI value for balloon implant is 25 kg/m^2, after failure of clinical treatment.

- *Patients with BMI > 35 kg/m²* as a bridge to surgery (bariatric or other surgery) in order to reduce > surgical and anesthesiologic risks and the incidence of post-operative complications.
- *Patients with BMI > 35 kg/m* who refuse bariatric surgical procedure, in order to achieve a satisfactory weight loss or, at least, weight stability.
- Preventing or delaying the natural history of weight gain in obese patient.

At the moment there are no specific recommendations as regards age limits. The device could, therefore, also be used for children over 12 years, after established puberty, with multidisciplinary evaluation, and parental consent [13, 40]. There is no maximum age limit for implants in elderly persons, each patient being evaluated individually.

IGB: Contraindications

IGBS placement is absolutely contraindicated in case of:

- Voluminous hiatal hernia (> 5 cm)
- Esophageal varices
- Active gastric or duodenal ulcer
- Previous gastric surgery
- Gastric varices
- A coagulation disorder or potential bleeding conditions of the upper gastrointestinal tract
- Patients with major or non-collaborative psychiatric disorders
- Alcoholism or drug addiction
- Certified pregnancy or desire to become pregnant
- Breastfeeding
- Severe liver disease

IGBS placement is relatively contraindicated in case of:

- Eosinophilic esophagitis
- Previous abdominal surgery
- HIV positive (immunocompetent)
- Psychiatric disorders without control or treatment
- Inflammatory bowel disease (e.g., Crohn's disease, etc.)
- Non-steroidal anti-inflammatory drug use

IGB: Pre-procedure Assessment and Multidisciplinary Follow-Up

All the patients should perform the following tests or undergo counseling before IGB placement: a complete blood analysis (including metabolic evaluation), ECG and cardiologic videat, endocrinological and dietologic examinations, psychiatric clinical evaluation in select cases, and lung function test (spirometry and sleep study) in obese patients with a BMI > 50 kg/m^2 or in high-risk obese patients (regardless of BMI). The pre-treatment endoscopy is worldwide considered useful but not

mandatory in order to exclude intraluminal disease that could contraindicate the IGB placement. Prior endoscopy, according to some users, can be avoided performing a good and complete evaluation of patient clinical history and upper GI symptoms assessment [35]. In preparation for balloon implant, fasting for 8 h is recommended.

IGB: Post-placement Management

Pharmacological Treatment of Symptoms

Pharmacological treatment of symptoms should be considered as part of a comprehensive strategy for IGB management. During the first 2–3 days, the device placement induces accommodative symptoms such as nausea, regurgitation or vomiting, and cramp-like epigastric pains. These tend to last only for a short period after balloon insertion and are usually self-limiting.

In order to reduce or prevent these adverse effects, all patients must receive adequate medication based on fluids hydration, proton pump inhibitors, and antispasmodic and antiemetic drugs. In our clinical experience, aprepitant (125 mg orally once daily) is also used as premedication 4 h before procedure and continued for 2 days after IGB placement (80 mg/daily). Daily intake of proton pump inhibitors should be maintained throughout IGB treatment.

Post-placement Diet

The post-placement IGB diet should be divided into three phases: during the first day, patient should take fluids only, and from the second and up to the 6th–7th, a semi-liquid diet could be introduced (yoghurt, mashed potatoes, puréed vegetables). Generally, as of the second week, patient returns to a normal textured diet, though with caution. The dietetic program, elaborated by a physician specialized in clinical nutrition, consists of a daily intake of about 1000–1200 Kcal (including at least 1 g protein/Kg ideal weight), consumed over three main meals and two small snacks. Although indications have not yet been fully standardized, this nutritional schedule could reduce the symptoms related to IGB placement.

IGB: Patient Follow-Up

A closed follow-up is mandatory to prevent and identify possible adverse events.

Before discharge the patient is made aware of the importance of adequate hydration (water at least 1.5 L/day to sip slowly) and of ongoing urine checks, in order to report quickly the premature rupture of the IGB or a possible valve leak. In case of complications (e.g., blue urine, recurrent vomiting), an immediate clinical evaluation and X-ray or endoscopic evaluation may be needed in order to exclude possible complication (migration of the deflated balloon and bowel obstruction, balloon hyperinflation, gastric dilation, etc.). Finally, prompt removal within six, or different, months from the time of insertion is recommended to enhance the safety profile and utilization of available IGB technologies [3].

The information in this chapter is mainly referred to FDA-approved intragastric balloons, available on the US market: ORBERA® Intragastric Balloon System, RESHAPE DUO Intragastric Balloon, and OBALON Balloon System. Two other

Table 1 Space-occupying devices: total body weight loss percentage (TBWL%) and aide adverse effects (no longer on the market since 2019)

