

Endoluminal Bariatric Interventions : Where do we stand ? Where are we going ?

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Abstract

Background : Obesity is an epidemic leading to high morbidity, mortality, and therefore health-related costs. Thus, there is a huge need for development of safe and effective treatments. Even though success rates of conservative methods are highly limited, the surgical approaches lead to major complications in as many as 25% of the patients. In this study, we aimed to review the currently available, less-invasive, endoscopic bariatric techniques which provides an option to reduce the risks of the patients and the medical costs.

Methods : A systematic literature review through Pubmed and Medline was performed to find the studies on this topic, and all controlled clinical trials, case reports, and case series were reviewed.

Results : Endoluminal bariatric interventions include restrictive, malabsorptive approaches, and other techniques including transpyloric shuttle, botulinum toxin, gastric pacing and vagal nerve stimulation. Restrictive procedures act by limiting the gastric volume and leading to early satiety, while malabsorptive procedures create a malabsorption state. Transpyloric shuttle is a device decreasing the rate of gastric emptying. Botox injection causes a delay in gastric emptying, and vagal nerve stimulation modulates eating behavior.

Conclusion : Endoluminal bariatric techniques can become the primary choice of therapy in the near future for bariatric care. (*Acta gastroenterol. belg.*, 2015, 78, 415-423).

Key words : bariatric, endoluminal, endoscopic, obesity, surgery.

Introduction

Obesity is a complex disease associated with metabolic, gastrointestinal and cardiovascular disorders. It has been a pandemic leading to high morbidity, mortality, and therefore health-related costs. Hence, there is an increasing demand for safe and effective treatments.

While the success of conservative methods is highly limited, the surgical approaches lead to major complications in as many as 25% of the patients. Recently, the need of less invasive, safer, reversible and cost effective interventions such as endoscopic procedures has been addressed. Endoscopic techniques may be used as stand-alone procedures for weight loss or as an adjunct to surgery or for revision after bariatric surgery. A less invasive surgical technique, Natural Orifice Transluminal Endoscopic Surgery (NOTES), was introduced and started to be used in obesity, however the difficulty of the technique and complications after procedure remains as a challenge (1-4). Less invasive techniques are needed to reduce the risks of the patients and also the medical costs (5-8). Although there have been several reports on

novel endoscopic interventions and devices over the past decade, none of them have been formally approved for use in the USA. This paper reviews the various endoscopic bariatric techniques and devices that are currently available.

Methods

A bibliographic research through Pubmed and Medline was performed to find the studies on this topic ; the following keywords were used alone or in combination : 'endoscopic', 'bariatric', 'intra-gastric', 'balloon', 'suture', 'staple', 'botulinum toxin', 'vagal stimulation', 'bypass sleeve', 'pacing', 'transpyloric shuttle', 'gastric', 'gastro-enteric', and 'duodenojejunal'. Controlled clinical trials, case reports, case series and preliminary reports of clinical trials were used for search, and references, titles, abstracts and articles were all reviewed with careful examination of the data to avoid from double counting of patients between series. A total of 63 articles were found after a comprehensive literature research according to given criteria and after the exclusion of unrelated studies and reviews, 26 articles were included in the study and the corresponding tables in this manuscript.

Restrictive approaches

Intra-gastric Balloon

The intra-gastric balloon (IGB) is a reversible endoscopic technique for the treatment of obesity. Its principle is based on partially occupying a space in stomach and therefore causing early satiety. The IGBs were only air-filled e larger capacity and may be filled with air or saline solution (9). Although early trials failed to show a significant efficacy but complications including small bowel obstruction due to balloon deflation, bleeding, and gastric mucosal ulceration and perforation, recent studies have demonstrated the efficiency and safety of IGBs compared to sham procedures (10-12).

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The average durability of IGBs is 3-6 months which can be prolonged to 12 months with repetitive procedures (13,14). The most successful results of weight loss have been reported to be in the first 3 months. Weight loss at 6 and 12 months were more likely in the patients who lost weight more than 6.5 kg within 3 months after the procedure. When the procedure is repeated for the patients who successfully lost weight in the first months, an additional weight loss of 20.5% was seen at the end of first year (15). In 2008, a metaanalysis with 3608 patients showed a mean excess body weight (EBW) loss of 14.7 kg (32.1%). Moreover, progress in patients with type 2 diabetes mellitus, hypertension, obstructive sleep apnea, and lipid metabolism abnormalities was shown (16).

