BARIATRIC ENDOSCOPY

ADVANCES IN MINIMALLY INVASIVE ENDOSCOPIC PROCEDURES FOR WEIGHT LOSS

Bryan Feyen DO
INTRODUCTION

• Overview of obesity
• Medical therapy
• Surgical
• Endoscopic
• The future
Medical Complications of Obesity

- Coronary Heart Disease 
  & Stroke
- Insulin resistance 
  B-cell failure 
  (Diabetes)
- Atherogenic 
  Dyslipidemia
- Nonalcoholic fatty 
  liver disease
- Pulmonary disease
  Hypertension
- Gall bladder disease
- Gastroesophageal reflux disease
- Gynecologic abnormalities
- Osteoarthritis
- Gout
- Phlebitis
  Venous stasis
- Cancer
  Cognitive dysfunction
Genes
- Monogenic
- Polygenic

Environment
- Food availability
- Diet content
- Physical activity
- Friends
- Drugs

Pathway Adjustment
- Development
- Postnatal factors
- Epigenetic

Gut Bacteria

Psychology
- Behavior patterns
- Culture
- Hedonics
- Stress
Obesity Treatment Pyramid

- Surgery
- Endoscopic Therapy?
- Pharmacotherapy
- Lifestyle Modification
  - Diet
  - Physical Activity
Dark blue >35%

Story and Johnson 25%
Controlled Trials

- 20 trials weight loss
- Maintenance

Exercise alone

Drugs

Meal replacement

### FDA-Approved Drugs for Weight Loss

<table>
<thead>
<tr>
<th>Year Approved</th>
<th>Generic Name</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1947</td>
<td>Desoxynorphedrine/methamphetamine</td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td>Phenmetrazine</td>
<td></td>
</tr>
<tr>
<td>1959</td>
<td>Phentermine</td>
<td></td>
</tr>
<tr>
<td>1959</td>
<td>Diethylpropion</td>
<td></td>
</tr>
<tr>
<td>1959</td>
<td>Phendimetrazine</td>
<td></td>
</tr>
<tr>
<td>1960</td>
<td>Benzphetamine</td>
<td></td>
</tr>
<tr>
<td>1972</td>
<td>Fenfluramine</td>
<td>Withdrawn 1997</td>
</tr>
<tr>
<td>1973</td>
<td>Mazindol</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>Dexfenfluramine</td>
<td>Withdrawn 1997</td>
</tr>
<tr>
<td>1997</td>
<td>Sibutramine</td>
<td>Withdrawn 2010</td>
</tr>
<tr>
<td>1999</td>
<td>Orlistat</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>Phentermine-Topiramate</td>
<td>Most effective</td>
</tr>
<tr>
<td>2013</td>
<td>Lorcaserin</td>
<td>5-HT-2C receptor agonists</td>
</tr>
<tr>
<td>2014</td>
<td>Bupropion-Naltrexone</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>Liraglutide</td>
<td>Delayed gastric emptying</td>
</tr>
</tbody>
</table>
SURGICAL OPTIONS

• Indicated
  • BMI > 40, or BMI >35 with two co morbid conditions due to obesity

• Types
  • Gastric bypass
  • Sleeve gastroplasty
  • Duodenal switch
  • Lap Band
## Current Surgical Treatments

### Invasiveness

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Restrictive</th>
<th>Malabsorbptive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adj. Gastric Band</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Gastric Sleeve</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Roux-en-Y</td>
<td>40</td>
<td>&lt;5</td>
</tr>
<tr>
<td>BPD/DS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Performance Measures

<table>
<thead>
<tr>
<th></th>
<th>Percentage</th>
<th>EWL @ 1 yr [%]</th>
<th>Mortality [%]</th>
<th>SAEs* [%]</th>
<th>GI Symptoms [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adj. Gastric Band</td>
<td>5</td>
<td>49.5</td>
<td>0.1</td>
<td>&lt;0.5</td>
<td>7.0</td>
</tr>
<tr>
<td>Gastric Sleeve</td>
<td>50</td>
<td>60</td>
<td>0.3</td>
<td>1.0</td>
<td>10</td>
</tr>
<tr>
<td>Roux-en-Y</td>
<td>40</td>
<td>70.1</td>
<td>0.5 (0.3 HVC)</td>
<td>1.8</td>
<td>16.9</td>
</tr>
<tr>
<td>BPD/DS</td>
<td></td>
<td>71.7</td>
<td>1.1</td>
<td>1.8</td>
<td>37.7</td>
</tr>
</tbody>
</table>