SPACE-OCCUPYING DEVICES	DEVICE	CHARACTERISTICS	% TBWL	SIDE EFFECTS			
				% Nausea	% Vomiting	% Abdominal pain	% Gastric ulcer
BALLOON	**Orbera Intragastric Balloon** (Apollo Endosurgery, Austin, TX)	Soft and smooth silicone sphere, **endoscopically placed,** filled with **400–700 mL of saline**, with optional methylene blue to detect spontaneous deflation. **6 months treatment; endoscopically removed.** FDA APPROVED	10.2[a]	75.6[a]	86.8[a]	57.5[a]	0[a]
	ReShape Integrated Dual Balloon System (ReShape Medical, San Clemente, CA)	Two silicone spheres interconnected by a flexible wire; **endoscopically placed**. The **2 balloons** are independently filled with up to **450 mL of saline** each with methylene blue to detect early deflation. **6 months treatment; endoscopically removed.** FDA APPROVED	6.8[a]	61.0[a]	86.7[a]	54.5[a]	10[a]
	Obalon Balloon System (Obalon Therapeutics, Carlsbad, CA)	A **swallowable Intragastric Balloon System**, consisting of three nylon polyethylene blend balloons, each filled with **250 mL of a nitrogen mix gas**; **endoscopically removed**. **6 months treatment** from the first balloon placement. FDA APPROVED	6.6[a]	56.0[a]	17.3[a]	72.6[a]	0.9[a]
	Spatz Balloon 3 (Spatz FGIA, Great Neck, NY)	Spherical silicone balloon with an extractable and flexible tube for endoscopic volume adjustment while the balloon is in place. **Adjustable fluid filled IGB with saline, endoscopically placed and removed. 12 months treatment.** NOT FDA APPROVED	16.3	92[b]	21[b]	24[b]	3.03[b]
	Elipse Balloon (Allurion Technologies, Wellesley, MA)	Spherical balloon made of a film, filled with **550 mL of saline**; **swallowed in a capsule** for placement with gastric location verified by fluoroscopy; **complete deflation** after planned valve release at **4 months** and subsequent passage through the GI tract. NOT FDA APPROVED	14.2[c]	---	---	---	---
NON BALLOON	**The Transpyloric Shuttle** (TPS; BARONova Inc, San Carlos, CA)	Two bulbs connected by a flexible silicone tether which facilitates partial gastric obstruction to reduce gastric emptying; **endoscopically placed and removed. 12 months treatment.** FDA APPROVED	9.51[d]	63.1[d]	58.1[d]	70.0[d]	10.3[d]

[a]Sullivan et al. [45]
[b]Usuy and Brooks [48]
[c]Ienca et al. [23]
[d]ENDObesity® II Study: TransPyloric Shuttle® System for Weight Loss (https://clinicaltrials.gov/ct2/show/NCT02518685)

balloons are currently under FDA investigation for approval: the Spatz Adjustable (Spatz Medical, Great Neck, NY) and the Elipse Balloon (Allurion, Natick, MA). The main characteristic of these devices is shown in the Table 1.

ORBERA® Intragastric Balloon System

The ORBERA® balloon (Apollo Endosurgery, Austin, TX, USA) had begun development in the 1990s and was commercially launched outside the USA in 2004. More than 277,000 ORBERA® balloons have been distributed globally (www.apolloendo.com). It was FDA approved on August 6, 2015, for use in the USA. It is the most commonly used IGB, with over 230 peer-reviewed publications around the globe on over 8000 patients [7, 44]. The ORBERA® balloon (formerly BioEnterics) is an endoscopically implanted spherical silicone elastomer device (Fig. 3).

The procedure can be performed in conscious (diazepam or midazolam) or in unconscious sedation (propofol), or (rarely) with orotracheal intubation and lasts on average 15 min. The balloon is placed in the gastric fundus and then filled with 500–750 mL saline and 10 mL methylene blue (which alters urine color in case of balloon perforation or valve leaks). This dye is contraindicated in patients with glucose-6-

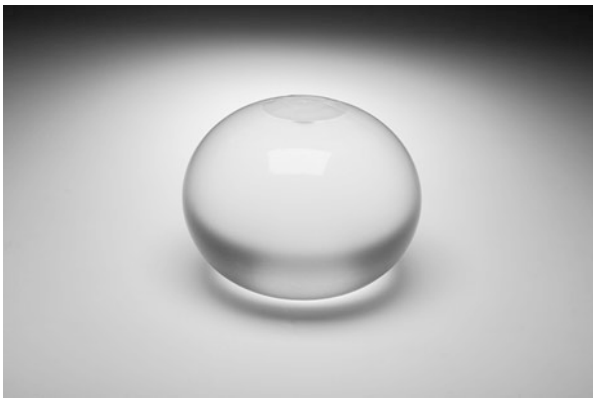

Fig. 3 ORBERA® Intragastric Balloon

phosphate-dehydrogenase (G-6-PDH) deficit, due to the risk to hemolysis crisis in case of its release. The balloon is resistant to gastric acid and is indicated for insertion for up to 6 months [27].

Due to the delayed gastric emptying achieved with the balloon, the removal procedure should be preceded by at least 2 days of liquid diet, in order to avoid "ab ingestis," chiefly when the procedure is performed in unconscious sedation. Through an esophagogastroduodenoscopy, the ORBERA® is identified and is removed with a dedicated "grasper" after the completed deflation. Stomach observation is necessary to exclude possible mucosal lesions. Rarely, gastroduodenal ulcers, Mallory-Weiss tears, and esophagitis have also been reported after balloon placement despite aggressive proton pump inhibitor therapy [3]. Apollo Endosurgery has released a new ORBERA Balloon, ORBERA 365®, so called as it can stay inside the stomach for 1 year. No clinical data have been published up to know.

A large meta-analysis of 3698 patients showed a mean reduction of 14.7 kg, 12.2% of initial weight, 5.7 kg/m^2 point of BMI, and 32.1% of excess weight loss (EWL) [24].

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee performed a direct meta-analysis including 1683 patients to assess the ORBERA® performance in weight loss. The results indicated that %TBWL was 13.16% and 11.27% at 6 and 12 months after IGB implantation, respectively, and % EWL was 25% at 12 months [5].

More recently, a large (5549 patients) systematic review of studies investigating the use of the ORBERA® for obesity treatment reported that %TBWL at 6 months was 13.2% [28].

To date, the largest European experience on ORBERA® was published in 2005 by the Italian LAP-BAND® and BIB® group (GILB). In this clinical trial, accounting for 2515 patients with a mean initial BMI of 44.4 kg/m^2 and a mean excess weight of 59.5 kg, %EWL was 33.9% after the 6-month IGB treatment [18].

The long-term weight loss trend after removal of the ORBERA balloon was assessed in 500 patients, with a mean BMI 43.7 kg/m^2. At the time of balloon

removal, 83% patients had reached a successful> result (defined as ≥20% EWL), with a mean BMI loss 8.3 kg/m^2. In 41% patients available 5 years after balloon treatment, the successful group showed an average loss of 7.3 ± 5.4 kg and an average BMI loss of 2.5 kg/m^2 [26]. Another long-term multicenter European study showed an EWL of 29.1% ± 60.3% at 3 years after balloon placement (Genco et al. 2013).