Studies with results of 6 months after IGB placement demonstrates 15 kg of mean weight loss or 34% excess weight loss (EWL) ($P < 0.001$) (5,15,17,18). Moreover, although a study with a follow up time of 12 months failed to show weight loss in 15% of the patients (15,16), an average of 24 kg weight loss was succeeded (13).

IGB placement is a procedure that requires the removal of the gastric balloon after a certain amount of time. Therefore, weight regain after removal has become a major concern. In a study, the average weight loss at removal time is demonstrated as 12.6 kg. However, only 24% of the patients were able to maintain over 10% of EWL. Forty percent of the patients required a surgical bariatric procedure at the 5th year of balloon removal (14,19). In addition, another meta-analysis showed that 133 of 143 patients regained 39.6% of the weight loss 1-year after balloon removal (16).

Although there are studies showing the success of IGB procedures over laparoscopic gastric bypass (LGBP) at 12 and 18 months of follow up (20), common conception is that LGBP results in greater weight loss compared to IGB (16,21). While LGBP leads to a mean weight loss of 25 kg (21), at 6 months post-IGB removal the mean weight loss is 14.7 kg (16). While LGBP procedures allow patients to maintain their weight loss for long years, weight regain after a transient weight loss is a major issue in IGBs (14,21). Therefore, IGB placement as a pre-treatment may be an option for patients with high surgical risks (22).

The most common complications of IGB are esophagitis (1.27%), gastric perforation (0.21%), gastric outlet obstruction (0.76%), gastric ulcer (0.2%), balloon rupture (0.36%), and death (0.07%) (5,23,24).

Currently, there are several different IGBs on the market. Below, the brief explanations of the procedures are given. Results from essential studies for each technique are illustrated in table 1.

BioEnterics Intragastic Balloon (BIB)

BIB (The Orbera by Allergan) is the most preferred IGB which is made of silicone and filled with saline and methylene blue. Placement location of BIB is gastric fundus and in case the balloon deflates due to a rupture, the

methylene blue is released causing the urine to change its color (25-27).

Heliosphere Bag

This is another endoscopic IGB which is filled with air and has an interior lining of gold to avoid a possible air leakage. This IGB was reported for problems with placing the balloon at the right location. In a study comparing BIB and HB, the patients that underwent a HB procedure showed more complications than the patients with a BIB (28-30).

Spatz Adjustable Balloon System

This is an endoscopic IGB that allows physicians to adjust the volume of the balloon. Reduction of the volume is done in case of intolerance and when the patients' weight loss plateaued an elevation of the volume is preferred (Fig. 1) (13).

Stationary Antral Balloon

This is a pear shaped balloon that has a stem for duodenum and filled with saline. A metallic weight is attached to the balloon on it to keep its position in the antrum leading to a sensation of satiety (31).

Reshape Duo

This is an IGB designed as a double balloon in order to avert migration to small bowel and causing an obstruction in case of deflation (32).

Endoluminal Vertical Gastroplasty (EVG)

Also known as endoluminal suturing, the purpose of this procedure is basically creating a gastric pouch that impedes the food intake and causes a sensation of fullness. EndoCinch and Transoral Gastric Volume Reduction are explained below and results from different studies are demonstrated in table 2. Although there are currently no meta analysis showing the overall outcomes, endoluminal vertical gastroplasty (EVG) stays as an alternative to endoscopic IGB procedures.

EndoCinch

This procedure was first used for the treatment of gastroesophageal reflux and then for the repair of gastrogastric fistulas (33,34). It has been used for obesity since 2008. The procedure involves continuous cross-link sutures running from proximal fundus to distal body (Fig. 2). At EndoCinch procedure in the study of Fogel R et al, sham procedure was not present (35).

