# Factors That Will Make or Break Bariatric Embolization for the Treatment of Obesity

The importance of defining clinical efficacy and safety in larger cohorts, determining the appropriate patient population, evaluating cost-effectiveness, and integrating bariatric embolization into the obesity care pathway.

**BY GODWIN ABIOLA, BA, AND CLIFFORD R. WEISS, MD, FSIR, FCIRSE**

Obesity is a burgeoning epidemic with staggering effects both on human health and health care costs worldwide. Treatment of obese patients requires multiple strategies for management. For most patients, the initial approach to weight loss involves lifestyle management, which includes diet changes, exercise, and behavioral interventions. Although effective for some patients, these interventions either fail from the outset or over the long term for the majority of patients. Forty percent of patients only achieve a 5% weight loss after 1 year, and as many as 50% of patients return to their original weight within 3 years after implementing lifestyle changes.[1,2] Typically, the next phase of treatment is pharmacotherapy with any number of agents that are currently available on the market, such as phentermine or orlistat. The magnitude of effect of this treatment is largely based on patient compliance and tolerance of side effects. However, the efficacy of these noninvasive and pharmacologic interventions are modest if used in isolation, with expected weight loss of 2 to 7 kg.[3,4]

More invasive approaches to initiate and maintain weight loss can be pursued in appropriately selected patients, usually in those who are severely obese. Minimally invasive endoscopic and bariatric surgical strategies aim to restrict meal size and/or absorption by altering the patient's anatomy. The most common minimally invasive endoscopic approaches include intragastric balloon placement and endoscopic sleeve gastrectomy, while common bariatric surgical approaches are the Roux-en-Y gastric bypass, sleeve gastrectomy, and gastric banding.[5-7] Bariatric surgical strategies tend to result in higher weight loss percentages, with losses as high as 36% with Roux-en-Y, and have the added benefit of correcting metabolic derangements such as diabetes and hyperlipidemia.[7] However, more invasive approaches carry a risk of morbidity and mortality that is further exacerbated by the fact that patients with obesity tend to have higher rates of surgical morbidity and mortality.[8] Thus, there is still much room in the field for an effective yet minimally invasive way to treat obesity.

Bariatric embolization is a relatively new, image-guided endovascular technique that may provide an alternative solution for weight loss in obese patients. This technique involves embolization of the arteries supplying the gastric fundus using an embolic agent, with the goal of inducing ischemia of the gastric fundus, the region mediating appetite-stimulating endocrine functions within the stomach. There is a growing body of evidence that bariatric embolization is efficacious for both weight loss and regulation of appetite-stimulating hormones, with minimal complications in select patients with obesity.[9-15]

Briefly, the current literature shows that bariatric embolization results in 7% to 17% weight loss and

appears to be well tolerated, with the most severe reported complications being gastric ulceration and epigastric discomfort.[9-15] Our pilot data demonstrate that bariatric embolization is technically feasible, well tolerated, and relatively effective. However, given that this procedure is still in its early phases, there is a paucity of studies and patients, variable prospective and retrospective study designs, and a lack of randomized controlled trials. As such, there is still much to learn about the procedure before we can draw definitive conclusions and determine whether it should be broadly adopted. Key factors in this decision include selecting the ideal patient population, standardizing the procedure, selecting clinically meaningful outcomes to determine efficacy, determining cost-effectiveness, and aligning with referring clinicians to help these patients with complicated cases.

## WHOM ARE WE TREATING?

To date, data are only available for a small number of patients who have undergone bariatric embolization, and considering the variability of the studies, it is difficult to draw definitive conclusions regarding safety and efficacy. There are published results from 41 patients at varying time points in prospective trials, and this number increases to 99 when retrospective studies are included. There are also a number of single-arm studies that are currently underway. In particular, patient inclusion and exclusion criteria have differed among the studies. For example, Bai et al included patients with a body mass index (BMI) ≥ 30 kg/m$^2$ in China, whereas trials performed by Weiss et al and Syed et al included patients with a BMI of 40 to 60 kg/m$^2$ in the United States.[11-13] Weiss et al[12] excluded patients with diabetes, while others did not, and Kipshidze et al[14] and Pirlet et al[10] specifically included patients with cardiovascular disease. Although interesting weight and metabolic changes were observed when patients were stratified according to different factors, statistically significant conclusions could not be drawn from these studies due to the small number of patients involved.