Moreover ORBERA® is a temporary and repeatable treatment, with a time interval after the first placement. The effectiveness of a second ORBERA® balloon insertion has been investigated in clinical trials. Although the second ORBERA® therapy resulted in a continuous weight loss, its magnitude was smaller than that of the initial therapy [30].

The metabolic effects of ORBERA® treatment have been examined in several studies.

Data from the Italian LAP-BAND® and BIB® group (GILB) showed that diabetic patients undergoing treatment achieved a resolution or improvement in 32.8% and 54.8%, respectively. At the 3-year mark, Genco et al. reported complete resolution of the following outcomes: diabetes (in 33% patients), hypertension (44%), hypercholesterolemia (34%), dyslipidemia (45%), osteoarthropathy (47%), and respiratory disorders (100%) (Genco et al. 2013). The incidence of metabolic syndrome declined from 34.8% (at baseline) to 14.5%, 13%, and 11.6% at removal, at the 6-mo follow-up, and at the 1-year follow-up, respectively. The incidence of type 2 diabetes mellitus dropped from 32.6% to 20.9%, 22.5%, and 21.3%, respectively. Likewise, the occurrence of hyperuricemia, hypertriglyceridemia, and hypercholesterolemia significantly decreased with respect to baseline [11]. A prospective study by Forlano et al. analyzed the metabolic effect of the device on improving various components of the metabolic syndrome in 130 obese patients. The results showed a significant improvement of blood glucose, insulin, triglycerides, and ALT and of the value of the HOMA index [15].

Interestingly, a longitudinal and interventional study on 40 obese/overweight patients found a statistically significant improvement regarding the metabolic syndrome parameters and pulmonary function variables, leading to a reduction of the restrictive ventilatory defect [32].

A multicenter study presented data following treatment with the ORBERA intragastric balloon in obese/overweight populations. The percentage of patients with comorbidities at baseline and at the 3-year follow-up was 29% and 16% for hypertension, 15% and 10% for diabetes mellitus, 20% and 18% for dyslipidemia, 32% and 21% for hypercholesterolemia, and 25% and 13% for osteoarthropathy, respectively (Genco et al. 2013).

All IGB were associated with a high incidence of accommodative symptoms, such as nausea, vomiting, or abdominal pain. These symptoms are self-limiting without sequelae within 3–7 days of device placement.

A recent systematic review showed the ORBERA balloon to carry the highest percentage of nausea and vomiting when compared to Elipse (Allurion Technologies, Wellesley, MA), Obalon balloons (Obalon Therapeutics, Carlsbad, CA), and

ReShape (ReShape Medical, San Clemente, CA). However, such data derive from non-comparative studies which significantly limit the strength of these results [47].

Other serious adverse events (SAEs) in ORBERA included one gastric outlet obstruction with diffuse gastritis, one gastric perforation with sepsis, one aspiration pneumonia, two esophageal tears, one laryngospasm, and one infected balloon [45].

The incidence of GERD, gastric ulcers, and balloon migration was 18.3%, 2%, and 1.4%, respectively, while the prevalence of small bowel obstruction, perforation, and death was 0.3%, 0.1%, and 0.08%, respectively (Abu [1]).

Up-to-date information regarding SAEs reported to the FDA can be seen on the Manufacturer and user Facility Device Experience (MAUDE) database, which can be accessed at: http://www.accessdata.fda.gov/scripts/drh/cfdocs/cfMAUDE/Search.cfm.

RESHAPE DUO Integrated Dual Balloon System

RESHAPE DUO (ReShape Medical, San Clemente, CA, USA) consists of a double balloon>, filled with a total > 900 ml saline solution (mixed with methylene blue), attached one to the other by a flexible tube to prevent migration if one balloon deflates. It is endoscopically placed in the stomach and retrieved following 6 months treatment.

In July 2015, FDA approved this device as weight loss procedure for people with mild-to-moderate obesity. This balloon was removed from the market in 2019 following the acquisition of ReShape by Apollo Endosurgery.

The REDUCE trial was the first large multicenter prospective, randomized, sham-controlled study examining the efficacy and safety of the ReShape dual balloon. This study, including 326 obese with a BMI between 30 and 40 kg/m^2, randomized patients to endoscopic ReShape Duo balloon placement plus diet and exercise (DUO patients) vs. sham endoscopy plus diet and exercise alone (DIET patients). After 24 weeks, the findings showed that the DUO patients had a 25.1 ± 1.6%EWL vs. 11.3 ± 1.9%EWL of the DIET patients ($p = 0.004$). Comorbid conditions, such as glucose and lipid profile, blood pressure, and waist and hip circumference, showed a significant improvement through the completion of the 48-week follow-up. During the study there were no deaths, no intestinal obstruction, and no gastric perforation. In 6% of DUO patients, device deflation was observed, without device migration. Gastric ulcerations were found in 35% of the treated patients. This rate significantly decreased after a modification to the device's distal tip, and then the incidence of gastric ulceration dropped to 10% [41]. The most recent data was published by Agnihotri et al. in [2]. The authors evaluated 202 adult patients (mean BMI f 36.8 + 8.4 kg/m^2) who underwent ReShape Duo IGB insertion, and over a 12 months (mo) period, they determined %TBWL and %EWL.

