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REVIEW

Efficacy of Intragastric Balloons for Weight Loss in Overweight and Obese Adults: a Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Intragastric balloons (IGB) are the most widely used endoscopic bariatric and metabolic therapies. We aimed to evaluate the efficacy of IGB in comparison with sham or lifestyle interventions for weight loss in overweight and obese patients. This systematic review and meta-analysis was performed following the PRISMA guidelines. Electronic searches were performed to identify randomized controlled trials, which compared IGB with sham or lifestyle intervention. Thirteen RCTs with 1523 patients were included. The difference in mean %EWL and %TWL at follow-up was 17.98%, and 4.40%, respectively, which was significantly higher in the IGB group. Similarly, the difference in mean AWL and BMIL was 6.12 kg, and 2.13 kg/m^2, respectively. IGB therapy is more effective than lifestyle intervention alone for weight loss in overweight and obese adults.

Keywords Intragastric balloon · Obesity · Overweight · Systematic review · Meta-analysis

Introduction

More than 1.9 billion adults are overweight, and 650 million are obese globally, and yet these overwhelming statistics continue to rise [1]. Excess weight predisposes to chronic diseases, mental health issues, and higher mortality. In 2015, overweight and obesity were responsible for about 4 million deaths and 120 million disability-

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adjusted life years (DALY), and 39% of these deaths and 37% of these lost years occurred in overweight people [2]. Nevertheless, obesity is an underdiagnosed and undertreated condition [3]. Physicians should discuss weight loss options and offer a multidisciplinary obesity treatment.

The weight loss approach starts with lifestyle interventions (LI) with a balanced diet and increased physical activity. Lifestyle interventions can be complemented with pharmacological therapy, but their efficacy is limited, and most patients fail to achieve sustained weight loss [4]. Bariatric surgery is the most effective method for weight loss in severe obesity resulting in a percentage of excess weight loss ranging from 60 to 87% in randomized controlled trials [5]. However, surgery is not indicated for overweight and obesity class I patients, and only less than 1% of obese patients who qualify for bariatric surgery undergo the procedure because of the patient refusal, lack of access to surgery, high costs, perceived risks of postoperative complications and mortality, among others [6–11]. Studies have shown that even 5% total weight loss can result in multiple health benefits, including improvement or prevention of metabolic disease [12]. Therefore, minimally invasive therapies may be useful for patients who have failed conservative treatment and do not meet the criteria for surgery or do not want to undergo the operation.

Endoscopic bariatric and metabolic therapies (EBMTs) have emerged as promising minimally invasive procedures to complement the obesity management [13, 14]. Several endoscopic procedures have been described, including intragastric balloon (IGB), endoscopic sleeve gastroplasty, gastric aspiration, duodenal sleeve, and duodenal mucosal resurfacing. Among these gastric and small bowel interventions, IGBs are the most studied and widely used therapy for obesity. These space-occupying devices emerged in the 1980s with the Garren-Edwards gastric bubble [15] and have evolved over the years to become more effective and safe. Currently, many IGBs are available in clinical practice (Table 1). These IGBs may differ in the method of insertion, removal, filling volume, adjustability, and duration of implantation.

A meta-analysis of randomized controlled trials (RCTs) provides superior evidence and is a vital component of evidence-based medicine. Therefore, we aimed to perform a comprehensive systematic review and meta-analysis of RCT to assess the efficacy of currently available IGBs in comparison with the control group (sham/LI) for weight loss in overweight and obese patients. We also performed a subgroup analysis to compare different types of balloons.

Table 1 Characteristics of currently in use IGB

Balloon	ORBERA® Intragastric Balloon System (Apollo Endosurgery Inc, Austin, Texas, USA)	Heliosphere Bag®, (Helioscopie, Vienne, France)	ReShape Integrated Dual Balloon System™ (ReShape Medical Inc, San Clemente, CA, USA)	Obalon Balloon System™ (Obalon Therapeutics Inc, Carlsbad, CA, USA)	Spatz3™ Adjustable Balloon System (Spatz Medical, Great Neck, NY, USA)	Elipse Balloon™ (Allurion Technologies, Wellesley, MA, USA)
Material	Silicone	Polyurethane and silicone	Silicone	Gelatin capsule	Silicone	Polymer film
Shape	Spherical	Spherical	Bi-lobal	Spherical	Spherical with an inflation tube	Spherical
Number of balloons	1	1	2	Up to 3	1	1
Fulfillment	Saline	Air	Saline + methylene blue	Nitrogen-sulfur hexafluoride gas	Saline + methylene blue	Proprietary solution
Capacity	400–700 mL	550 mL	900 mL (450 mL each balloon)	250–450 mL	400–700 mL	450–550 mL
Insertion	Endoscopically	Endoscopically	Endoscopically	Deglutable	Endoscopically	Deglutable
Retrieval	Endoscopically	Endoscopically	Endoscopically	Endoscopically	Endoscopically	Natural excretion
Duration	6 months	6 months	6 months	12–26 weeks	12 months	4 months
FDA-approved	Yes	No	No	Yes	No	No
CE-approved	Yes	Yes	Yes	Yes	Yes	Yes

Materials and Methods

Protocol and Registration

The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registry number CRD42019137271). This study was approved by the ethics committee of Hospital das Clínicas, Faculty of Medicine, University of São Paulo. As this study is a systematic review with meta-analysis, the informed consent does not apply.

