

Intragastric balloon for weight loss: results in 100 individuals followed for at least 2.5 years

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Background and study aims: To determine long-term outcome after treatment with an intragastric balloon for 6 months, with no structured weight maintenance program offered after balloon removal.

Patients and methods: 100 consecutive overweight/obese individuals (mean body mass index [BMI] 35.0 ± 5.6 kg/m²) were prospectively followed after endoscopic implantation of a saline-filled intragastric balloon; 97 completed final follow-up at a mean of 4.8 ± 1.6 years. Successful intragastric balloon therapy was defined as weight loss at 6 months of $\geq 10\%$ of weight at baseline, that remained $\geq 10\%$ until 2.5 years, without bariatric surgery. All analyses followed intention-to-treat principles.

Results: At 6 months, mean weight loss was 12.6 ± 8.3 kg, 63 individuals had $\geq 10\%$ baseline weight loss; no severe morbidity was detected. During

the first and second years following intragastric balloon removal, mean body mass increased by 4.2 ± 6.8 and 2.3 ± 6.0 kg, respectively ($P < 0.001$ for both year-on-year comparisons). At 2.5 years, intragastric balloon therapy had been successful in 24 participants. At final follow-up (4.8 ± 1.6 years), 28 had $\geq 10\%$ baseline weight loss, 35 had undergone bariatric surgery (60% had preoperative mass higher than baseline), and 3 were lost to follow-up; the 34 remaining had lost 1.5 ± 5.8 kg compared with baseline. During follow-up, 13 had a second intragastric balloon implanted and 13 took sibutramine for short periods.

Conclusion: Intragastric balloon therapy was relatively innocuous and associated with successful weight loss and maintenance at 2.5 years in a quarter of participants. It represents a valid option for weight loss.

Introduction

According to current guidelines [1,2] weight loss efforts in overweight and obese individuals should include an initial 6-month period of weight loss followed by a second phase of weight maintenance, which is usually assessed over 24 months. The goal of the weight loss phase is to reduce body weight by approximately 10% from baseline because this is associated with the prevention and improvement of obesity-related comorbidities and may be sustained. For this purpose, the National Institutes of Health (NIH) recommends low-calorie diets, physical activity, behavior therapy, pharmacotherapy (for those with a body mass index [BMI] ≥ 30 kg/m², or ≥ 27 kg/m² if obesity-related risk factors or diseases are present), and bariatric surgery (in carefully selected individuals with clinically severe obesity). Another option, the intragastric balloon, has received more attention since the publication of these recommendations because an intragas-

tric balloon model devoid of most of the shortcomings present in original models has been made available [3].

Randomized sham-controlled trials have shown that the current, liquid-filled, intragastric balloon model decreases preprandial hunger, increases postprandial satiety, and promotes weight loss in the short term [4–6]. Additionally, the intragastric balloon is thought to help individuals to modify their eating habits by providing a self-education tool [7]. However, results after more than 1 year following intragastric balloon extraction have not been reported to date.

We have prospectively followed a cohort of individuals treated with the intragastric balloon to induce weight loss but having no structured weight maintenance program offered after the weight-loss phase. The aim of this study is to describe the results in 100 consecutive individuals with a minimum follow-up of 2.5 years after intragastric balloon implantation.

Materials and methods

Patients

Consecutive individuals who were screened at endoscopy for intragastric balloon implantation between June 25 1999 and June 21 2005 at the Erasme University Hospital were included, after exclusion of eight participants who received intragastric balloon therapy to facilitate bariatric surgery [8]. All individuals had experienced failed previous attempts to lose weight; these included dietary guidance from a dietician ($n = 97$); a structured commercial weight-loss program that included a food plan, a physical activity plan, and a behavior-modification plan ($n = 56$) [9]; and pharmacotherapy (sibutramine, $n = 20$; orlistat, $n = 3$). All of them had pre-screening independent evaluation by a gastroenterologist and a dietician (plus a bariatric surgeon and a psychologist if appropriate) [1,2]. As previously reported [10], inclusion criteria were mainly based on the BMI and on associated co-morbidities (they did not take into account the eating pattern); exclusion criteria were strictly observed except that a history of appendectomy or of laparoscopic cholecystectomy was not considered to be a contraindication. Overweight individuals were included if they had co-morbidities likely to improve with weight loss ($n = 9$) or a BMI in excess of 29.0 kg/m^2 at the time of evaluation and $\geq 30.0 \text{ kg/m}^2$ during the preceding year ($n = 6$).