Mean %TBWL at 1, 3, 6, 9, and 12 months was 4.8%, 8.8%, 11.4%, 13.3%, and 14.7%, respectively; 60.4% of patients achieved more than 10% TBWL and 55.4% more than 25% EWL. Common SAEs included nausea, vomiting, and abdominal pain, occurring in 149 (73.8%), 99 (49%), and 51 (25.2%) patients. One patient reported small bowel obstruction, requiring surgical removal. Secondary endpoints such as systolic and diastolic blood pressure, hemoglobin a1c, fasting blood sugar,

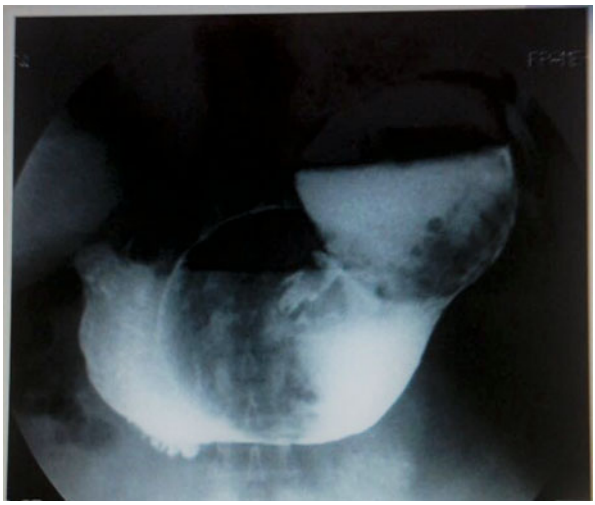

Fig. 4 RESHAPE DUO Integrated Dual Balloon System

and total cholesterol were found, statistically, to be significantly lower at balloon removal than at baseline [2] (Fig. 4).

OBALON Balloon System

The swallowable gas-filled intragastric balloon system (Obalon; Obalon Therapeutics, Carlsbad, CA; OBS) was approved by the FDA in September 2016 and in January 2017 was made commercially available in the USA.

The OBS, a gas-filled balloon indicated for a BMI of 30–40 kg/m^2, does not require endoscopy to be inserted. However, an endoscopic removal under monitored anesthesia care or conscious sedation is performed at the end of treatment. The OBS consists of three nylon polyethylene blend balloons with a radiopaque metal self-sealing valve attached to a small diameter (3 French) catheter and filled with 250 ml of a nitrogen mix gas. Each balloon is folded within a hard gelatin US Pharmacopeia grade capsule. A catheter is attached to the capsule at the metal self-sealing valve for device administration and inflation. Once swallowed, the balloon location is confirmed in the stomach radiographically and then inflated with a nitrogen mix gas using an Inflation Dispenser. The Inflation Dispenser is battery-powered and contains a pressure gauge and regulator to control and monitor inflation pressure. Three balloons are typically placed within the first 3 months. All balloons are removed endoscopically 6 months after placement of the first balloon [37].

To support FDA approval, the OBS was evaluated in a 15-center, double-blind, randomized, sham-controlled pivotal trial of the OBS plus lifestyle therapy compared with lifestyle therapy plus sham device in 387 participants in the USA (Six-Month Adjunctive Weight Reduction Therapy [SMART] Study). The results showed a %TBWL of 7.1 $\pm$ 5.0%, with a BMI change of 2.5 $\pm$ 1.8 kg/m^2; at least 66.7% patients lost $\geq$5% TBWL. The author also reported significant improvement

in fasting glucose, low-density lipoprotein cholesterol, systolic blood pressure, and triglycerides at the 24th week. AEs occurred in 91.1% patients, but >99% of those events were classified as mild or moderate. One bleeding ulcer and one balloon deflation occurred [46].

A smaller, clinical study, including 17 overweight or obese patients (BMI 27–35 kg/m^2), showed that 98% of balloons were swallowed successfully, with an average of 36.2% EWL at 12 weeks. Abdominal pain (in 76%) and nausea (in 41%) were the most frequent SAEs. At 12 weeks, all balloons were removed endoscopically, under conscious sedation [36].

The most recent study, published in 2019, reported a retrospective analysis of a prospective registry of 1343 patients with body mass index (BMI) ≥25 kg/m^2. The weight loss for patients with intended use of OBS (BMI 30–40 kg/m^2 with 3 balloons for ≥20 weeks of therapy) was 10.0 ± 6.1%TBWL and 38.3 ± 25.3%EWL; weight loss in other BMI categories was 8.2 ± 5.6 kg or 10.3 ± 7.0%TBWL for BMI 25 to 29.9 kg/m^2 and 11.6 ± 7.8 kg or %TBWL 9.3 ± 6.0 for BMI >40 kg/m^2. The weight loss for all patients treated with three balloons (n = 1177 patients; 87.6%) was 9.6 ± 6.5 kg, 9.6 ± 6.2%TBWL, and 42.4 ± 61.7%EWL. There were 308 non-serious AEs reported in 14.2% of patients. The most frequent AEs reported were abdominal pain (5.29%), nausea (4.69%), vomiting (2.31%), and abdominal distension (1.04%). There were seven balloon deflations, none caused obstruction [37] (Fig. 5).

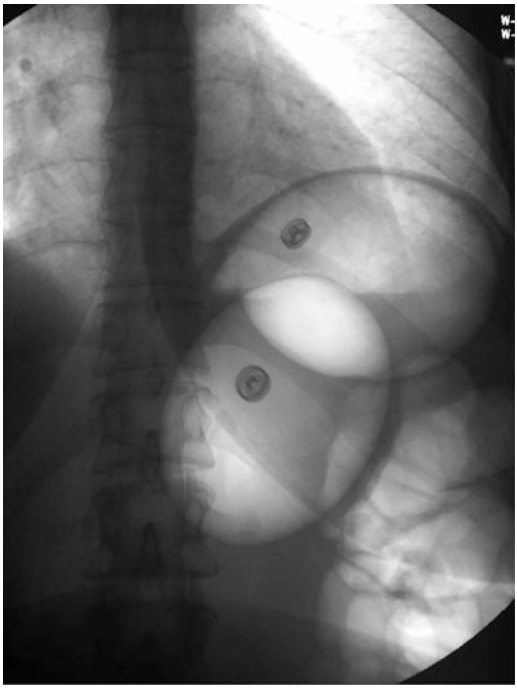

Fig. 5 OBALON Balloon System

Other IGBs are available worldwide but not currently approved in the USA.

