Bariatric Gastric Artery Embolization For Weight Management: How Is It Done: How Effective Is It (The LOSE-IT RCT) And Will It Replace Bariatric Surgery
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Potential conflicts of interest
Dr. Nickolas Kipshidze:
I have the following potential conflicts of interest to report:
• Founder and significant equity holder of EndoBar Solutions LLC

Obesity, An Epidemic!
• WHO: 1.5 billion overweight; 500 million obese
• Major risk factor for Diabetes, CAD, Stroke, Cancer
• Billions in healthcare economic burden
• Fifth leading risk for death globally

Weight and cardiovascular disease

<table>
<thead>
<tr>
<th>BMI range (kg/m²)</th>
<th>Relative risk of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean</td>
<td>1.0</td>
</tr>
<tr>
<td>Overweight</td>
<td>1.4</td>
</tr>
<tr>
<td>Obese</td>
<td>2.2</td>
</tr>
</tbody>
</table>


How Much Weight Loss Is Needed to Prevent T2DM–Not Very Much: The DPP Experience

Change in Weight from Baseline (kg) 0 5 10 15 20 25 30
How effective enough for many people

Diet and Lifestyle 5% 10% 15%
Lap Band 20% 25%
Gastric Bypass 30% 35%
Too risky for many people

The Treatment Gap in Bariatric Therapy

% Effective weight loss

Incidence Rate per 100 Person-Years

Ghrelin: The Hunger Hormone

Ghrelin is a hormone produced mainly by P/D1 cells lining the fundus of the human stomach and epsilon cells of the pancreas that stimulates hunger.

- The most potent appetite stimulant
- Levels rise before meals
- Levels fall after eating
- Levels increase with dieting

Can we target Ghrelin for weight control?

Transcatheter Approach
The Left Gastric Artery

- 90% Ghrelin is produced in the stomach fundus
- The left gastric artery (LGA) is the principal source of arterial supply to the gastric fundus.
- Arterial embolization procedures are well characterized and safe
- LGA embolization can reduce ghrelin production, potentially leading to weight loss.

Bariatric Surgery Options

<table>
<thead>
<tr>
<th>Bariatric Surgery Options</th>
<th>Component</th>
<th>Technique</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustable Gastric Banding</td>
<td>Component</td>
<td>Endoscopy</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Sleeve Gastrectomy</td>
<td>Component</td>
<td>Minimally Invasive</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Roux-en-Y Gastric Bypass</td>
<td>Component</td>
<td>Open Surgery</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Biliopancreatic Diversion/Duodenal Switch</td>
<td>Component</td>
<td>Colonoscopic</td>
<td>Weight Loss</td>
</tr>
</tbody>
</table>

Bariatric Embolization: From Theory to Practice

- 2002: Cummings described role of the ghrelin hormone in bariatric therapy
- 2012: Olu reported significant weight loss after gastric embolization for bleeding in patients
- 2012: Kipshidze. First-in-man study (Georgia and Germany)
- 2014-2017 U.S. physician sponsored IDEs to study LGA embolization for weight loss; ongoing

Concept Validation in Animals (well studied): Summary of Gastric Embolization Preclinical Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Embolic Agent</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arepally</td>
<td>2007</td>
<td>6</td>
<td>Morrhuate Sodium</td>
<td>Weight Gain</td>
</tr>
<tr>
<td>Arepally</td>
<td>2008</td>
<td>10</td>
<td>Morrhuate Sodium</td>
<td>Weight Gain</td>
</tr>
<tr>
<td>Bawudun</td>
<td>2012</td>
<td>10</td>
<td>PVA 500-700μ</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Paxton</td>
<td>2013</td>
<td>12</td>
<td>Particles 40μ</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Kipshidze</td>
<td>2012</td>
<td>18</td>
<td>Particles 300-500μ</td>
<td>Weight Loss</td>
</tr>
</tbody>
</table>

* Less non-target embolization and greater weight loss and decreases in serum ghrelin levels with PVA particles.
** Significant incidence of ulcers, gastritis, and esophageal strictures.

Significant Side Effects: Non-Target Embolization

- Ulcers in 2/6 (33%) animals
- Gastritis in 6/6 (100%) animals
Gastric embolization with commercially available catheter: antegrade and retrograde reflux

Animal Study Angiographic Results with Endobar

No reflux, no distal distribution microspheres

Why size of particles matters?