Data collected prospectively included baseline body height, weight and co-morbidities, duration of intragastric balloon therapy, number of visits with the dietician, details of endoscopic procedures, durations of hospital stays, potential complications and body weights at 6, 18 and 30 months after intragastric balloon implantation as well as at intragastric balloon extraction and in November 2007 – January 2008.

The study was approved by the institutional ethics committee. This was an investigator-initiated study with no industry involvement in any part of the study.

Interventions

Only Bioenterics intragastric balloons (Allergan, Irvine, California, USA) were implanted during the study period. Placement was performed as previously described [6] with patients under sedation ($n = 80$) or general anesthesia ($n = 20$), immediately after upper gastrointestinal endoscopy if this revealed no contraindication (e.g., potentially bleeding lesion, large hiatal hernia). The balloon was inflated with 500–650 ml saline mixed with 10 ml methylene blue.

Patients were instructed: (i) to expect nausea, vomiting, and abdominal cramps during the following 72 hours (to be treated with hyoscine-N-butylbromide, lorazepam, and paracetamol, preferably via the rectal or sublingual route); (ii) to follow a reliable (nonoral) contraceptive method; (iii) to take a liquid diet for 72 hours, including protein-rich drinks (e.g., Clinutren; Nestlé, Vevey, Switzerland) and, starting at day 4, to progressively follow a personalized balanced-deficit diet of 1000 kcal per day less than their usual intake, with approximately 15% of energy derived from proteins, 30% or less from fats, and the remainder from carbohydrates; and (iv) to present for a visit with the gastroenterologist and the dietician 2 weeks later. All individuals were encouraged to see the dietician at least once a month. During visits with the gastroenterologist and the dietician, individuals were encouraged to set realistic goals, to record their food intake, to drink no or little alcohol, to choose high-fiber food, to have moderate-intensity exercise ≥ 30 min daily, and to weigh themselves weekly. Between visits, participants were contacted by phone calls

from the dietician. No weight-loss medication was allowed during intragastric balloon therapy.

Potential complications were recorded after clinical examination 2 weeks after intragastric balloon implantation as well as during scheduled or unscheduled follow-up visits.

Participants had a visit with the gastroenterologist about 2 weeks before the intragastric balloon extraction that was scheduled for 6 months after implantation. The extraction was performed at endoscopy under sedation ($n = 86$) or general anesthesia ($n = 13$), using a specifically designed retrieval kit (Allergan, Hoeilaart, Belgium), and was immediately followed by upper gastrointestinal endoscopy to detect potential lesions in all cases. In six individuals, the intragastric balloon was exchanged with a new one during this procedure; this was done because of spontaneous intragastric balloon deflation ($n = 1$, with total duration of intragastric balloon treatment of 6 months in this patient), or to prolong intragastric balloon therapy ($n = 5$) beyond the 6-month period recommended by the manufacturer.

No structured weight maintenance program was proposed after intragastric balloon extraction, but participants were strongly recommended to attend monthly visits with the dietician for 6 months.

Definitions and study end points

The definition of successful intragastric balloon therapy was derived from US NIH guidelines [2], and consisted of weight loss at 6 months of $\geq 10\%$ of weight at baseline, maintained without bariatric surgery during the subsequent 2 years. Ideal body weight was calculated according to the Lorentz equation [11]. Full-course therapy was defined as the presence of the balloon in the stomach for ≥ 4 months, and complications were assessed according to international definitions [12].

Durations of hospital stays between the day of intragastric balloon implantation until that of hospital discharge after intragastric balloon extraction were calculated (including hospitalizations for complications), and weights at yearly intervals between 2.5 years and the end of follow-up were obtained by extrapolation. The “whole study population” refers to the 100 patients included in the study. For individuals who were lost to follow-up or who underwent bariatric surgery, the last observation (at the time of operation in case of bariatric surgery) was carried forward up to the end of follow-up (“last observation carried forward”, or LOCF analysis).