The **Spatz Adjustable Gastric Balloon** (Spatz Medical, Great Neck, NY, USA) is an endoscopically placed IGB with a unique design allowing for volume adjustment. This device consists of a spherical silicone balloon around a curved catheter extending outside the balloon, through which more or less saline solution (adjustable) can be added or removed to induce a lower rate of accommodative symptoms or an increased sense of fullness [44]. Due to curved catheter and not smooth surface, the safety of Spatz balloon is still under evaluation (Fady et al. 2016). The Spatz Adjustable Gastric Balloon is currently under FDA study, and preliminary data suggest satisfactory results. Prior generations of the Spatz Adjustable Balloons resulted in up to 20% TBWL at 12 months but showed device-related complications, such as ulcer formation and adjustment catheter impaction requiring surgical removal [8].

The most recent study analyzed the results of 165 (BMI $>$ 26.5 kg/m^2) Spatz3 patients retrospectively reviewed in two Brazilian centers. After 12 months, the authors reported a mean 16.3% TBWL, a mean 67.4% EWL, and a responder rate (>25%EWL; 10%TBWL) of 88.5%. As regards the length of implantation, 21 patients (12.7%) had their balloons extracted prior to 4 months; 17 of the 21 refused down adjustments; 116 out of 165 patients (70.3%) completed at least 8 months balloon treatment. Down adjustments were performed in 20 patients, and up adjustments were performed in 64 patients.

The incidence of nausea and vomiting was lower in patients receiving aprepitant and ondansetron medication. One gastric perforation (0.6%) occurred in a patient who experienced abdominal pain for 2 weeks. Five patients with small ulcers did not require balloon extraction [48].

A multicenter trial is currently underway in the USA to determine safety and efficacy [45] (Fig. 6).

Elipse™ Intragastric Balloon (Allurion Technologies, Wellesley, MA, USA) is a polyurethane balloon not requiring endoscopic placement and removal. To date,

Fig. 6 Spatz Adjustable Gastric Balloon

the pre-treatment endoscopy is still under evaluation by physician user. This device is enclosed in a dissolvable capsule, easily swallowable by the patient and attached to a thin catheter (about 75 cm long) used for filling. The Elipse contains a radiopaque ring that can be used to confirm the correct positioning of the balloon in the stomach through an abdominal X-ray, before filling it with 550 ml of dedicated fluid. After 16 weeks, the valve, consisting of a patented degradable component, is designed to dissolve, then the liquid is dispersed, and the balloon evacuated spontaneously through the gastrointestinal tract.

In a pilot, non-randomized study, eight patients (mean BMI = 31.0 kg/m^2) successfully swallowed the device. There were no serious adverse events during the 6 weeks treatment, and the balloon was safely excreted through the gastrointestinal tract (Machytka et al. 2015).

In a multicenter, prospective study, 135 patients were enrolled, with a BMI ranging from 25 to 45 kg/m^2. After 16 weeks, the mean %TBWL was 15.1%. Regarding accommodative symptoms, the authors reported 2.2% > early removal due to intolerance, 2.2% early deflation, 21.5% of patients experienced abdominal pain in the week of balloon deflation, and 1 patient experienced small bowel obstruction after which the balloon was removed via laparoscopic enterotomy [4].

In a prospective Italian clinical trial, Elipse treatment resulted to be a safe and effective to induce an 11.6% TBWL, a mean EWL 26%, and a mean BMI reduction of 4.2 kg/m^2 points from baseline. There was also a significant reduction in major comorbidities related to metabolic syndromes (MS): blood pressure, waist circumference, triglycerides, blood glucose, and HOMA-IR index. No deflation or other serious adverse event was shown [19]. Similar results were reported on Italian obese patients who, at the start of the Elipse treatment, met the criteria for metabolic syndrome (91%). At the conclusion of the study, only 27.5% of patients met the criteria for MS, without SAEs. This study showed statistically significant, and clinically relevant, improvements in the comorbidities related to metabolic syndrome [14].

One study evaluated weight result at 12 months after Elipse placement [42], reporting that the mean %EWL and %TBWL were 50.2% and 14.6%, respectively, at balloon excretion and 17.6% and 5.9% at 12 months. There were also statistically significant improvements in patients' body fat% and rate of metabolic syndrome parameters at balloon excretion. All balloons were excreted safely, and there were no serious adverse events. These results were recently confirmed by M.H. Jamal et al. who have concluded that with patients following the complete Allurion program 72% of the weight loss was sustained over 1 year after the passage of the Elipse balloon. This study reported one bowel obstruction (0.9%) [25].

In a multicenter, prospective, non-randomized, open label registry study, 1770 overweight patients (BMI > 27 Kg/m^2) achieved a statistically improvement in term of weight loss, %TBWL (14.2%) and EWL (67.0%), from baseline value. There were no bowel obstructions from 2017 onward with the introduction of the current generation device [23] (Fig. 7).

Fig. 7 Elipse™ Intragastric Balloon

TransPyloric Shuttle

The **TransPyloric Shuttle** (TSP, BAROnova, Inc., Goleta, CA, USA) consists of a large spherical silicone bulb connected to a smaller cylindrical silicone bulb by a flexible catheter. The device is placed through an overtube with the weight pre-filled into the silicone skin, and the silicone cord coiled into the ball end of the silicone skin after the skin has been advanced into the stomach. This unique design allows the device to assume transpyloric positioning creating an intermittent seal resulting in delayed gastric emptying and early satiety. This device is indicated for weight reduction in obese adult patients with a BMI of 35.0–40.0 kg/m^2 or a BMI of 30.0–34.9 kg/m^2 with one or more obesity-related comorbid conditions [20, 45].

A small study with 20 obese patients (BMI, 36.0 ± 5.5 kg/m^2), using a previous generation of TPS, demonstrated 8.9% TBWL at 3 months and 14.5% TBWL at 6 months. In total, 10 of the 20 subjects developed gastric ulcers as SAEs [22].