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

Source: Buchwald 2004, Maggard 2005
<table>
<thead>
<tr>
<th></th>
<th>Roux-en-Y Gastric Bypass (RYGB)</th>
<th>Laparoscopic Adjustable Gastric Band (LAGB)</th>
<th>Biliopancreatic Diversion with or without Duodenal Switch (BPD &amp; BPD/DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolved</td>
<td>84% (829/989)</td>
<td>48% (98/205)</td>
<td>98% (282/288)</td>
</tr>
<tr>
<td>Resolved/improved</td>
<td>91% (115/127)</td>
<td>80% (174/217)</td>
<td>88% (89/101)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolved/improved</td>
<td>94% (117/125)</td>
<td>71% (303/426)</td>
<td>99.5% (199/200)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolved/improved</td>
<td>95% (417/439)</td>
<td>78% (18/23)</td>
<td>99.7% (1234/1238)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolved/improved</td>
<td>94% (255/271)</td>
<td>77% (10/13)</td>
<td>100% (588/588)</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolved</td>
<td>75% (1594/2115)</td>
<td>38% (232/604)</td>
<td>81% (629/774)</td>
</tr>
<tr>
<td>Resolved/improved</td>
<td>87% (379/435)</td>
<td>72% (490/685)</td>
<td>92% (718/782)</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolved</td>
<td>87% (776/896)</td>
<td>95% (53/56)</td>
<td>95% (157/165)</td>
</tr>
<tr>
<td>Resolved/improved</td>
<td>95% (167/176)</td>
<td>56% (10/18)</td>
<td>87% (144/166)</td>
</tr>
</tbody>
</table>

* Data from a meta-analysis (90) and the “Resolution” and “Resolution/Improvement” categories do not always include the same studies so the denominator is different between these two columns and in a few cases, such as resolution or improvement of diabetes with BPD with or without DS and of obstructive sleep apnea with LAGB, the frequency of “Resolution” is higher than that of “Resolution/Improvement”. No studies were available to include Sleeve Gastrectomy in this analysis.
BALLOONS

• BMI 30-40

• Most involve endoscopic placement and removal
  • Requires lifestyle changes to effective
  • Very low complication rates
  • On average 25% EWL
    • Better results in Europe

• No insurance coverage currently

• Outpatient procedure
CONTRAINdications

- Previous gastric surgery
- Cirrhosis
- Large hiatal hernia
- Coagulopathy
- Unwilling to take a PPI for six months
- History of an eating disorder
- Unwilling to participate in the lifestyle modification counseling
- GI inflammatory disease
- GI bleeding conditions
Garren-Edwards Gastric Bubble

- First obesity device approved by the FDA, on September 17, 1985
- Cylinder-shaped elastomeric polyurethane balloon with a hollow central channel through which fluid/food could pass
<table>
<thead>
<tr>
<th>Intragastric Balloons (IGB)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Orbera</strong></td>
</tr>
<tr>
<td>Apollo Endosurgery</td>
</tr>
<tr>
<td>Elastic spherical balloon made from silicone and filled with about 500-700 ml of saline. It is inserted and retrieved endoscopically.</td>
</tr>
<tr>
<td><strong>ReShape Duo</strong></td>
</tr>
<tr>
<td>ReShape Medical</td>
</tr>
<tr>
<td>Saline solution-filled, dual intragastric balloon system with 2 balloons attached to each other by a flexible tube. Each balloon has independent channels so that unintentional leaks or deflation in 1 balloon do not to impact the other balloon.</td>
</tr>
<tr>
<td><strong>Spatz Adjustable Balloon System</strong></td>
</tr>
<tr>
<td>Spatz Medical</td>
</tr>
<tr>
<td>Saline filled intragastric balloon with an extractable inflation tube for volume adjustment, while the IGB remains in the stomach.</td>
</tr>
<tr>
<td><strong>Obalon Gastric Balloon</strong></td>
</tr>
<tr>
<td>Obalon Therapeutics</td>
</tr>
<tr>
<td>Gas-filled balloon with a maximal volume of 250ml. It is compressed, folded, and fitted in a large gelatin capsule. Once the capsule is ingested, the catheter extends from the stomach to outside the body through the esophagus and the mouth. After balloon inflation, the catheter is detached and removed. One or more balloon can be swallowed during the same session.</td>
</tr>
</tbody>
</table>