This systematic review and meta-analysis was performed in accordance with The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.

Eligibility Criteria

Only RCTs published or presented in abstract form in the English language were included; however, there was no restriction on publication year. RCTs with the following characteristics were included: (1) participants: patients with body mass index (BMI) > 27 kg/m^2; (2) intervention: currently used IGB with or without LI for at least 12 weeks; (3) comparison: sham *or* LI or both; and (4) outcomes: absolute weight loss (AWL), body mass index loss (BMIL), percentage of excess weight loss (%EWL), and percentage of total weight loss (%TWL).

The exclusion criteria were as follows: (1) studies using non-human subjects; (2) trials that included IGBs no longer available in the market (Ballobes, Garren-Edwards); and (3) trials comparing different IGBs or IGBs with pharmacological therapy, hyaluronic acid injection, and botulinum toxin injection.

Search and Study Selection

We searched electronic databases (MEDLINE, EMBASE, Cochrane, and Lilacs/Bireme) from their inception to November 2019. The search strategy was highly sensitive for Embase, and MEDLINE was “Gastric Balloon OR Gastric Balloons OR Intragastric Balloon OR Intragastric Balloons OR Gastric Bubble OR Gastric Bubbles OR Intragastric Bubble OR Intragastric Bubbles.” Simpler strategies were used for searching other databases.

Two independent investigators conducted the screening for eligibility. Any disagreements were resolved by consensus or by consultation with a third reviewer.

Data Collection Process

Two independent reviewers (APSTK and IBR) extracted and organized relevant data in the form of tables. For crossover trials, we collected data only for the first period (before the crossover of patients). The primary outcomes were %EWL and %TWL, and secondary outcomes were AWL and BMIL at the time of IGB removal.

Risk of Bias in Individual Studies

The risk of bias was assessed by version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB2). This tool is structured into five domains of bias: (1) randomization process; (2) deviations from intended interventions; (3) missing outcome data; (4) measurement of the outcome; and (5) selection of the reported results. The risk of bias of each domain reveals an overall result that can be categorized as "low", "some concerns", and "high." We analyzed the risk of bias for each outcome of every included study. In order to simplify the analysis, we also assessed the overall risk of bias of the enrolled trials using the same domains of the RoB2.

Summary Measures, Synthesis of Results, and Evidence Quality

As our outcomes were continuous variables, differences between their measures were calculated using the mean difference (using the mean, standard deviation, and sample size of each group). When studies did not report mean and variance, we estimated them from the median, range, and sample size.

Statistical analyses were performed with the Review Manager software, version 5.3 (RevMan 5.3; Cochrane Collaboration, Oxford, UK), using the inverse variance (IV) method. We used a 95% confidence interval, and the level of statistical significance was set at a P value of less than 0.05. Heterogeneity was calculated using the method by Higgins (I-square). Meta-analyses were performed using a random-effects model, given the degree of heterogeneity in the included studies. The results of each outcome are graphically analyzed using a forest plot.

Evidence quality was analyzed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group.

Results

Study Selection

Figure 1 details the process of study selection. A total of 13,448 citations were identified through the database search. After the removal of duplicate records, titles and abstracts were reviewed for 6520 records. We identified 37 citations for full-text review. One study was not an RCT, seven studies did not have a sham or lifestyle intervention control group, seven studies used IGB no longer used in clinical practice, one study had duplicate patients, and eight studies were ineligible for quantitative synthesis because there was insufficient data for analysis. After excluding these studies, 13 studies were finally included in the meta-analysis. The characteristics of the included studies are summarized in Table 2.