Transoral Gastric Volume Reduction (TRIM)

This is an endoscopic device with an endoscope that holds a device capsule and suturing system to create a restrictive gastric pouch. This system is also known as Restore Suturing System (36,37).

Endoluminal stapling

This is another endoscopic procedure that takes a different approach to create a restrictive pouch by gastric

Table 1. — Summary of the studies on BioEnterics IntraGastric Balloon, Heliosphere Bag, Spatz Adjustable Balloon System, Stationary Antral Balloon, and Reshape Duo

Method	Studies	Subjects	Results	Complications	Metabolic Outcomes
BIB	Genco A. <i>et al.</i>	130	% Excess BMI loss at 6 months BIB = 38.5 conservative methods = 18.6	Balloon deflation and distal migration - Small bowel obstruction - Patient discomfort - Esophageal Perforation	None
	Crea N. <i>et al.</i>	143	Body weight loss percentage at IGB removal time (BWL%) = 29.3 Partial weight regain was observed at 12 months after IGB removal		Change in incidence from pre IGB to 12 months after IGB removal: metabolic syndrome (34.8% to 11.6%) T2DM (32.6% to 21.3%) hypertriglyceridemia (37.7% to 17.4%) hypercholesterolemia (33.4% to 18.9%) blood hypertension (44.9% to 34.8%)
	Milone L.	77	% Excess weight loss (% EWL) of Laparoscopic Sleeve Gastrectomy (LSG) and BIB at 6 months LSG = 35% BIB = 24%		Decreased comorbidities by 90% in both patient groups
Heliosphere Bag	Forestieri P. <i>et al.</i>	100	Mean weight loss at 6 months after HB replacement with a 1000 kcal diet = 17.5 kg	Balloon deflation and distal migration - Small bowel obstruction - Patient discomfort	None
	De Castro M.L. <i>et al.</i>	33*	Weight loss is not different between HB and BIB procedures at 6 months		None
Spatz Adjustable Balloon System	Machytka E. <i>et al.</i>	18	% EWL at 24 months: 26.4% % EWL at 52 months: 48.8%	Nausea - Vomiting - Distal Migration	None
Stationary Antral Balloon	Lopasso F.P. <i>et al.</i>	26	Median weight reduction = 6.5 kg Median weight loss in patients with initial body weight of > 90 kg = 8.1 kg < 90 kg = 4.5 kg	Small Bowel Obstruction - Rectal Expulsion	None
Rehsape Duo	Ponce J. <i>et al.</i>	30	Mean % EWL at 24 weeks after the procedure = 31.8% Treatment Group maintained 64% of their weight loss at 48 weeks	Nausea - Vomiting	None

* 18 patients were implanted with HB balloons and 15 were implanted with BIBs for comparison of outcomes.

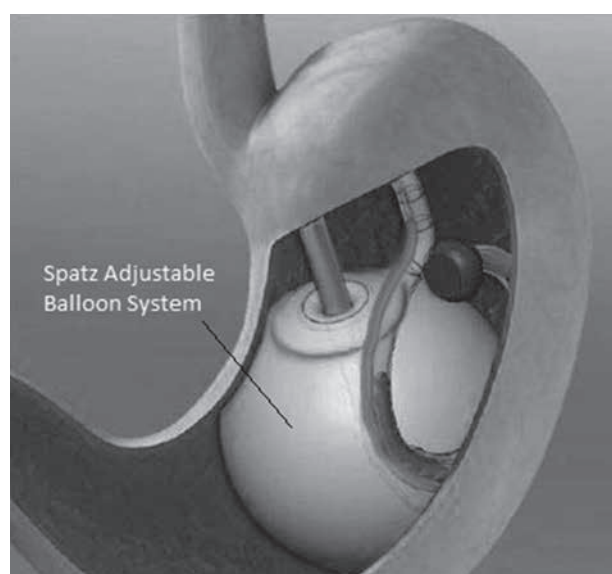


Fig. 1. — Spatz Adjustable Balloon System

stapling instead of suturing. This method has been used for obesity since 2007. Different methods of endoluminal stapling are defined below (Table 3).

