



## Intra-gastric balloons – The past, present and future

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### ABSTRACT

Obesity is a complex metabolic illness that is interrelated to a plethora of complications that predispose to avoidable morbidity and mortality. The considerable impact of obesity has invited various therapies ranging from lifestyle advice, pharmacotherapy, endoscopic bariatric therapy and ultimately surgery. Intra-gastric balloons are space-occupying therapies that aim to increase satiety through mechanical and neuroendocrine mechanisms. Their prevalence is owed to their ease of administration and general safety. However, long term data concerning safety and efficacy is scarce when considering the various types of balloons in use. In this review, we discuss the intra-gastric balloon comprehensively in terms of efficacy, safety, limitations and future direction.

### 1. Introduction

Obesity represents a global public health burden. It is typically interrelated to a plethora of complications that predispose to avoidable morbidity and mortality [1]. The rates of obesity have been shown to have tripled over the past 35 years [2], and while lifestyle intervention is a cornerstone and remains a sturdy bedrock for the management of excess weight, it is limited to approximately 5–10% weight loss in 50% of obese patients and relies on strict patient cooperation [3]. Obesity remains an underdiagnosed and undertreated condition, with patients receiving overdue advice once complications present [4]. (see [Tables 1 and 2](#))

The propensity for obesity to adversely affect life expectancy has invited various therapies over the past few decades [4]. Classically, treatment is initiated from least invasive and may be escalated towards pharmacotherapy, endoscopic bariatric interventions and lastly, surgical intervention.

Multiple pharmacotherapies exist, yet their efficacy in weight loss is limited to 5–10% total body weight loss [12,13]. At present, the gold standard treatment for unsuccessful medical treatment of obesity is surgical intervention, providing unrivalled weight loss. These interventions include, but are not limited to; the adjustable gastric band, sleeve gastrectomy and Roux-en-Y gastric bypass [13,14]. Despite providing considerable weight loss, only about 1% of obese patients undergo bariatric surgery [14,15]. Perhaps this may be in part, due to high cost, concerns related to the surgical intervention and lack of access to bariatric centres.

Endoscopic bariatric therapy offers a less invasive option for patients reluctant to go under the knife and includes various procedures such as; space-occupying devices, restrictive procedures, and aspiration therapies. Space occupying devices refer to Intra-gastric balloons [IGB] that are usually temporary, endoscopically placed air or fluid-filled balloons, resulting in mechanical and metabolic effects that target weight loss. These therapies aim to bridge a treatment gap, referring to management between pharmacotherapy and surgery, and additionally provide care to a subset of overweight or obese patients that are not eligible for bariatric surgery. In this review, we focus on intra-gastric balloons and their applications, efficacy, and role in managing obesity.

#### 1.1. History and course

In 1985 the Garren-Edwards gastric bubble was the first intra-gastric balloon (IGB) to receive approval from the US Food and Drug Administration (FDA). This balloon was designed by 2 gastroenterologists; Lloyd R. Garren and his wife Mary L. Garren, and was manufactured by American Edwards Laboratories of Santa Ana California [16]. The balloon was cylindrical in shape with a hollow central channel and designed to be inserted and retrieved endoscopically. Upon insertion the balloon is inflated with 200 cc of room air and is left in the stomach for 4 months [16]. Weight loss results were unsatisfactory [17] and its associated complications [18–20] led to its withdrawal from the market in 1992.

In 1987, a comprehensive workshop was held in Tarpon Springs Florida [21]. International experts established the characteristics of the

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“ideal intra-gastric balloon”. Their definition described a; spherical silicone balloon, that was saline-filled, smooth, included a radio-opaque marker and has an adjustable volume between 400 and 500 cc. IGBs were to be used in patients whose BMI did not qualify for surgery yet wished to lose weight or resolve an obesity-associated condition. Furthermore, IGBs could apply to patients with extremely high BMI; to reduce the risk of surgery or when the patient was deemed surgically “unfit” [21].