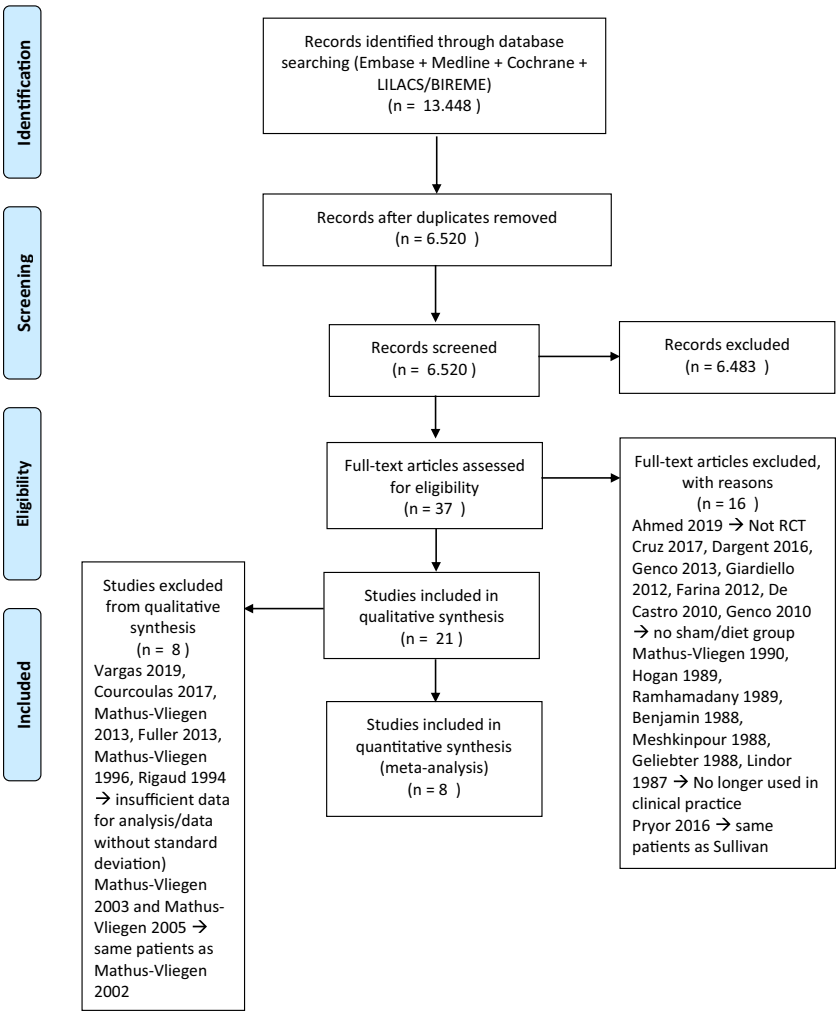

Fig. 1 PRISMA flow diagram detailing the process of study selection

Risk of Bias Within Studies

Five studies had a "high" overall risk of bias, one study had a "some concerns" risk of bias, and six studies attained all requirements for a high-quality study. The overall risk of bias for each study is shown in Fig. 2. The detailed risk of bias for each outcome is described in the Supplementary Material.

Results of Individual Studies

Weight-loss outcomes for individual studies are summarized in Table 3.

Synthesis of Results

Mean Difference in %EWL Between IGB and Control Group

Five studies [16–20] with a total of 903 patients (506 in the IGB group and 397 in the control group) were included in the meta-analysis of %EWL outcomes. The mean %EWL difference between the groups was 17.98% (95% CI, 8.37 to 27.58) $P < 0.00001$), significantly in favor of the IGB group over sham/LI. The heterogeneity was 98% ($Tau^2 = 106.61$; $Chi^2 = 215.15$, df = 4 ($P < 0.00001$); $I^2 = 98\%$) in a random-effect analysis model. (Fig. 3).

In subgroup analysis, there was no significant difference between balloon types for this outcome.

This outcome has a low certainty of the evidence (GRADE) (Annex 5).

Mean Difference in %TWL Between IGB and Control Group

Five studies [18, 19, 21–23] with a total of 1084 patients (611 in the IGB group and 473 in the control group) were included in the meta-analysis of %TWL outcomes. The mean %TWL difference between the groups was 4.40% (95%CI, 1.37 to 7.43) $P < 0.00001$), significantly higher in IGB group compared with sham/LI. The heterogeneity was 97% (heterogeneity: $Tau^2 = 11.29$; $Chi^2 = 139.72$, df = 4 ($P < 0.00001$); $I^2 = 97\%$) in a random-effect analysis model (Fig. 4).

In subgroup analysis, this effect was predominantly determined by the Spatz balloon (11.30 [9.77, 12.83]) although

Table 2 Baseline characteristics of the studies included in the meta-analysis (mean ± standard deviation)