The ENDObesity 1 study was conducted in Australia with 20 patients and a mean BMI of 36 kg/m^2. All patients had the transpyloric shuttle inserted and follow-up at 3 and 6 months. Three-month patients had mean %EWL of 25.1% and mean % TBWL of 8.9%. Six-month patients had mean %EWL of 41.0% and mean %WL of 14.5%. All patients also tolerated the device, while 15 patients had evidence of mucosal erosion. Early device removal occurred in two patients due to symptomatic gastric ulcerations, resolved after device removal [33]. A follow-up double-blind, sham-controlled trial (ENDObesity II) has recently been completed. The authors enrolled a total 270 patients, with BMI 30–40 kg/m^2, and randomized in 2:1 ratio to TPS placement or Control arm. At 12 months the mean %TBL was 9.5% in the TPS Group compared to 2.8% for the control group; the %EWL was 30.9% vs. 9.8% in the TPS and control group, respectively. TPS treatment also produced greater improvements in various cardio-metabolic risk markers. The most commonly reported adverse events were gastrointestinal symptoms, and 91% of all adverse events were mild-to-moderate in severity; 10.3% patients had TPS removed before

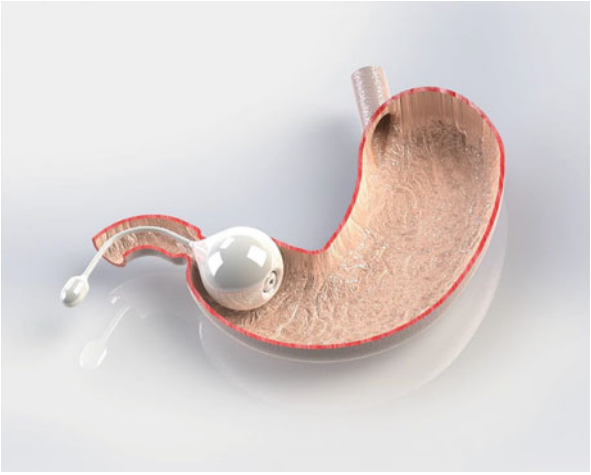

Fig. 8 TransPyloric Shuttle

12 months due to an adverse event. Device- and/or procedure-related serious adverse events were 2.5% in the TPS group. Endoscopic observation of gastroduodenal ulcers occurred in 10.3% of TPS patients without bleeding or perforation (https://clinicaltrials.gov/ct2/show/NCT02518685) [44] (Fig. 8).

The Future

A new concept of IG is the "Sleeveballoon" (Keyron Ltd., London, UK), a new device combining an intragastric balloon traversed by a channel that permits the passage of a limited amount of food. The channel continues with a connecting sleeve, which covers the duodenal and proximal jejunal mucosa. Its very important hormonal and weight reduction results are due to restrictive and malabsorptive effects. In a recent experimental study, Sleeveballoon reduces peripheral and hepatic insulin resistance, blood glycaemia, body weight, and ectopic fat deposition to a similar level as Roux-en-Y gastric bypass [10] (Fig. 9).

The intragastric balloon represents an important therapeutic option of obesity in patients no longer able to lose weight under guided diet program and lifestyle modification. The possibility of complication even using devices less invasive than bariatric surgery suggests its use under multidisciplinary team control and by a follow-up properly managed.

As obesity is a chronic disease and the space occupying devices are made for temporary treatment, all intragastric devices have to be used as soon as possible and earlier, in terms of age and BMI, in order to perform the prevention and not the cure of morbid obesity.