The primary end point was the proportion of participants in whom intragastric balloon therapy was successful. Secondary end points included: the changes in weight and the performance of weight-directed therapies throughout the follow-up; comparison of weight losses at 6 months and 2.5 years between BMI categories; morbidity; and assessment of factors associated with $\geq 10\%$ baseline weight loss at 6 months and with successful intragastric balloon therapy.

Statistical analysis

All analyses were carried out on an intention-to-treat basis including all 100 patients. Continuous variables were described by their means \pm SD (or by their medians with interquartile range [IQR] if they were found to be non-normally distributed after Shapiro–Wilk normality test using a P value < 0.05); for graphical representations, they were presented as means \pm SE. Comparisons of categorical data were done using Fisher’s exact test. Comparisons of body weight in the same participants at different time points were done using the paired t test, and weight loss compar-

isons between participant groups were done using the Kruskal–Wallis test (the Tukey–Kramer honestly significant difference [HSD] test was used to describe significant differences between specific participant groups). In a Kaplan–Meier analysis of bariatric surgery during follow-up, patients who died or were lost to follow-up without bariatric surgery were censored at the time of last contact.

We also examined which of the following factors were associated with $\geq 10\%$ baseline weight loss at 6 months and with successful intragastric balloon therapy: age, sex, baseline BMI, intragastric balloon fill volume, number of visits with the dietician, complete vs. incomplete intragastric balloon therapy, weight loss at 3 months, moderate-intensity exercise ≥ 30 minutes daily, and intake of a fiber-enriched, fat-restricted diet during intragastric balloon therapy. The analysis for successful intragastric balloon therapy included the factors cited above plus weight loss at 3 and 6 months, maintenance of a fiber-enriched, fat-restricted, diet during follow-up, and repeat intragastric balloon implantation, as well as intake of weight-loss drugs during follow-up. All tests were two-sided; P values < 0.05 were considered statistically significant. Analyses were performed using JMP software (version 5.1.2, SAS, Cary, North Carolina, USA).

Results

Participants' baseline characteristics are presented in **Table 1**. A total of 86 individuals completed a full-course therapy; in the remaining 14, intragastric balloon extraction was performed after a median of 32 days (IQR 8–84), mostly on account of digestive intolerance or participants' perception of insufficient effects on satiety (**Fig. 1**).

At 6 months after intragastric balloon implantation, mean weight loss in the 100 participants was 12.6 ± 8.3 kg ($P < 0.001$ compared with baseline), corresponding to $38.3\% \pm 26.9\%$ of excess weight, and they had attended 4.9 ± 2.8 visits with the dietician. Endoscopic intragastric balloon extraction was successful in all of 99 attempted cases (one intragastric balloon had been spontaneously eliminated), at a mean of 5.9 ± 2.4 months. Total hospital stay duration was 1.3 ± 1.1 days.

Primary end point (2.5-year analysis)

Intragastric balloon therapy was successful in 24 individuals: among 63 who had achieved weight loss of $\geq 10\%$ baseline value at 6 months, 24 (38%) maintained their weight below this threshold during the 2 following years (36 during the first year only), 29 regained weight above this threshold, 9 underwent bariatric surgery, and 1 was lost to follow-up because of moving from the area.

In the whole population, mean weight loss from intragastric balloon implantation to 2.5 years was 5.8 ± 9.6 kg (LOCF analysis; $P < 0.001$), corresponding to $16.3\% \pm 30.5\%$ excess weight. No significant difference in absolute weight loss was found between individuals from different baseline BMI categories (**Fig. 2**).

Secondary end points

Final visit. At 58.1 ± 19.5 months after intragastric balloon implantation, mean weight loss in the whole population was 4.6 ± 11.8 kg (LOCF analysis; $P < 0.001$), corresponding to $12.6 \pm 37.8\%$ excess weight. Three individuals were lost (moving away from area, $n = 2$; death from decompensated heart failure 5 years after intragastric balloon implantation, $n = 1$), 35 had un-

Table 1 Participants' baseline characteristics ($n = 100$).