	Study		Study design	Intervention	Control	N (M/F) (TG)	N (M/F) (CG)	Age (TG)	Age (CG)	Balloon type (volume)	Balloon duration
1	Abu Dayyeh 2019	Abstract	RCT	Spatz 3	Lifestyle therapy	187	101	22–64	22–64	Fluid-filled adjustable (400–700 mL)	32 weeks (8 months)
2	Sullivan 2018	Full-text	RCT	Swallowable gas-filled Obalon + lifestyle therapy	Sham + lifestyle therapy	198 (27 M/171F)	189 (19 M/70F)	42.7 ± 9.6	42.5 ± 9.3	3 swallowable gas-filled capsule (250 mL each)	24 weeks (6 months)
3	Vicente 2017	Full-text	RCT	Orbera + diet/exercise	Diet/exercise	32 (11 M/21F)	34 (10 M/24F)	43 ± 10.2	42.6 ± 9.2	500 mL (BMI 35–40), 600 mL (BMI 40–50) and 700 mL (BMI > 50)	6 months
4	Coffin 2017	Full-text	RCT	27 Orbera/28 Heliosphere	Standard medical care	55–27 fluid/28 air (13 M/42F)	60 (17 M/43F)	40.5 ± 12.3	40.1 ± 11.6	Fluid filled 600 mL Air filled 650 mL	6 months
5	Ponce 2015	Full-text	RCT	Dual balloon system (ReShape Duo) + diet/exercise	Diet/exercise	187 (9 M/178F)	139 (7 M/32F)	43.8 ± 9.5	44.0 ± 10.2	ReShape Duo Fluid filled 900 mL/750 mL (short stature patients)	6 months
6	Mohammed 2014*	Full-text	RCT	Orbera	Conservative therapy (diet and physical exercises)	84 (48 M/36F)	44 (26 M/18F)	44 ± 5.64	41 ± 6	Fluid filled 500 mL	6 months
7	Mathus-Vliegen 2014	Full-text	RCT	Orbera 13 weeks	Sham 13 weeks	19	21	37.7 ± 10.9	45.0 ± 9.5	Fluid filled 500 mL	13 weeks (3 months)
8	Ponce 2013	Full-text	RCT	ReShape Duo + diet + exercise	Diet + exercise	21 (4 M/17F)	9 (0 M/9F)	38.9 ± 9.1	45.3 ± 6.6	ReShape Duo Fluid filled 900 mL	24 weeks (6 months)
9	Lee 2012	Full-text	RCT	Orbera + diet + exercise	Diet + exercise	8 (3 M/5F)	10 (8 M/2F)	43 median	47 median	Fluid filled 500 mL	6 months
10	Konopko-Zubrzycka 2009	Full-text	RCT	Orbera + diet + exercise	Diet + exercise	21 (11 M/10F)	15 (6 M/9F)	41 ± 11.9	42.8 ± 9.4	Fluid filled 500 mL	6 months
11	Martinez-Brocca 2007	Full-text	RCT	Orbera + diet	Sham + diet	11 (3 M/8F)	11 (2 M/9F)	34.8 ± 10.8	37.7 ± 8.8	Fluid filled 600 mL	4 months
12	Genco 2006	Full-text	RCT	Orbera	Sham	16 (4 M/12F)	16 (4 M/12F)	36.2 ± 5.2	36.3 ± 5.9	Fluid filled 500 mL	3 months
13	Mathus-Vliegen 2002	Full-text	RCT	Orbera	Sham	20 (4 M/16F)	23 (3 M/20F)	41.4 (22–64) 41.4 ± 10.5	41.4 (22–64) 41.4 ± 10.5	Fluid filled 500 mL	13 weeks (3 months)

RCT randomized controlled trial, *TG* treatment group, *CG* control group, *w* weeks, *m* months, *N/A* not available, *M* male, *F* female, *mL* milliliters, *BMI* body mass index

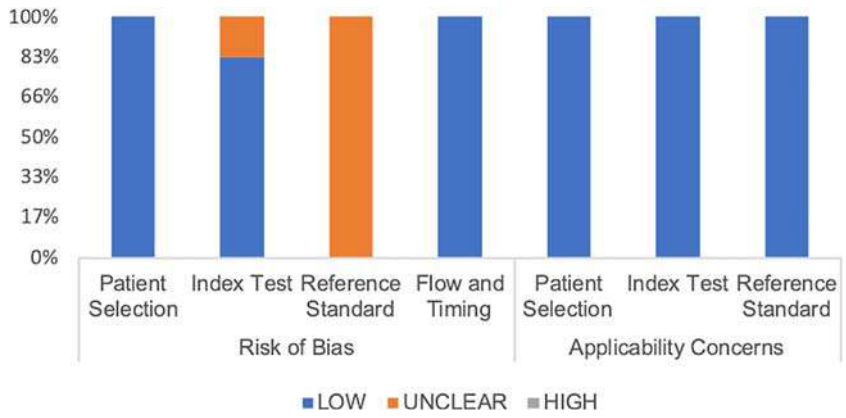

Fig. 2 The overall risk of bias for each study (RoB2)

other balloons (Obalon, Orbera, and ReShape Duo) also had favorable outcomes. The heterogeneity was 97.9% (test for subgroup differences: $Chi^2 = 139.70$, df = 3 ($P < 0.00001$), $I^2 = 97.9\%$).

This outcome has a very low certainty of the evidence (GRADE) (Annex 5).

Mean Difference in AWL Between IGB and Control Group

Seven studies [16, 18, 19, 22, 24–26] with a total of 1005 patients (552 in the IGB group and 453 in the control group) were included in the meta-analysis of AWL outcomes. The mean difference in AWL between the groups was 6.12 kg (95%CI, 3.80 to 8.44) $P < 0.00001$), significantly in favor of the IGB group (heterogeneity: $Tau^2 = 6.73$; $Chi^2 = 35.93$, df = 6 ($P < 0.00001$); $I^2 = 83\%$).

In subgroup analysis, this effect was predominantly determined by the Orbera balloon (7.88 [3.81, 11.95]), although other balloons (Obalon and ReShape Duo) also showed favorable outcomes (heterogeneity: test for subgroup differences: $Chi^2 = 4.58$, df = 2 ($P = 0.10$), $I^2 = 56.4\%$). The forest plot for this outcome is included in Supplementary Material (Annex 3).