To better inform our colleagues and patients on the benefits and risks of bariatric embolization, it is important to carefully select patients to study in larger cohorts. For example, studies could target patients who fall into a narrow BMI range (similar to studies on endoscopic devices for obesity), are diabetic or prediabetic (to assess the effects on metabolic syndrome), are ineligible for bariatric surgery, or are seeking to lose a moderate amount of weight to become eligible for other procedures. Importantly, reducing the number of variables and comorbid conditions in study subjects needs to be a priority in order to determine the efficacy of bariatric embolization and eventually expand the procedure to other populations. Although it may be difficult to find patients without comorbid conditions in this population, it is critical that we understand which patients would benefit most from this procedure and for whom this procedure may be unsafe.

## HOW ARE WE TREATING?

Ensuring patient safety includes not only defining the target patient characteristics but also determining the technical aspects of the procedure and periprocedural care, including nonprocedural weight management strategies. Although the goal of bariatric embolization is to induce ischemia to the gastric fundus, studies have varied in the embolic materials and sizes used, anatomic targets and degree of embolization, periprocedural management and patient follow-up, and assessment of gastric function after the procedure. It is important to work toward standardizing the procedure to establish safety and efficacy and eventually for broader adoption.

The retrospective and prospective studies thus far have used a variety of embolic materials of different sizes, including coils, Gelfoam (Pfizer, Inc.), and glue in retrospective studies and polyvinyl alcohol, Embosphere microspheres (Merit Medical Systems, Inc.), and Bead Block (BTG International) in prospective studies.[11-14] Of note, the retrospective literature included patients who experienced incidental weight loss after embolization for the treatment of gastrointestinal bleeding.[15-17] Because these were clinical cases and not part of controlled studies, embolic selection and delivery site were determined based on operator experience and clinical need.[15,18] Differing embolic sizes and materials can lead to differences in ischemia in the target tissue, thus contributing to variability in the treatment effect and safety profile.

Studies have also varied in which vessels were embolized (left gastric vs left gastric and distal gastroepiploic), which might have implications for procedural efficacy and safety. Although the left gastric artery is always embolized in bariatric embolization, other arteries may contribute to the fundal supply. This variation is compounded by individual differences in patient anatomy. For example, the Uflacker system classifies up to eight variants just for the celiac artery.[19] In addition, the endpoint of embolization affects the degree of induced ischemia. Weiss et al established the endpoint as complete lack of perfusion of a vessel, defined as no observable flow after five cardiac beats on angiography.[12] Other trials, including both prospective and retrospective studies, have taken embolization to stasis or near stasis without clear definitions for those terms.

Further aspects that have varied among studies are periprocedural management and patient follow-up.

Many studies have not fully considered to what degree comprehensive weight management plays a role in the outcomes for these patients. Most trials recruited patients who had failed multiple weight loss attempts; however, a majority of studies made no mention of whether other weight loss strategies were followed in addition to the procedure. This factor can significantly confound the data, given the number of weight management strategies available to patients.

Finally, assessment of gastric function after bariatric embolization has not been consistent across pilot trials. Preclinical data have shown evidence of ulceration and gastritis after the procedure.[20,21] In addition, there have been varying reports of superficial gastric ulceration and no reports of changes in gastric mechanical function.[20,21] However, because bariatric embolization is a new procedure, it is important to continually and consistently monitor changes with tests such as endoscopy. More data on metabolic and hormonal changes after the procedure should also be acquired. Bariatric embolization is thought to work primarily by decreasing the amount of ghrelin production, thus suppressing appetite, although a few trials have shown inconsistent results. Ghrelin is not the only metabolic hormone involved in appetite, as other hormonal changes have been observed as well.[22] Future trials should incorporate a range of appetite-related hormones, including ghrelin, leptin, peptide YY, and others, to gain a full understanding of the effects of this procedure.

## WHY ARE WE TREATING?

When establishing outcome measurements, the goals of the treatment should be clarified, such as weight loss, adherence to a diet program, or other measures. Thus far, studies on bariatric embolization have reported weight loss as total weight loss, relative loss from baseline weight, or loss of excess weight from an "ideal weight."[23] Other reported measures have included abdominal waist circumference, abdominal adipose content, changes in BMI, quality-of-life assessments, and changes in hunger/satiety. Interestingly, the reported outcomes thus far have been relatively consistent, given the early stage of the current data.