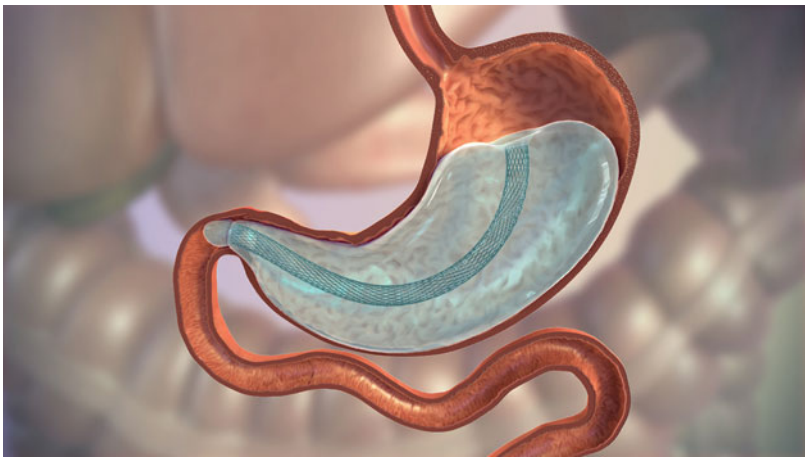

Fig. 9 Sleeveballoon

References

1. Abu Dayyeh BK, Eaton LL, Woodman G et al (2015) A randomized, multi-center study to evaluate the safety and effectiveness of an intragastric balloon as an adjunct to a behavioral modification program, in comparison with a behavioral modification program alone in the weight management of obese subjects. Gastrointest Endosc 81:AB147
2. Agnihotri A, Xie A, Bartalos C, et al (2018) Real-world safety and efficacy of fluid-filled dual intragastric balloon for weight loss [Published correction appears in Clin Gastroenterol Hepatol 2018;16(9):1538. Sullivan, Shelby [added]]. Clin Gastroenterol Hepatol 16(7):1081–1088.e1. https://doi.org/10.1016/j.cgh.2018.02.026
3. Ali MR, Moustarah F, Kim JJ, American Society for Metabolic and Bariatric Surgery Clinical Issues Committee (2016) American Society for Metabolic and Bariatric Surgery position statement on intragastric balloon therapy endorsed by the Society of American Gastrointestinal and Endoscopic Surgeons. Surg Obes Relat Dis 12(3):462–467. https://doi.org/10.1016/j.soard.2015.12.026
4. Alsabah S, Al Haddad E, Ekrouf S, Almulla A, Al-Subaie S, Al Kendari M (2018) The safety and efficacy of the procedureless intragastric balloon. Surg Obes Relat Dis 14(3):311–317. https://doi.org/10.1016/j.soard.2017.12.001
5. ASGE Bariatric Endoscopy Task Force and ASGE Technology Committee, Abu Dayyeh BK, Kumar N et al (2015) ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. Gastrointest Endosc 82(3):425–38.e5. https://doi.org/10.1016/j.gie.2015.03.1964
6. ASGE Bariatric Endoscopy Task Force, ASGE Technology Committee, Abu Dayyeh BK et al (2015) Endoscopic bariatric therapies. Gastrointest Endosc 81(5):1073–1086. https://doi.org/10.1016/j.gie.2015.02.023
7. Behary J, Kumbhari V (2015) Advances in the endoscopic management of obesity. Gastroenterol Res Pract 2015:757821. https://doi.org/10.1155/2015/757821
8. Brooks J, Srivastava ED, Mathus-Vliegen EM (2014) One-year adjustable intragastric balloons: results in 73 consecutive patients in the U.K. Obes Surg 24(5):813–819. https://doi.org/10.1007/s11695-014-1176-3

9. Buchwald H, Oien DM (2013) Metabolic/bariatric surgery worldwide 2011. Obes Surg 23(4): 427–436
10. Casella-Mariolo J, Castagneto-Gissey L, Angelini G et al (2019) Simulation of gastric bypass effects on glucose metabolism and non-alcoholic fatty liver disease with the Sleeveballoon device. EBioMedicine 46:452–462. https://doi.org/10.1016/j.ebiom.2019.07.069
11. Crea N, Pata G, Della Casa D et al (2009) Improvement of metabolic syndrome following intragastric balloon: 1 year follow-up analysis. Obes Surg 19(8):1084–1088. https://doi.org/10.1007/s11695-009-9879-6
12. Daniel F, Abou Fadel C, Houmani Z, Salti N (2016) Spatz 3 adjustable intragastric balloon: long-term safety concerns. Obes Surg 26(1):159–160. https://doi.org/10.1007/s11695-015-1897-y
13. De Peppo F, Caccamo R, Adorisio O et al (2017) The Obalon swallowable intragastric balloon in pediatric and adolescent morbid obesity. Endosc Int Open 5(1):E59–E63. https://doi.org/10.1055/s-0042-120413
14. Ernesti I, Ienca R, Basciani S, Mariani S, Genco A (2018) Effect of a new Swallowable intragastric balloon (Elipse™) on weight loss and metabolic syndrome. J Obes Nutr Disord: JOND-120. https://doi.org/10.29011/JOND-120. 100020
15. Forlano R, Ippolito AM, Iacobellis A et al (2010) Effect of the BioEnterics intragastric balloon on weight, insulin resistance, and liver steatosis in obese patients. Gastrointest Endosc 71(6): 927–933. https://doi.org/10.1016/j.gie.2009.06.036
16. Genco A, Dellepiane D, Baglio G et al (2013) Adjustable intragastric balloon vs non-adjustable intragastric balloon: case-control study on complications, tolerance, and efficacy. Obes Surg 23(7):953–958. https://doi.org/10.1007/s11695-013-0891-5
17. Genco A, López-Nava G, Wahlen C et al (2013) Multi-centre European experience with intragastric balloon in overweight populations: 13 years of experience. Obes Surg 23(4): 515–521. https://doi.org/10.1007/s11695-012-0829-3
18. Genco A, Lorenzo M, Baglio G et al (2014) Does the intragastric balloon have a predictive role in subsequent LAP-BAND(®) surgery? Italian multicenter study results at 5-year follow-up. Surg Obes Relat Dis 10(3):474–478. https://doi.org/10.1016/j.soard.2013.10.021
19. Genco A, Ernesti I, Ienca R et al (2018) Safety and efficacy of a new Swallowable intragastric balloon not needing endoscopy: early Italian experience. Obes Surg 28(2):405–409. https://doi.org/10.1007/s11695-017-2877-1
20. Glass J, Chaudhry A, Zeeshan MS, Ramzan Z (2019) New era: endoscopic treatment options in obesity-a paradigm shift. World J Gastroenterol 25(32):4567–4579. https://doi.org/10.3748/wjg.v25.i32.4567
21. Hales CM, Carroll MD, Fryar CD et al (2017) Prevalence of obesity among adults and youth: United States, 2015–2016. NCHS Data Brief 288:1–8
22. Haskins O (2013) TransPyloric Shuttle demonstrates weight-loss. Bariatric News. Available at: http://www.bariatricnews.net/?q¼node/1236
23. Ienca R et al (2020) The procedurless Elipse gastric balloon program: multicenter experience in 1770 consecutive patients. Obes Surg 30(9):3354–3362. https://doi.org/10.1007/S11695-020-04539-8
24. Imaz I, Martínez-Cervell C, García-Alvarez EE, Sendra-Gutiérrez JM, González-Enríquez J (2008) Safety and effectiveness of the intragastric balloon for obesity. A meta-analysis. Obes Surg 18(7):841–846. https://doi.org/10.1007/s11695-007-9331-8
25. Jamal MH, Almutairi R, Elabd R, AlSabah SK, Alqattan H, Altaweel T (2019) The safety and efficacy of procedureless gastric balloon: a study examining the effect of Elipse intragastric balloon safety, short and medium term effects on weight loss with 1-year follow-up post-removal. Obes Surg 29(4):1236–1241. https://doi.org/10.1007/s11695-018-03671
26. Kotzampassi K, Grosomanidis V, Papakostas P, Penna S, Eleftheriadis E (2012) 500 intragastric balloons: what happens 5 years thereafter? Obes Surg 22(6):896–903. https://doi.org/10.1007/s11695-012-0607-2