This outcome has a very low certainty of the evidence (GRADE) (Annex 5).

Mean Difference in BMIL Between IGB and Control Group

Six studies [18, 19, 22, 27–29] with a total of 978 patients (483 in the IGB group and 495 in the sham/LI group) were included in the meta-analysis. The mean BMI loss difference between the groups was 2.13 (95%CI, 0.57to 3.68) $P < 0.00001$) in favor of IGB group (heterogeneity: $Tau^2 = 4.31$; $Chi^2 = 522.98$, df = 6 ($P < 0.00001$); $I^2 = 99\%$).

In subgroup analysis, this effect was predominantly determined by the Orbera balloon (2.49 [0.19, 4.80]) although other IGBs (Obalon, Heliosphere, and ReShape Duo) also showed favorable results (heterogeneity: test for subgroup differences: $Chi^2 = 21.45$, df = 3 ($P < 0.0001$), $I^2 = 86.0\%$). The forest plot for this outcome is included in Supplementary Material (Annex 4).

This outcome has a very low certainty of the evidence (GRADE) (Annex 5).

Discussion

IGBs are the most widely used EBMT. The balloon is an artificial bezoar that occupies space in the stomach, reducing food intake and inducing satiety, thus resulting in weight loss [30]. This restrictive method has the advantage of being reversible and not altering gastrointestinal anatomy. IGBs are primarily indicated for patients with BMI > 30 kg/m^2 in the USA or BMI > 27 kg/m^2 internationally who have failed lifestyle interventions. Besides weight loss, these devices induce a significant decrease in hepatic steatosis, insulin resistance, and improvement in other obesity-associated comorbidities [16, 31, 32].

Currently, there is no consensus on the proportion of weight loss that should be achieved with endoscopic therapies to incorporate them into clinical practice. However, ASGE and ASMBS joint task force recommended that the mean %EWL difference between a primary EBMT and control groups should be a minimum of 15% EWL and be statistically significant [33]. Our analysis revealed a %EWL mean difference between the IGB and control group of 17.98% in favor of the IGB group, indicating that IGB is appropriate to be incorporated into clinical practice. We also found a mean %TWL difference between the groups of 4.40% in favor of the IGB group. Similarly, the subgroup analysis also showed favorable results for all balloon types (Orbera, Obalon, ReShape, and Spatz). Secondary outcomes AWL and BMIL also indicated that the use of IGBs is significantly more effective than sham/ lifestyle interventions treatment. Our results are consistent with the largest reported case series, a Brazilian consensus based on practice of experts and scientific literature that comprised data of over 40,000 IGB cases reported by 37 endoscopists. A total of 78.2% of the devices were Orbera,

Table 3 Summary of outcomes at balloon removal of the studies included in the meta-analysis (mean ± standard deviation)

	Study	Initial BMI (TG)	Initial BMI (CG)	Final BMI (TG)	Final BMI (CG)	BMI loss (TG)	BMI loss (CG)	Initial weight (TG)	Initial weight (CG)
1	Abu Dayyeh 2019	30–40	30–40	N/A	N/A	N/A	N/A	N/A	N/A
2	Sullivan 2018	35.2 ± 2.7	35.5 ± 2.7	N/A	N/A	2.3 ± 1.8	1.2 ± 1.8	98.1 ± 13.2 kg	98.8 ± 11.9 kg
3	Vicente 2017	46.4 ± -6.9	46 46.4 + -6.9	40.0 ± 6.2	44.3 ± 5.5	N/A	N/A	129.2 ± 19.2	125.0 ± 18.5
4	Coffin 2017	53.9 ± 6.5	54.7 ± 10.3	N/A	N/A	2.8 ± 1.125	0.4 ± 0.475	148.3 ± 24.3	153.9 ± 36.2
5	Ponce 2015	35.3 ± 2.8	35.4 ± 2.6	N/A	N/A	2.7 ± 1.9	1.3 ± 2.3	94.89 ± 11.7	96.7 ± 11.56
6	Mohammed 2014	47.87 ± 1.080	47.46 ± 1.85	42.92 ± 4.2	46.25 ± 3.7	N/A	N/A	136.94 ± 7.97	137.80 ± 9.80
7	Mathus-Vliegen 2014	43.0 ± 5.5	43.2 ± 7.1	38.5 ± 4.9	39.4 ± 7.2	4.6 ± 1.9	3.7 ± 2.0	124.0 ± 21.1	122.5 ± 19.0
8	Ponce 2013	34.7 ± 2.6	35.6 ± 2.0	N/A	N/A	N/A	N/A	100.8 ± 11.6	96.9 ± 10.7
9	Lee 2012	30.3 ± 5.7	32.4 ± 9.1	28.7 ± 8.1	31.6 ± 9.5	1.69 ± 0.89	0.54 ± 0.54	N/A	N/A
10	Konopko-Zubrzycka 2009	47.3 ± 5.7	47.1 ± 6.9	N/A	N/A	N/A	N/A	138.5 ± 26.2	138.9 ± 18.2
11	Martinez-Brocca 2007	50.2 ± 9.6	51.3 ± 6.1	45.7 ± 9.7	48.2 ± 7.8	N/A	N/A	143.8 ± 31.2	138.8 ± 24.5
12	Genco 2006	43.9 ± 1.1	43.6 ± 1.8	38.0 ± 2.6	43.1 ± 2.8	5.8 ± 0.5	0.4 ± 0.2	N/A	N/A
13	Mathus-Vliegen 2002	43.0 ± 1.26	43.6 ± 1.58	38.4 ± 1.12	39.8 ± 1.52	N/A	N/A	124.0 ± 4.83	125.9 ± 4.72