If the goal of the procedure is to achieve long-term weight loss, primary efficacy endpoints should include at least mean percent loss of baseline body weight and categorical changes in body weight. Specifically, the FDA considers a technique to be efficacious for weight management if the difference in mean weight loss between the active product- and sham-treated groups is at least 5% and the difference is statistically significant. Further, the proportion of patients who lose ≥ 5% of baseline body weight in the active product-treated group should be at least 50% and approximately double the proportion in the placebo-treated group, and the difference between groups should be statistically significant when measured 1 year after the procedure.[24,25] If the goal of the procedure is to achieve short-term weight loss, such as to qualify for another procedure (orthopedic, transplant), then the weight loss target may shift. Finally, if the goal of bariatric embolization is to improve a patient's ability to adhere to an existing diet program, changes in appetite, satiety, and quality-of-life measures may be paramount.

Secondary endpoints may include metabolic changes (hemoglobin A1c, fasting glucose and insulin levels, lipid levels), hemodynamic changes (blood pressure, resting heart rate), and waist circumference (indirect measure of visceral fat). These measures of course can be tailored to specific questions, but in the early phases of development, we recommend a comprehensive approach to data collection in all study subjects.

## IS IT SAFE?

The focus of the pilot trials on bariatric embolization thus far has been primarily short-term safety and efficacy, with the longest trial to date having followed patients for up to 1 year postprocedure. So far, this procedure has been demonstrated to be relatively well tolerated, with superficial gastric ulceration, transient abdominal pain, nausea, and vomiting as the most reported complications. In theory, the most severe potential complication is gastric perforation; however, this has not been reported to date nor have any other major adverse events. That being said, it is not yet possible to declare this procedure to be "safe" due to the small number of patients in the pilot studies and variation among the studies in patient populations, technique, and periprocedural assessments. One concern raised by some surgeons is whether bariatric embolization may preclude patients from future bariatric surgery. Although this is not likely to be the case, studies will need to be performed to confirm this. Until then, a desire to undergo future bariatric surgery should be considered a contraindication to bariatric embolization.

## WILL IT BE COST-EFFECTIVE?

A question that has not yet been addressed is how bariatric embolization will fit within the financial scheme of weight loss therapy, as reported data have only been collected as part of research protocols or for gastrointestinal bleeding. It may be a possible therapy for those who have attempted noninvasive techniques with limited success and do not want to or are unable to undergo a more invasive option. Conversely, bariatric embolization may be deemed more cost-effective

for patients who need to undergo rapid weight loss in a limited amount of time to qualify for other critical surgeries. Relative efficacy and cost-effectiveness studies comparing bariatric embolization to other weight loss procedures will need to be performed once efficacy and safety are established.

## HOW WILL BARIATRIC EMBOLIZATION BE INTEGRATED INTO THE OBESITY CARE PATHWAY?

Interventional radiologists will need to align themselves with obesity medicine specialists, dieticians, gastroenterologists, and surgeons to provide optimal treatment for obese patients. How these specialists collaborate will ultimately affect whether bariatric embolization becomes a viable procedure. As previously discussed, bariatric embolization may be appropriate for patients with certain classes of obesity or degrees of metabolic derangements, or it may be another tool to work in synergy with existing therapies. Either way, obesity and its complications are so prevalent, dangerous, and costly that collaborative care is a necessity. Working together with other clinicians will help us achieve the best tailored care for patients based on their personal obesity profiles. Just as we have with cancer, interventional radiologists should become educated about obesity, become actively involved in multidisciplinary obesity clinics, and provide valuable options for their patients.

## CONCLUSION

Bariatric embolization has shown promising initial results, including weight loss and correction of metabolic derangements. The hope is that this procedure will become an effective and widely used part of our tool kit to fight the growing obesity epidemic. Although bariatric embolization appears to be technically feasible, well tolerated, and demonstrates a degree of efficacy, many steps are still needed for safe, widespread adoption. The next stage will be challenging, as we endeavor to define true clinical efficacy and safety profiles, determine the most appropriate patient population for this treatment, calculate costs and payment schemas, and integrate this procedure with those of other weight loss clinicians. With progressive, careful, and collaborative research, the future of interventional radiology's role in the treatment of obesity is bright. ■

*Acknowledgments: The authors would like to acknowledge Christopher Bailey, MD, for his assistance with manuscript preparation and editing.*

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*Disclosures: Grant support from BTG, Siemens Healthcare, Merit Medical Systems, Inc., Medtronic; consultant to Medtronic and BTG.*