Endoscopic Treatment of Obesity

Philippe Saniour, MD
LSGE, November 2014
Some facts

- Obesity is a CHRONIC, LIFE LONG DISEASE causing morbidities and premature death
- 5% weight loss improves QOL and ovarian function
- 10% weight loss improves BP, lipid profile and diabetes control
- 10-20% weight loss reverses the high mortality risk in diabetes
Can we squeeze in?

• Behavioral modifications, energy restricted diet, physical exercise first
• Pharmacotherapy is indicated for BMI > 30 or >27 with co-morbidities
• Bariatric surgery is indicated for BMI > 40 or > 35 with co-morbidities
• The intermediate group of failed conservative approach and not yet surgical candidate should be taken care of, at least partially by GI
Can we squeeze in?

- Patients with BMI between 30 and 40 who failed the conservative approach
- Obese patients who refuse surgery
- BMI > 40 who are poor surgical candidates
- Super-obese, BMI > 50 who need some pre-op weight loss to decrease surgical difficulties and morbidity
- A stratification tool predicting post sleeve successful weight loss?
Endoscopic techniques

- Gastric distention and space occupying devices: Balloons et al
- Delayed gastric emptying: BoTox
- Gastric restrictions: Suturing and plication techniques
- Malabsorptive and duodenal exclusion techniques: ValenTx and EndoBarrier
- The Roman decadent technique: Aspiration therapy
Endoscopic techniques

- Gastric distention and space occupying devices: *Balloons et al*
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Intra gastric Balloons

Balloons and prosthesis

- Orbera Intragastric Balloon
- Ullorex Intragastric Balloon (Swallowable balloons)
- Spatz Adjustable Intragastric Balloon
- Heliosphere Bag
- Semistationary Antral Balloon
- Reshape Duo™ Intragastric Ballon
- Endogast-ATIIP (Adjustable Totally Implantable Intragastric Prosthesis)
## Intra gastric Balloons: Results

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<th>Duration</th>
<th>Average weight loss</th>
<th>Average EWL %</th>
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Bioenteric Intragastric Balloon

- Efficacious
- Improvement of metabolic morbidities
- Over placebo weight loss of 6-7 kgs
- Possibility of back to back balloons
- 4-5% early removal and < 1-2% major morbidities, few cases of deaths reported
- Major drawback: WEIGHT REGAIN after 1 and 2 years of retrieval: Only half retain > 10% body weight loss

Mathus-Viegen EM, Obes Surg 2008
Dumonceau JM, Obes Surg 2008
Spatz Adjustable Balloon

• Similar results to back to back BIB: 55% EWL
• More complications:
  - Early removal: 15 %
  - Surgery for related complications: 5 %

Experts opinion: Needs improvement to decrease failures and complications

Genco A, Obes Surg 2013
ReShape Duo

- Results of the REDUCE trial (Obesity week 2014, top 10 papers)

326 pts, BMI 30-40, 95% f
139 Duo v/s 187 sham procedure
25.1% v.s 11.7% EWL, Half > 25% EWL
Simple, without major complications but early removal in 15%, and gastric ulcers (majority small and superficial) in 10%

FDA decision for approval in 2015
Malabsorptive Techniques

ValenTx

EndoBarrier
Duodenojejunal bypass sleeve
Duodenojejunal Bypass Sleeve

- Currently launched for BMI > 30 AND DM 2 for 12 months placement duration
- 4 RCTs and 6 open label studies: 12-22% excess weight loss in Gr II obesity
- Most recent (Koehestanie P, Ann Surg 2014): 32% EWL compared to 16.4% in diet arm
  HbA1c 7.0% v/s 7.9%

DeJonge C, Obes Surg 2013
Duodenojejunal Bypass Sleeve

- Mode of action:
  Food bypass proximal small bowel without mixing with biliary and pancreatic secretions

  Less Glucagon and GIP secretions due to the absence of food in the proximal intestine:
  The foregut theory

  More GLP-1 and Incretins due to more undigested food in the distal intestine:
  The hindgut theory

Consequence: Glycemic control and weight loss
Duodenojejunal Bypass Sleeve

- Safety and feasibility:
  282 pts
  Failure of placement in 18 (+ 5)
  60 early explantations (migration, dislocation, obstruction, bleeding ...)