	Final weight (TG)	Final weight (CG)	Absolute weight loss (TG)	Absolute weight loss (CG)	%EWL (TG)	%EWL (CG)	%TWL (TG)	%TWL (CG)
1	N/A	N/A	N/A	N/A	N/A	N/A	14.9 ± 7.2	3.6 ± 5.8
2	N/A	N/A	6.6 ± 5.3	3.3 ± 5.1	23.9 ± 19.2	12.4 ± 18.8	6.6 ± 5.1	3.4 ± 5.0
3	112.8 ± 26.4	121.3 ± 20.5	16.2 ± 9.8	4.7 ± 8.7	N/A	N/A	N/A	N/A
4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
5	N/A	N/A	7.21 ± 5.39	3.53 ± 6.39	25.1 ± 1.6%	11.3 ± 1.9	7.6 ± 5.5	3.6 ± 6.3
6	122.65 ± 12.6	131.41 ± 8.54	14.33 ± 11.37	6.40 ± 5.87	21.5 ± 16.75%	4.2 ± 21.5%	N/A	N/A
7	111.0 ± 20.2	111.9 ± 19.8	13.1 ± 5.2	10.6 ± 5.8	N/A	N/A	10.6 ± 3.8	8.8 ± 4.9
8	N/A	N/A	N/A	N/A	31.8 ± 21.3	18.3 ± 20.9	N/A	N/A
9	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
10	N/A	N/A	17.1 ± 8	3.5 ± 6.4	N/A	N/A	12.3%	2.3%
11	131.1 ± 32.6	129.9 ± 25.6	2.7 ± 5.6	8.9 ± 9.2	N/A	N/A	N/A	N/A
12	N/A	N/A	N/A	N/A	34.0 ± 4.8	2.1 ± 1	N/A	N/A
13	111.0 ± 4.63	114.7 ± 4.54	N/A	N/A	N/A	N/A	10.59 ± 0.88	8.98 ± 0.99

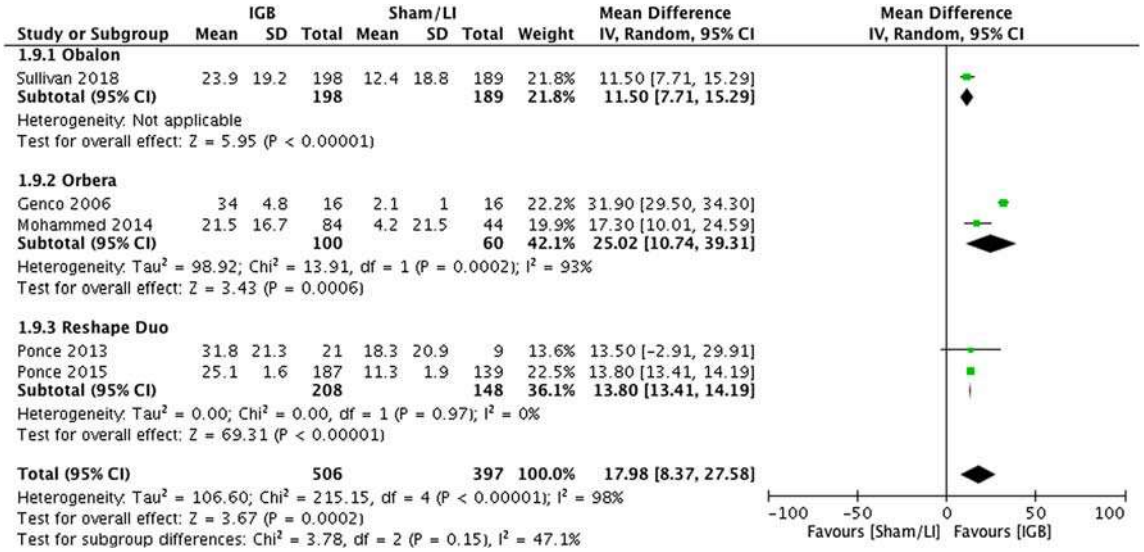

Fig. 3 Forest plot of studies reporting %EWL using a random-effect model and inversed variance method. CI, confidence interval; SD, standard deviation; IGB, intragastric balloon; LI, lifestyle intervention

2.5% were Heliosphere Bag, 2.4% were Spatz, and 16.9% were other similar balloons (Medicone Corporea and Silimed) [34].