Age, mean \pm SD, years	39.2 \pm 11.2
Female sex, n	86
Body weight, mean \pm SD, kg	96.5 \pm 18.8
BMI, mean \pm SD, kg/m ²	35.0 \pm 5.6
Excess weight, mean \pm SD, kg	36.9 \pm 16.5
BMI category, n	
28.0–29.9	15
30.0–34.9	43
35.0–39.9	28
≥ 40.0	14
Comorbidities, n	
Dyslipidemia	24
Arterial hypertension	15
Osteoarthropathy	11
Diabetes mellitus	9
Sleep apnea	5
Nonalcoholic steatohepatitis	2

SD, standard deviation; BMI, body mass index.

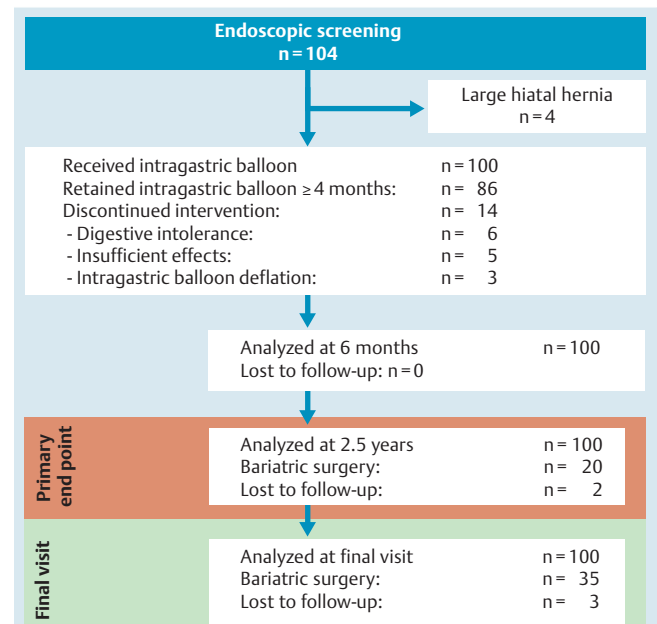


Fig. 1 CONSORT flowchart showing the participants' course during the study. For participants who underwent bariatric surgery or were lost to follow-up, the last observation (at the time of operation in the case of bariatric surgery) was carried forward up to the end of follow-up ("last observation carried forward", LOCF analysis).

dergone bariatric surgery, and the remaining 62 had a mean weight loss of 8.7 ± 10.2 kg (28 of them with $\geq 10\%$ baseline weight loss).

LOCF analysis of the whole study population showed that weight regain was statistically significant during the first and second years following intragastric balloon extraction (4.7 ± 6.8 kg and 2.3 ± 6.0 kg, respectively; $P < 0.001$ for both year-on-year comparisons) (**Fig. 3**).

Weight-directed therapies during follow-up. After intragastric balloon extraction, participants followed no structured weight maintenance program; they attended 1.1 ± 0.3 visits with a dietician, and 13 of them took sibutramine for intermittent, ≤ 2 -month, periods. A second intragastric balloon was implanted in 13 individuals (excluding one intragastric balloon exchange for spontaneous intragastric balloon deflation), and repeat intragas-

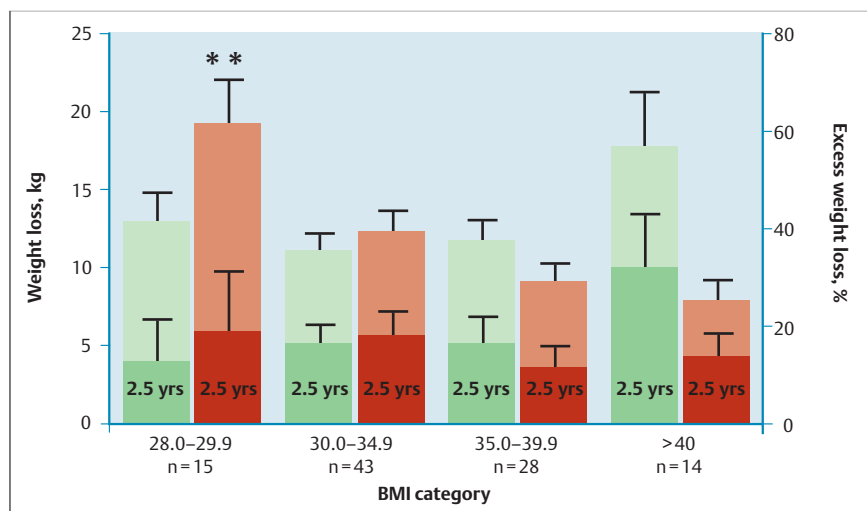


Fig. 2 Weight loss (mean \pm SE) at 6 months and 2.5 years (top and bottom bars, respectively), according to body mass index (BMI) categories. For each BMI category, left and right bars indicate absolute and relative weight loss, referring to left and right y axis, respectively. ** $P < 0.001$ for comparison with all other BMI categories (Tukey–Kramer test).

