Endoscopic Therapies for Obesity: where we are and where we go?

Gregory G. Ginsberg, M.D.
Professor of Medicine
University of Pennsylvania Perelman School of Medicine
Gastroenterology Division
Director of Endoscopic Service
PENN Medicine
Abramson Cancer Center

DISCLOSURE

Relevant Financial Relationship(s)
None

Off Label Usage
None
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

Obesity: Global Problem

- 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
Obesity in the United States


Rural and urban

Centers for Disease Control and Prevention

Body Mass Index Vs. Mortality

Exponential Increase in Risk

Relative Mortality Rate

BMI (kg/m²)

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

Biology Is Against Us

- “The essence of all living things is to obtain energy and reproduce”
  - Dean Robert Chase, Biol. Lafayette Col
- We evolved to crave sweet, salty, and fatty foods
- Biology does not have to be our destiny
Diets and Medications Have Limited Efficacy

- **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**


Bariatric Surgical Approaches

- **Lower Morbidity / Lower Risk**
  - Less Effective
- **Higher Morbidity / Higher Risk**
  - More Effective
Obesity

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

Class | BMI Kg/m²
--- | ---
Underweight | 18
Normal | 18-24.9
Overweight | 25-29.9
Obesity I | 30-34.9
Obesity II | 35-39.9
Obesity III | >40

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.

<table>
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<th>No. Examined</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
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<td>176</td>
<td>156</td>
<td>138</td>
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<td>124</td>
<td>122</td>
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<tr>
<td>Vertical-banded gastroplasty</td>
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<td>2162</td>
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<td>2174</td>
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<td>Gastric bypass</td>
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<td>106</td>
<td>86</td>
<td>66</td>
<td>46</td>
</tr>
</tbody>
</table>

T 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
Endoscopic Bariatric Therapy in the USA

- The following is a list of EBT currently approved for use in the USA:
  - 
  - 
  - 
  - 
  - 

Endoscopic Bariatric Therapies

- Why should you care?
  - Obesity is an epidemic with real negative societal impact
  - Opportunity to
    - address an unmet need
    - achieve a good on behalf of society
    - expand the endoscopic armamentarium
  - Millions of healthcare and related $$ at stake
  - We have a responsibility to do so
Endoluminal Bariatric Therapies Task Force

The ASGE is dedicated to advancing patient care and digestive health by promoting excellence in gastrointestinal endoscopy.

The ASMBS is dedicated to improving public health and well-being by lessening the burden of the disease of obesity and related diseases.

- **ASGE**
  - Gregory G. Ginsberg
  - Steven A. Edmundowicz
  - Christopher C. Thompson
  - Gregory A. Cote'

- **ASMBS**
  - Bipan Chand
  - Ninh T. Nguyen
  - Aurora Pryor
  - Ramsey M. Dallal

ASGE/ASMBS EBT Task Force

**Mission:**

- 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**
- **Other…**
- **NOTES**

Devices to Treat Obesity


- **Restrictive Devices**
  - Transoral Gastroplasty (TOGA)
  - RESTORE Suturing System™
- **Artificial Fullness Devices**
  - Reshape Duo intragastric balloons
  - Polymer pills
  - Full Sense Device
- **Malabsorption Devices**
  - GI Dynamics’ EndoBarrier
  - Gastrx Sleeve-like Device
  - ValenTx Sleeve
  - Aspire aspiration therapy
- **Devices to Control Gastric Emptying**
  - TransPyloric Shuttle BAROnova Therapeutics
  - BaroSense’s TERIS (Trans-oral Endoscopic Restrictive Implant System)
  - Endoscopic Intragastric Injection of Botulinum Toxin
  - EndoVx EUS guided HIFU vagotomy (TEVx)
- **Appetite Suppressive Devices**
  - MetaCure’s Tantalus System
  - EnteroMedics’ Maestro System for VBLOC
  - Silhouette Medical’s nObese RF Ablation Device
- **Gastric Electrical Stimulation**
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ACG 2013

ACG Postgraduate Course • October 12-13, 2013
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Dental Implants

- **Intra-oral weight loss device**

- **Removable, custom-made, oral device that slows food intake**
New Obesity Procedure Categories

- Bridge
- Early Intervention
- Primary Therapy
- Metabolic

Key Features:
- Rapid effect
- Moderate to high weight loss
- Short term durability
- No permanent anatomic alteration

