Introduction

Obesity is clearly the pandemic of the 21st century and is associated with considerable morbidity and mortality\(^1\). Management of obesity depends on body mass index (BMI) as well as the presence of co-morbidities, including heart disease, diabetes, hypertension, dyslipidemia, osteoarthritis, and sleep apnea.\(^2\)

Approximately 1.6 billion adults are overweight; at least 400 million adults are obese. World Health Organization (WHO) further projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. Once considered a problem only in high-income countries, overweight and obesity are now dramatically on the rise in low- and middle-income countries, particularly in urban settings.\(^3\)

The only effective therapy for morbid obesity, as defined by Body Mass Index (BMI) of 40 kg/m\(^2\) or more, or by a BMI of 35 kg/m\(^2\) or more in the presence of co-morbidities, is currently surgery\(^4\). It has been shown effective on the long term and significantly reduces the risk of mortality associated with this disease. In the US, the number of indications for bariatric surgery has increased by 80% between 1998 and 2004\(^5\) and in terms of health care demand, it clearly will represent the pandemic of the 21st century.

Bariatric surgery for morbidly obese patients has demonstrated significant clinical benefits. It induces and maintains satisfactory weight loss while decreasing co-morbidities associated with the patient’s overweight.\(^6\) Efficacy varies with the type of procedure, which can be divided into restrictive (lap band, vertical gastroplasty, sleeve gastrectomy), malabsorptive (biliopancreatic diversion) or a combination of both (gastric bypass). The first and the latter type of operations are currently the most frequently performed sometimes as an optional 2 steps procedure starting with gastric restriction.

Although very effective, laparoscopic and surgical bariatric procedures have complication rates of 3% to 20% and mortality rates of 1%.\(^7\) Cardiopulmonary events and anastomotic leaks are the major sources of severe morbidities.

The demand for less invasive therapy for obesity in the last years lead to emergence of endoscopic technology potentially characterized by less invasiveness and less post procedures complications.

Indeed, endoluminal surgery, performed entirely through natural orifice, offers the potential for a less invasive weight loss procedure, possibly performed on an ambulatory basis, and might find its place in the current armamentarium or morbid obesity treatment, extending indication to patients with severe co-morbidities, older age or even non morbid obese patients. We review the various endoluminal techniques which are currently ei-
ther in routine use or in clinical evaluation, and will also address the role of endoscopy in management of complications occurring after bariatric surgery.

**Endoscopic options for endoluminal primary treatment of obesity.**

1. **Intragastric Balloon.**

   The use of intragastric device to induce weight loss in obese patients was first described in 1982. Since then, numbers of intragastric balloons have been in use worldwide, and several have been withdrawn from the market. With a spherical shape and larger capacity than earlier models, the BioEnterics Intragastric Balloon (BIB, Allergan, Irvine, CA) is the one which has been the most extensively studied. Among the recently improved minimally invasive procedures, intragastric balloon has been one temporary nonsurgical option that can promote weight loss in obese patients by partially filling their stomach and inducing a sense of early satiety. One of the major drawbacks of balloon implantation is weight regain after balloon removal. In this line, two recent studies help to better understand what can be expected from balloon implantation.

   Mathus-Vliegen et al. included patients who had participated in a randomized controlled trial comparing balloon versus sham for a 3 months period, into an additional trial including 9 months of balloon treatment and follow-up for 1 year after removal. They excluded 8 patients who had not met the weight loss goal during the first 3 months (N=5) or who did not tolerate the balloon (N=3). Although there was no difference between sham and balloon during the first 3 months, after 1 year of balloon treatment, a mean weight loss of 21.3 kg (17.1%) was achieved in all patients of which 12.6 kg (9.9%) was maintained at the end of the second balloon free year. Overall, 47% of patients sustained a 10% weight loss at the end of 2 years follow-up. Although this study could not demonstrate an independent benefit of balloon treatment beyond diet, exercise, and behavioral therapy in the first treatment, balloon treatment for 1 year, in those patients who tolerated the treatment, resulted in substantial weight loss, a significant part of which was maintained during the first year after removal of the balloon.

   Another recently published study looked at the long-term outcome after treatment with an intragastric balloon for 6 months, with no structured weight maintenance program after balloon removal.

   Hundred consecutive morbidly obese individuals were prospectively followed after BIB placement (Allergan, Irvine, CA); 97 patients completed final follow up at a mean of 4.8 years.

   While, after 6 months, 63% of patients had more than 10% baseline weight loss, there were only 28% at final follow up. At that time, 35 patients had undergone bariatric surgery and 34 patients had no significant weight change from baseline. These studies further confirm that balloon implantation may be of some help in a minority of patients for long term weight loss. It is a potential option for patients unwilling bariatric surgery or not candidate for bariatric surgery, and could also be used as a temporary measure in super obese patients, in order to induce weight loss and decrease the risk of complications associated with further bariatric surgery.