Transluminal Oral Gastroplasty (TOGA)

This is a method where a sail septum is used to maintain the desired position of stomach, a part of gastric mucosa is suctioned and stapled to create a gastric pouch for the limitation of food intake (Fig. 3) (38-41).

Transoral Endoscopic Restrictive Implant System (TERIS)

This is a device that is used to place anchors into the gastric cardia firstly by transmural plication stapling. Lastly a diaphragm for restriction is attached to the anchors (Fig. 4). The anchors are designed to be enduring and adjustable if needed (38,40,42,43).

Stomaphy X

This technique is commonly used following failed vertical banded gastroplasty (VBG) for the augmentation

Table 2. — Summary of the studies on EndoCinch and Transoral Gastric Volume Reduction

Method	Studies	Subjects	Results	Complications	Metabolic Outcomes
EndoCinch	Fogel R. <i>et al.</i>	64	% EWL at 1 month = 21.1 +/- 6.2, at 3 months = 39.6 +/- 11.3 at 12 months = 58.1 +/- 19.9	Loosening and breaking of the sutures on repeat endoscopy	None
Transoral Gastric Volume Reduction (TRIM)	Brethauer S.A. <i>et al.</i>	18	Number of plications = 4-8 (average of 6) at 12 months follow up (14 patients) % EWL = 27.7 ± 21.9% The proportion of patients with an EWL of ≥ 20% or ≥ 30% was 57% and 50%, respectively	Nausea - Vomiting - Abdominal discomfort - Partial or complete release of plications	The mean decrease in blood pressure Sistolic = 15.2 mm Hg Diastolic = 9.7 mm Hg

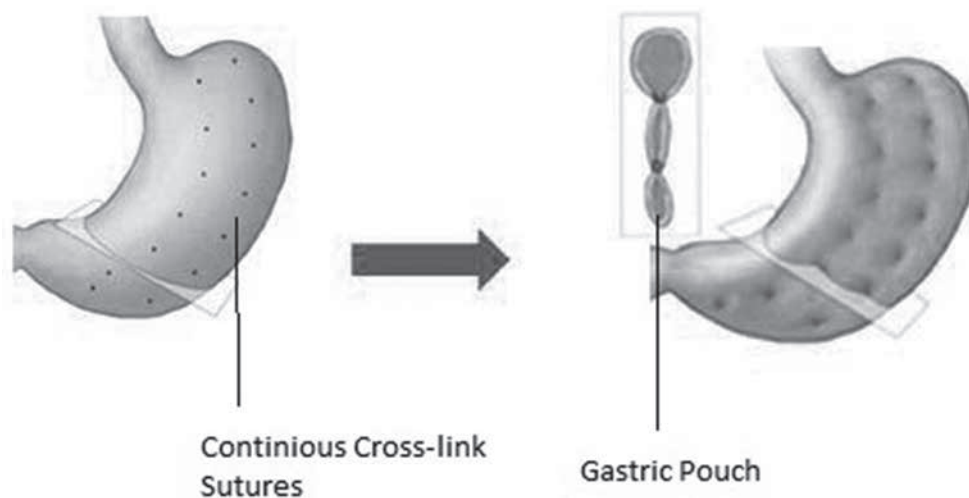


Fig. 2. — EndoCinch Suturing Procedure

of restriction by approximating the gastric or gastroenteric tissues (44).

Expandable Tissue Anchors

This is a promising new method that involves two expandable anchors that allows more restriction than that can be achieved by staples or sutures. The anchors are flexible and attached to a polyester suture on both sides. One advantage of this procedure is that it maintains its hold to the tissue while accommodating post-operative inflammation (45).

Malabsorptive Approaches

Endoluminal Bypass

Open Gastric Bypass surgeries such as Roux-en-Y gastric bypass were proven to be effective in weight loss and showed improvements in the patients with hypertension, T2DM and obstructive sleep apnea. The biggest problem with these surgeries was post and intra-operative complications (46). Therefore, with the new endoscopic techniques evolving, less invasive methods have been developed such as EndoBarrier Gastric Liner and ValenTx bypass sleeve (Table 4).

