Comparative Studies and Metabolic Effects of Sleeve Gastrectomy

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- Allergan: consulting agreement
Body Weight Is Highly Regulated

- **Counter Regulation:**
- Changes in appetite and metabolic rate proportional to the change in body weight work to maintain weight within a set range.

<table>
<thead>
<tr>
<th>Usual weight</th>
<th>Weight gain</th>
<th>Weight loss</th>
<th>Counter regulation</th>
<th>Counter regulation</th>
</tr>
</thead>
</table>
Counter Regulation: The “Adipostat”

- Brain
- Circulating Signal
- Caloric Intake
- Body Fat Stores
“Obesogenic” Environment

Eat more:

**Increased food availability**
- calories/person/day has increased 15% since 1970
- % of food $ spent outside the home has doubled since 1970

**Increased portion size**
- in the 1950’s a 12 oz soda at McDonalds was king-sized; now it’s child size

**Increased energy density (kcal/g)**
- high fat foods; low fat/low cal foods

Do less:

**Increased sedentary leisure time activities**
- TV, computers, video games; cutbacks in mandatory PE

**Decreased occupational physical activity**

**Increased use of automobiles**
Over the next 20 years obesity will be the #1 health problem in the world.
The Elusive Magic Pill for Obesity
Bariatric Mechanisms of Weight Loss

- The key question is, how does bariatric surgery overcome an individual's adipostatic compensatory mechanisms and maintain significant weight loss?
- Changes in the entero–encefalic endocrine axis may offer part of the explanation.
Objectives

• To challenge **caloric restriction** as the only mechanisms of weight loss and comorbidities resolution after the two most common restrictive procedures:
  • Laparoscopic Adjustable Gastric Banding (LAGB)
  • Laparoscopic Sleeve Gastrectomy (LSG)

• To Review Components Changes of the Entero–Encephalic Endocrine Axis (**Metabolic Effects**) after these procedures.
Laparoscopic adjustable gastric banding (LAGB)

- A silicon band attached to a subcutaneous port is placed around the proximal stomach
- Injection of isotonic fluids into the port hydraulically inflates the band

**Advantages**
- Reversible and adjustable
- Low operative complication rate
- Lower risk of gallstones
- Return to work 1 week after surgery

**Disadvantages**
- Requires an implanted medical device
- Easier to ‘cheat’
- Risk of slippage or erosion
LAGB and conventional therapy for T2D: A randomized controlled trial

- First RCT to compare surgically induced weight loss versus conventional therapy in the management of T2D
- First RCT to study patients with T2D and obesity
- Participants: 60 obese patients (BMI 30–40) with recently diagnosed (<2 years) diabetes
- Outcome measures:
  - Primary: remission of T2D as measured by fasting plasma glucose (FPG) <126 mg/dL and HbA₁c <6.2%
  - Secondary: weight loss and components of the metabolic syndrome

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Adjustable Gastric Banding and Conventional Therapy for Type 2 Diabetes: A Randomized Controlled Trial

- **Context**: Observational studies suggest that surgically induced weight loss may be effective therapy for type 2 diabetes.
- **Objective**: To determine if surgically induced weight loss results in better glycemic control and improved diabetes medication requirements compared to weight loss and diabetes control.
- **Design, Setting, and Participants**: Unblinded, randomized controlled trial conducted from December 2004 to December 2006 at the University of Sydney, Australia, with general community recruitment to established treatment programs. Participants were 60 obese patients (BMI >30 and <40) with recently diagnosed (<2 years) type 2 diabetes.
- **Interventions**: Conventional diabetes therapy with a focus on weight loss by lifestyle change vs laparoscopic adjustable gastric banding with conventional diabetes care.

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Shaded area indicates Position of picture box

Study Design

Maximise current management

Weight loss surgery and conventional therapy for T2D n=30

Regular review 4–6 weeks

Conventional therapy for T2D n=30

2 years

LAGB placed by 1 of 2 surgeons via Pars Flaccida technique

Best available medical practice

LAGB induces loss of excess weight*

*Excess weight calculated using BMI 25 as the ideal

p<0.001

LAGB induces T2D remission

Dixon: Conclusions

- Mean HbA$_{1c}$ and FPG levels were significantly lower in the surgical group at 2 years versus the conventional therapy group ($p<0.001$)
- Significant reduction in use of medications for glycemic control in the surgical group compared versus the conventional therapy group at 2 years
- Significantly fewer subjects had metabolic syndrome in the surgical group (30%) versus the conventional therapy group (87%) at 2 years ($p<0.001$)
- The surgical group had a significantly greater improvement in insulin resistance, levels of triglycerides and high-density lipoproteins than the conventional therapy group