**Elipse Balloon – Allurion**
Orbera Intragastric Balloon

- AKA Bioenterics Intragastric balloon (BIB) – available OUS for over 10 years
- Single Balloon
- Fluid filled/Methylene Blue
- Variable fill: 500 ml to 800 ml (average 600-650)
- Removal after 6 months
Peri-Procedure Treatment

- Anti-emetics
  - Peri-Procedure: Scopolamine patch prior to procedure, IV Decadron, IV Zofran, Emend
  - Post-Procedure: Sublingual Zofran post-procedure, PO Ativan, SL Levsin, Lortab elixir for pain, PO Reglan used in the trial, but only for 24-48 hours
  - Hydration: IVF: 2-3L NS or ½ NS

- Diet: 24-48 hours clear liquids, 2 weeks full liquids
- Expected rate of 3-7.5% of patients will request early removal due to accommodative symptoms
- Avoid NSAIDs, maintain on PPI
- Patient education on evidence of balloon deflation: urine will turn green
Meta Analysis - BIB

- 1638 patients average percent excess weight loss (%EWL) at 12 months (6 months after balloon removal): 25%
- Three randomized controlled trials the difference in %EWL between active and control patients: 26.9%

Gastrointest Endosc 2015; 81(5) : 1073-86
Orbera IGB Adverse Events
n=8500

Gastrointest Endosc 2015; 81(5) : 20151073-86
ReShape Duo® Integrated Dual Intragastric Balloon

- Two silicone balloons connected by a flexible shaft
- Trans-oral endoscopic delivery over a guidewire
- Inflated with saline / methylene blue solution by a powered pump to a total volume of 750 – 900ml
- Average placement procedure time: 8 minutes
Adverse Events: ReShape

- In 264 dual balloon-implanted subjects:
  - No deaths, migrations, obstructions or surgery
- Most AEs were related to accommodative symptoms, mild/moderate in severity, Resolved within days
- Gastric ulcers were due to distal balloon tip design, minor modification during the trial reduced incidence to 10%, and most were not clinically significant
- Deflations occurred, but no balloons migrated into the small bowel

Surg Obes Rel Dis. 2015;11(4): 874-881
Obalon
Obalon Pivotal Trial

- 366 subjects with ≥ 2 balloons, ≥ 18 weeks of therapy
- 1:1 randomization
- Balloons placed at weeks 0, 3 and 9-12
- Baseline BMI 35.2 ± 2.7
- Early balloon removals 4.5% (preference, intolerance)
- Deflation rate 0.13% (one patient 21 weeks)
- One bleeding gastric ulcer (on NSAIDS), two other gastric ulcers

Shelby Sullivan, MD. Presented at DDW 2016
Obalon Data

- Administration time 9.5 ± 4.1 min
- Removal Time 16.9 ± 8.5 min

<table>
<thead>
<tr>
<th></th>
<th>Balloon</th>
<th>Sham</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBWL</td>
<td>6.81 ± 5.1%</td>
<td>3.59 ± 5.0%</td>
<td>0.0338</td>
</tr>
<tr>
<td>Responder rate</td>
<td>64.3 %</td>
<td>32.0 %</td>
<td></td>
</tr>
</tbody>
</table>

- Improvements in systolic blood pressure, fasting glucose, LDL cholesterol, and triglycerides occurred in the treatment group.

Shelby Sullivan, MD. Presented at DDW 2016
Spatz 3 Adjustable Balloon
### Spatz Adjustable Intragastric Balloon

<table>
<thead>
<tr>
<th>Implantation Time (# of patients)</th>
<th>Wt Loss (kg)</th>
<th>% wt loss</th>
<th>% EWL</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Months (158)</td>
<td>12.5 kg</td>
<td>11.7 %</td>
<td>28.8 %</td>
</tr>
<tr>
<td>6 Months (158)</td>
<td>16.2 kg</td>
<td>16.7 %</td>
<td>35.3 %</td>
</tr>
<tr>
<td>9 Months (94)</td>
<td>23.2 kg</td>
<td>20.4 %</td>
<td>44.9 %</td>
</tr>
<tr>
<td>12 Months (48)</td>
<td>24.1 kg</td>
<td>20.6 %</td>
<td>48.1 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#</th>
<th>Mean Volume (range) ml</th>
<th>Mean Time (months)</th>
<th>Weight loss after adjustment (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down Adjustment 11</td>
<td>100</td>
<td>0.3</td>
<td>15.3 kg</td>
</tr>
<tr>
<td>Upward Adjustment 38</td>
<td>327 (150-500)</td>
<td>4.1 months</td>
<td>8.7 kg</td>
</tr>
</tbody>
</table>