EndoBarrier Gastric Liner (EGL)

This method is done by a 60cm long sleeve attached to duodenum and runs distally until proximal jejunum. The sleeve, therefore, limits the absorption between duodenum and proximal jejunum (Fig. 5) (47-49).

ValenTx Bypass Sleeve

This adjustable device is very similar to EGL in principle. However, unlike EGL its sleeve is 120 cm and it is anchored to distal esophagus mimicking the final anatomical structure created by Roux-en-Y gastric bypass surgery. While this procedure still requires laparoscopic approach with endoscopy, it is planned to be performed exclusively with endoscopic methods in the future (50).

Other approaches

Examples of studies of techniques that potentially affect gastric function are given in table 5.

Transpyloric Shuttle

This is a removable and replaceable device that can place itself across pylorus decreasing the rate of gastric emptying. This method works by enabling a prolonged satiety rather than causing an early satiation (51).

Table 3. — Summary of the studies on Transluminal Oral Gastroplasty and Transoral Endoscopic Restrictive Implant System and Stomaphyx

Method	Studies	Subjects	Results	Complications	Metabolic Outcomes
Transluminal Oral Gastroplasty	Moreno C. <i>et al.</i>	11	Mean % EWL at 1 month = 19.2% at 3 months = 33.7% at 6 months = 46.0%	Nausea - Vomiting - Abdominal discomfort	None
	Familiari P. <i>et al.</i>	67	Excess BMI loss at 3 months = 33.9% at 6 months = 42.6% at 12 months = 44.8% Excess BMI loss at 12 months (53 pts) Patients with a baseline BMI of < 40.0 = 52.2% Patients with a baseline BMI of ≥ 40.0 = 41.3%	Respiratory insufficiency - Asymptomatic pneumoperitoneum - Esophageal perforation	At 12 months Hemoglobin A(1c) levels decreased from 7.0% at baseline to 5.7% ; Triglyceride levels decreased from 142.9 mg/dL to 98 mg/dL High-density lipoprotein levels increased from 47.0 mg/dL to 57.5 mg/dL*
	Nanni G. <i>et al.</i>	79	BMI respectively at 12 and 24 months TOGA® (29 pts) = 34.5 and 35.5 kg/m ² , with 44 and 48.3% of patients with BMI < 35 LGBP group (20 pts) = 30.7 and 29.2 kg/m ² , with 80 and 85% of patients with BMI < 35. BPD group (30 pts) = 30 and 29.6 kg/m ² , with 100 and 93.3% of patients with BMI < 35	Nausea - Vomiting - Abdominal discomfort	None
Transoral Endoscopic Restrictive Implant System	de Jong K. <i>et al.</i>	13	At 3 months postprocedure Median% EWL = 28 Median BMI decreased from 42.1 to 37.9 kg/m ²	Gastric perforation - Pneumoperitoneum - Throat pain - Fever - Epigastric pain - Back pain - Vomiting - Thrombophlebitis - Reflux - Pneumoperitoneum - Perforation	None
	Biertho L. <i>et al.</i>	20	Median% EWL at 3 months = 21% at 6 months = 26%	None**	None
StomaphyX	Manouchehri N. <i>et al.</i>	14	- BMI pre-op vs. post-op (mean follow up= 126 days) Pre-op = 43.4 ± 9.7 kg/m ² Post-op = 39.8 ± 9.1 kg/m ² - Weight pre-op vs. post-op Pre-op = 119.5 ± 25.9 kg Post-op = 109.6 ± 24.4 kg	Headache - Backpain	None

* Information related to metabolic outcome is only for 54 patients and follow up of 12 months was not possible for 14 patients in this study.

** Complication information was available only for one case.

Botulinum Toxin

Botox, by its anticholinergic effect, causes a delay in gastric emptying and allows a prolonged feeling of fullness (52). Studies demonstrated that while toxin injection to prepyloric antral gastric wall was ineffective for causing a weight loss (53), injection to both antrum and fundus showed to reduce BMI significantly more compared to sham procedures (54).

