GASTRIC BYPASS:
THE FUTURE OF TYPE II DIABETES TREATMENT

James Cromie
The Arguments:

- T2DM - tremendous economic burden globally
- Lifestyle / Pharm Rx:
  - INEFFECTIVE and UNSUSTAINED
- Bariatric surgery is an **Effective** and **Durable** treatment option
  - Well established for BMI > 35
  - Effective for BMI > 25
- Surgery is a **Cost Effective** and **Safe** option
> 30% of American population obese (BMI > 30)
  - By 2030
    - 90% of adult Americans projected to be overweight / obese (> 50% obese)
    - US Obesity-related medical spending: $956 billion dollars

8.3% of Americans have type II DM
  - BMI > 40: 7X more likely to develop T2DM than normal BMI

285 million people worldwide with T2DM
  - 438 million projected for 2030 (WHO)
2010: US spent $198 billion on DM treatment
  - $9677 per patient diagnosed
  - $58 billion in lost earnings / decreased productivity

By 2030: Global expenditure for DM treatment and prevention will be $490 billion
  - 12% of worldwide healthcare expenditure spent for DM

### Table I. The ABCs of diabetes care: treatment targets as recommended by the American Diabetes Association.³

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA₁c</td>
<td>&lt;7.0% in general; &lt;6.0% in selected individuals</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>&lt;130/80 mm Hg</td>
</tr>
<tr>
<td>Cholesterol</td>
<td></td>
</tr>
<tr>
<td>LDL-C</td>
<td>&lt;100 mg/dL (&lt;70 mg/dL in very high-risk patients)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>&gt;40 mg/dL in men; &gt;50 mg/dL in women</td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>&lt;130 mg/dL (&lt;100 mg/dL in high-risk patients)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&lt;150 mg/dL</td>
</tr>
</tbody>
</table>

HbA₁c = glycosylated hemoglobin.
National Health and Nutrition Examination Survey (NHANES); 2006
- 88% fail to achieve all 3 ADA standards
- 44% fail to achieve HbA1C < 7%

Complete remission of hyperglycemia and metabolic consequences is rare
- Metformin / sulfonylureas → progressive loss of β-cell function.

Am J Med. 2006; 122:443-453
Follow up (yrs) | % Failing Monotherapy
---|---
3 | 50%
9 | 75%

608 patients, using current NIH inclusion criteria
- RYGB
- 14 yr Follow up

82.9% DM resolution in those with T2DM dx.
98.7% normalization in those with pre-diabetes

Correction of T2DM occurs within days of the operation before weight loss occurs

Effects are maintained long-term, though patients remain overweight / obese

DM “cure” less likely for older patients or those with DM for > 5 – 10 years (due to lower B-cell reserve)
Utility of bariatric surgery well established for DM in morbidly obese patients (BMI >35)
- 92% DM-related mortality reduction compared to medical management

In 2000: NIH recommendation:
- BMI > 40
  - Or,
- BMI > 35 AND:
  - DM, HTN, OSA, GERD, etc.

In 2009, centers for Medicare and Medicaid services provided coverage for bariatric surgery for above indications
- Lap adjustable gastric band
- Sleeve gastrectomy
- Roux-en-Y gastric bypass
  - Restrictive-Malabsorptive
  - Most common technique
  - 30cc gastric pouch
  - 100 – 150cm roux limb
- Biliopancreatic diversion
  - Restrictive-malabsorptive
  - 200-500cc gastric pouch
  - 50cm common limb
International meta-analysis.

- 22,094 patients with T2DM in 136 studies:
  - 84% remission rate overall, 2 yr f/u
    - BPD / DS: 95.1%
    - RYGB: 80.3%
    - Gastoplasty: 79.7%
    - LAGB: 56.7%

Effect of DM duration:

- 95% remission when DM < 5 years
- 54% remission if DM > 10 yrs

Modest weight loss can result in 20% reduction in all-cause mortality

Long term results: gastric bypass for BMI > 35

- 312 patients with T2DM
- BMI 50 +/- 9
- 10 year follow up. None on antidiabetic Rx.

