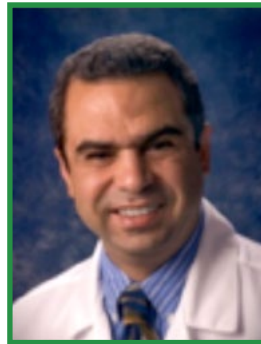


Gastric Embolization to Treat Obesity



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In 2008, more than 1.6 billion adults were overweight (body mass index [BMI] ≥ 25), with more than 400 million considered obese (BMI ≥ 30). Currently, more than one-third of adults in the United States are obese, and by 2030, it is expected that more than 42% of Americans will be obese. This trend is not exclusive to adults. In 2010, more than one-third of children and adolescents were overweight or obese, and since 1980, obesity rates have almost tripled. The prevalence of obesity has increased in both males and females across all ages, education levels, and racial and ethnic groups. **Obesity is on course to overtake tobacco as the main cause of preventable death in the United States.** Being overweight and obese is associated with an increased risk of several diseases, including diabetes, cardiovascular disease (ie, heart disease and stroke), endometrial cancer, breast cancer, colon cancer, sleep apnea, and osteoarthritis. Of these obesity-related conditions, diabetes may be the most closely linked to obesity. Type 2 diabetes mellitus (T2DM) affects 25.8 million Americans (8.3% of the population). In 2010, there were approximately 1.5 million new cases of T2DM in patients over 45 years of age. T2DM is associated with a two- to fourfold increase in the risk of heart disease or stroke and is a leading cause of new blindness. Following a healthy lifestyle can prevent individuals from becoming overweight and obese. Diet, exercise, and behavioral modification have long been the mainstay of weight loss plans. The National Institutes of Health (NIH) advises a 1,000 to 1,200 kcal/day diet for most women and a 1,200 to 1,600 kcal/day diet for most men, with a gradual weight loss goal of 1 to 2 lbs per week until weight is within

a healthy BMI category (18.5–24.9). Safe weight loss can occur with diet, exercise, and behavioral modification, but it is typically only maintained for 1 to 5 years.

Pharmacological interventions are rapidly being investigated. The current criteria used by the US Food and Drug Administration to demonstrate efficacy is a statistically significant weight reduction of 5% greater than the placebo group. **Patients who are unable to lose weight with diet, exercise, and behavioral modification and have a BMI ≥ 30 (or ≥ 27 with a comorbid medical condition) are eligible for drug treatment.** Examples of drugs used to treat obesity include sibutramine and orlistat. Sibutramine exerts its effects by inhibiting the reuptake of norepinephrine, serotonin, and dopamine; this product was removed from the market in 2010 due to adverse events. Orlistat works by inhibiting the action of gastric and pancreatic lipases. The short-term weight loss associated with these drugs is typically 5% to 10% of total body weight. Orlistat has common side effects, including flatulence and loose stools.

Bariatric surgery is indicated in patients with morbid obesity (BMI ≥ 40 or a BMI ≥ 35 with comorbid conditions). There are two general types of operations performed: those that restrict gastric volume (banded gastroplasty and sleeve gastrectomy) and those that alter digestion (Roux-en-Y gastric bypass). Bariatric surgery is considered the best long-term treatment for weight loss in these patients and also causes significant improvement in comorbid conditions, including T2DM, hypertension, and sleep apnea. In morbidly obese patients, bariatric surgery significantly reduced global, cardiovascular, and all-cause mortality.

