Metabolic Surgery – Where Does It Fit In?

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Presenter Disclosure Information

In compliance with the accrediting board policies, the American Diabetes Association requires the following disclosure to the participants:

Presenter: Mary-Elizabeth Patti MD

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Consultant: Eiger
Metabolic Surgery is a Treatment Option for T2D!
Metabolic Surgery…Not Just Bariatric Surgery!

- Normal Anatomy
- Roux-en-Y Gastric Bypass (RYGB)
- Vertical Sleeve Gastrectomy (VSG)
- Adjustable Gastric Band (LAGB)

228,000 in 2017 in US (ASMBS)

18%  59%  3%  14% - revisions
Glucose metabolism is profoundly altered by upper gastrointestinal surgery.
Altered Glucose Patterns after Upper GI Surgery

Spike after eating

Nadir

RYGB

Normal fasting glucose

Nonsurgical

Salehi 2014
Altered Postprandial Metabolism after Mixed Meal after Bariatric Surgery

Spike after eating

↑ Glc Absorption

↑ Insulin Levels

↑ Insulin Secretion

↑ GLP-1 Levels

Similar patterns after SG
Salehi 2014
Upper GI Surgery

Rapid delivery of nutrients to foregut

Early & high peak of glucose

↑ Postprandial secretion of GLP1 (10x)

↑ Insulin secretion in postprandial state

• ↓ suppression of insulin secretion with hypoglycemia
• ↓ clearance of insulin

• Reduced counterregulatory hormones
• ↑ Insulin-independent glucose uptake
• Neural effects

Lowering of Glucose
Type 2 Diabetes – What Should I Do?

- Surgery?
- Medical Management?
TOUGH DECISIONS AHEAD
Goals of Therapy for T2D?

Improve glucose control – YES!

A1c

Danger!

Caution!

Success

↓ Average Glucose

Glycemic Variability
Other Critical Goals of Therapy for T2D

**Improve overall metabolic health**
- obesity, insulin resistance, physical fitness

**Prevent T2D and obesity complications**
- Neuropathy, retinopathy/visual loss, nephropathy
- NAFLD
- Cancer
- Pregnancy complications, effects on offspring

**Cardiovascular disease**

**Slow progression of T2D?**
- Extend lifespan?

**Optimize quality of life**
- reduce disease burden

**Safety, reversibility**
- if side effects develop

**Affordability**
- personal, societal
How Can We Best Achieve These Goals?

**Surgical Tools**

- Alter Gut-Brain Axis
- ↑ Incretin Secretion
- ↑ Insulin Secretion
- ↑ Insulin Sensitivity
- ? Endoscopic Approaches

**Medical Tools**

- Lifestyle modification
- ↓ Overnutrition
- ↑ Activity & fitness
- Technology
  - Activity, glucose monitors (CGM)
  - Closed loop pumps
- Medications:
  - Diabetes
  - Obesity
What are the Current Data?

Surgical

Medical
Randomized Clinical Trials of Metabolic Surgery vs. Medical Management for T2D

Cleveland Clinic
Joslin / BWH
University of Washington
University of Pittsburgh

Funding: NIH U01
Sustained Weight Loss & Remission of DM after Surgery at 3 Years – SLIMM Trial

**Sustained Weight Loss**

![Graph showing sustained weight loss](image)

**Sustained ↓HgbA1c**

![Graph showing sustained decrease in HgbA1c](image)

**↓ DM Medication Use**

![Graph showing decrease in DM medication use](image)

Simonson Diabetes Care 2018; SOARD 2019 in press

*Why Wait – intensive lifestyle and medical intervention program at Joslin also decreased BP & lipid med use*
**Sustained Weight Loss**

**Diabetes Remission**

Remission:
- A1c < 6.5%
- FPG 100-125 mg/dl on no Rx

MED

RYGB

37% remission on no meds at 5 years!

**Diabetes Medications**

Mingrone et al Lancet 2015
5 Year Followup from Larger Randomized Trial (STAMPEDE) Shows Sustained Weight Loss and DM Control

*Medical vs. Sleeve vs. RYGB*

At 5 years, how many are off all DM meds?
- Medical therapy: 2%
- Sleeve: 25%
- Gastric Bypass: 45%

Average 8.5 yrs of DM, 44% on insulin preop
Similar data for BMI <35 at study entry
What About the Long Term?
Sustained Improvement in Diabetes Control in SOS Observational Study

Prevalence of Diabetes Remission (FPG<110, no meds)

Await longer-term results of randomized trials...

SOS, Sjostrom et al. JAMA 2014
Impact on Diabetes Complications?
Long-Term Observational Study Reveals ↓ Complications

**Macrovascular**
- 32% risk reduction

**Microvascular**
- 56% risk reduction

Meta-analyses of observational studies show risk reduction for microvascular disease favoring metabolic surgery

*SOS, Sjostrom JAMA 2014; Merlotti, Obesity Rev 2017, Upala SOARD 2016*
Impact of bariatric surgery on existing diabetic nephropathy

101 patients with T2D and albuminuria pre-surgery (single center)

Adapted from Young L, Surgical Endoscopy, 2018
What about macrovascular disease?