<table>
<thead>
<tr>
<th></th>
<th>Prior to BPD</th>
<th>At 1 year</th>
<th>At 2 years</th>
<th>At 3 years</th>
<th>At 5 years</th>
<th>At 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>312</td>
<td>305</td>
<td>300</td>
<td>290</td>
<td>272</td>
<td>243</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>135.4 ± 25.6</td>
<td>88.9 ± 20.9</td>
<td>84.3 ± 16.5</td>
<td>88.2 ± 18.3</td>
<td>85.8 ± 18.3</td>
<td>86.6 ± 18.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>50.1 ± 9.0</td>
<td>32.8 ± 7.4</td>
<td>31.1 ± 6.5</td>
<td>32.1 ± 7.0</td>
<td>31.6 ± 6.4</td>
<td>32.0 ± 6.7</td>
</tr>
<tr>
<td>GL (mg/dl)</td>
<td>178 ± 61</td>
<td>84 ± 15</td>
<td>85 ± 18</td>
<td>84 ± 14</td>
<td>86 ± 18</td>
<td>89 ± 24</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>220 ± 155</td>
<td>120 ± 55</td>
<td>124 ± 107</td>
<td>96 ± 61</td>
<td>83 ± 36</td>
<td>82 ± 35</td>
</tr>
<tr>
<td>CHOL (mg/dl)</td>
<td>222 ± 75</td>
<td>136 ± 34</td>
<td>133 ± 33</td>
<td>126 ± 32</td>
<td>126 ± 31</td>
<td>113 ± 29</td>
</tr>
</tbody>
</table>

Growing evidence base for similar benefits for BMI 25 – 35

Sporadic case reports of gastric resection in non-obese diabetic patients resulting in T2DM remission

1998: Noya et al.
- First clinical report of Biliopancreatic diversion in BMI 24 - 38
- 10 patients with uncontrolled T2DM and hypercholesterolemia
- 18 month follow up
- 9/10 achieved normoglycemia
- 100% normalized cholesterol / triglycerides
- 100% normalized BP

Obesity Surgery 1998; 8: 67 - 72
117 patients with DM, 84 patients with pre-diabetes
- Lap mini-gastric bypass surgery
  - BMI > 35 vs < 35

5-yr follow up.
0.12% mortality, 2.2% complications

Baseline:
- Glucose: 158 mg/dl
- Cholesterol: 200 mg/dl
- LDL: 142 mg/dl
- HbA1C: 7.2%

Achieving ADA guidelines (1yr)

- **A1C < 7%; LDL < 100 mg/dl; Triglyceride < 150 mg/dl**

- BMI < 35: 76.5%
- BMI 35-45: 88.9%
- BMI > 45: 100%

Compare:
- 12% of those medically managed, meeting ADA standards
- (NHANES 2006)
- Asia-Pacific bariatric guidelines
  - BMI 27 definition of obesity in Taiwan
  - 90% of T2DM cases in Taiwan have BMI < 30
- Modified to include BMI > 32 with T2DM:
200 patients, BMI < 35
- Lap RYGB: 86%
- L AGB / SG: 14%

1 year follow-up
- 72.4% overall diabetes resolution
  - DM < 5 yrs: 90.3% remission
  - DM > 10 yrs: 62.5% remission

1% major complication (anastomotic leakage, requiring surgical revision)

Retrospective, 7 patients, on medication for DM

BMI 32 – 34.6

Mean follow up: 13 years (10 – 18 years)

10 year follow up

- ADA criteria
  - Triglycerides: 100%
  - BP control: 86% (No medications)
  - HbA1c not reported (Glucose < 126): 40%

*long term remission for those with DM < 4 yrs

Safety

- **Bariatric Outcomes Longitudinal Database (BOLD)**
  - 55,000 patients
  - All cause 30 day mortality: 0.09%