2. **Gastric Restriction.**

   A. **Endoluminal vertical gastroplasty using EndoCinch**

   The EndoCinch Suturing System (C.R. Bard, Murray Hill, NJ) was initially designed for the endoscopic treat-
ment of GERD. This system allows the placement of series of stitches in the lower esophagus to create a pleat in the sphincter. This pleat alters the gateway between the stomach and esophagus and potentially prevents acid from flowing out of the stomach. Although associated with encouraging early results, the EndoCinch for the treatment of GERD has been called into questions due to the lack of retention of plications in the long term.14

Fogel et al15 first described the use of this technology for the treatment of obesity in 64 patients. His technique consisted in the deployment of 7 sutures in a continuous and cross-linked design from the proximal fundus to the distal body. The result of the treatment is suggested to be a significant decrease in distensibility of the stomach. The procedure was performed ambulatory and out of the 59 patients followed for 12 months, the percentage excess weight loss reported was 21% at 1 month and 58% at 12 months. Only a minority of patients (N=14) underwent repeated endoscopy in the follow up. In 11 of them, the suture line was reported as completely or partially intact.

A randomized controlled trial is ongoing in the US to further investigate this technique and hopefully will also provide long-term data that are the major matter of concern both clinically and anatomically.

B. Transoral gastroplasty

Transoral gastroplasty (TOGa System; Satiety, Inc, Palo Alto, CA) recently emerged as a new and apparently safe technique for the endoluminal surgical treatment of obesity. It uses the first endoscopic stapling device in
order to create a full-thickness plication in the proximal stomach, with a strictly endoluminal approach. The purpose is, like for other restrictive procedures, to induce an early satiety due to the reduction of the stomach capacity.

The system consists of the TOGa Sleeve Stapler, a flexible 18 mm diameter shaft device, which rides over a guide wire for introduction.

It is specifically designed for the procedure and accommodates a standard endoscope up to 8.6 mm diameter and creates a full-thickness plication of the anterior and posterior walls of the stomach, which are acquired using vacuum pots located parallel to the staple line (Fig. 1). The stapling allows a serosa to serosa apposition and is performed via 2 successive applications of staple lines of 5 cm each.

In the first evaluation, this procedure is completed by the placement of restriction in the distal part of the pouch, using a dedicated stapling device also based on vacuum acquisition of the tissues.

Only 2 human series are currently published as full paper. The first one was performed in 21 patients with a mean BMI of 43.3 kg/m². The mean excess weight loss was 16, 23 and 25% at 1, 3 and 6 months post-treatment. No severe adverse event was reported and, at 6 months endoscopy, Gaps between the 2 staple lines were evidenced in 13 of 21 patients. After this first evaluation, the technique was improved, especially concerning the successive application of the 2 staple lines and the device has been modified. Using this later, a second human pilot series was reported in 11 patients, showing better results with mean excess weight loss of 19, 34 and 46% at 1, 3 and 6 months, respectively. Another 300 patients were included in a multicentric randomized sham controlled trial. This study showed a significant but modest advantage over the sham procedure but was judged insufficient by the FDA, a feature which led to closure of the company. The interest of these studies was however to show that these transoral techniques are not more difficult to perform in heavily obese patients and recovery is very fast and the procedure could be performed on an outpatient basis.

The revisional surgery after TOGa was evaluated in a recent study showing that the conversion of TOGa into a laparoscopic Roux-en-Y gastric bypass (LRYGBP) was easy and performed over the same duration as a primary LRYGBP, without the excess time and difficulty usually needed for conversion of a restrictive procedure into a LRYGBP.

C. The POSE procedure

The POSE (USGI medical, USA) procedure includes a multi-lumen access device, an endoluminal tissue approximator and suture anchors and consists in performing multiple transmural plicatures into the fundus and the distal body of the stomach (Fig. 2). The first pilot study included 45 patients with an initial BMI of 37. As an outpatient procedure with a mean OR time of 1 hour, the authors achieved a 49% EWL at 6 months. Larger randomized studies are awaited to evaluate the time efficacy of this promising technique.

D. Duodenojejunal bypass sleeve.

This technique has to be put in line with the development of metabolic surgery and particularly with the clinical observation that bypassing the proximal bowel improves type 2 diabetes and induces weight loss, a feature which, at least in part, explains the greater improvement of diabetes observed in patients undergoing a LRYGBP, for the same weight loss, compared with a pure restrictive procedure.