In accordance with the characteristics set in the conference, the BioEnterics Corporation developed a balloon in 1991 that contains a saline-methylene blue mixture, and is to remain intra-gastric for 6 months. It was promoted and used in Europe, South America, Asia and the Middle East, however its application in USA and Canada failed at the time [16,22]. In 2015, the balloon received its FDA approval, marketed as the Orbera, becoming the first intra-gastric balloon to be approved in the U.S. From 2015 onwards, the ReShape and Obalon balloons received FDA approval.

Several other intra-gastric balloons were developed afterwards; however, only the three aforementioned balloons have FDA approval. The trend towards less invasive procedures continues with the development of balloons that can be swallowed, and are only inflated once they are in position; Eclipse™ and Obalon™. For the purpose of the review we focus mainly on FDA-approved balloons and review a number of Conformité Européenne (CE) approved balloons.

## 1.2. Physiology

A number of physiological mechanisms have been implicated in IGB-induced weight loss, ultimately aimed at increasing satiety. Satiety is a complex process regulated by the gut-brain axis. Intra-gastric balloons may increase satiety by; the mechanical effect of the balloon in reducing free gastric volume, altering gastrointestinal (GI) hormones and increasing gastric emptying time (GE) [23–28].

Firstly, IGBs reduce the capacity of the stomach to accommodate more food, thus reducing the amount consumed per meal and hence calorie intake. Additionally, stretching the gastric wall may potentially alter the release of gastro-intestinal peptides involved in satiety and energy balance [23].

Ghrelin is a 28 amino-acid peptide secreted primarily by the stomach fundus, levels of plasma ghrelin increase pre-prandial and decrease post-prandial, acting as one of the many mechanisms to regulate satiety [24]. The role of ghrelin in IGB-associated weight loss is contentious, levels have been shown to decrease during IGB treatment, with conflicting results on it being the main mechanism involved in weight loss [25,26].

According to Mion et al., IGB resulted in a decrease in ghrelin levels and a delay in gastric emptying. However, ghrelin was not affected in the absence of food. It was noted that IGB coupled with caloric intake would reduce ghrelin levels and result in weight loss [25]. This is supported by Ly et al. which stated that the mechanical effects of balloon inflation alone did not reduce plasma ghrelin levels, but caloric intake is a mandatory signal for ghrelin induced sensation of satiety [26].

Lastly, the presence of an IGB delays GE, leading to sustained gastric

**Table 2**

Displaying effect of intra-gastric balloons on weight loss.

Balloon products	Type of study	Sample size	TBWL (%)	EWL (%)	References
FDA + CE approved					
Reshape Duo™	Randomised controlled pivotal trial	326	7.6	25.1	[5]
Orbera™	Meta-Analysis (17 studies)	1683	13.16	25.44	[6]
Obalon™	Randomised controlled trial	387	7.1	26	[7]
CE Approved only					
Eclipse™	Meta-Analysis (6 prospective studies)	2016	14.2	67	[8]
Spatz™	Prospective cohort	73	20.1	45.8	[9]
End-Ball™	Retrospective Analysis	114	17.1	36.5	[10]
Heliosphere bag™	Prospective cohort	82	13.4	33.2	[11]

TBWL – Total body weight loss; EWL – Extra body weight loss.

distention. Consequently, gastric mechanoreceptors are stimulated sending afferent signals to the brain stem triggering satiety [28,29,30]. This is evident by testing scintigraphic gastric emptying time, which is increased in the presence of IGB and correlates positively with weight loss [31]. Su et al. demonstrated that solid and liquid scintigraphic GE half-times were significantly longer after IGB placement, with a positive correlation between longer GE times and body weight loss [27]. Gomez et al. also demonstrated that IGB resulted in a delay in GE, with slower emptying associated with greater %TBWL and a return of GE to normal after removal of IGB [28].

## 1.3. Indications

The intra-gastric balloon could offer a minimally invasive option for the management of obesity. Multiple indications exist, IGBs may be used in patients with a BMI of >27 kg/m<sup>2</sup> to induce weight loss or to treat obesity-related medical conditions [32]. In patients that qualify for bariatric surgery but have a BMI; 45–50, surgery and anesthesia may carry potential risks. IGB may be used as bridging therapy prior to undergoing surgery; justified by reducing BMI and simultaneously reducing surgical and anesthesia-related complications. Weight loss preoperatively may diminish hepatomegaly and avoids possible technical difficulty [33]. It is prudent to approach the application of intra-gastric balloons as a case-by-case basis. The indications may overlap and due to the lack of a clear consensus, the provider must be clear on the aim of treatment, whether; bridging therapy for bariatric procedures, weight loss induction or combination therapy.