In 2016, Moura et al. [35] published a meta-analysis, including 9 RCTs that demonstrated IGB was effective in reducing weight and BMI. In our analysis, we included 13 studies and excluded trials with insufficient data to perform meta-analysis and trials with obsolete devices. The previous review only included a single fluid-filled balloon and air-filled balloon. Our analysis, in addition, also included swallowable and adjustable IGBs. Another systematic review by Saber et al. [36] based on 20 RCTs comparing IGB (including devices no longer used) with a sham procedure, behavioral modifications, and pharmacotherapy also showed that the IGB was superior weight loss therapy. In our study, we excluded trials with IGBs no longer available in the market (Ballobes, Garren-Edwards) and studies that included pharmacological therapy in an attempt to assess the efficacy of commercially available IGBs accurately. Nonetheless, our results were similar and favored IGB for the treatment of weight loss. In

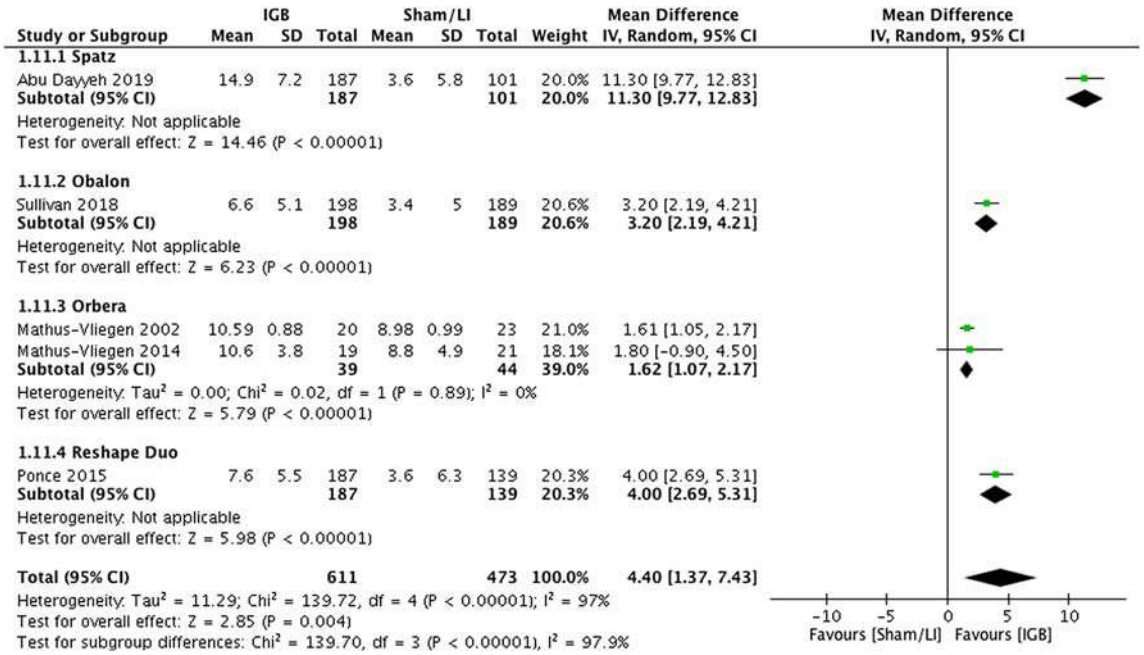

Fig. 4 Forest plot of studies reporting %TWL using a random-effect model and inversed variance method. CI, confidence interval; SD, standard deviation; IGB, intragastric balloon; LI, lifestyle interve

another systematic review, including 10 randomized controlled trials (RCT) and 30 observational studies, Popov et al. [37] found that IGBs are more effective than diet in improving obesity-related metabolic comorbidities. Recently a network meta-analysis [38] including 15 RCTs comparing IGBs with a sham procedure, behavioral modifications, and another IGB-type found that fluid-filled IGBs were superior to gas-filled IGBs or lifestyle intervention. Our study excluded RCTs comparing IGB versus another IGB and only included studies with sham or LI control groups.

When analyzing each type of IGB, it is notable that the ORBERA® Intragastric Balloon System (Apollo Endosurgery Inc., Austin, Texas, USA) [39] is the most widely used and studied IGB. It is a single spherical IGB made of silicone and filled with 400 to 600 mL of saline solution. It is inserted and removed endoscopically and typically remains in the stomach for 6 months. Our results revealed favorable weight-loss outcomes with statistical significance for Orbera IGB. Analysis of patients that received Orbera showed a mean difference in AWL of 7.88 kg, BMIL of 2.49 kg/m^2, %EWL of 25.02%, and %TWL of 1.62% over the control group.

The Heliosphere Bag®, (Helioscopie, Vienne, France) [40] is a single spherical air-filled IGB made of polyurethane and silicone that weighs less than 30 g. The volume of the IGB is 550 mL. It is inserted and removed endoscopically and has an implantation duration of 6 months. This IGB is better tolerated, but disadvantages include difficulty in implantation of the IGB through gastric cardia, and lack of methylene blue makes the diagnosis of IGB deflation difficult, thus increasing the risk of intestinal obstruction [40, 41]. Our results with the Heliosphere were favorable with statistical significance for the studied outcome (mean difference in BMIL of 2.40 kg/m^2 over the control group).

