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## Best Practice & Research Clinical Gastroenterology



## Endoscopic treatment: The past, the present and the future



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Keywords: Endoscopy Intragastric balloons Gastric bubble Duodenojejunal bypass sleeve Duodenojejunal bypass liner Botulinum toxin A Gastric suturing Gastric stapling Aspire bariatrics system

## ABSTRACT

The obesity epidemic asks for an active involvement of gastroenterologists: many of the co-morbidities associated with obesity involve the gastrointestinal tract; a small proportion of obese patients will need bariatric surgery and may suffer from surgical complications that may be solved by minimally invasive endoscopic techniques; and finally, the majority will not be eligible for bariatric surgery and will need some other form of treatment. The first approach should consist of an energy-restricted diet, physical exercise and behaviour modification, followed by pharmacotherapy. For patients who do not respond to medical therapy but are not or not yet surgical candidates, an endoscopic treatment might look attractive. So, endoscopic bariatric therapy has a role to play either as an alternative or adjunct to medical treatment. The different endoscopic modalities may vary in mechanisms of action: by gastric distension and space occupation, delayed gastric emptying, gastric restriction and decreased distensibility, impaired gastric accommodation, stimulation of antroduodenal receptors, or by duodenal exclusion and malabsorption. These treatments will be discussed into detail.

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Abbreviations: EVG, endoluminal vertical gastroplasty; POSE, primary obesity surgery endolumenal; TGVR, transoral gastric volume reduction; TRIM, transoral gastric volume reduction intervention for weight management; TOGA, transoral gastroplasty; TERIS, transoral endoscopic restrictive implant system; ACE stapler, articulating circular endoscopic stapler.

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Obesity is a chronic, lifelong, multi-factorial and genetically related disease of excessive fat storage, which in addition to how the fat is distributed, places the individual at risk of premature death and obesity-associated diseases. Almost every organ system is affected by obesity, the gastrointestinal tract is involved as well [1,2]. This is the first reason why gastroenterologists should take care of the obese patient. In the second place, the gastrointestinal tract is involved in the regulation of the energy balance and many treatments will concentrate on the digestive tract. The third reason is the burgeoning interest in bariatric surgery. The widespread use of bariatric surgery means that a significant proportion of patients will suffer from surgical complications that may be solved by minimally invasive endoscopic techniques.

Authoritative institutions such as The National Heart, Lung and Blood Institutes, the World Health Organization and the National Institute for Health and Clinical Excellence (NICE) have documented that weight loss reduces many of the risk factors for increased death and obesity-related diseases [1-3]. The initial goal of weight loss is to reduce body weight by approximately 5-10% from baseline. A reasonable timeline for a 10% reduction in body weight is 6 months. Although this weight loss may appear insignificant, it is associated with a fall in systolic blood pressure of 10 mmHg and in diastolic blood pressure of 20 mmHg [1]. Dyslipidemia is corrected by a decrease of 10% in total cholesterol, 15% in LDL-cholesterol, 30% in triglycerides and an increase of 8% in HDL-cholesterol. A 10–20% weight loss is associated with improved glycaemic control and a weight loss of 15–20% is able to reverse the elevated mortality risk of diabetes. Ovarian function and quality of life is improved by a 5% weight loss [1]. After 6 months of effective weight loss, treatment efforts to maintain the weight loss over a period of at least 1–2 years, but preferentially lifelong, should be instituted.

Based on evidence-based guidelines, the first approach should consist of an energy-restricted diet, physical exercise and behaviour modification [1–3]. When motivated patients have seriously attempted but failed to achieve weight loss, pharmacotherapy is recommended. Drugs should always be embedded in an intensive lifestyle programme. One of the few available drugs, Orlistat, acts on the digestive system by inhibiting gastric and pancreatic lipase. Pharmacotherapy is indicated in subjects with a BMI > 30 or a BMI  $\geq$ 27 kg/m<sup>2</sup> in the presence of obesity-associated comorbidity. A surgical approach is restricted to very obese subjects (BMI > 40 kg/m<sup>2</sup> or BMI > 35 kg/m<sup>2</sup> with obesity-associated co-morbidity). Yet, only approximately 1% of eligible individuals with morbid obesity in the US receive bariatric surgery [4].

Notwithstanding these treatment options, there is an intermediate group of patients who do not respond to medical therapy but are not or not yet surgical candidates. Some patients refuse surgery because of its invasiveness and fear of complications. For this group, an endoscopic treatment might look attractive. The same holds true for severely obese patients with a BMI  $> 40 \text{ kg/m}^2$ , being poor surgical candidates for elective surgery, and for patients with a BMI > 50 kg/m<sup>2</sup>, being bariatric surgical candidates, in whom the achievement of a moderate preoperative weight loss might reduce anaesthesia risks and surgical complications and might allow to better visualise the operative field as a bridge to surgery. So, endoscopic therapy, often labelled endoscopic bariatric therapy (EBT), has a role to play in the treatment of obesity either as an alternative or adjunct to medical treatment [5–9]. The different endoscopic modalities may vary in mechanisms of action: by gastric distension and space occupation, delayed gastric emptying, gastric restriction and decreased distensibility, impaired gastric accommodation, stimulation of antroduodenal receptors, or by duodenal exclusion and malabsorption. Vagal signalling to the hypothalamus and hormonal influences may play a role as well. Only treatments will be discussed that are covered in peer reviewed articles. One should realise that these developments are very costly and several companies went bankrupt. Except for intragastric balloons, the duodenojejunal bypass liner and the aspiration therapy, most of the other endoscopic tools are still investigational or under further development or refinement. None of the endoscopic modalities are available in the US and are elsewhere often not reimbursed.

Roughly, the interventions can be separated into

- 1. early intervention in obese patients (BMI  $\ge$  30 kg/m<sup>2</sup>) to provide weight loss;
- primary intervention in subjects eligible for surgery but who refuse surgery or have no access to surgery;
- 3. secondary intervention as a bridge to elective surgery in those with  $BMI \ge 40 \text{ kg/m}^2$  or as a bridge to bariatric surgery in those with  $BMI \ge 50 \text{ kg/m}^2$ ;

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