**Table 1**

Displaying summary of intra-gastric balloon characteristics.

Balloon products	Manufacturer	Material (filled)	Number of balloons	Duration (months)	Insertion/removal method
FDA + CE approved					
Reshape Duo™	ReShape Medical	Silicone (Saline 450 ml)	2	6	Endoscopic/Endoscopic
Orbera™	Apollo Endosurgery	Silicone (Saline 400–700 ml)	1	6	Endoscopic/Endoscopic
Orbera 365™	Apollo Endosurgery	Silicone (Saline 400–700 ml)	1	12	Endoscopic/Endoscopic
Obalon™	Obalon Therapeutics	Gelatin capsule (Gas 250 ml)	Up to 3	3–6	oral/Endoscopic
CE Approved					
Eclipse™	Allurion Technologies	Polymer Film (fluid filled 450–550 ml)	1	4	Oral/natural excretion
Spatz™	Spatz Medical	Silicone (adjustable)	1	12	Endoscopic/Endoscopic
End-Ball™	Endalis	Polyurethane (Air/Fluid 700 ml)	1	6	Endoscopic/Endoscopic
Heliosphere bag™	Helioscopie	Polyurethane and silicone (Air 550 ml)	1	6	Endoscopic/Endoscopic

### 1.4. Contra indications

A thorough history and physical exam is imperative to identify whether the patient has any contraindications to the procedure. There is currently no clear consensus on the method of patient work-up. While each intra-gastric balloon is variable in its design and application, contraindications may similarly differ. The contraindications below are commonly applied to the Orbera IGB [33,34].

Absolute	Relative
Previous Gastric surgery	Previous abdominal surgery
Coagulation disorder	hiatal hernia
Bleeding lesion in upper GIT	Inflammatory bowel disease
Pregnancy	Chronic non-steroidal anti-inflammatory use
Hiatal hernia >5 cm	Esophagitis
Alcoholism or drug abuse	Psychiatric disorder
Severe liver disease	

### 1.5. Efficacy of intra-gastric balloons

IGBs have been shown to improve metabolic parameters in people who successfully lose weight [35], but there is no long term data evaluating these parameters. In a systematic review published in 2017 which incorporated 10 RCTs and 30 observational studies and included 5668 patients, IGBs were shown to decrease mean difference (MD) fasting glucose [-12.7 mg/dl] MD in triglycerides [-19 mg/dl] MD in waist circumference [-4.1 cm] MD in diastolic blood pressure [-2.9]. Additionally, the odds ratio of diabetes remission after 6 months was 1.4, odds ratio for hypertension remission was 2.0 and the odds ratio dyslipidemia remission was 1.7 [36].

Weight loss is usually measured by calculating percentage of excess weight loss (%EWL), which is defined by the total weight loss/(patient current weight - ideal body weight). Saber et al. conducted a meta-analysis in 2017 including 20 RCTs and 1195 patients; demonstrating 11–14 %EWL overall after intra-gastric balloon treatment [37]. In a retrospective analysis on 1221 patients by Armijo et al., patients reached 50% of their target weight loss within 30 days of intra-gastric balloon insertion (6.2% TBWL). However, it was also noted that weight loss in the first 30-days after the procedure was most likely due to dehydration [38]. A meta-analysis published by the American society for Gastrointestinal Endoscopy and Bariatric Endoscopy (ASGE) suggested that the Orbera Intra-gastric balloon leads to an overall %TBWL of 13.16% after 6 months [6]. Additionally, a RCT by Courcoulas et al. showed similar effective weight loss at 3 and 6 months post-removal of the balloon [39].

