Endoscopic Advances for the Management of Obesity

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Obesity

- Obesity is a metabolic disease
  - Severe toll of co-morbid illness
- Defined as BMI ≥ 30
- A modern problem
  - Statistics for it did not even exist 50 years ago
- Increase of
  - Convenience foods
  - Labor-saving devices
  - Motorized transport
  - More sedentary lifestyles
High-, mid- and low-income countries; more prevalent than hunger
By 2015, ~2.3 billion adults overweight & > 700 million obese
In 2005, 20 million children < 5 yr old overweight globally
Body Mass Index vs. Mortality

Exponential Increase in Risk

BMI (kg/m²)

Relative Mortality Rate

0 50 100 150 200 250 300 350 400

16 19 22 25 28 31 34 37 40 45

High risk
Medium risk
Low risk

Courtesy, David Metz, MD

Obesity-Related Co-Morbidities

- All-cause mortality
- Heart disease
- Hypertension
- Stroke
- Dyslipidemia
- Cholelithiasis
- Type II diabetes
- Osteoarthritis
- Sleep apnea
- Malignancies
- Reduced QOL
- Social marginalization

Not only the human toll, but their associated costs for diagnosis, management, and disability
Lifestyle: TWL 4kg
- diet, counseling and exercise
- 3-5% of maintain weight loss for 5 years

Medications achieve better weight loss than diet/exercise alone (3-5 kg)
- High rates of attrition (30-40%)
- Cost of medications (lifelong?)
- Adverse events

Cost of ineffective therapy

Obesity

NIH Consensus Conference, 1985
NIH Clinical Guidelines pub# 98-4083, Sept 1998

<table>
<thead>
<tr>
<th>Class</th>
<th>BMI Kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>18</td>
</tr>
<tr>
<td>Normal</td>
<td>18-24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25-29.9</td>
</tr>
<tr>
<td>Obesity I</td>
<td>30-34.9</td>
</tr>
<tr>
<td>Obesity II</td>
<td>35-39.9</td>
</tr>
<tr>
<td>Obesity III</td>
<td>&gt;40</td>
</tr>
</tbody>
</table>

Qualify for surgery
BMI ≥ 35 with co-morbid illness
BMI ≥ 40

Courtesy, Christopher Thompson, MD

Bariatric Surgical Outcomes

Figure 1. Mean Percent Weight Change during a 15-Year Period in the Control Group and the Surgery Group, According to the Method of Bariatric Surgery. 1 bars denote 95% confidence intervals.
Limitations of Bariatric Surgery

- 20 million Americans are heavy enough to qualify for bariatric surgery (Andrew Pollack, NYTimes, 3/16/2011)
  - Only 200,000 have operations each year
  - Morbidity 3-20%; Mortality 0.1-0.5%
  - Many patients unfit or unwilling to undergo surgery
  - Current cost $12,000 to $30,000
  - What about the other 99%?

The Case for Endoluminal Bariatric Procedure(s)

- Obesity problem is increasing
- Considerable obesity related morbidity, mortality, and costs
- Lifestyle and medication therapies under-perform
- Operative interventions are effective but with limited in applicability and associated with considerable risk and cost
ASGE/ASMBS EBT Task Force

• Establish thresholds for
  • Safety
  • Efficacy

• Guide
  • Development
  • Investigation
  • Training
  • Adoption

“A pathway to endoscopic bariatric therapies”

Endoluminal Bariatric
Procedure Concepts

• Restrictive
  • Space occupying or volume reducing

• Malabsorptive
  • Bypass or barrier to intestinal contact

• Neurohumeral
  • Satiation and other effects

• Combinations of the above
### New Obesity Procedure Categories

<table>
<thead>
<tr>
<th>Bridge</th>
<th>Key Features:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>To more definitive bariatric surgery</td>
</tr>
<tr>
<td>Early Intervention</td>
<td>Other surgery</td>
</tr>
<tr>
<td></td>
<td>Ortho, Card, TXP</td>
</tr>
<tr>
<td>Primary Therapy</td>
<td>Rapid effect</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Moderate to high weight loss</td>
</tr>
<tr>
<td></td>
<td>Short term durability</td>
</tr>
<tr>
<td></td>
<td>No permanent anatomic alteration</td>
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</tbody>
</table>

### New Obesity Procedure Categories

<table>
<thead>
<tr>
<th>Bridge</th>
<th>Key Features:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Modest weight loss and/or</td>
</tr>
<tr>
<td>Early Intervention</td>
<td>Prevention of weight gain</td>
</tr>
<tr>
<td>Primary Therapy</td>
<td>High safety profile</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Durable and/or repeatable</td>
</tr>
<tr>
<td></td>
<td>Adolescents??</td>
</tr>
</tbody>
</table>
New Obesity Procedure Categories