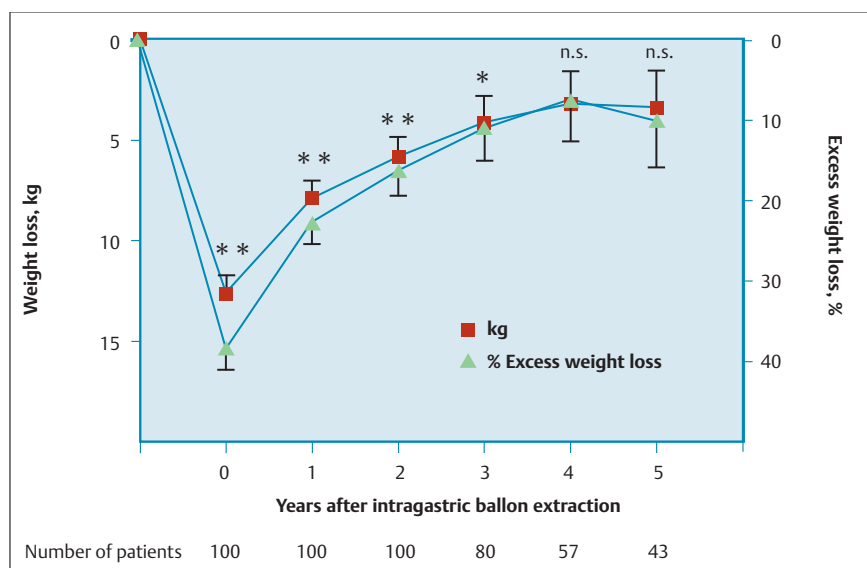


Fig. 3 Weight loss (mean \pm SE) from baseline, absolute and relative, left and right y axis, respectively. Comparison with baseline body weight: * $P < 0.005$; ** $P < 0.001$; n.s., not significant.

tric balloon therapy was associated with a median weight loss of 10.0 (IQR 2.8–13.0) kg.

Bariatric surgery was performed in 35 individuals. At the time of surgery (23.5 ± 16.2 months after intragastric balloon extraction), mean weight regain was 14.3 ± 9.4 kg and 21 of these participants (60%) had a weight greater than baseline. Kaplan–Meier estimates indicate that the rates of bariatric surgery steadily increased from 9.2% at 1 year after intragastric balloon extraction to 46.8% at 6 years (► Fig. 4), without significant difference between baseline BMI categories (log-rank test, $P = 0.603$). Among these participants, 11 had a preoperative BMI between 30.0 and 34.9 kg/m²; this definitely did not meet standard BMI criteria for bariatric surgery and these individuals underwent operation outside of our institution.

Parameters associated with $\geq 10\%$ baseline weight loss at 6 months and successful intragastric balloon therapy. The weight loss at 3 months, diet, and full-course (≥ 4 months) intragastric balloon therapy were the single factors that were independently associated with $\geq 10\%$ baseline weight loss, at 6 months. Performance of moderate-intensity exercise ≥ 30 minutes daily and the intragastric balloon fill volume were associated with $\geq 10\%$ baseline weight loss at 6 months, but these associations became weaker ($P = 0.104$ and $P = 0.751$, respectively) after inclusion of

the diet, initial weight loss, and full-course intragastric balloon therapy in the stepwise analysis (► Table 2).

Maintenance of a fiber-enriched, fat restricted, diet during follow-up and weight loss at 6 months were independently associated with successful intragastric balloon therapy at 2.5 years. The association with weight loss at 3 months became not significant after inclusion of weight loss at 6 months in the stepwise analysis (► Table 3).