Submucosal arteries 200-300 microns in ID

Mucosal arteries 50 microns in ID

Precise Selective Embolization of Submucosa

First-In-Man study of Left Gastric Artery Embolization for treatment of obesity

Study details

Methods:
• 5 obese patients underwent left GAE.
• Gastroscopy was performed before and after GAE and at 1 week
• Blood Ghrelin level was measured at baseline and at follow up.
• Weight loss measured at 30 days

Patient demographics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>n = 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender female/male (%)</td>
<td>20/80%</td>
</tr>
<tr>
<td>Age female/male (years)</td>
<td>44.7 ± 7.4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>128.1 ± 24.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>42.2 ± 6.8</td>
</tr>
<tr>
<td>Ghrelin (pg/ml)</td>
<td>473.4 ± 189.1</td>
</tr>
</tbody>
</table>

Results:
• No periprocedural complications
• 3 / 5 patients experienced acute epigastric pain
• No ulceration, abnormalities per gastroscopy
• Significantly decreased appetite, weight loss and ghrelin suppression in all patients
Weight in kilograms over time in months

*Individual weights are outlined via dashed lines and average weight (with standard deviation) in a solid line.

Mean change in weight loss

Mean change in weight loss

LGA Embolization

Before embolization: catheter at mid portion of LGA
After embolization: Absence of flow in distal LGA

Preliminary Results of Clinical Studies

<table>
<thead>
<tr>
<th>Number</th>
<th>Follow-up</th>
<th>Before</th>
<th>After</th>
<th>Weight Loss Mean</th>
<th>Minor Adverse Events</th>
<th>Major Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>24 mos</td>
<td>16%</td>
<td>0</td>
<td>9%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>20 mos</td>
<td>9%</td>
<td>0</td>
<td>6%</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>3-6 mos</td>
<td>8%</td>
<td>0</td>
<td>8%</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>6 mos</td>
<td>6%</td>
<td>0</td>
<td>1-1.5kg/mos</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>12 months</td>
<td>6%</td>
<td>0</td>
<td>6%</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>9 mos</td>
<td>9%</td>
<td>0</td>
<td>9.5%</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>2 mos</td>
<td>9%</td>
<td>0</td>
<td>9%</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>62</td>
<td>2-24 mos</td>
<td>10%</td>
<td>0</td>
<td>10%</td>
<td>35.4%</td>
<td>0</td>
</tr>
</tbody>
</table>

Early Work Lessons

- Bariatric embolization is technically feasible and effective
- Ghrelin suppression and weight reduction demonstrated extensively
- Use of embolic spheres/particles is more clinically relevant: size and location are critical to procedural effectiveness and safety
- Concern over non-target embolization and high level of FDA required safety profile limits generalization of procedure with off the shelf devices
- Clinical generalization of Bariatric Embolization requires the development of a dedicated micro-catheter and infusion system
Next Steps

- Diabetic Patients
- Randomized Study using dedicated device
- Multidisplinary Obesity Team

Efficacy and Safety of EndoBar Bariatric Embolization for Weight Management in People with Obesity

- Prospective sham controlled, single-blind 12-month trial with 1:1 randomization
- PI – Martin Fried, MD
- Co-PI – Vivek Reddy, MD
  Robert Rosen, MD
  Peter Neuzel, MD
  Homolka Hospital, Prague, Czech Republic
  OB Klinika, Prague, Czech Republic

OUS Clinical Study (January 2017):
Efficacy and Safety of EndoBar Bariatric Embolization for Weight Management in People with Obesity

Key Inclusion Criteria
- Patients with BMI >35
- with crossover to therapy for sham group at 6 months

Primary Endpoints

- **EFFICACY ENDPOINTS:**
  - Primary efficacy endpoint of the study was difference in percent of total body weight loss at 6 months.
- **SAFETY ENDPOINTS:**
  - 1. Incidence of device-, procedure- and therapy-related adverse events
  - 2. Incidence of device related, or unrelated, serious adverse events, including unanticipated adverse device effects

SECONDARY OUTCOMES:

- **SECONDARY OUTCOMES:**
  - The secondary outcomes measured at 6-months are:
    - Percent excess weight (%EWL) at 6 months. Percent total body weight loss from baseline at 12 months
    - Proportion of subjects who achieve ≥5% and ≥10% total body weight loss from baseline
    - Percent change in selected coronary heart disease risk factors: plasma triglyceride and HDL-cholesterol, and systolic and diastolic blood pressure
    - Success of performing the radiological procedure

Additional Endpoints of Interest (assessed at baseline and at 6 months)

- Changes in mood (depression/anxiety)
- Change in quality-of-life
- Change in eating behavior
- Change in gastric emptying of liquids and solids
- Change in volume of Ensure consumed to achieve satiation
- Change in plasma ghrelin and glucagon-like peptide 1 concentrations
- Change in oral glucose tolerance and insulin sensitivity