

# Obesity and weight management: What can we do as gastroenterologists?



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Received 14 February 2020

Available online 29 July 2020

**Keywords:** Obesity; Practice guide on obesity and weight management, Education, and resources; Bariatric endoscopy

## Obesity may be one of the biggest health problems in the future

Obesity is a chronic, relapsing, multifactorial pandemic defined as the excessive or abnormal accumulation of body fat due to genetic, biological, microbial, and environmental factors that promote a positive energy balance mainly associated with increased intake and reduced consumption.<sup>1–3</sup> Obesity is the consequence of enormous multisystem disorders, including cardiovascular disease,<sup>4</sup> type 2 diabetes,<sup>5</sup> tumors,<sup>6</sup> sleep apnea,<sup>7–10</sup> etc., significantly increases mortality rate,<sup>11–13</sup> and accounts for substantial elevation in health expenditures.<sup>14</sup> Compared with Western countries, central obesity is more typical in Chinese individuals with a higher waist-to-hip ratio (waist circumference > 102 cm or waist-to-hip ratio > 0.9 in men and waist circumference > 88 cm

or waist-to-hip ratio > 0.85 in women) when the body mass index (BMI) is the same. As an independent risk factor of mortality,<sup>15</sup> central obesity is more closely linked to associated medical problems that place a heavy burden on China's health care system. Most comorbidities, especially nonalcoholic fatty liver disease and gastroesophageal reflux disease (GERD), can be considerably improved with weight loss alone. Nowadays, the well-known approaches mainly consist of lifestyle interventions, pharmacotherapy, or bariatric surgery, but merely result in slight weight loss or unfavorable side effects. Recently, we have discovered that obesity-related gastrointestinal disorders tend to be more frequent and present even sooner than type 2 diabetes mellitus and cardiovascular disease. Thus, gastroenterologists have an opportunity to fully participate in obesity management and provide effective therapy in advance by updating the current theoretical knowledge.

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Peer review under responsibility of Chinese Medical Association.



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## Obesity management: Practice Guide on Obesity and Weight Management, Education, and Resources (POWER)

The American Gastroenterological Association (AGA) has proposed a new care model for obesity treatment strategy and weight management, the POWER program guide, which is based on a continuum

<https://doi.org/10.1016/j.cdtm.2020.07.001>

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of 4 phases: (1) obesity assessment, (2) intensive weight loss intervention, (3) weight stabilization and re-intensification when needed, and (4) prevention of weight regain.<sup>6,16</sup>

### *Obesity assessment*

#### *Readiness*

Before initiating a treatment plan, it is essential for the clinician to assess whether the patient is motivated and ready to undertake the necessary weight loss measures. The modified 5 A's (Ask, Advise, Assess, Assist, and Arrange) for interviewing could serve as an effective tool for obesity counseling.

#### *Medical evaluation*

An assessment for underlying etiologies (family history, sleep disorders, medications, etc.), contributing factors of secondary weight gain, and identification of symptoms suggestive of cardiovascular diseases and other obesity-related complications, especially obesity hypoventilation syndrome, is needed in the medical evaluation of obese patients. It is necessary for all patients to cooperate with the evaluation of BMI and waist circumference, as well as a complete physical examination and basic laboratory evaluation. Doctors should bear in mind that severe obesity is associated with a high risk of symptoms, even though the screening guidelines do not distinguish patients based on their BMI.

#### *Nutrition evaluation*

As many obese individuals have a calorically dense intake but with insufficient micronutrient content. However, they are malnourished and have multiple nutrient deficiencies and insufficient muscle. Assessment of a patient's ability and willingness to keep food logs, read food labels, and prepare meals to make better food choices is helpful. Moreover, we could formulate a personalized care plan with the assistance of commercial programs and software for food tracking and calorie counting to facilitate and supervise the treatment process.

#### *Psychosocial evaluation*

A patient's psychosocial status, including eating triggers, body image disturbances, and maladaptive eating patterns should be screened, considering that behavioral modification is a critical component to successful obesity management.

### *Intensive weight loss intervention*

*The cornerstones: reduced calorie diet, physical activity, and behavior change*

Lifestyle modification is the key to long-term successful weight management based on a low-caloric diet and regular physical activity, but most patients have poor compliance with long-term persistence. Considering appetite is associated with emotions and mental disorders, active psychological measures should be taken by psychologists to correct the behaviors and mentalities that lead to obesity. Moreover, a registered dietitian is needed to design a nutrition intervention tailored to the unique needs and circumstances of each patient in a way that the individual is likely to follow. Regular physical activity is also essential; aerobic exercises such as swimming, cycling, brisk walking, jogging, and rowing can increase metabolism and help individuals achieve weight loss quickly, and participating in higher intensity exercise 200–300 minutes per week promotes the constant maintenance of low body weight. Notably, the rapid acceleration and emergency stop in many ball sports have a significant impact on the joints and ligaments, as well as the internal environment of the knees and ligaments and their special structures, which makes it difficult to recover quickly after injury; therefore, patients should be informed that these types of activities are not recommended.