The ReShape Integrated Dual Balloon System ™ (ReShape Medical Inc., San Clemente, CA, USA) [19] has two fluid-filled IGBs made of silicone with a total capacity of 900 mL (450 mL each). It is inserted and removed endoscopically and has an implantation duration of 6 months. The main advantage of the ReShape Integrated Dual Balloon System™ is that if one IGB ruptures, the second will keep the IGB in the stomach and allow the patient to return to the endoscopist for device removal, avoiding small bowel obstruction [20]. Our results showed favorable weight-loss outcomes with statistical significance for ReShape balloon. Patients that received this IGB had a pooled mean difference in AWL of 3.68 kg, in BMIL of 1.40 kg/m^2, in %EWL of 13.80%, and a %TWL of 4.00% over the control group. In 2018, Apollo Endosurgery purchased the ReShape Balloon and discontinued selling this product to focus exclusively on the Orbera.

The Obalon Balloon System™ (Obalon Therapeutics Inc., Carlsbad, CA, USA) [18] is a gelatin capsule device that is swallowed with a catheter and insufflated with 250 cm of nitrogen-sulfur hexafluoride gas after fluoroscopic confirmation of placement. Up to three IGBs can be placed, and all IGBs are removed endoscopically after 6 months of insertion of the first IGB. It has the advantage of implantation without an endoscopy; however, endoscopy is required for removal. Our results for Obalon were favorable, and patients that received this IGB had a pooled mean difference in AWL of 3.30 kg, in BMIL of 1.10 kg/m^2, in %EWL of 11.50%, and a %TWL of 3.20% over the control group.

The Spatz3™ Adjustable Balloon System (Spatz Medical, Great Neck, NY, USA) [42] is a single silicone spherical IGB with a catheter that allows adjustments. It is inserted endoscopically and filled with 400 to 700 ml of saline. The volume can be adjusted downward to improve tolerability or upward in an attempt to improve weight loss. It has an implantation duration of up to 12 months and is removed endoscopically. Our results showed favorable weight-loss outcomes with statistical significance for the Spatz3 (mean difference in %TWL of 11.30% over the control group). The better results of this IGB may be related to its volume readjustment capability allowing the maintenance of weight loss and keeping the patient close to the follow-up program. A recently described technique to modify a conventional non-adjustable IGB into an adjustable IGB may be an alternative in cases where the Spatz adjustable balloon is not available [43].

A new procedure-less IGB, Elipse balloon ™ (Allurion Technologies, Wellesley, MA, USA) [44], is now available. It is a single spherical polymer film IGB filled with 450 to 550 ml of proprietary fluid, consisting of distilled water and food preservative potassium sorbate and citric acid. This IGB is swallowable, degradable, and excretes naturally after 4 months and, therefore, does not require sedation and invasive procedures for placement and removal. Thus, complications associated with endoscopic IGB removals such as laceration, esophageal perforation, and aspiration pneumonia are avoided [44]. The disadvantage is that it lasts only up to 4 months, and its safety profile concerning small obstruction is still unclear. This IGB was not included in this analysis because there are no randomized controlled trials yet.

The safety profile of IGB is well established. A systematic review [45] evaluated adverse events related to the use of IGB. The most common adverse event was nausea and vomiting (23.3%) and abdominal pain (19.9%), followed by gastroesophageal reflux (14.3%), diarrhea or constipation (10.4%), and gastric stasis (8.3%). Early removal occurred in 3.5% and was mostly related to abdominal pain and nausea and vomiting. The mortality rate was 0.05%.

We performed a rigorous analysis adhering to the PRISMA statement and selected RCTs with good methodological quality. We did not include studies using obsolete devices. However, our study has some limitations. The majority of RCTs were performed using one fluid-filled IGB. There was significant heterogeneity between studies that can be explained by the following reasons: firstly, the BMI range in the included studies was wide;

secondly, the duration of follow up after device implantation varied between 3 months and 8 months. We did include an abstract in our analysis. However, the abstract showed the required data, including mean and standard deviation, and thus met the inclusion criteria. Another limitation of this study is that long-term efficacy after IGB withdrawal cannot be assessed due to a lack of follow-up data.

In conclusion, our meta-analysis of RCTs shows that IGB therapy is more effective than lifestyle intervention alone for weight loss in overweight and obese adults. An intragastric balloon is a valuable option beyond lifestyle modifications for the treatment of obesity.

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Compliance with Ethical Standards

Conflict of Interest Dr. Moura reports personal fees from Boston Scientific, personal fees from Olympus, outside the submitted work. All other authors declare that they have no conflict of interest.

Ethical Statement This study was approved by the ethics committee of Hospital das Clínicas, Faculty of Medicine, University of São Paulo.

Consent Statement As this study is a systematic review with meta-analysis, the informed consent does not apply.

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