## Weight control hormones that have been studied after LAGB

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Origin</th>
<th>Mechanism of action in obesity</th>
<th>Effect on weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghrelin</td>
<td>Primarily stomach fundus</td>
<td>Stimulates GH release</td>
<td>Stimulates appetite</td>
</tr>
<tr>
<td></td>
<td>Pancreas</td>
<td>Opposes leptin actions</td>
<td>Reduces metabolic rate</td>
</tr>
<tr>
<td></td>
<td>Intestine</td>
<td></td>
<td>Reduces fat catabolism</td>
</tr>
<tr>
<td>PYY</td>
<td>Enteroendocrine L cells of ileum and colon</td>
<td>Associated with IR and insulin secretion</td>
<td>Induces satiety</td>
</tr>
<tr>
<td>Leptin</td>
<td>Adipocytes</td>
<td>Inhibits NPY and activates POMC neurons</td>
<td>Anorectic</td>
</tr>
</tbody>
</table>
Effect of LAGB on Adiponectin

Effect of LAGB on Leptin

Effect of LAGB on PYY and Ghrelin

Summary for LAGB

- The effect LSG on patients’ metabolic profile is exerted by caloric restriction and changes in circulating and hepatic levels of Adiponectin and Leptin.

- LAGB does not induce any significant changes in PYY, Ghrelin, GLP-1, and GIP peptides.

- LSG is categorized as a restrictive operation, however its metabolic effect clearly extend beyond caloric restriction through changes in adipokine profiles.
Gastric sleeve resection

• The fundus and body of the stomach are excised, leaving a tube with reduced volume [1]

• Advantages: [2]
  – Good weight loss
  – No ‘dumping’ syndrome

• Disadvantages: [3]
  – Major surgery with associated risks such as staple line bleeding and leakage
  – Increased risk of gallstones

Ghrelin Levels after LSG and LAGB

Langer et al., Obesity Surgery 2005

Table 1. Demographic data of the study population

<table>
<thead>
<tr>
<th></th>
<th>Sleeve gastrectomy</th>
<th>Gastric banding</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Sex (f / m)</td>
<td>9/1</td>
<td>9/1</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.3±11.7</td>
<td>38.5±13.6</td>
<td>0.796 (n.s.)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>133.8±16.3</td>
<td>135.5±16.3</td>
<td>0.684 (n.s.)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>48.3±5.7</td>
<td>46.7±3.5</td>
<td>0.393 (n.s.)</td>
</tr>
<tr>
<td>Super-obese</td>
<td>5 (50%)</td>
<td>1 (10%)</td>
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</table>
Metabolic Changes after LSG


Karamanakos, S; Vagenas, K; Kalfarentzos, F; Alexandrides, T

<table>
<thead>
<tr>
<th>TABLE 1. Patient Characteristics at Baseline</th>
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<tr>
<td></td>
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<tr>
<td>N</td>
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<tr>
<td>----</td>
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<tr>
<td>RYGBP</td>
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<tr>
<td>Sleeve gastrectomy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 4. Body Mass Index, % Excess Weight Loss, Ghrelin, and PYY Changes Before and 1, 3, 6, and 12 Months After Sleeve Gastrectomy</th>
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</thead>
<tbody>
<tr>
<td>Pre (mean ± SD)</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
</tr>
<tr>
<td>EWL%</td>
</tr>
<tr>
<td>Fasting ghrelin (pg/mL)</td>
</tr>
<tr>
<td>Fasting PYY (pg/mL)</td>
</tr>
</tbody>
</table>
Meal induced changes in ghrelin and PYY levels in 6 patients after LRYGBP (A) and 6 patients after LSG (B). Fasting (black bar) and postprandial (white bar) ghrelin values.
Summary for LSG

- The effect LSG on patients’ metabolic profile is exerted primarily by caloric restriction and ghrelin's' reduction after fundus removal.
- Meal stimulated PYY is significantly higher after LSG however gradually decreases over time, due to physiologic adaptation of the gastric remnant leading to better digestion. Therefore the long-term efficiency of LSG on appetite suppression is under question.
- LSG is categorized as a restrictive operation, however its ability to extend beyond caloric restriction through changes in gut hormone profiles raises a promise that it will play a leading role in the future of bariatric surgery.