- Orbera

The Orbera is currently the most comprehensively studied intra-gastric balloon. A systematic review published in 2017 which included 44 studies on the Orbera Balloon showed a %TBWL at 6 months of 13.2% [95% CI 12.3–14] [40]. Genco et al. conducted a randomized controlled cross-over trial comparing Orbera IGB to sham (endoscopy) and behaviour modification, at three months, the treatment group achieved significant %EWL when compared to control group (34% vs 2.1%). At three months after cross-over, the original treatment group lost 31% vs 4.6% %EWL [41]. A long term study by Kotzampassi et al. included approximately 400 patients that were followed up for 5 years post IGB removal who lost >20%EWL during their treatment with IGB, showed that a similar degree of weight loss was maintained in 53, 27 and 21% of patients at one, two and five years respectively [42]. In a meta-analysis conducted in 2008 involving 3608 patients the Orbera balloon resulted in a median %EWL of 32.1% (CI 26.9–37.4) and a median % total weight loss (%TWL) 12.2% (CI 10–14.3) at 6 months after implantation [43]. In 2015, a meta-analysis of including 1683 patients demonstrated an 11.5% TBWL and a 25.4% EWL at 12 months after balloon placement [6]. Weight loss from the Orbera is also

associated with improvement in weight-related comorbid conditions such as hypertension, type 2 diabetes, and hyperlipidaemia [44].

- ReShape

The REDUCE pivotal trial which was a retrospective study of 326 patients with a BMI 30–40kg/m<sup>2</sup>, that were randomized to ReShape Balloon for 6 months and sham endoscopy plus diet, showed that those who were assigned to Reshape balloon had greater weight loss [25.1% vs 11.3% EWL] [5]. In another observational study conducted on 60 patients, with average BMI 38.8kg/m<sup>2</sup> followed for at least 6 months, results show a decrease for %EWL of 47.1% [45] Two other small studies showed promising results; a retrospective study of 34 patients with BMI 27.6–49.17 showing a %TBWL of 6.8% and a mean BMI decrease of 7% after 6 months [46]. Another prospective randomized study showed promise with a trend towards greater %EWL in the treatment group however due to the small sample size, this was not deemed statistically significant [47].

- Obalon

A 12-week uncontrolled pilot study of 17 adults who received Obalon intragastric balloons resulting in a 5.8% TBWL [48]. Sullivan et al. conducted a multi-centre randomized sham-controlled trial in 2018 on 387 patients with BMI 30–40kg/m<sup>2</sup>, showed that treatment group with gas filled balloon and lifestyle changes resulted in twice as much weight loss compared to the control group [%TBWL of 7.1% vs 3.6%] [7].

- Spatz

In a 12-month pilot study, Machytka et al. implanted the Spatz balloon for eighteen patients and demonstrated a mean %EWL of 48.8% [49]. Two other studies reported a %EWL of 45.7% and 42.9%, respectively [9,50]. Genco et al. conducted a case-control study comparing Orbera to Spatz and demonstrated comparable results in terms of weight loss [51]. A cross-sectional study by Schwaab et al., in 2020, demonstrated weight loss comparable to the Orbera balloon as well [52]. There is, however, a need to study the long-term safety of the balloon [53].

- Ellipse

In a systematic review and meta-analysis published in 2020 that included 6 prospective cohort studies including 2016 patients with a BMI ranging 30.6–36.2 kg/m<sup>2</sup>, results demonstrated %TWL of 12.8% at 4–6 months and 10.9% at one year. Unfortunately, there are only two studies that reported long term follow-up of 12 months, thus more long term studies are needed [8].

### 1.6. Complications

The majority of patients experience non-serious adverse events including; nausea, vomiting and abdominal pain after insertion of the IGB. This is usually secondary to gastric accommodation. The rates of adverse events vary greatly between studies depending on the scope of the study. Trang et al. published a meta-analysis which included 938 patients reporting the adverse events of IGB, which showed 63% of the patients reporting nausea, 55% reported vomiting, 58% reported abdominal pain and 20% reported gastro-oesophageal reflux (GERD) symptoms [54].

Early balloon removal is usually required if symptoms persist [34, 43]. The rates of early balloon removal for the Orbera, ReShape and Ellipse are 7, 9 and 2.6% respectively [6,5,8]. In a systematic review which included 26 studies, most of which were case series, reported that early balloon removal was 3.5% and was mostly commonly due to abdominal pain [55].