- Bridge
- Early Intervention
- Primary Therapy
- Metabolic

Key Features:
- Weight loss profile to approach that of bariatric surgery
- Safety profile to exceed that of bariatric surgery

New Obesity Procedure Categories

- Bridge
- Early Intervention
- Primary Therapy
- Metabolic

Key Features:
- Minimal or modest weight loss
- Emphasis on measurable reduction in comorbid conditions
- DM, HTN, HLD, NASH

Patients who lose 5% of their total body weight have significant reductions in diabetes and cardiovascular risk factors.
Intagastric balloons
Endoluminal gastroplasty
Barrier sleeves
Aspiration devices

Intragastric Balloon (IGB) Therapy

- Space occupying/restrictive effect
- Checkered history…
  - Garren-Edwards Gastric Bubble
    - GIE 1988;34:463–467
- Two with FDA approval
  - Adults with a BMI of 30 to 40 kg/m² [and 1 or more obesity-related conditions (HTN, HLD, DM)] in patients who have failed previous attempts at weight loss through diet and exercise alone.
- 6 month duration
Single Balloon IGB

- 20 yr. OUS experience, CE Mark 1997
- > 230 publications; 220K balloons placed
- US Pivotal trial
- ASGE PIVI Systematic review and meta-analysis*

Safety and Effectiveness of the Intragastric Balloon for Obesity. A Meta-Analysis

- Multicenter, prospective, randomized, non-blinded, controlled trial
- 1:1 randomization SIGB + Behavioral Modification versus Behavioral Modification alone)
- 448 subjects enrolled; 273 patients randomized; 15 sites
- 12 month follow-up

Inclusion Criteria
- BMI ≥ 30 and ≤ 40
- Ages 18 – 65
- History of obesity for at 2+ years
- Failed more conservative weight-reduction alternatives

Primary Objective
- Evaluate the safety and effectiveness of the device as an adjunct to behavioral modification for patients with a BMI ≥ 30 and ≤ 40

*ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies

Volume 82, No. 3 : 2015 GASTROINTESTINAL ENDOSCOPY 425
SIGB Pivotal Study: Subject Disposition & Demographics

- Enrolled: 448
- Randomized: 273
- Screen Failures: 131
- Run-In (planned 46): 44
- Treatment: 137
- Treatment After Randomization: 12
- D/C Before Week 52: 27
- Control: 136
- Drop-Outs After Randomization: 6
- Completed Study – w52: 98
- Completed Study – w52: 93

Demographics:
- 90% female
- Mean age = 38.7 years
- 81% Caucasian
- 70% married
- Mean excess weight = 78.8 lbs
- Mean BMI = 35.2

Greater Weight Loss in SIGB Group through 12 months

- Mean %TBWL (95% CI)
  - Month 0: 0 %
  - Month 3: 3.3%
  - Month 6: 3.4%
  - Month 9: 3.1%
  - Month 12: 4.5%

SIGB provided 3.1x weight loss vs. diet & exercise alone
Mean EWL at 6 months: 38%
SIGB Global Meta-Analysis (2015) - Efficacy

- 82 OUS Publications reviewed based on following criteria:
  - Peer-reviewed journal
  - English
  - Human Trial
  - Inclusion of %EWL, %TBWL or adverse events

- OUS experience is similar to the US Pivotal Study but demonstrates on average slightly higher weight loss

Two Studies included %TBWL at 36 months: 6.0% (2.4%-9.7%)
Comorbidity resolution

- Italian assessment of metabolic syndrome with 1 year follow up
  - 143 Patients (Mean BMI: 36.2)
  - Improvement: 67% - 43% - 53% - 23% - 35%

- Multi-center EU experience w/ 3yr follow-up
  - 261 Patients (Mean BMI: 28.6)
  - Improvement: 29% - 32% - 21% - 20% - 26%

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DUAL BALLOON IGB

- Two connected, independently sealed, saline-filled balloons.
  - SATIETY – With the capacity to hold up to 900 cc of saline, offers more gastric filling than any single balloon device.
  - COMFORT – Conform to the patient’s anatomy and enhance tolerability.
  - SAFETY – Individual balloon leakage or deflation, the independently sealed balloons are designed to minimize risk of migration or obstruction.
The REDUCE pivotal trial: a prospective, randomized controlled pivotal trial of a dual intragastric balloon for the treatment of obesity