The first strictly endoluminal device used to bypass the proximal small intestine is the duodeno-jejunal by-
The POSE system, including multi-lumen device (A), Tissue approximator (B), Tissue anchor (C) and schematic view of the stomach after treatment (D).

**Fig. 2.** The POSE procedure.

**Fig. 3.** (A) Duodenojejunal sleeve. (B) Schematic representation of the sleeve in place in the proximal jejunum.

pass (DJBS), also called "the EndoBarrier" (GI Dynamics Inc, Watertown, MA). It is composed of a self expanding implant that seats in the duodenum and has anti-migration features. It is attached to a 60 cm plastic sleeve that extends into the proximal jejunum and works by creating a physical barrier between food that has been ingested and both the intestinal wall and biliopancreatic secretions (Fig. 3). The device is left in place for a maximum of 3 to 6 months and is removed with a dedicated and relatively easy system. Three trials demonstrated the potential benefit of DJBS. In the first one,\(^1\) it was successfully deployed in 12 patients in less than 30 minutes (and required approximately 40 minutes to be removed). With the exception of pain prompting early removal, it was associated with a significant drop in HbA1C, compared with a control group. A second multicenter trial, from Chile, showed, at 12 weeks, a weight loss significantly higher in 24 patients treated with the
Table 1. Available and post bariatric endotherapy technology

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EndoBarrier system compared to the died control group in a preoperative setting. The last available study is a sham-controlled trial with 24 patients treated and 13 undergoing the sham procedure, with a 12 weeks study design. Excess weight loss (11.9% versus 2.7%) and loss of more than 10% excess weight (62% versus 17% of patients) were all in favor of the DJBS. However, 7 subjects terminated earlier because of GI bleeding (N=3) or device intolerance (pain and/or vomiting, N=4), showing that the technological developments are still to be done. Although these techniques still suffer from the need for the implantation of a foreign body and the limited duration of indwell, they clearly deserve further technical improvement and clinical investigation since they could be those impacting the most on co-morbidities and might be of particular interest in diabetic obese patients. Other implantable devices, potentially mimicking more closely RYGBP are currently in development (Valentx Inc, Carpinteria, CA) but no clinical data are currently available.

Table 1 summarizes the current techniques of bariatric endotherapy for which clinical data are available. No doubt that other will come and that the role of endotherapy will be increasing in the management of bariatric patients, rendering necessary the integration of endotherapy into the armamentarium of multidisciplinary groups treating these patients.

E. Transoral endoscopic restrictive implant

If the duodenojejunal sleeve may be seen as the endoscopic counterpart of RYGBP, the TOGa, as the one of sleeve gastrectomy or vertical banded gastroplasty, a recently reported endoscopic implantable device (Transoral Endoscopic Restrictive Implants System (TERIS), Barosense, Redwood City, CA) may be seen as an endoscopic equivalent to gastric banding. A phase I pilot trial has been recently reported. Successful placement has been achieved in 12 of 13 patients with complications (including perforation) in 3 of them. This system is obviously currently technically demanding (22 mm insertion tube, 142 min median procedural time) but an interesting excess weight los of 28% was observed at 3 months, suggesting that provided technical improvements are made, it could become another option in the endoscopic armamentarium. This procedure is associated with the placement of an implant which means that it offers the potential advantage of being removable (the drawback being like with other implants the long-term durability of the procedure which will only be demonstrated by long-term follow-up). The company recently closed and sold its assets to Boston Sc.
Revisional endoscopy after bariatric surgery

Besides the primary treatment of obesity and the treatment of bariatric complications, another area of growing interest is the management of failed bariatric procedures. The RYGBP has become the most common procedure performed for the surgical treatment of morbid obesity and, therefore, encountered by gastroenterologists. Reintervention on these patients is associated with very high morbidity, in case of failure for obtaining weight loss after bariatric surgery. This failure may be attributed to dietetic problem but several anatomic factors such as staple line disruption, pouch dilation or band sleepage, may be also, at least partly, responsible.

Staple line disruption resulting in gastrogastric fistula is a classical cause of weight regain in these patients. Besides the classical surgical reintervention, endoscopic suturing or fibrin glue application have been successfully reported in small series. Endoscopic suturing (Endocinch, Bard Inc USA) or volume reduction by dedicated devices (Stomaphyx, Endogastric Solutions, Seattle USA) has also been reported in patients having an enlarged pouch or anastomosis after RYGBP. Although the currently reported series are uncontrolled, they have reported significant weight loss at follow-up of 6 to 12 months. This is potentially an interesting option for patients who are at high risk of complications and often desperate after failure of bariatric surgery.

Finally, while these techniques are being assessed in the setting of clinical research, Endotherapy already plays a major and established role in the management of post bariatric complications including fistulae, leaks and migrated bands and rings.

References