Complications

Complications were observed in 12 individuals and were graded as minimal ($n = 9$) or mild ($n = 3$) [12]. These consisted of abdominal pain, nausea and vomiting (digestive intolerance, $n = 7$), spontaneous intragastric balloon deflation ($n = 4$), and mild acute pancreatitis ($n = 1$). All complications resolved with analgesic/antiemetic drugs alone ($n = 1$) or intragastric balloon elimination (through vomiting [$n = 1$] or endoscopic extraction [$n = 10$]), associated with intravenous KCl administration ($n = 1$) or intragastric balloon replacement ($n = 1$) in two individuals. Additionally, unexpected pregnancy led to the extraction of one intragastric balloon at 4.2 months after implantation (infant normal at birth).

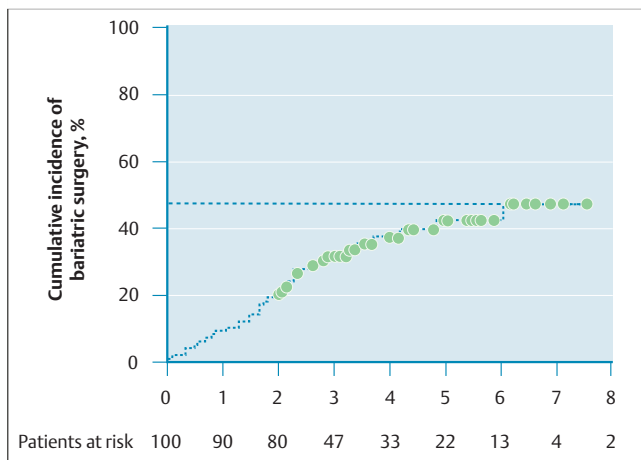


Fig. 4 Kaplan–Meier cumulative-event curve of bariatric surgery. Circles indicate censored cases.

Table 2 Logistic regression analysis of variables associated with weight loss $\geq 10\%$ baseline weight, at 6 months.

Variable	P value
Weight loss at 3 months	< 0.001
Fiber-enriched, fat-restricted, diet	< 0.001
Full-course intragastric balloon therapy	< 0.001
Moderate-intensity exercise ≥ 30 min daily	0.014
Intragastric balloon fill volume	0.031
Number of visits with the dietician	0.064
Age	0.651
Baseline BMI	0.854
Gender	0.964

Table 3 Logistic regression analysis of variables associated with successful intragastric balloon therapy.

Variable	P value
Maintenance of a fiber-enriched, fat-restricted, diet during follow-up	< 0.001
Weight loss at 6 months	< 0.001
Weight loss at 3 months	0.002
Age	0.067
Full-course intragastric balloon therapy	0.101
Gender	0.128
Baseline BMI	0.367
Repeat intragastric balloon implantation during follow-up	0.593
Intake of weight-loss drugs during follow-up	0.723

The incidence of abnormal endoscopic findings after intragastric balloon extraction (mostly esophagitis) was not different between participants who did or did not have digestive intolerance (1/7 vs. 15/92; $P = 1$).

Discussion

We found that, after temporary intragastric balloon implantation in overweight or obese individuals, a weight loss that was $\geq 10\%$ of weight at baseline and sustained at 2.5 years was achieved in 24% of participants. Given the ease and reproducibility of the method, these results are encouraging because they are at least

equivalent to those reported with therapies recommended for weight loss or maintenance [1,2]. In particular, dietetic counseling or behavioral therapy allows 15%–30% of obese individuals to achieve $\geq 10\%$ baseline weight loss at 1 year [13–15], compared with 63% at 6 months and 36% at 18 months in the present series. Also in intention-to-treat analysis, maintenance of 10% weight loss for 18 months (after successful weight loss) is achieved by fewer than 30% of individuals assigned to sibutramine [16], compared with 57% at 1 year and 38% at 2 years in the present series.

Our short-term results were similar to those previously reported with the Bioenterics intragastric balloon with, at 6 months, a mean weight loss of 12.6 kg (12.0–15.2 kg in four large series) [8,17–19], and a $\geq 10\%$ baseline weight loss in 63% of participants [6]. Short-term weight loss might have been higher with more frequent encounters with the dietician (eg, weekly rather than monthly scheduled visits) as, in dietary-based lifestyle-modification programs, more frequent scheduled support meetings are an independent predictor of greater weight loss [20]. However, this remains to be demonstrated in the setting of intragastric balloon therapy and, in our patients, the association between the actual number of visits and weight loss at 6 months was not statistically significant.