*Second-level therapy: medications, endoscopy, and surgery*

Pharmacotherapy, bariatric endoscopy, and bariatric surgery as second-level therapy can be used separately, sequentially, or in combination, to achieve significantly sustained weight loss. It should be emphasized to patients that the application of these three interventions alone cannot completely address obesity, and that lifestyle modification is what ultimately results in success. It can be an option for obese patients who have failed to lose weight by barely adjusting their lifestyle or have weight-related comorbidities.<sup>17</sup> Furthermore, adverse events are inevitable; pharmacotherapy is prone to relapse after withdrawal with varying degrees of liver and kidney damage and necessitates the regular evaluation of efficacy and safety. Bariatric endoscopy and surgery are associated with relatively high medical expenditure and with high incidence of complications, we need rigorous preoperative evaluation according to the criterion for indications and contraindications, what is more, after the bariatric endoscopy and surgery, patients require multidisciplinary postoperative care and

nutritional support also needs to be fully guaranteed. Moreover, there are numerous misunderstandings regarding the use of liposuction to achieve weight loss and gain health benefits. The crucial pathogenic factor of related comorbidities is visceral fat, including mesenteric and perihepatic fat, which has little relation to subcutaneous fat; therefore, liposuction cannot be used as a shortcut to help us address obesity.

#### *Weight loss maintenance intervention and therapy for relapse*

It is of vital importance in this phase to expose the patient to the attitudes and behaviors that may promote the long-term maintenance of weight loss and prevent its associated consequences with a comprehensive and sustained effort, which involves devising an individualized, appropriate approach to nutritional support, behavior and physical activities. Doctors must recognize that weight regain is an opportunity to learn and adjust compounding therapy, and patients should be encouraged to set reasonable goals and reliable support systems within the social environment and the community. From clinical experiences, we emphasize that weight management is a multiphase, systematic project. Like with many other chronic diseases, therapy alone often results in weight regain; therefore, multidisciplinary cooperation between gastroenterologists, bariatric surgeons, endoscopists, nursing staff, nutrition specialists, psychologists, sports rehabilitation specialists, and clinical pharmacists is required. Gastroenterologists could participate in obesity treatment with the technologies they have (medicines, endoscopy, nutrition, etc.) or could provide endoscopic support and a remedy for bariatric surgery or could be leaders of the multidisciplinary team.

#### **Development and classification of bariatric endoscopy**

Nowadays, a variety of endoscopic bariatric therapies have achieved potential progress among patients who are ineligible for bariatric surgery in combination with a well-structured multidisciplinary weight loss program.<sup>18</sup>

##### *Intragastric balloons*

###### *Orbera*

The Orbera Intragastric Balloon (Apollo Endosurgery, Austin, Tex, USA) is the earliest bariatric endoscopy tool to help achieve weight loss by reducing the limited volume of the stomach. The Food and Drug Administration (FDA) approved it as a tool for the

temporary treatment of obesity, applicable to patients with a BMI 30–40 kg/m<sup>2</sup>, with or without comorbidities. A single deflated balloon is placed in the fundus accurately, and 400–700 ml saline with methylene blue is injected through the external port of the catheter under direct endoscopic visualization. A broken balloon can be detected by green urine. The balloon is then deflated and retrieved endoscopically up to 6 months later. A meta-analysis of 17 studies showed that the pooled percentage of total body weight loss as a result of using this tool was 13.16% and 11.27% at 6 and 12 months after insertion.<sup>19</sup> Because of a high incidence of esophagitis, perforation, and gastric outlet obstruction,<sup>19,20</sup> a new balloon is now available.

