Endoscopic Approaches to the Management of Obesity

Steven A. Edmundowicz MD FASGE
Professor of Medicine
Chief of Endoscopy
Washington University School of Medicine
St. Louis, Missouri
Primary Endoscopic Bariatric Therapies

- Endoscopic gastric restriction
- Balloons
- Aspiration Therapy
- Sleeve’s
The shape of things to come
An Obesity Epidemic

• 78 million U.S. adults are obese
  – 17% of U.S. children
• Estimated 32 million more people will be obese in 2030 (42% of US population)
  – Severe obesity (> 100 pounds overweight) expected to double (11% of US population)
• Costs
  – Obesity accounts for at least 9% of health spending → $150 billion
  – Incremental cost of $1,429/obese person

CDC, “Weight of the Nation,” May, 2012
Obesity Trends Among U.S. Adults (BMI ≥ 30)

- **1990**
- **2000**
- **2010**

www.cdc.gov
# Current Surgical Treatments

<table>
<thead>
<tr>
<th>Invasiveness</th>
<th>Adj. Gastric Band</th>
<th>Gastric Sleeve</th>
<th>Roux-en-Y</th>
<th>BPD/DS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>30</td>
<td>&lt;5</td>
<td>60</td>
<td>&lt;5</td>
</tr>
<tr>
<td>EWL @ 1 yr [%]</td>
<td>49.5</td>
<td>60</td>
<td>70.1</td>
<td>71.7</td>
</tr>
<tr>
<td>Mortality [%]</td>
<td>0.1</td>
<td>0.3</td>
<td>0.5 (0.3 HVC)</td>
<td>1.1</td>
</tr>
<tr>
<td>SAEs* [%]</td>
<td>&lt;0.5</td>
<td>1.0</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>GI Symptoms [%]</td>
<td>7.0</td>
<td>10</td>
<td>16.9</td>
<td>37.7</td>
</tr>
</tbody>
</table>

*Major AEs include leak, blockage, bleeding, reoperation, medical (stroke, cardiac, etc.)*

Source: Buchwald 2004, Maggard 2005
Longevity of Weight Loss

Sjostrom, et al, NEJM 2004
Demand for endoscopic therapies

- Limited efficacy and durability of lifestyle interventions and pharmacotherapy
- Arguments against surgery
  - 20% of obese Americans have class II-III obesity (BMI > 35)
  - Significant morbidity (3-20%) and mortality (0.1-0.5%)
    - Only 1 in 400 class III individuals undergo bariatric surgery in the U.S.

Concept of endoluminal therapy for morbid obesity

- Flexible endoscopic procedure
- Safer with less morbidity than lap surgery
- Alters or effects GI tract to result in weight loss that is long lasting
  - Amount of weight loss can be less than surgery
  - Weight loss would lead to a documented improvement in comorbidities
  - Weight loss should be durable (with or without reapplication of an endoscopic procedure)
Obesity Treatment

- Bariatric Surgery
- Bariatric Endoscopy
- Pharmacotherapy
- Lifestyle Therapy

Risk

Weight Loss
Endoscopic Treatment of Obesity

• Gastric Balloons
<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
<th>Design</th>
<th>Fill</th>
<th>Placement/Retrieval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORBERA (formerly BioEnterics Intragastric Balloon)</td>
<td>Apollo Endosurgery, Austin, TX</td>
<td>500ml Silicone balloon</td>
<td>500 ml Saline with methylene blue</td>
<td>Endoscopic/Endoscopic 6 month duration</td>
</tr>
<tr>
<td>ReShape Duo Balloon</td>
<td>ReShape Medical, San Clemente, CA</td>
<td>Two 450ml Silicone balloons tethered to a flexible silicone shaft</td>
<td>375-450 ml Saline with methylene blue</td>
<td>Endoscopic/Endoscopic 6 month duration</td>
</tr>
<tr>
<td>Heliosphere Bag</td>
<td>Helioscopie Medical Implants, Vienne, France</td>
<td>550 cm³ polyurethane and silicone sphere</td>
<td>550 ml Air</td>
<td>Endoscopic/Endoscopic 6 month duration</td>
</tr>
<tr>
<td>Spatz Adjustable Gastric Balloon</td>
<td>Spatz FGIA, Jericho, NY</td>
<td>800ml Silicone Balloon mounted on a catheter, adjustable after initial placement</td>
<td>500-800 ml Saline</td>
<td>Endoscopic/Endoscopic 12 month duration</td>
</tr>
<tr>
<td>MedSil Balloon</td>
<td>MedSil, Moscow, Russia</td>
<td>700 ml Silicone Balloon</td>
<td>400-700 ml Saline</td>
<td>Endoscopic/Endoscopic 6 months</td>
</tr>
<tr>
<td>Silimed Gastric Balloon</td>
<td>Silimed Industria de Implantes, Rio De Janeiro, Brazil</td>
<td>650 ml Silicone balloon</td>
<td>632 ml saline, 20 ml Iopamiron contrast, 10 ml 2% methylene blue</td>
<td>Endoscopic/Endoscopic 6 months</td>
</tr>
<tr>
<td>Obalon</td>
<td>Obalon Therapeutics, Carlsbad, CA</td>
<td>250 ml porcine protein balloon, up to 3 placed sequentially</td>
<td>Nitrogen gas</td>
<td>Swallowed Pill/Endoscopic 3 months</td>
</tr>
</tbody>
</table>
Intragastric balloons