Although bariatric surgery in general has low perioperative risks, complications vary significantly with weight and the overall health of the individual. In young patients without comorbidities and with BMI ≤ 50 , mortality rates are quoted at $< 1\%$. In patients with BMI ≥ 60 with diabetes, hypertension, and cardiopulmonary failure, mortality rates range from 2% to 4%. In addition, there are significant potential long-term complications, including development of incisional hernias, gallstones, dumping syndrome, and vitamin and mineral deficiencies. In certain populations, the role of bariatric surgery is not clearly defined, including



those with class I obesity (BMI = 30–35), very obese patients (BMI > 60), morbidly obese adolescents, and obese patients requiring weight reduction for another procedure. Despite the efficacy of bariatric surgery, it is currently utilized in $< 1\%$ of patients who meet the NIH criteria of BMI ≥ 35 . Weight gain after bariatric surgery can occur when patients fail to exercise and return to old eating habits. Recently, the peptide ghrelin was identified as a regulator of long-term appetite regulation and energy homeostasis. Ghrelin is a powerful appetite stimulant that is produced in the mucosa of the gastric fundus in response to hunger and starvation, signaling the brain to stimulate feeding. Ghrelin release results in increased growth hormone secretion, increased gastric acid secretion, gastric motility, and decreased gastric emptying. Ghrelin administration results in increased appetite and adiposity. Ghrelin levels have been shown to be associated with obesity.

The stomach typically receives its arterial supply via the celiac axis (Figure 1). The left gastric artery most commonly arises directly from the celiac axis and supplies the superior portion of the lesser curvature of the stomach, as well as the distal esophagus; it is the primary supply to the fundus of the stomach. The right gastric artery most commonly arises from the proper hepatic artery (or, less commonly, from the common hepatic artery) and supplies the inferior portion of the lesser curvature of the stomach to the pylorus. It can also arise from the gastroduodenal or left hepatic artery. The right gastroepiploic artery is a terminal branch of the gastroduodenal artery and supplies the inferior portion of the greater curvature of the stomach. The left gastroepiploic artery is the largest branch of the splenic artery and supplies the superior portion of the greater curvature of the stomach. The short gastric arteries are small branches arising from the splenic artery to supply

the greater curvature of the stomach, anastomosing with the left gastric and left gastroepiploic arteries. Embolization has been employed in the upper gastrointestinal (GI) tract since the 1970s for the management of GI bleeding. Ischemic complications rarely occur, as a result of the foregut's rich collateral blood supply. With this background in mind, it has recently been suggested that catheter-directed gastric embolization could serve as a treatment option for bariatric patients. The rationale behind this idea is that left gastric artery embolization can cause localized ischemia in the region of ghrelin production, which can therefore reduce ghrelin levels and reduce appetite. This idea has been supported by several preclinical studies.

In March 2013, the results of a first-in-human study performed by Kipshidze et al in Tbilisi, Georgia, were presented. These authors reported the results of left gastric artery embolization performed in five patients. Bead Block microspheres (BTG International, West Conshohocken, PA), PVA-hydrogel microspheres measuring 300 to 500 μm in diameter, were used for embolization. Endoscopy and ghrelin levels were obtained before and after embolization. All patients reported decreased appetite during the first week after the procedure. Weight loss was observed in all patients at 1-month follow-up. The mean initial weight decreased from 128 kg to 114 kg, and the mean initial BMI decreased from 42.3 to 37.9 between initial measurement and 1-month follow-up. No complications were observed in this population of patients. Even though this is only a small sample of patients, this study does demonstrate the potential efficacy of this procedure.

Finally, in 2013, Gunn et al presented the results of a retrospective study evaluating patients who underwent left gastric embolization for GI bleeding. When comparing patients undergoing this procedure with a matched control group, they found that patients undergoing embolization lost an average of 7.9% of their body weight within 3 months. The control group lost 1.2% of their body weight during the same amount of time, which was a statistically significant difference. Although this last study was not well controlled, it does provide additional signal in support of this procedure.

Gastric embolization is potentially an exciting advance in the treatment of obesity for patients who are not considered appropriate candidates for bariatric surgery. It is clear that we need a better understanding of this procedure and its safety, efficacy, and relationship to hormone reduction. The minimally invasive nature of the procedure, its safety and short hospital stay makes it a potential cornerstone in the treatment of obesity.