###### *ReShape Duo*

The *ReShape Duo* (*ReShape Medical*, San Clemente, CA, USA) is a dual-balloon system connected by a flexible silicone rod that has been recently approved by the FDA for patients with a BMI 30–40 kg/m<sup>2</sup> and more than 1 obesity-related comorbidity. Unintentional leakage of one balloon will not lead to migration and obstruction because of the independent channels of each balloon. Approximately 900 ml methylene blue-tinted saline is injected into the balloons, and leakage can be detected by green urine. The device is then deployed and retrieved endoscopically 6 months later. The mean percentage of weight loss resulting from this system was higher in the *ReShape Duo* group (8.4% and 7.5% at 6 and 9 months, respectively) than in the lifestyle intervention group (5.4% and 4.6% at 6 and 9 months, respectively) according to the REDUCE trial.<sup>21</sup> With different migration-hindering mechanisms, the obstruction rate was decreased substantially, but deflation or retrieval for non-ulcer intolerance still occurred.<sup>22</sup>

##### *Adjustable balloon system*

The Spatz Adjustable Balloon System (Spatz Medical, Great Neck, NY, USA) is a new intragastric silicone device developed with unique design features based on the original endoscopically placed intragastric balloon, that aims to address the abovementioned limitations. It was manufactured with characteristics that permit the inflation and deflation of the balloon with an extractable filling tube to improve patient efficacy and tolerance by adjusting the amount of saline solution filled in the intragastric balloon to prolong its 12-month implantation in the stomach with a loop remaining in the gastric lumen preventing balloon migration despite an eventual deflation. However, the complication rate reported in a case–control study was considerably high,<sup>23</sup> consisting of proximal small intestine

perforation in severe cases, which restricts the widespread promotion and application of this system. More research is needed to confirm the safety and efficacy of this system in a wider series.

### *Obalon*

The Obalon gastric balloon (Obalon Therapeutics Inc., Carlsbad, CA, USA) is a new device further proposed by researchers to reduce discomfort and complications of treatment and is approved by the FDA for patients with a BMI 30–40 kg/m<sup>2</sup>. The balloon is folded, compressed, and fitted in a swallowable gelatin capsule connected to a thin catheter, and 200 ml of a nitrogen-based mixed gas is injected through the catheter under X-ray surveillance after the capsule is ingested and proceeds to the gastric fundus. Up to 3 balloons can be deployed simultaneously within 6 months but still need to be removed endoscopically with general anesthesia at the end of treatment. This device is a valuable option and can be easily administered to both child and adolescent patients with appreciable weight loss and almost no sudden or serious adverse events.<sup>24</sup>

### *Eclipse*

The removal of balloons endoscopically can be unsafe and have several serious complications,<sup>22</sup> including esophageal perforation, aspiration pneumonitis, and anesthetic-related adverse events. Therefore, the Eclipse Balloon (Allurion Technologies, Wellesley, MA, USA) was further designed as a procedureless device that resides in the stomach for a scheduled period of several months without the requirement of endoscopy for placement and removal. It is folded into a vegetarian capsule and connected with a thin delivery catheter with a self-sealing valve. The capsule dissolves rapidly after being swallowed to the stomach; 550 ml of supplied filling solution fills the balloon through the catheter, and an abdominal X-ray or ultrasound is performed to confirm its position. The detachable catheter is then retrieved by simple pulling without sedation. The retained balloon was designed to be emptied when the valve is released 4 months later and spontaneously excreted from the gastrointestinal tract. The Eclipse is the first procedureless gastric balloon reported to have demonstrated clinically significant efficacy similar, or even favorable, to the outcome of previous endoscopically placed balloons.<sup>25,26</sup> Common adverse events include nausea, vomiting, acid reflux, and abdominal pain, which are either self-limiting or resolved with medication. It is still in clinical trials and currently has no FDA approval.

Different types of balloons have different capacities due to various materials and designs. The contents

generally include methylene blue-tinted normal saline in case the balloon is ruptured, as the methylene blue saline leakage will alert the clinician through the color change of urine and stool. Complications reported of intragastric balloon techniques mainly consist of nausea, vomiting, and abdominal discomfort, usually occurring within 3–7 days after placement and may be improved by treatment during hospitalization without early removal. From the comparison of these balloons, it is evident that Reshape balloons have a higher incidence of ulcers, while Orbera balloons have the highest incidence of GERD.

### *Aspiration therapy*

The AspireAssist System (Aspire Bariatrics, Inc., Kings of Prussia, PA, USA) is a novel obesity treatment approach approved by the FDA for patients older than 22 years with a BMI of 35.0–55.0 kg/m<sup>2</sup> who have failed to lose weight without surgery. Similar to percutaneous gastrostomy, this device permits the disposal of partial gastric contents by perfusing fluid into the stomach. Under normal circumstances, aspiration is performed approximately half an hour after the consumption of one meal to restrict energy absorption, generally there will be 25%–30% ingested calories removed with the device aspirating up to 3 times per day. A specially designed diet with proper eating habits is required for the normal and long-term manipulation of the device. Main adverse events, such as peritonitis, gastric ulcer, and abdominal pain, can be alleviated after treatment.<sup>27,28</sup>