Gastric Pacing

Gastric Pacing (Laparoscopic implantable gastric stimulation) is a technique where bipolar leads are placed in the seromuscular layer of gastric wall to generate pulses along the lesser curvature. The primary goal of this

method is to create an early satiety rather than gastric restriction or intestinal malabsorption (55). Results of the studies have been highly variable to decide whether or not it is effective to lose weight in obese patients (56-60).

Vagal Nerve Stimulation

Vagal nerve stimulation (VNS) is achieved by placing an electrode subcutaneously to give pulses to vagal nerve in order to lose weight and decrease sweet craving (61-63). Despite several studies, ideal positioning of the electrode and the frequency of the blocking algorithm remains unclear (60,62,64). Since this method was first introduced to be used in the treatment of epilepsy (65) and resistant depression (66), its application may be

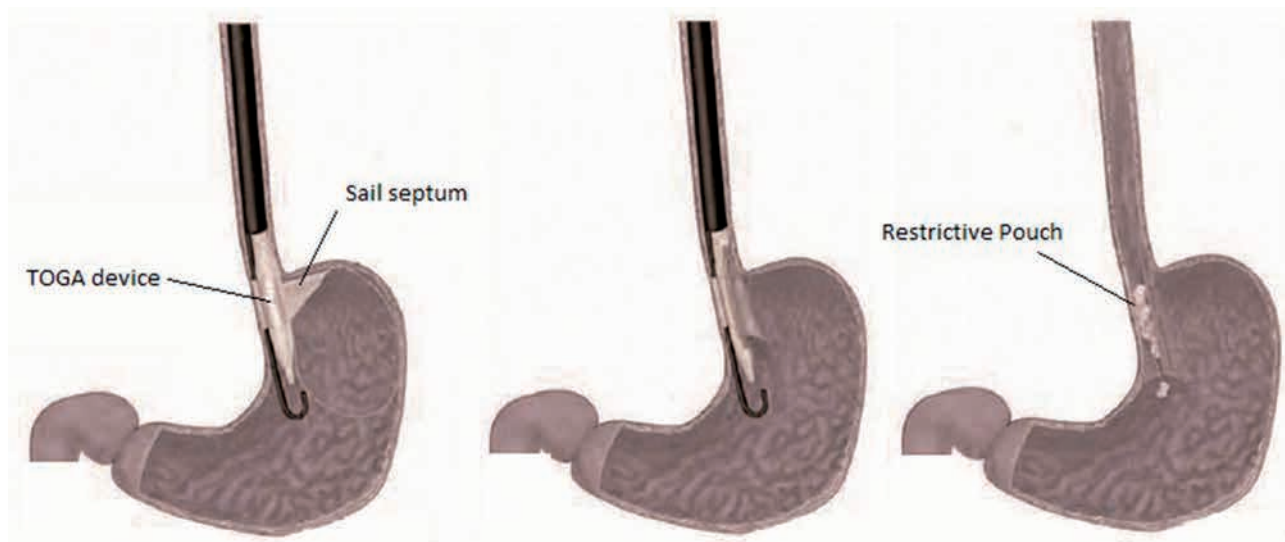


Fig. 3. — Transluminal Oral Gastroplasty (TOGA)

Table 4. — Summary of the studies on Endobarrier Gastric Liner and ValenTx Endoluminal Bypass Sleeve

Method	Studies	Subjects	Results	Complications	Metabolic Outcomes
Endobarrier Gastric Liner (EGI)	Rodriguez-Grunert L. <i>et al.</i>	12	At week 12 (10 pts) Mean EBW Loss = 23.6%	Abdominal pain - Nausea - Vomiting - Partial Pharyngeal Tear	All 4 diabetic patients had normal fasting plasma glucose levels without antihyperglycemic medication for the entire 12 weeks. Of these 4 patients, 3 had decreased hemoglobin A(1c) of > or = .5% by week 12.
	Gersin <i>et al.</i>	37	% EWL at 12 weeks EGI group (13) = 11.9% Sham group (24) = 2.0%	GI bleeding - Abdominal pain - Nausea - Vomiting	None
	Schouten R. <i>et al.</i>	41	Mean % EWL at 3 months EGI group (22/30 pts) = 19.0% Diet group (11 pts) = 6.9%	Migration - Dislocation of the anchor - Sleeve obstruction - Continuous epigastric pain - Nausea	Improvement in 7 out of 8 type 2 diabetes mellitus patients during the study period (lower glucose levels, HbA1c, and medication requirements).
ValenTx Endoluminal Bypass Sleeve	Sandler B.J. <i>et al.</i>	24	at week 12 (17 pts)% EWL = 39.7%	Inflammation at the gastroesophageal junction - Postoperative dysphagia	All 7 patients with preoperative diabetes mellitus had normal blood glucose levels without antihyperglycemic medications for the entire 12 weeks . All 4 patients with elevated hemoglobin A1c levels at the time of implantation showed improvement by the end of the trial.