Bridge: To Decrease Surgical Risk

- Morbid obesity with its co-morbid illness (OSA, DM, CAD) is a known risk factor for surgical complications
  - DVT, PE, atelectasis, renal failure, wound infection, prosthesis failure
- Cardiac
- Orthopedic
- Cancer
- Transplant
- Bariatric

Modified from Christopher Thompson, MD
Intragastric Balloon Therapy

- Short-term weight loss of 14-18 kg in 6 months
- Relatively safe
- Weight loss does not last
- Patients regain weight
- 20% to 40% of patients fail to achieve any meaningful weight loss

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

Intragastric balloon significantly improves nonalcoholic fatty liver disease activity score in obese patients with nonalcoholic steatohepatitis: a pilot study

Yin-Mei Lee, MD,1 How Cheng Low, MD,1 Lee Guan Lim,1 Yock Young Dan,1 Myat Oo Aung, MD,1 Chee Leong Cheng,2 Aileen Wee,3 Seng Gee Lim, MD,3 Khok Yu Ho, MD3

Gastrointest Endosc 2012;76:756-60

Figure 1. BMI drop in treatment and control. BMI, body mass index.

Figure 2. NAS, nonalcoholic fatty liver disease activity score.

Metabolic therapy...
New Obesity Procedure Categories

- Bridge
- Early Intervention
- Primary Therapy
- Metabolic

Key Features:
- Modest weight loss
- Prevention of weight gain
- High safety profile
- Durable and/or repeatable

Modified from Christopher Thompson, MD
New Obesity Procedure Categories

- Bridge
- Early Intervention
- Primary Therapy
- Metabolic

Key Features:
- Modest weight loss
- Prevention of weight gain
- High safety profile
- Durable and/or repeatable

Modified from Christopher Thompson, MD

Some Sewing Tools

- NDO
- OverStitch
- SafeStitch
- EndoCinch
- TAS
- StomaPhyx
- G-Prox
- Eagle Claw
- Spiderman

Courtesy, Rich Rothstein, MD
**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

Modified from Christopher Thompson, MD
Transoral gastroplasty for morbid obesity: a multicenter trial with a 1-year outcome

Pietro Familiar, MD,1 Guido Costamagna, MD,1 Daniel Béreo, MD, PhD,2 Olivier Le Moine, MD, PhD,2 Vincenzo Perri, MD,1 Ivo Boskoski, MD,1 Emmanuel Coppens, MD,2 Marie Barca, MS,2 Amerigo Iaconelli, MD,4 Gertrude Mingrone, MD,2 Christophe Moreno, MD, PhD2 Jacques Devière, MD, PhD2

Gastrointest Endosc 2011;74:1248-58

TOGa: A Cautionary Tail

- Prospective, multicenter, single arm trial, 53 patients

| TABLE 3. Results: average %EBMIL, %EWL, and weight loss after TOGA procedure |
|-----------------|---------|---------|---------|
|                 | 3 mo    | 6 mo    | 12 mo   |
| %EBMIL          |         |         |         |
| All patients    | 33.9% ± 13.7 | 42.6% ± 18.3 | 44.8% ± 20.0 |
| Group 1 (BMI < 40.0) | 40.3% ± 16.8 | 52.2% ± 22.3 | 52.2% ± 23.6 |
| Group 2 (BMI ≥ 40.0) | 31.1% ± 10.9 | 38.5% ± 14.4 | 41.3% ± 17.0 |
| %EWL (all patients) | 20.3% ± 11.6 | 36.8% ± 15.7 | 38.7% ± 17.1 |
| Weight loss     | 15.1 kg ± 6.3 | 19 kg ± 8.5 | 19.5 kg ± 9.2 |

%EBMIL, percentage of excess BMI loss, compared with an ideal BMI of 25 kg/m²; %EWL, percentage of excess weight loss, compared with an ideal weight measured according to 1983 MustLifts Height-Weight Tables—midpoint of medium frame; TOGA, transoral gastroplasty; BMI, body mass index.
TOGa Pivotal Trial: Weight Loss

- Mean %EWL of 25%
- "Roll in" subjects (N=18) did better than the rest
- While statistically significant, less than 50% achieved threshold response
- Cross-over patients with only 8%EWL

Courtesy Sriram Machineni MD

Based on disappointing results, FDA application was withdrawn and the company was disbanded

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New Obesity Procedure Categories

- Bridge
- Early Intervention
- Primary Therapy
- Metabolic
  - Minimal or modest weight loss
  - Emphasis on measurable reduction in comorbid conditions

Modified from Christopher Thompson, MD

Patients who lose 5% of their total body weight have significant reductions in diabetes and cardiovascular risk factors.

