Role and Long-Term Effects of Metabolic Surgery

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No Disclosures
History of Bariatric Surgery

Current Metabolic Surgical Alternatives
Roux-en Y Gastric Bypass: 1971-Present

- Reduced calorie intake
- Dumping syndrome
- Nutrient diversion but Malabsorption minimal
- %EWL @ 1 yr ~ 70%
- 45% of current procedures
Adjustable Gastric Band: 1993-Present

- Stoma diameter is adjustable but generally smaller than in gastric bypass
- Distal stomach and small intestine are unaltered
- Reduced calorie intake
- No malabsorption
- No dumping syndrome
- %EWL @ 1-yr ~ 40%
- 5% of current procedures
Duodenal Switch: 1990-Present

- Biliopancreatic diversion with duodenal switch

- Reduced calorie intake
- Significant malabsorption
- No dumping syndrome
- Loss of 80% of excess weight
- <5% of bariatric procedures
Sleeve Gastrectomy: 2003-Present

- Intermediate operative risks and weight loss
- Reduced calorie intake
- No malabsorption and no dumping
- Resection of source of Ghrelin
- %EWL @ 1 yr ~55%
- 45% of bariatric procedures
Mechanisms of Metabolic Effects

- All bariatric surgeries have profound neural, hormonal and metabolic effects
- Some of these effects result in weight loss
- Some are likely the result of weight loss
- Some are independent of weight loss
- Many but not all effects are beneficial

Mechanisms of Metabolic Effects

- Reduced caloric intake due to enhanced satiety
- Changes in tastes/food choices
- Reduction in fat mass
- Malabsorption
  - Duodenal switch
- Altered absorption/digestion
  - Gastric bypass and duodenal switch
- Resection of hormonally active tissue
  - Sleeve gastrectomy and duodenal switch
Postop Calorie Intake


Changes in Taste

Pepino et al, Obesity, 2014
Reduction in Fat Mass

Weight Loss: SOS study

Sjostrom et al, JAMA, 2012
Resting Energy Expenditure

- 31 RYGB pts REE and body composition at baseline and 6 months (29% wt loss)
- Fat mass loss was 77% of total wt loss
- REE/FFM ratio decreased ~10% relative to baseline

Carrasco et al, Obes Surg, 2007

Mortality and Bariatric Surgery

- Reduced long term mortality
  - Cardiovascular/Diabetes
  - Cancer

Sjostrom et al, NEJM 2007
Adams et al, NEJM 2007
Diabetes Remission

- SOS study patients with DM at baseline
- Remission OR 40 at 2 yrs dropping to 6 at 15 yrs
- Remission more likely with short duration of DM
- Diabetes complications reduced:
  - Microvascular HR 0.44,
  - Macrovascular HR 0.68
  Sjostrom et al, JAMA, 2014

Diabetes Incidence

- SOS study pts without DM at baseline
- DM incidence over 15 yrs:
  - Control 28/1000person-yrs
  - Surgery 7/1000 person-yrs
  - HR 0.17
  Carlsson et al, NEJM, 2012
Changes in Cardiovascular Risk Factors: Gastric Bypass

- 949 RYGB pts w/ mean f/u 1 yr
- Reduction in prevalence of CV risk factors
  - HTN 20%
  - DM 71%
  - High TG 93%
  - High LDL 48%
  - Low HDL 30%

Dallal et al, SOARD, 2012

Changes in Cardiovascular Risk Factors: Sleeve Gastrectomy

- 52 Sleeve pts w/ 6 & 12 mo f/u
- Reduction in prevalence of CV risk factors
  - Metabolic syndrome
    - 56% reduction
  - Most benefit by 6 mo

To et al, Exp Clin Endocrin Diab, 2012
Comparison of Medical and Surgical Therapy for DM

- Randomized 150 DM pts to:
  - 50 RYGB, 50 SG, 50 Intense Medical Therapy
  - Mean DM duration 8 yrs, 44% on Insulin
- Primary end-point HgbA1c < 6 at 12 mo
- No Mortality
- Mean BMI 37
- Surgical pts lost more wt

Schauer et al, NEJM, 2012

Comparison of Medical and Surgical Therapy for DM

- Surgery reduced DM medications
- Surgery reduced HgbA1c 37-42% vs 12% w/ IMT
- No differences in wt loss or HgbA1c between RYGB and SG
  - Beta cell function improved only in RYGB

Schauer et al, NEJM, 2012
Kashyap et al, Diab Care, 2013
HOMA IR Changes After Bariatric Surgery

- 660 pts: 78% IR preop
- 544 GB
- 116 AGB

Lee et al, Obes Surg, 2008

Antidiabetic Mechanism of Action

- Weight or Fat mass loss
- Caloric Restriction (Flux)
- Incretin changes related to altered nutrient flows
  - Gut hormones released by contact of nutrients with GI mucosa that stimulate insulin release
    - GIP (proximal SB), GLP-1 (ileum), ghrelin (stomach and duodenum)
  - Rapid or early delivery of nutrients in bypass procedures
Is Nutrient Diversion Important

- 10 RYGB, 10 AGB non-diabetic pts
- Measured at baseline and at 20% wt loss
  - 22wks AGB, 16 wks RYGB
- Euglycemic-Hyperinsulinemic Clamp
  - HOMA-IR
  - Insulin mediated glucose disposal
    - Skeletal muscle insulin sensitivity
- Mixed Meal Tracer Study
  - Disposition Index: Beta cell function
  
Bradley et al, JCI, 2012

Is Nutrient Diversion Important

- Improved Peripheral Insulin sensitivity and Improved beta cell function at 20% wt loss
- RYGB and AGB similar
- At same degree of wt loss, nutrient diversion may not be needed for increase in insulin sensitivity
Response to a mixed meal
Is Nutrient Diversion Important

- Metabolic response to a mixed meal is altered by RYGB but not by AGB
- Nutrient diversion profoundly affects rates of glucose absorption, endogenous glucose production, insulin secretion and GLP-1 secretion during a meal

Procedure Differences in Insulin Sensitivity Changes

- 10 GB, 8 BPD and 20 lean controls
- Insulin clamp

Muscetti et al, Am J Med, 2005
Long-term Effects on Lipids

- 94 RYGB pts with hyperlipidemia
- Beneficial trends

Jamal et al, SOARD, 2011

Lipid Kinetics after RYGB

- 7 RYGB pts studied at baseline, 6 & 12 mo
- Lipid precursor tracers
- Palmitate Ra decrease 50%
  - Insulin level decreased 70%
  - Adipocyte insulin sensitivity increased
- VLDL-TG secretion decreased

Klein et al, Gastroent, 2006
Metabolic Surgery

- RYGB, SG, AGB, and DS all have profound effects on caloric consumption, and fat mass
- These mechanisms result in long lasting changes in insulin sensitivity, co-morbidities, cardiovascular risk factors, lipid metabolism and mortality risk
- Other mechanisms include altered nutrient absorption that affects metabolic response to meals – some of which may be non-weight loss related