‘While promising, the DJBL is not recommended for routine use but should be restricted to research settings only’

Zechmeister-Koss, Obes Surg 2014
Duodenojejunal Bypass Sleeve

- Important limiting factor

Over placebo weight loss: 6 kgs

Device price: 4500 $
Procedures fees: 1500 $

Cost per kg lost: 1000 $
Endoscopic Suturing Technique

**ENDOLUMINAL VERTICAL GASTROPLASTY (EVG)**

*EndoCinch*

**Fogel R et al.**

*GIE 2008;68(1):51-8*

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**Follow-up** | **Excess Weight Loss (%EWL)**
---|---
1m | 21.1±6.2
3m | 39.6±11.3
12m | 58.1±19.9
Endoscopic Suturing Technique

TRIM procedure
Restore Suturing System
Brethauer SA et al, 2012

12 months FU (18/14) Number of plications: 6
Mean procedure time: 2.1h (range 1.5–2.8).
Decreases:
Mean weight (-11.0±10.0kg) P = .0006
Mean BMI (-4.0±3.5kg/m²) P = .0006
Mean waist circumference (-12.6±9.5cm) P = .0004
Mean excess weight loss: (27.7±21.9%)
Endoscopic Stapling Technique

Multicenter pivotal trial (300 pts) showed significant but modest effect vs Sham procedure and 2% severe complications.

The company developing TOGA closed down and sold its assets end of 2010.
Endoscopic Restrictive Technique

Transoral Endoscopic Restrictive Implant System (TERIS)

- EWL at 3 months: 28%.
- BMI decreased from 42.1 to 37.9
- Gastric perforation (N=1); pneumoperitoneum (N=2)
- TERIS system is not being developed further due to unacceptable durability of lesser curvature anchor point and alternative implant design and plication patterns are being studied.
Aspiration Therapy

- PEG tube and an AspireAssist siphon to remove gastric content 20 mn after a meal
- One study randomizing 18 pts for Aspire vs life style change:
  After 1 year, 18.6% wt loss (49% EWL) vs 6% wt loss (15%EWL) in control arm
- Problem of acceptance and long term results after removal (and maybe peristomal infections, leakage, fistula...)

Shelby Sullivan et al, Gastroenterology 2013;145
Why are we failing

• Cherchez les hormones (et la microbiota ?)
  - Obesity is a chronic disease
  - After weight loss: adaptation with less Leptin, PYY, Insulin, CCK and more Ghrelin
  - After Bypass and Sleeve, the Incretins (PYY and GLP-1) increase, consequently causing less Glucagon and more Insulin secretion
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of Action</th>
<th>Results</th>
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<tr>
<td>Orlistat</td>
<td>Inhibits gastric and pancreatic lipase</td>
<td>3 kg weight loss (Fear of soiling)</td>
</tr>
<tr>
<td>Lorcanerin</td>
<td>5-HT2c agonist Reduces food intake and food reward</td>
<td>52 wks, 10 mg BID: 2.9-3.6% extra weight loss over diet</td>
</tr>
<tr>
<td>Phentermine-Topiramate (fixed dose combination)</td>
<td>Phentermine: Sympathomimetic effect Topiramate: Antiepileptic, unknown mechanism for weight loss</td>
<td>High dose combination: 7.5-8.7% placebo adjusted weight loss Currently low dose combo</td>
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Liraglutide (Victosa)
GLP-1 analog

- Incretin, GLP-1
- Stimulates insulin release
- Inhibits glucagon release
- Lowering of blood glucose
- DPP-4 enzyme inactivates GLP-1
- DPP-4 inhibitors (drugs) block DPP-4 and decrease glucose
Liraglutide (Victosa)

- At 1.8 mg daily, modest effect on weight loss
- Currently, 4 phase III clinical trial at 3 mg/d studying effect on weight loss (the SCALEs)
- Overall, 6-8% extra weight loss over placebo

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<th>Priority Area 10: Obesity</th>
<th>High-Impact Potential</th>
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<tr>
<td>1. Aspiration system (AspireAssist) for treatment of obesity</td>
<td>No high impact potential at this time</td>
</tr>
<tr>
<td>2. *Controlled-release phentermine-topiramate (Qsymia) for treatment of obesity</td>
<td>Moderate</td>
</tr>
<tr>
<td>3. *Intragastic dual balloon (ReShape Duo) for treatment of obesity</td>
<td>Lower end of the high-impact-potential range</td>
</tr>
<tr>
<td>4. *Liraglutide (Victoza) for treatment of obesity</td>
<td>Moderate</td>
</tr>
<tr>
<td>5. *Lorcaserin (Belviq) for treatment of obesity</td>
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Please, can we squeeze in?
Conclusion

- We do not have yet a technique that is simple with a long term benefit.
- Most probably there is more to come:
  - Obesity is pandemic.
  - Obesity is a chronic disease.
  - Endoscopic treatment is an ideal first line approach that does not compromise further surgery.
  - Interest of the developers remain high.