N=5301 bariatric, 14,934 matched nonsurgical pts
Fisher et al JAMA 2018
 Metabolic Surgery is Effective for T2D Prevention

**COMPARE:** Pooled results from diabetes prevention trials:
Lifestyle intervention ↓ risk of developing DM by 36%

SOS, Carlsson NEJM 2012; Barry BMJ 2017
## Complications?

<table>
<thead>
<tr>
<th>Bariatric Surgery</th>
<th>Medical Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative morbidity</td>
<td>Side effects of meds - GI</td>
</tr>
<tr>
<td>similar to cholecystectomy!</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Iron, B12, D deficiency</td>
<td>Weight gain with insulin</td>
</tr>
<tr>
<td>Other nutrient / protein deficiencies</td>
<td>Clinical inertia</td>
</tr>
<tr>
<td>Need for multiple vitamins</td>
<td>Need for multiple medications</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Some injectable</td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>Chronic costs</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Difficulty with maintaining lifestyle changes</td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>Difficulty with weight loss and maintenance</td>
</tr>
<tr>
<td>Marginal ulcers</td>
<td>Chronic disease burnout</td>
</tr>
<tr>
<td>Post-bariatric hypoglycemia</td>
<td></td>
</tr>
<tr>
<td>Weight regain</td>
<td></td>
</tr>
<tr>
<td>Revisional surgery</td>
<td></td>
</tr>
<tr>
<td>Loss of glycemic control</td>
<td></td>
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<tr>
<td>Addiction/EtOH abuse</td>
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</tr>
</tbody>
</table>
Effective DM control & modest weight loss

• Limited by clinical inertia in real world

More effective sustained weight loss & DM control

• 5-15 yrs
• Erosion of remission over time

Not readily reversible

Need chronic nutrition monitoring & care

Insufficient data BMI < 35

Complications:
• ↓ CVD in observational studies
• Controlled trials in progress

Variable access

Cost

Medical

Effective DM control & modest weight loss

• Limited by clinical inertia in real world

Reversible

Fewer early side effects

Abundant data BMI<35

Complications:
• ↓ CVD & microvascular complications in controlled trials

Variable access

Cost

Surgery

More effective sustained weight loss & DM control

• 5-15 yrs
• Erosion of remission over time

Not readily reversible

Need chronic nutrition monitoring & care

Insufficient data BMI < 35

Complications:
• ↓ CVD in observational studies
• Controlled trials in progress

Variable access

Cost

Results of randomized trials for complications endpoints unknown

Impact of either surgery or medical Rx in combination with newer, more effective DM / obesity meds unknown

Uncertainties in 2019
BMI ≥ 40* should be recommended for Surgery.

BMI 35-40** should be considered if Rx and lifestyle inadequate or not durable.

BMI 30-35*** should be considered if Rx and lifestyle inadequate or not durable.

ADA Standards of Medical Care in Diabetes—2019
*BMI >37.5 in Asian Americans. **32.5-37.4, ***27.5-32.4
Metabolic Surgery is a Potent Approach to T2D
…But We Still Need More Data!!!

Direct comparison of surgery vs. *current* pharmacotherapy options for T2D & obesity

Impact on T2D with BMI < 35!

Identify new targets for non-surgical therapy
Can We Predict Success of Surgery for DM Remission Preoperatively?

Key factors:
- Age
- duration of DM
- use of insulin
- poor metabolic control

Scoring systems: ABCD, DiaRem, Ad-DiaRem, DiaBetter

Physiology:
- ↓likelihood of β-cell functional recovery →
- ↓likelihood of remission
Using Ad-DiaRems to Predict Remission

**Table 2: Ad-DiaRems Scoring System**

<table>
<thead>
<tr>
<th>Prediction Factor</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
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</tr>
<tr>
<td>15-41</td>
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</tr>
<tr>
<td>42-52</td>
<td>3</td>
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<tr>
<td>53-69</td>
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<tr>
<td>HbA1c (%)</td>
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<td>45-6.9</td>
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<td>7.0-7.4</td>
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<td>7.5-18.4</td>
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<td>Insulin</td>
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<tr>
<td>No</td>
<td>0</td>
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<tr>
<td>Yes</td>
<td>3</td>
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<tr>
<td>Other glucose-lowering agentsa</td>
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<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Number of glucose-lowering agentsb</td>
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<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
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<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>≥3</td>
<td>3</td>
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<tr>
<td>Diabetes duration (years)</td>
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</tr>
<tr>
<td>0-6.9</td>
<td>0</td>
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<tr>
<td>7.0-13.9</td>
<td>3</td>
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<tr>
<td>≥14</td>
<td>5</td>
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<tr>
<td>Ad-DiaRem overall score</td>
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<tr>
<td>(sum of the above six components)</td>
<td>0-21</td>
</tr>
</tbody>
</table>

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**Impact of Med #**

- **Age (years)**
- **A1c**
- **Rx with insulin**
- **Other Rx for DM**
- **Total # Rx for DM**
- **DM Duration**

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*Aron-Wisnewsky et al. Diabetologia 2017*
FINAL THOUGHTS

• Metabolic surgery is one part of our toolbox for T2D
• Consider in everyone
• Identify surgical colleagues
• Personal decision for patient requiring careful consideration
• Not an easy solution!
• Major lifelong commitment
• But...we need to consider and discuss surgical options with our patients with T2D
• Don’t wait until it’s too late!
• Type 1 DM? No!
Thank You!

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