### *Endoscopic sleeve gastropasty*

Endoscopic sleeve gastropasty (ESG) is an incisionless transoral bariatric procedure defined as endoscopic endoluminal greater curvature plication using an FDA-approved and commercially available endoscopic suturing device (OverStitch; Apollo Endo-surgery, Austin, TX, USA). The reduction of gastric capacity starts at the pylorus and extends proximally to the gastroesophageal junction with a series of full-thickness running sutures. Compared with the gastrectomy procedure, a restrictive sleeve is created to maintain the structural integrity, neuronal innervation, and blood supply of the gastric wall. Recent studies have demonstrated the technical safety, durability, and effect of long-term weight loss of ESG, as well as statistically significant physiologic changes, including increased insulin sensitivity, delayed gastric emptying, and improved metabolic profile.<sup>29–32</sup> The adverse events associated with this procedure are usually minor and include peri-gastric fluid, bleeding, pneumoperitoneum, and pneumothorax. A reverse

surgery is also available in case of postoperative intolerance occurrence, which makes ESG a desirable alternative for selected patients with obesity.

#### *Transoral outlet reduction*

Apart from direct interventions to address obesity, endoscopic technology, such as transoral outlet reduction (TORe), is also performed as a surgical remedy. An interrupted or purse-string suture is placed to reduce the anastomosis aperture after Roux-en-Y gastric bypass surgery with the help of an endoscopic suturing device to prevent long-standing weight regain. Symptoms of sore throat, nausea, vomiting, and epigastric pain are frequently mentioned among patients who undergo TORe, but serious adverse events such as leaks, bleeding, and mortality are rare.<sup>33,34</sup>

#### *Endoscopic duodenal-jejunal bypass sleeve*

The Endobarrier (GI Dynamics, Lexington, MA, USA) is a duodenojejunal bypass sleeve that mainly achieves weight loss by preventing normal gastrointestinal digestion and absorption. A 60 cm impermeable sleeve extends from the duodenal bulb to the duodenal and proximal jejunum, while the nitinol crown is anchored to the wall of the duodenal bulb, creating an isolated barrier that not only prevents the chyme from contacting with pancreaticobiliary secretions until in the uncovered intestine but also accelerates the speed of food passing through the duodenum and proximal jejunum. Recent studies have indicated that the bypassing effect of the Endobarrier may contribute to significant improvements in glucose homeostasis in type 2 diabetic patients by suppressing the secretion of certain hormones related to insulin resistance.<sup>35,36</sup> However, even with promising outcomes, a high incidence of early removal and separate serious adverse events, including esophageal perforation, make further prospective trials necessary to validate its safety.

#### **Bariatric endoscopy will become a hotspot of endoscopic technology**

Bariatric endoscopy remains an effective and durable treatment option, bridging the current gap in our management approach to obesity with emerging endoscopic technologies. Intra-gastric balloons are currently widely used in many countries due to their simplicity and relatively few complications, but often require a high demand of balloon material and volume. Moreover, ESG has

rigorous technical requirements for both equipment and operators with a limited number of clinical samples in China at present, and its effects and safety profile necessitate further research and observation. Aspiration therapy devices and endoscopic duodenal-jejunal bypass sleeves restrict the absorption of essential nutrients with the potential occurrence of postoperative malnutrition and the lack of trace elements, which still require diet regulation and long-term follow up.

In general, bariatric endoscopy is now established as a minimally invasive, potentially cost-effective, safe, and reversible procedure in the treatment of obesity with lifestyle interventions. With the continuous improvement of surgical methods as well as the enhancement of materials and equipment, bariatric endoscopy may become a research hot spot of endoscopy technology with broader prospects in the future.

#### **Summary and prospect**

As one of the leading chronic diseases worldwide, obesity is the underlying factor for many neglected gastrointestinal disorders, and patients with more severe obesity are at increased risk. Successful treatment and prevention require multidisciplinary participation, which is a long-term systematic project. The AGA recommends that physicians use the POWER program as a guide, to implement comprehensive and innovative personalized care for obese patients in addition to lifestyle modifications, including a reduced-calorie diet and physical activity as the cornerstones of treatment, and new medications, bariatric endoscopy, and surgery as important tools to achieve weight management safely and effectively. As internists and specialists in digestive disorders, endoscopists and gastroenterologists are in a unique position to play an important role in obesity treatment. It is important to pay attention to gastrointestinal symptoms and other comorbidities of obese patients, and even more important to implement health education and advocate a regular lifestyle before obesity occurs so that realistic goals may be achieved by multidisciplinary teams.

#### **Conflicts of interest**

None.

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