Poster, Canadian DDW Conference, February 2014
## Complications Spatz 3

<table>
<thead>
<tr>
<th>16,000 Cases (2012 -2015)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve Issues (1) 0.007%</td>
</tr>
<tr>
<td>Catheter Entry into Duodenum (20) occasionally symptomatic with nausea or vomiting, no ulcers or need for balloon extraction 0.13%</td>
</tr>
<tr>
<td>Ulcers (22) 0.14%</td>
</tr>
<tr>
<td>Balloon Deflation (32) 0.2%</td>
</tr>
</tbody>
</table>

Data provided by Jeffrey Brooks MD, Spatz
Complications – cont’d

| 16,000 Cases (2012-2015) |   
|--------------------------|---
| Perforations (4)         | 0.025%  
| Untreated gastric ulcer for 5 months (1) |   
| Gastric perf spontaneous (2) |   
| Gastric perf – previous gastric surgery (1) |   
| SBO/Surgery (2)          | 0.012%  

**Total** 0.51%

Data provided by Jeffrey Brooks MD, Spatz
Elipse™: the first procedure-less gastric balloon for weight loss
Elipse Intragastric Balloon Technologies

1. Balloon Film
   - 85% thinner than silicone balloons
   - Flexible enough to fold into capsule and safely pass GI tract
   - Durable enough to spend months in stomach

2. Swallowing
   - Balloon is rolled into a capsule and swallowed along with a thin Delivery Catheter for filling

3. Fill Valve
   - Made from thin film
   - Seals shut after Delivery Catheter is pulled out

4. Release Valve
   - Made from thin film
   - Only exposed to inside of device
   - Weakens over time, then opens catastrophically, allowing balloon to empty
Elipse™ Weight Loss: on par with Orbera®

Elipse™ (Athens Cohort; n=11); Totie et al. Obes Surg. 2001. Orbera 16-week weight loss interpolated

Ram Chuttani, MD. Presented at DDW 2016
Concept

- Percutaneous Endoscopic Gastrostomy tubes
  - Used for feeding in patients unable to eat
  - Used for removal of gastric fluid in patients with intestinal obstruction

- AspireAssist System
  - Used for Aspiration Therapy (AT): removal of a portion of gastric contents after a meal for weight loss
AspireAssist System (Aspire Bariatrics)

- Placed using standard pull technique in patients with BMI <55 kg/m²
- Aspirate gastric contents ~20 minutes after meals 2-3 x/day
- Removes 25-30% of calories consumed at that meal
- Accounts for 50-80% of weight loss – lifestyle and mealtime behaviors reduce overall food intake
Percent Total Body Weight Loss: BMI 35-55 kg/m² and >55 kg/m²

- AT 52 week completers n=10
- AT 104 week completers n=7
- Europe Completers n=22
- Mexico n=9 week 26, n=6 week 52
- Super Obese n=11 week 52, n=8 week 76, n=6 week 104
- US Control n=4
## US Trial: Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects Affected</th>
<th>Number of Reports</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain &gt; 4 wks after placement</td>
<td>10</td>
<td>35</td>
<td>Min-Mod</td>
</tr>
<tr>
<td>Peristomal dermatitis</td>
<td>6</td>
<td>9</td>
<td>Min-Mod</td>
</tr>
<tr>
<td>Leakage</td>
<td>1</td>
<td>1</td>
<td>Minimal</td>
</tr>
<tr>
<td>Peristomal Bleeding</td>
<td>5</td>
<td>9</td>
<td>Min-Mod</td>
</tr>
<tr>
<td>Peristomal Infection</td>
<td>3</td>
<td>3</td>
<td>Min-Mod</td>
</tr>
<tr>
<td>Nausea +/- Vomiting</td>
<td>7</td>
<td>11</td>
<td>Min-Mod</td>
</tr>
<tr>
<td>Anemia</td>
<td>4</td>
<td>4</td>
<td>Minimal</td>
</tr>
<tr>
<td>Persistent Fistula after tube removal</td>
<td>1/4</td>
<td>1</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

*One episode of hypokalemia (3.4 mEq/L) in noncompliant subject. Average serum K = 4.2 ± 0.3 meq/L*
Patient Acceptability

Overall Satisfaction

- Very dissatisfied: 2%
- Somewhat dissatisfied: 3%
- Neither satisfied nor dissatisfied: 69%
- Somewhat satisfied: 23%

Willingness to Recommend

- Very unlikely: 3%
- Somewhat unlikely: 27%
- Neither likely nor unlikely: 66%
- Somewhat likely: 1%
- Very likely or already have recommended: 23%

Overall, how satisfied are you with your experience with the AspireAssist?

