Research progress of bariatric embolization for treatment of obesity

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To the Editor: The prevalence of obesity, defined as body mass index (BMI) ≥30 kg/m^2, is increasing worldwide and has been identified that obesity is a risk factor for several kinds of chronic diseases.[1] According to the severity of obesity, associated coexisting chronic diseases, and functional limitations, therapies for obesity include lifestyle intervention (eg, diet and exercise), pharmacotherapy, endoscopic bariatric therapies, bariatric surgery, and bariatric embolization (BAE).

Patients who fail to lose weight by lifestyle intervention but are not candidates for bariatric surgery have few other treatment options. Except pharmacotherapy and endoscopic bariatric therapies mentioned earlier, BAE, a minimally invasive technique performed by interventional radiologist under the imaging guidance has been introduced.

Since about 90% of ghrelin was produced from the fundus of the stomach, embolization of the blood supply of the fundus through left gastric artery (LGA) and, to a lesser extent, the gastroepiploic artery (GEA) should lead to ghrelin decrease ideally. Obese patients fail to suppress ghrelin levels after eating food and lead to overeating. By making ischemia in the gastric fundus, BAE destructs the ghrelin-producing cells to decrease ghrelin production and control body weight.[2]

The first animal study of BAE was performed by Arepally *et al*.[3] The study showed that ghrelin levels could be significantly altered with embolization of the gastric artery using morrhuate sodium. After that, a series of early animal studies performed in growing swine and obese dogs showed a decrease in serum ghrelin levels as well as an increased absolute weight loss or decreased weight gain when compared to the control group.

With a relatively short period of clinical investigations of BAE, the clinical data in this field are limited[4-10] [Table 1]. Gunn and Oklu[4] and Anton *et al*[5] reported their retrospective studies regarding BAE in 2014 and 2015, respectively, with preliminary positive treatment efficacy and safety observed. Three prospective studies were then reported also with promising treatment safety and short-term efficacy.[6-8]

To date, there are two ongoing clinical trials focusing on BAE, both of which have reported and published their preliminary results.[9,10] Among them, the first reported study is the Bariatric Embolization of Arteries for the Treatment of Obesity (BEAT Obesity) trial carried out by Weiss *et al* at Johns Hopkins Hospital in the United States.[9] Five severely obese patients (four women, one man) with a mean BMI of 43.8±2.9 kg/m^2 without clinically important comorbidities were enrolled in the preliminary study. The results showed that no major AEs occurred. Regarding to treatment efficacy, there was 5.9% excess weight loss at the 1-month time point (n=5) and 9.0% at the 3-month time point (n=4), respectively. Mean fasting serum ghrelin was relatively unchanged from baseline at weeks one and two during the follow-up. It increased by 8.7% and decreased by 17.5% from baseline at 1 and 3 months, respectively. The preliminary results of BEAT Obesity trial demonstrated that BAE is safe and has potential efficacy for the treatment of obesity.

The latest published preliminary study of an ongoing trial is the one carried out by Bai *et al* in China.[10] The preliminary study included five obese patients whose BMI were higher than 30 kg/m^2. The mean BMI of the included patients was 38.1 kg/m^2. No serious AEs were observed. In terms of efficacy, the mean body weight loss at 3, 6, and 9 months after BAE was 8.28, 10.42, and 12.90 kg, respectively, showing a continuous loss during the follow-up. Serum ghrelin levels decreased by 40.83%, 31.94%, and 24.82% at 3, 6, and 9 months after BAE, respectively. Similar to BEAT Obesity trial, this Chinese trial demonstrated safety and potential efficacy regarding BAE.

Weiss and Teng updated their studies' 1-year outcome in two international academic meetings in 2018. With the

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Table 1: Characteristics and treatment outcomes of clinical studies.

First author/year	Sample size, *n*	Embolic agent	Embolic size (μm)	Diabetes	Follow-up (months)	Primary endpoint	AEs	Pre-procedure BMI (kg/m^2)	Pre-procedure Weight (kg)	Post-procedure weight (kg)	Latest updated weight* (kg)
Gunn and Oklu/2014[4]	19	Coils, gelfoam, PVA	300–500 500–710 710–1000	Unknown	13.6	Weight loss	Unknown	30.3	Unknown	Unknown	N/A
Anton *et al*/2014[5]	10	Coils, gelatin sponge pledget suspension	Unknown	Included	12	Weight loss	Unknown	31	97.3	Unknown	N/A
Kipshidze *et al*/2015[6]	5	BeadBlock	300–500	Unknown	24	Weight loss	Mild transient epigastric discomfort	42.2	128.1	106	N/A
Syed *et al*/2016[7]	4	BeadBlock	300–500	Included	6	Safety	Mild nausea, occasional vomiting, mild epigastric discomfort	42.4	117.6	108.4	N/A
Pirlet *et al*/2018[8]	7	PVA	300–500	Included	12	Feasibility and safety	None	52	160	147	N/A
Weiss *et al*/2017[9]	5	Embosphere	300–500	Excluded	3	30-day AEs	Transient pancreatitis, asymptomatic superficial ulcer	43.8	127.8	123.1	120.2
Bai *et al*/2017[10]	5	PVA	500–710	Included	9	Safety	Superficial linear ulceration, hematoma in puncture site	38.1	102.0	89.1	90.1

*Updated weight loss at 12 months post-procedure. AEs: Adverse events; BMI: Body mass index; PVA: Polyvinyl alcohol.

latest reported data of two ongoing trials in this updated review, we found that the intermediate results (1 year) regarding safety and efficacy on BAE are positive and promising. Compared to bariatric surgery and endoscopic therapy, the mean excess weight loss of BAE is lower (up to 30% *vs*. about 10%) and BAE procedure seems safer, with fewer complications occur. Therefore, several key questions regarding BAE should be answered before it becomes a widely accepted treatment approach for obesity.

First, although obvious weight loss at 1-year follow-up, there were both slight weight regain when compared it to the last follow-up point (6 and 9 months, respectively) of the BEAT Obesity trial and Chinese trial. Repeat embolization such as transarterial chemoembolization for hepatocellular carcinoma or whether BAE should be supplemented with other treatments, such as banding and pharmacology, needs to be explored in the near future.

Second, the ideal candidate for BAE is unclear. The patients' BMI in the GET LEAN and BEAT Obesity trials was no less than 40 kg/m^2, and it was no less than 30 kg/m^2 for patients included in the Chinese trial. The difference in BMI can be attributed to cultural differences and all three trials demonstrated a similar range of weight loss, with the highest decrease level in Chinese trial. The results of these three trials suggest that BAE may be more effective in treating obese, but not severely or morbidly obese patients.

Third, does BAE have an effect on diabetes? With a clinically significant effect observed in one patient in the GET LEAN trial and a general reduction in HbA1c observed in the BEAT Obesity trial, it is interesting to find out whether BAE has an effect on diabetes with larger sample in the near future.

Last, what is the standard way to perform BAE? Different kinds of embolic agents with different diameters have been applied in the previous animal and human studies. Moreover, the embolized blood vessels and the embolization endpoints also varies. LGA is the most common main target for embolization. However, In the BEAT Obesity trial, the embolization target was "fundal arteries," which included LGA branches, as well as the distal GEA, if it was considered a significant source of fundal perfusion.

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Conflicts of interest

None.

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