- EWL: 28% vs 12% medically supervised diet & exercise alone (2x).
- 55% of patients lost at least 25% of their excess weight.
- Significant and sustained improvements in co-morbidities (HLD, HTN)
- 2/3 of mean weight loss achieved during the treatment phase was maintained for the 24 weeks after removal.
- Favorable safety profile, with no migrations or obstructions reported. 9% intolerance.
- 66% of trial patients would do it again

Surgery for Obesity and Related Diseases 11 (2015) 874–881
Some Sewing Tools

NDO
OverStitch
SafeStitch
EndoCinch
TAS
StomaPhyx
G-Prox
Eagle Claw

Courtesy, Rich Rothstein, MD

The Primary Obesity Surgery Endolumenal (POSE) procedure: one-year patient weight loss and safety outcomes

Gontrand López-Nava, M.D.*, Inmaculada Bautista-Castaño, M.D., Ph.D.,
Amaya Jimenez, M.D., Teresa de Grado, M.D., Juan Pedro Fernandez-Corbella, M.D.

Changes in weight parameters after the Primary Obesity Surgery Endolumenal (POSE) procedure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>3 months (mean ± SD) n = 147</th>
<th>6 months (mean ± SD) n = 131</th>
<th>12 months (mean ± SD) n = 116</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>106.8 ± 18.2</td>
<td>95.7 ± 15.9</td>
<td>92.2 ± 14.8</td>
<td>91.6 ± 15.2</td>
</tr>
<tr>
<td>Total weight loss (kg)</td>
<td>11.1 ± 5.6</td>
<td>14.83 ± 8.0</td>
<td>16.6 ± 9.8</td>
<td>15.1 ± 7.8</td>
</tr>
<tr>
<td>% of initial weight loss</td>
<td>10.2 ± 4.5</td>
<td>13.6 ± 6.4</td>
<td>15.1 ± 7.8</td>
<td></td>
</tr>
<tr>
<td>% change in weight loss</td>
<td>32.1 ± 14.8</td>
<td>42.10 ± 21.8</td>
<td>44.9 ± 24.4</td>
<td></td>
</tr>
</tbody>
</table>

*Total weight was significantly different at 3, 6, and 12 months compared with initial weight (Student's t test for dependent samples).

Surgery for Obesity and Related Diseases 11 (2015) 861–865

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Endoscopic Barrier Sleeves

- An anchoring mechanism secures the device in place in the duodenum but permits removal.
- A soft, flexible barrier sleeve positioned below the pylorus diverts until the jejunum.
- Delays metabolic and endocrine processes.

Duodenojejunal Bypass Sleeve (DJBS)

- 60-cm long impermeable plastic sleeve anchored to duodenal bulb.
- Placed and removed endoscopically.
- Short term (3 month) comparative trials +/- sham.
  - m %EWL 19% v 7% (p<.002)
  - m 8.2 kg v 2.1 kg (p<0.5)
  - Poor patient tolerance.

ASGE SER Endoluminal bariatric techniques. GIE 2012;76:1-7
DJBS Improves HbA1c

- Week 12
  - N=9
  - N=4
  - EndoBarrier: -1.3
  - Sham: -0.8

- Week 30
  - N=8
  - N=3
  - EndoBarrier: -2.9
  - Sham: -0.76

*Week 30 p=0.004


Aspiration Therapy

- Modified PEG
- 20 min after meal
- Water lavage
- 30% of caloric intake
Aspiration Therapy
US Pivotal Trial

- Trial: 175 patient trial, 11-center trial
- Patients randomized 2:1 AT to Control (Lifestyle Therapy)
- BMI: 35-55 kg/m²

Limitations to Endoscopic Bariatric Therapies

- Motivated patient
- Only effective when combined with a fully developed nutrition and life-style modification program
- Best done in a center with integrated multidisciplinary management of obesity
- Education and training
- Endoscopy unit and clinic space designed for obese patients and their families

Financial Implications of Endoscopic Bariatric Therapy

- No CPT code
- No commercial payers
- Cash upfront enterprise
  - Plastic Surgery Model
  - $5,000 - $10,000
  - Device and accessories
  - Insertion
    - Facility, Professional, Anesthesiology
  - Aftercare
    - Phone calls, IVF, etc.
- Diet and life-style counseling
- Removal
- Not for the uncommitted

The Battle Against Obesity

- Medical therapies
- Bariatric surgery
- Culture change
  - Education
  - Access to healthy foods
  - Realignment of government subsidies
  - Societal initiatives
- Endoscopic Bariatric therapies
  - Association for Bariatric Endoscopy (ABE), a Division of ASGE