If the AspireAssist were available, how likely would you be to recommend it to a close friend or relative who was interested in losing weight?

N=64 Subjects, 34 subjects completed/exited study before survey was implemented; 13 subjects failed to take survey due to coordination error/decline. Survey was not mandatory.
COSTS

- Balloon ~ $6,000-10,000
- Gastric bypass in Iowa $ 25,000
- Lap band in Iowa $ 17,000
- Gastric sleeve $ 20,000
- Phenteramine 30 tablets of 37.5 mg ~ $18
- Phenteramine/topiramate (Qsymia) ~ $ 150/month
- Liraglutide ~ $ 3200/month
- Lorcaserin $ 230/ month
- Nutri systems- $ 240-300/month
FUTURE PROCEDURES

Endoscopic sleeve gastropasty

Gastric bypass revision

Odds and ends
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.
GI Dynamics Sleeve Endobarrier

- Higher than anticipated incidence of spontaneous hepatic abscesses detected in the treatment group especially with sleeves in place > 3 months
- Study put on enrollment hold by DSMB, FDA notified and could not come to agreement with GI Dynamics on mediation of this complication.
- Study stopped with incomplete enrollment
- Data analysis underway with primary endpoint of diabetes improvement (HgbA1c reduction).
- Unclear how the FDA will rule on the complication data
Compression Anastomosis


Human Magnetic Gastrojejunostomy


Tissue Remodeling

Tissue Necrosis

Tissue Remodeling
Bypass Animals Compared to Controls

Weight in kg

Control Pigs

Bypass Pigs

P = 0.001

GIE 2016;83:821
A Dual-path Enteral Bypass Procedure Created by a Novel Incisionless Anastomosis System (IAS): 6-month Clinical Results

- Presented at DDW 2016 (#103)
- 10 patients dual endoscopy, laparoscopic monitoring
- No major complications
- Weight loss at 6 months 10.6% TBWL (28.3% EWL)
- No Lifestyle Program
Gastroduodenojejunal bypass sleeve (ValenTx)

- Combined endoluminal-laparoscopic placement in the past
- Endoscopically placed sleeve from GEJ to jejunum
- In clinical trials at this time
- No data presented at DDW
Revita™ DMR Procedure

- Investigational, minimally invasive upper endoscopic therapy using novel balloon catheter
- Targets mucosal surface of the duodenum between ampulla of Vater and ligament of Treitz
- Procedural Steps
  - Size duodenum and lift submucosal space with saline injection to create protective barrier
  - Circumferential hydrothermal ablation of superficial mucosa to stimulate regeneration
  - Procedure duration ~60 minutes
- No implants, sutures or surgery
# Overview of Change in Metabolic Parameters: LS Cohort

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Screening</th>
<th>1 Month</th>
<th>3 Month</th>
<th>6 Month</th>
<th>Normal*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c - %</td>
<td>9.6±1.4</td>
<td>7.9±1.1</td>
<td>7.1±0.9</td>
<td>8.2±1.6</td>
<td>4.0-6.0</td>
</tr>
<tr>
<td>Weight - kg</td>
<td>86±11</td>
<td>82±11</td>
<td>83±12</td>
<td>85±11</td>
<td>--</td>
</tr>
<tr>
<td>ALT - IU/L</td>
<td>40±23</td>
<td>32±17</td>
<td>27±14</td>
<td>27±12</td>
<td>≤ 38</td>
</tr>
<tr>
<td>AST - IU/L</td>
<td>32±17</td>
<td>27±11</td>
<td>23±8</td>
<td>22±6</td>
<td>≤ 40</td>
</tr>
</tbody>
</table>

*Normal range based on ranges reported by lab that processed the samples. All numbers reported as mean ± SD.

Rajagopalan H, EASL 2016 & DDW 2016
SUMMARY

• Multiple new options for weight loss
  • Minimally invasive / outpatient
  • Insurance coverage ?
  • Metabolic outcomes ?
  • Many offer no change in anatomy
  • Fewer risks
QUESTIONS?

Thank you