EndoBarrier (GI Dynamics)

- Anchoring mechanism secures device in place in duodenum but permits removal
- Soft, flexible barrier sleeve positioned below pylorus diverts until the jejunum
- Delays metabolic and endocrine processes

Modified from Christopher Thompson, MD
**Duodenojejunal Bypass Sleeve**

- 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

---

**EndoBarrier™ Improves HbA1c**

<table>
<thead>
<tr>
<th>Week</th>
<th>N=9</th>
<th>N=4</th>
<th>N=8</th>
<th>N=3</th>
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<tr>
<td>% Change HbA1c</td>
<td>-1.3</td>
<td>-0.8</td>
<td>-2.9</td>
<td>-0.78</td>
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</tbody>
</table>

*Week 30 p=0.004

AspireAssist® Aspiration Therapy System

- Aspiration therapy
- 20 min after meal
- Water lavage
- 30% of caloric intake

Mean % Excess Weight Loss as a Function of Time

<table>
<thead>
<tr>
<th>Weeks</th>
<th>% Excess Weight Loss</th>
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<tr>
<td>0</td>
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<td>26</td>
<td>-10</td>
</tr>
<tr>
<td>52</td>
<td>-15</td>
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Threshold Analysis %EWL

<table>
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<th>Threshold (%EWL)</th>
<th>At 52 Weeks</th>
<th>At % Weeks</th>
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<tbody>
<tr>
<td>Percent of subjects losing at least 20%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Percent of subjects losing at least 25%</td>
<td>100%</td>
<td>56%</td>
</tr>
<tr>
<td>Percent of subjects losing at least 30%</td>
<td>50%</td>
<td>71%</td>
</tr>
<tr>
<td>Percent of subjects losing at least 50%</td>
<td>80%</td>
<td>57%</td>
</tr>
<tr>
<td>Percent of subjects losing at least 75%</td>
<td>10%</td>
<td>29%</td>
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%EWL over Time AT vs. Control Groups

<table>
<thead>
<tr>
<th>Visit</th>
<th>N (AT)</th>
<th>%EWL (AT)</th>
<th>N (Control)</th>
<th>%EWL (Control)</th>
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<tbody>
<tr>
<td>24 Weeks</td>
<td>10</td>
<td>20.3%</td>
<td>4</td>
<td>9.5%</td>
</tr>
<tr>
<td>52 Weeks</td>
<td>10</td>
<td>20.7%</td>
<td>4</td>
<td>14.9%</td>
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<tr>
<td>76 Weeks</td>
<td>8</td>
<td>25.0%</td>
<td>4</td>
<td>12.0%</td>
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<tr>
<td>96 Weeks</td>
<td>7</td>
<td>56.0%</td>
<td>4</td>
<td>26.9%</td>
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</table>

Percent weight loss in “Proof-of-Principle” subject
US Pivotal Trial

- Trial: 175 patient trial, 11-center trial
- Patients randomized 2:1 AT to Control (Lifestyle Therapy)
- BMI: 35-55 kg/m²
- Centers/ Investigators
  - Washington University: Steve Edmundowicz, Shelby Sullivan
  - Boston University: Carolyn Apovian, Chris Huang
  - Brigham & Women’s: Chris Thompson
  - Cornell: Louis Aronne, Mike Kahaleh
  - St. Mary’s: Alan Schorr, J. Matthew Bohning
  - Penn: Marion Vetter, David Jaffe, Gregory Ginsberg
  - Howard: Terry Fullum
  - Northwestern: Bob Kushner, John Martin
  - Mayo Clinic: Mike Jensen, Barham K Abu
  - St. Lukes (San Francisco): Nancy Bohanon
  - VA Center/ UC San Diego: Karen Herbst, Joe Glazer, Sam Ho

The Battle Against Obesity

- **Medical therapies**
- **Bariatric surgery**
- **Culture change**
  - Education
  - Access to healthy foods
  - Realignment of government subsidies
  - Societal initiatives
- **Endoscopic Bariatric therapies**
  - Future studies should objectively measure metabolic outcomes in addition to weight loss