Mean weight regain during the year following intragastric balloon extraction was 37%, compared with 28%–40% in previous reports [6,17], but we found that, during longer follow-up, participants continued to significantly regain weight and that 4 years after intragastric balloon extraction, mean weights were similar to baseline. We believe that the low frequency of meetings with the dietician after intragastric balloon extraction had little impact on our final results because a recent meta-analysis has found that, during the maintenance phase in dietary-based lifestyle-modification programs, the frequency of dietary counseling meetings was not predictive of weight change [20]. More recently, weight maintenance interventions with emphasis on daily self-weighing and access to an interactive website have been shown to yield significantly better results than control interventions [21,22]. Although the clinical significance of these results is questionable (the mean difference between intervention and control groups was 1.5 kg at 30 months), these techniques seem promising because they are more rewarding in a fraction of the participants than suggested by mean weight changes and they have the potential to be widely disseminated at a low cost. In our patients, we estimated that the cost-benefit ratio of maintenance programs was too high, particularly because $> 90\%$ of them had no diabetes [23].

During follow-up, the surgical option was chosen by an increasing proportion of participants (from 9% at 1 year after intragastric balloon extraction to $> 40\%$ after 5 years). Melissas et al. also reported a high surgery rate during follow-up after intragastric balloon extraction (32% at 18 months) even though all of their patients had refused bariatric surgery at the time of intragastric balloon insertion [24]. Intragastric balloon therapy was reported to “smooth the path to bariatric surgery” and surgery was finally chosen by a majority, 64%, of patients who had experienced initial weight loss followed by weight regain, compared with 33% of those patients who had not experienced a significant weight loss with the intragastric balloon and with 7% of those with successfully maintained weight loss. In our experience also, the choice of bariatric surgery was facilitated by intragastric balloon therapy for some individuals who were initially averse to surgery but who experienced temporary weight loss and the associated ben-

efits (the “scale up” process) [25]. At the time of operation, weight was greater than baseline in a majority of cases (although in some patients who underwent operation outside of our institution it remained lower than required according to standard BMI criteria).

The relatively high likelihood of bariatric surgery at distant follow-up in our series clearly underlines the necessity to improve results, including beyond the usual 2-year timeframe [26]. We think that possible avenues may include, in the short term, individual tailoring of the intragastric balloon fill volume, as intragastric balloon therapy ≤ 4 months was an independent predictor of short-term treatment failure, and early intragastric balloon extraction was related to gastric distension perceived as too severe or too mild by the patients in most cases [6,8,17,18,27], and, in the long term, combination with other therapies such as sibutramine [28]. The major problem with weight-loss drugs is the extremely high attrition rate ($>90\%$ in common clinical practice) [29,30].

The uncontrolled design of our study represents its major limitation. Steps taken to limit potential biases comprised the inclusion of consecutive individuals, a high (98%) retention rate, and the use of standard criteria to interpret results. We believe that this, together with the absence of exclusion criteria (except intragastric balloon placement intended to facilitate bariatric surgery, which could not be avoided), helped us to give a meaningful representation of intragastric balloon therapy in real life, which may be more difficult within the constraints of randomized controlled trials [31–33]. Recourse to nonsurgical weight loss therapies during follow-up was not “prohibited” (this is impossible), but this had little influence on the final results as mean weight loss was similar in patients who had or had not received treatment with a second intragastric balloon and/or sibutramine; this was true both at 2.5 years (5.9 ± 10.0 kg vs. 5.8 ± 9.6 kg) and at the final visit (5.0 ± 12.3 kg vs 4.6 ± 11.8 kg).

In conclusion, although the interpretation of these results is limited by the uncontrolled design of our study, intragastric balloon therapy is a significant addition to the different options available for weight loss. However, modifications are needed to improve both short- and long-term results, as testified by the relatively high likelihood of bariatric surgery during distant follow-up. In a significant proportion of patients, intragastric balloon therapy served as a bridge to bariatric surgery.

Competing interests: None

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