promising to be used in the obese patients with comorbidities including epilepsy or resistant depression.

Conclusion and Prospects for Future Research

With the rapidly evolving technology and research, endoluminal bariatric techniques could become the primary choice of therapy in the near future for bariatric care. However, while there is a search for endoscopic methods with lower risks and higher efficacy, different

techniques of endoluminal surgery and NOTES are also coming into practice (7,8). Therefore, a novel approach would derive from a combination of different surgical or endoscopic methods. As an example, the use of intra-gastric balloons prior to gastric bypass surgery was already suggested (22). Another similar approach is using endoluminal approaches as revisional therapy for weight regain after gastric bypass (67). Also, it may be possible, in the future, to use duodenojejunal sleeve with endoluminal stapling for better outcomes.

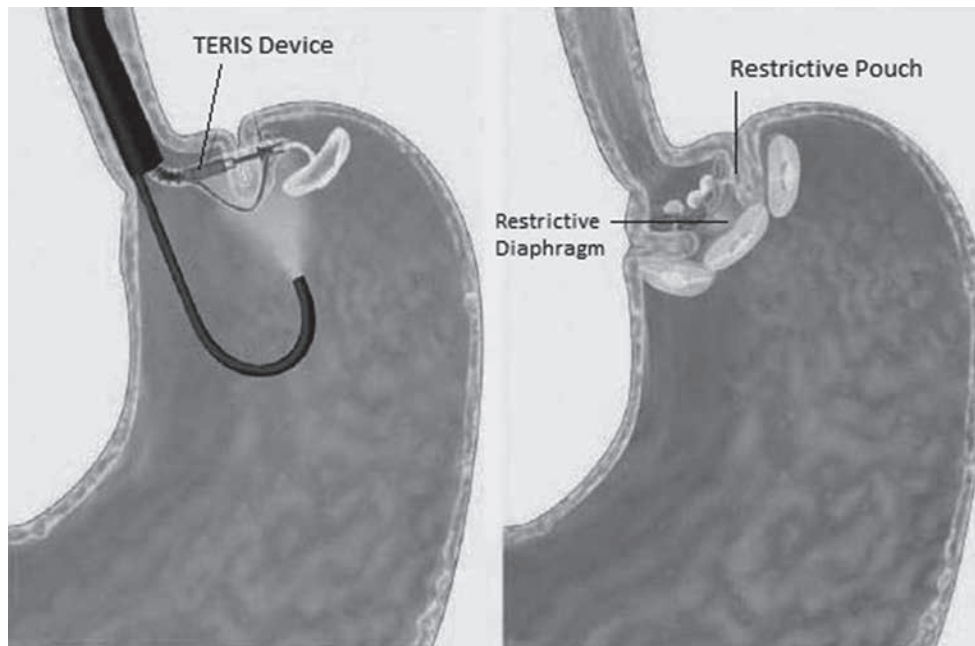


Fig. 4. — Transoral Endoscopic Restrictive Implant System (TERIS)

Table 5. — Summary of the Studies on TransPyloric Shuttle, Botulinum Toxin A Injection, Gastric Pacing and Vagal Nerve Stimulation