- Historical precedent: Garren-Edwards Gastric Bubble (GEGB), 1985 - 1988

Intragastric balloon

- Favorable short term (6 month) weight loss data
  - 2,515 patients (mean BMI 44.8 ± 7.8)
  - %EWL at six months 33.9 ± 18.7
    - Improvement/resolution of diabetes in 87%
    - Complication rate 2.8% (0.2% perforation)
- Cochrane meta-analysis of RCTs did not reveal a significant weight loss benefit of intragastric balloons

Intragastric balloon for treatment-resistant obesity: safety, tolerance, and efficacy of 1-year balloon treatment followed by a 1-year balloon-free follow-up

Elisabeth M. H. Mathus-Vliegen, MD, PhD, Guido N. J. Tytgat, MD, PhD


BioEnterics Intragastric Balloon
400-800ml adjustable

Plain abdominal radiograph showing balloon in body of stomach.
Duo balloon

Figure 1 Graphic of ReShape Duo™ Inserted in the Stomach

Table 1 OUS ReShape Percent Excess Weight Loss at 6 Months – Early Designs

<table>
<thead>
<tr>
<th>OUS Studies</th>
<th>Average BMI BMI ± SD (n) [95% CI]</th>
<th>Weight loss kgs ± SD (n) [95% CI]</th>
<th>Mean %WL % ± SD (n) [95% CI]</th>
<th>Mean %EWL % ± SD (n) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>900 ml early design</td>
<td>41.8 ± 3.8 (43) [40.6, 42.9]</td>
<td>23.3 ± 6.9 (35) [21.0, 25.7]</td>
<td>18.9 ± 5.1% (35) [17.1, 20.6%]</td>
<td>48.5 ± 14.5% (35) [43.5, 53.5%]</td>
</tr>
</tbody>
</table>

OUS = outside U.S., BMI = body mass index (kg/m²), CI = confidence interval, kg = kilogram, SD = standard deviation, n = number of subjects, %WL = percent weight loss, %EWL = excess weight loss.
ReShape Duo Balloon
US Multicenter Trial
Obesity Week November 2014

• The REDUCE Pivotal Trial was a prospective, sham-controlled, double-blinded, randomized multicenter clinical study
• 264 subjects BMI 30 – 40, (187 DUO and 77 DIET)
• 2 Primary Endpoints
  – mean %EWL between DUO and DIET subjects at 24 weeks with a minimum superiority margin of 7.5%.
  – The second endpoint was a comparison of the proportion of DUO subjects achieving at least a 25%EWL to a pre-specified performance goal of 35%.
• DUO subjects had a 25.1 ± 1.6(SE) %EWL and DIET subjects 11.3 ± 1.9(SE) %EWL (intent-to-treat basis, p value 0.0041 accounting for 7.5% superiority margin).
• The intent-to-treat proportion of DUO subjects who achieved a 25%EWL or greater weight loss at 24 weeks was 48.8%,
• Minor adverse events, 15% superficial ulcerations.
TransPyloric Shuttle BAROnova
Endoscopic Treatment of Obesity

- Gastric Balloons
- Aspiration Therapy
Aspiration Therapy Leads to Weight Loss in Obese Subjects: A Pilot Study

Shelby Sullivan, Steven Edmundowicz, Richard Stein, Sreenivasa Jonnalagadda, and Daniel Mullady,
AspireAssist System

Percutaneous Endoscopic Gastrostomy tubes commonly used for feeding in patients unable to eat and for removal of gastric fluid in patients with intestinal obstruction.

~20-min after meals, 2-3 x/day (5-15 minutes) Aspirate gastric contents

Removes ~ 25-30% of consumed calories
Randomized Control Trial

Control Group
Randomized n=7

Analyzied at week 52 n=4
Drop Out n=3

AT Group
Randomized n=11

15 Session diet and behavioral weight loss program

Analyzied at week 52 n=10
Drop Out n=1

PPI, Potassium

Analyzied at week 104 n=7
Effect of Aspiration Therapy on Body Weight

Percent Weight Loss

Time (Weeks)

0 24 52 76 104

Control

AT 52 week n=10

AT 104 week n=7

Percent Excess Weight Loss

Time (Weeks)

0 24 52 76 104

Control

AT 52 week n=10

AT 104 week n=7
Aspire Bariatrics current status

• CE approval and sales ongoing in Europe with an open label and registry study
• Pathway trial with US enrollment now complete in this RCT of 200 patients hoping to obtain FDA approval, final results in late 2015
Endoscopic Treatment of Obesity

- Gastric Balloons
- Aspiration Therapy
- Sleeve technologies
Duodeno Jejunal Bypass Sleeve

Nitinol anchor, barbs, retrieval drawstring. Impermeable fluoropolymer liner, 2 feet long.