27. Kumar N (2015) Endoscopic therapy for weight loss: Gastroplasty, duodenal sleeves, intragastric balloons, and aspiration. World J Gastrointest Endosc 7(9):847–859. https://doi.org/10.4253/wjge.v7.i9.847
28. Kumar N, Bazerbachi F, Rustagi T et al (2017) The influence of the Orbera intragastric balloon filling volumes on weight loss, tolerability, and adverse events: a systematic review and meta-analysis. Obes Surg 27(9):2272–2278. https://doi.org/10.1007/s11695-017-2636-3
29. Look AHEAD Research Group (2014) Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity (Silver Spring) 22(1):5–13. https://doi.org/10.1002/oby.20662
30. Lopez-Nava G, Rubio MA, Prados S et al (2011) BioEnterics® intragastric balloon (BIB®). Single ambulatory center Spanish experience with 714 consecutive patients treated with one or two consecutive balloons. Obes Surg 21(1):5–9. https://doi.org/10.1007/s11695-010-0093-3
31. Machytka E, Chuttani R, Bojkova M et al (2016) Elipse™, a procedureless gastric balloon for weight loss: a proof-of-concept pilot study. Obes Surg 26(3):512–516. https://doi.org/10.1007/s11695-015-1783-7
32. Mafort TT, Rufino R, Costa CH, Lopes AJ (2016) Obesity: systemic and pulmonary complications, biochemical abnormalities, and impairment of lung function. Multidiscip Respir Med 11:28. https://doi.org/10.1186/s40248-016-0066-z. Published 2016 Jul 12
33. Marinos G, Eliades C, Raman Muthusamy V, Greenway F (2014) Weight loss and improved quality of life with a nonsurgical endoscopic treatment for obesity: clinical results from a 3- and 6-month study. Surg Obes Relat Dis 10(5):929–934. https://doi.org/10.1016/j.soard.2014.03.005
34. Martinez-Brocca MA, Belda O, Parejo J et al (2007) Intragastric balloon-induced satiety is not mediated by modification in fasting or postprandial plasma ghrelin levels in morbid obesity. [Published correction appears in Obes Surg 2007;17(7):996]. Obes Surg 17(5):649–657. https://doi.org/10.1007/s11695-007-9109-z
35. Mathus-Vliegen EMH (2018) Is endoscopy really necessary for placing intragastric balloons? Obes Surg 28(1):169–175. https://doi.org/10.1007/s11695-017-2812-5
36. Mion F, Ibrahim M, Marjoux S et al (2013) Swallowable Obalon® gastric balloons as an aid for weight loss: a pilot feasibility study. Obes Surg 23(5):730–733. https://doi.org/10.1007/s11695-013-0927-x
37. Moore RL, Seger MV, Garber SM et al (2019) Clinical safety and effectiveness of a swallowable gas-filled intragastric balloon system for weight loss: consecutively treated patients in the initial year of U.S. commercialization. Surg Obes Relat Dis 15(3):417–423. https://doi.org/10.1016/j.soard.2018.12.007
38. Neto MG, Silva LB, Grecco E et al (2018) Brazilian Intragastric balloon consensus statement (BIBC): practical guidelines based on experience of over 40,000 cases. Surg Obes Relat Dis 14(2):151–159. https://doi.org/10.1016/j.soard.2017.09.528
39. Nieben OG, Harboe H (1982) Intragastric balloon as an artificial bezoar for treatment of obesity. Lancet 1(8265):198–199. https://doi.org/10.1016/s0140-6736(82)90762-0
40. Nobili V, Della Corte C, Liccardo D et al (2018) Obalon intragastric balloon in the treatment of paediatric obesity: a pilot study. Pediatr Obes 13(4):273. https://doi.org/10.1111/ijpo.12272
41. Ponce J, Woodman G, Swain J et al (2015) The REDUCE pivotal trial: a prospective, randomized controlled pivotal trial of a dual intragastric balloon for the treatment of obesity. Surg Obes Relat Dis 11(4):874–881. https://doi.org/10.1016/j.soard.2014.12.006
42. Raftopoulos I, Giannakou A (2017) The Elipse balloon, a swallowable gastric balloon for weight loss not requiring sedation, anesthesia or endoscopy: a pilot study with 12-month outcomes. Surg Obes Relat Dis 13(7):1174–1182. https://doi.org/10.1016/j.soard.2017.02.016
43. Schapiro M, Benjamin S, Blackburn G et al (1987) Obesity and the gastric balloon: a comprehensive workshop. Tarpon Springs, Florida, March 19–21, 1987. Gastrointest Endosc 33:323–327

44. Shahnazarian V, Ramai D, Sarkar A (2019) Endoscopic bariatric therapies for treating obesity: a learning curve for gastroenterologists. Transl Gastroenterol Hepatol 4:16. Published 2019 Mar 18. https://doi.org/10.21037/tgh.2019.03.01
45. Sullivan S, Edmundowicz SA, Thompson CC (2017) Endoscopic bariatric and metabolic therapies: new and emerging technologies. Gastroenterology 152(7):1791–1801. https://doi.org/10.1053/j.gastro.2017.01.044
46. Sullivan S, Swain J, Woodman G et al (2018) Randomized sham-controlled trial of the 6-month swallowable gas-filled intragastric balloon system for weight loss. Surg Obes Relat Dis 14(12): 1876–1889. https://doi.org/10.1016/j.soard.2018.09.486
47. Trang J, Lee SS, Miller A et al (2018) Incidence of nausea and vomiting after intragastric balloon placement in bariatric patients – a systematic review and meta-analysis. Int J Surg 57: 22–29. https://doi.org/10.1016/j.ijsu.2018.06.038
48. Usuy E, Brooks J (2018) Response rates with the Spatz3 adjustable balloon. Obes Surg 28(5): 1271–1276. https://doi.org/10.1007/s11695-017-2994-x
49. World Health Organization Obesity and overweight fact sheet. WHO. Available online: http://www.who.int/mediacentre/factsheets/fs311/en/