Method	Studies	Subjects	Results	Complications	Metabolic Outcomes
TransPyloric Shuttle	Marinos G. <i>et al.</i>	20	Mean % EWL Patients with follow-up time of 3 months (10 pts) = 25.1% Patients with follow-up time of 6 months (10 pts) = 41.0%	Symptomatic Gastric Ulceration	None
Botulinum Toxin A Injection (Into the Antrum and Fundus)	Foschi D. <i>et al.</i>	30	Body weight loss at 8 weeks Botulinum Toxin A (18 pts) = 11.8 +/- 0.9 kg Placebo (12 pts) = 5.5 +/- 1.1 kg BMI Loss at 8 weeks Botulinum Toxin A = 4.1 +/- 0.2 Placebo = 2.2 +/- 0.4	None	None
Gastric Pacing	De Luca M. <i>et al.</i>	69	The mean % EWL at 1 month = 8.6 +/- 1.8 at 3 months = 15.8 +/- 2.3 at 6 months = 17.8 +/- 2.6 at 10 months = 21.0 +/- 3.5 at 15 months = 21.0 +/- 5.0	Gastric penetration - Partial or complete dislodgment of the leads	In the 19 patients, despite weight reduction, ghrelin did not increase.
	Shikora S.A. <i>et al.</i>	190	% EWL at 12 months The control group = 11.7% +/- 16.9% Treatment group = 11.8% +/- 17.6% (Difference is not significant)	None	None
	Policker S. <i>et al.</i>	50	Mean weight loss at 24 weeks = 5.5 +/- 0.7 kg	None	HbA1c levels were reduced in 80% of the patients. Average drop in HbA1c = 1.1 +/- 0.1%
Vagal Nerve Stimulation	Pardo J.V. <i>et al.</i>	53	% EWL after 6 months of VNS = 14–23%	Changes in voice/speech - General pain - Throat or neck pain - Throat or larynx spasms - Headache - Insomnia	None

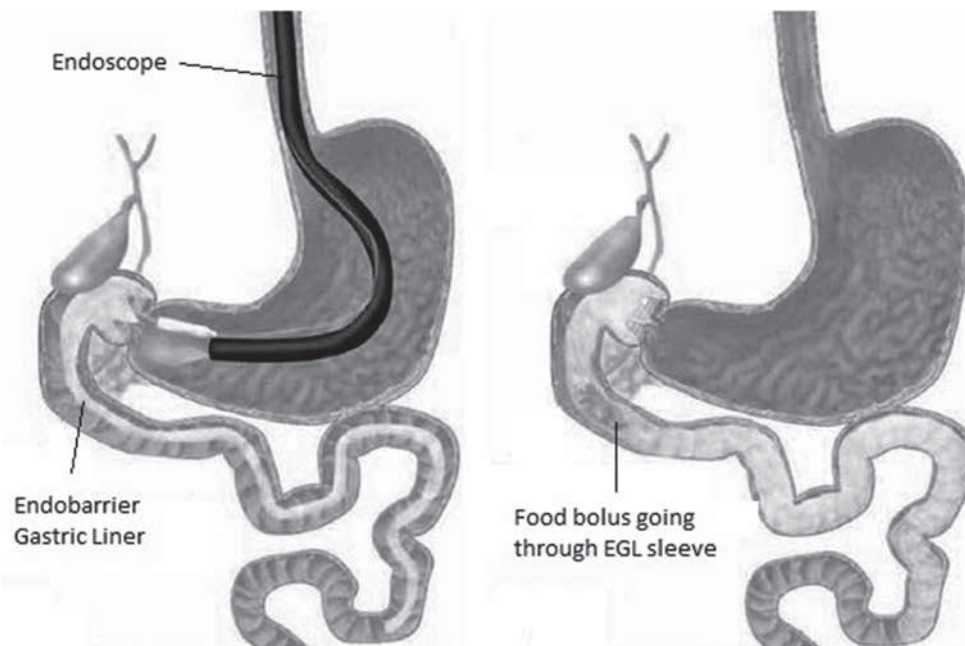


Fig. 5. — Endobarrier Gastric Liner (EGL)

Today, the endoscopic methods as well as surgical techniques for bariatric care require further developments. For this reason, gastroenterologists must improve their skills to be able to perform these techniques, while randomized prospective studies are performed for the evolving techniques.

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