The EndoBarrier™ is an investigational device. It is currently in clinical trials and is not yet commercially available.
Sleeve placement

DJBS Study - Chile

GI Dynamics Sleeve

- IPO in Australia raised funds for additional studies and attempt for FDA approval
- Improvement in HgbA1c noted in all diabetic patients with some durability after sleeve removal
- Ongoing >400 patient multicenter randomized sham study with primary endpoint of diabetes improvement (HgbA1c)
Gastroduodenojugal bypass sleeve (ValenTx)
Endoscopic Treatment of Obesity

• Gastric Balloons
• Sleeve technologies
• Endoscopic Gastroplasty
Figure 1. EVG stitching pattern. A, A frontal cross-section view of the stomach after all stitches were placed. B to D, Cross-sections of the stomach as the suture is pulled tight and secured to complete the EVG procedure. Fogel et al. GIE 2008;68:51-8
Figure 3. The percentage excess weight loss for the 64 patient population, segmented into subpopulations by BMI range: group I (BMI 40+ kg/m², n = 33), group II (BMI 35-40 kg/m², n = 19), and group III (BMI < 35 kg/m², n = 12).

Fogel et al. GIE 2008;68:51-8
Endoscopic Suturing
Endoscopic suturing

- Innovative device attaches to double channel endoscope for full thickness suturing.
- Allows the endoscopist the opportunity to close sizable defects.
Complications of Obesity Surgery: Gastrogastric Fistula

Devices in early clinical trials
Varied distribution of techniques

• **Endoluminal restrictive procedures**
  – Overstitch by Apollo endosurgery
    • Transoral Sleeve type gastroplasty
      – Registry trial beginning
  – G-Prox by USGI
    • Transoral Gastric Fundus reduction
    • Extensive use in Europe
    • RCT pivotal trial completed enrollment

• **Awaiting trials and long term results**
Endoluminal Therapies for Obesity

1. Complicated devices/procedures require intubation and general anesthesia, OR like environment with one to two operators.
   Compete with laparoscopic gastric bypass

2. Less complex devices that can be done in outpatient centers with MAC.
   Compete with Laparoscopic Adjustable Band

3. Simple devices that can be placed in outpatient centers with minimal sedation
   Compete with diet plans like weight watchers
Endoscopic Therapy of Obesity

- Devices are available outside of the USA
- Endoscopic suturing is available in the US today
- FDA will see and likely approve devices with obesity indications starting in 2015
  - Balloons
  - Other devices
    - Fundic plications (G-Prox)
    - Aspiration therapy
    - Duodenal sleeve
Endoscopic Bariatric Center

• Patient education and selection
• Lifestyle education
  – Diet
  – Exercise
  – Psychological support
• Physician education and leadership
  – Obesity training and education
  – Device training and education
Endoscopic Bariatric Center

Physical facility

- Mobility issues
  - Access, waiting room, bathroom, wheelchairs
- Scale, exam rooms, consultation rooms
- Anesthesia support
- Special endoscopes
- Observation area admissions (23 hour)
Endoscopic Bariatric Center

options to consider

• Work with an existing bariatric center that has the support services in place
  – Provide a specific treatment(s) through that center
    • Requires device specific training
    • Understanding of obesity related issues and expectations

• Develop an Endoscopic Bariatric Center
  – Develop your own expertise in obesity management
  – Develop expertise in techniques and devices
  – Develop complete support system for patients
  – Refer appropriate candidates to a surgical center
Multidisciplinary Weight Management Center

- Surgery
- Bariatric Endoscopy
- Pharmacotherapy
- Lifestyle Therapy
- Diet
- Physical Activity
- Behavior Modification
Education and Regulation

Development is beginning

• Education
  – Obesity management training
  – Lifestyle support training
  – Specific device training

• Regulation
  – Anticipate center of excellence type requirement
    • Must demonstrate ability to provide lifestyle support and procedures in an appropriate setting
    • Registry requirements for most of these procedures
    • Demonstration of success may be required
The Problem: Obesity

Thank You!
Thank you!

Visit us on the web at [http://ie.dom.wustl.edu](http://ie.dom.wustl.edu)

Washington University School of Medicine Interventional Endoscopy Section