Although uncommon, serious adverse events have been reported. IGBs remaining in situ for longer than recommended may result in balloon migration and perforation [56,57,58]. Thus, emphasizing close observation and timely follow-up.

A systematic review reported the rate of bowel obstruction in IGB as 0.8%, commonly related to the spontaneous collapse of the balloon, additionally it reported gastric perforation as 0.5% [55]. However, it was noted that higher balloon filling volumes >600 ml was associated with less incidence of balloon migration (2.26% vs 0.5%) [40].

A meta-analysis published on the Orbera which pooled data from 68 studies, reported a total of 4 deaths (0.08%) [6]. In another systematic review which included 20 studies on 1200 patients published in 2017 reported 0% mortality [37]. Since 2016, The US Food and Drug Administration (FDA) has issued multiple updates to alert healthcare providers of 18 reported deaths that occurred in patients using liquid filled IGB, three of which were secondary to gastric perforation and one secondary to oesophageal perforation [59].

Thorough patient education is necessary to avoid life threatening complications that may be brought upon by noncompliance to recommendations and lack of follow up [60,61,62]. Symptoms of persistent abdominal pain or intractable vomiting should always be investigated thoroughly to rule out serious complications.

## 2. Discussion

It is apparent from the existing literature that there is a considerable heterogeneity amongst studies. The majority of studies are observational and carried out retrospectively, inherently predisposing them to bias. With the rapid production of novel balloons, research on efficacy is falling behind. Long term efficacy is not clearly established in all existing devices at this point in time. The existing literature suggests that long term, significant weight loss is limited in comparison to conventional surgical methods, this knowledge must be conveyed to the patient. In addition to this, patients followed up have different eating habits and lifestyle factors that may be difficult to assess.

Currently, there is a necessity for long term studies following weight loss, metabolic parameters and hormonal effects. Additionally, cost-effectiveness should be studied to augment the providers approach to managing obesity. Finally, despite the commonly conceived safety of intra-gastric devices, it is important to note that there is likely a multifaceted cause for possible life-threatening complications; whether due to operator error, lack of follow up or patient in compliance.

Clearly, there a continuous drive towards non-invasiveness often favoured by both clinician and patient. Innovation and techniques to confront obesity are on the rise, various companies competing by innovating may prove useful. It is however, imperative that judicious research is carried out to establish safety and efficacy. Swallow-able balloons are noticeably gaining popularity due to their convenience and administration technique. Yet there is a clear lack of long term outcome studies. On deciding what treatment to recommend, intra-gastric balloons are undoubtedly valuable options that require a patient-centred, holistic approach to determine the likely yield of its application.

The trend towards ease of administration is clear, and it is possible that this will allow trained providers of various specialties to perform the procedure, possibly in an outpatient primary care setting. In recent years, we have seen novel innovations that endeavour to simplify administration, avoiding endoscopy and anesthesia. While still in the primary phases of research and development; the recent wireless, magnetically-assisted gastric capsule, demonstrates the familiar approach, whereby technology and innovation is incorporated into management [63,64,65].

## 3. Conclusion

At present, we believe that intra-gastric balloons are a valuable

adjunct to the provider's resources. They are however, relatively novel, and their use is escalating. While bariatric surgery provides unsurpassed weight loss, it is not without complications and risks. Endoscopic bariatric treatments are promising, especially in combination with lifestyle modification and pharmacotherapy. It may represent bridging therapy, for patients that cannot, should not or will not undergo major surgical procedures. Thus the option is worth considering and comprehensively discussing with patients.

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The study is exempt from ethical approval.

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## Author contribution

Eisa Lari Writing- Original draft preparation, Conceptualization, Methodology, Software, Writing- Reviewing and Editing, Waleed Burhamah Methodology, Data curation, Writing- Original draft preparation, Writing- Reviewing and Editing, Ali Lari Visualization, Investigation, Writing- Reviewing and Editing, Talal Alsaeed Supervision, Validation, Khalid Al Yaqout Supervision, Validation, Salman Al-Sabah Supervision, Validation.

## Registration of research studies

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

## Guarantor

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## Consent

No patient details are included in this paper.

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## Declaration of competing interest

No conflict of interest.

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