- **Longitudinal Assessment of Bariatric Surgery (LABS) Consortium**
  - 10 center prospective trial
  - 4776 morbidly obese patients
  - 0.3% 30-day post-op mortality
  - 4.3% complication rate (open & laparoscopic)
    - 3.1% Anastomotic leak (1.4% for laparoscopic)
    - 2.3% wound infection
    - 2.2% pulm. Events
    - 1.7% hemorrhage

- **BMI < 35 bariatric surgery review:**
  - 0.29% 30-day mortality
  - < 4% complication rate
Modeling Assumptions:
- Cost-effective QALY benchmark: $50,000

Takes into account:
- DM remission risk based on 2 and 10 year data
- Reduced risk related to:
  - Reduced BP
  - DM remission
  - Reduced cholesterol
- Costs of bariatric surgery

Evaluated effect of BMI 30 – 34 and > 35
- Modeled for BMI > 35
  - BMI 30 – 34 approximately doubled cost-effectiveness ratios ($ / QALY)
- RYGB is cost-effective, but not cost-saving

<table>
<thead>
<tr>
<th>Patients with newly diagnosed diabetes</th>
<th>Total costs*</th>
<th>Remaining life-years</th>
<th>QALYs*</th>
<th>Cost-effectiveness ratio ($/QALY)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>No surgery (standard care)</td>
<td>$71,130</td>
<td>21.62</td>
<td>9.55</td>
<td></td>
</tr>
<tr>
<td>Bypass surgery</td>
<td>$86,665</td>
<td>23.34</td>
<td>11.76</td>
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</tr>
<tr>
<td>Incremental (vs. no surgery)</td>
<td>$15,536</td>
<td>1.72</td>
<td>2.21</td>
<td>$7,000</td>
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<tr>
<td>Banding surgery</td>
<td>$89,029</td>
<td>22.76</td>
<td>11.12</td>
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</tr>
<tr>
<td>Incremental (vs. no surgery)</td>
<td>$17,900</td>
<td>1.14</td>
<td>1.57</td>
<td>$11,000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients with established diabetes</th>
<th>Total costs*</th>
<th>Remaining life-years</th>
<th>QALYs*</th>
<th>Cost-effectiveness ratio ($/QALY)†</th>
</tr>
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<tr>
<td>No surgery</td>
<td>$79,618</td>
<td>16.86</td>
<td>7.68</td>
<td></td>
</tr>
<tr>
<td>Bypass surgery</td>
<td>$99,944</td>
<td>17.95</td>
<td>9.38</td>
<td></td>
</tr>
<tr>
<td>Incremental (vs. no surgery)</td>
<td>$20,326</td>
<td>1.09</td>
<td>1.70</td>
<td>$12,000</td>
</tr>
<tr>
<td>Banding surgery</td>
<td>$96,921</td>
<td>17.80</td>
<td>9.02</td>
<td></td>
</tr>
<tr>
<td>Incremental (vs. no surgery)</td>
<td>$17,304</td>
<td>0.94</td>
<td>1.34</td>
<td>$13,000</td>
</tr>
</tbody>
</table>

*Diabetes care. 2010; 33(9):1933-1939*
- $15,000 - 20,000 per capita *excess* cost compared to standard care
  - Remaining life years in cost-effectiveness model: 20 years
- If we consider...
  - $58 billion annual indirect costs related to DM
    - (lost earnings and decreased productivity)
  - $2,233/yr per American with DM
    - X 10 yrs
- >$22,000 per capita lost earnings related to DM over 10 years

2010: 50 international delegates, Rome, Italy

Consensus Statement:

(A).* A surgical approach may also be appropriate as a non-primary alternative to treat inadequately controlled T2DM in suitable surgical candidates with mild-to-moderate obesity (BMI 30–35 kg/m²) (B). RYGB may be an appropriate surgical option for diabetes treatment in this patient population (C).
International Diabetes Federation

- March 2011:
  - Bariatric surgery should be an accepted option in people who have T2DM and BMI > 35
  - Surgery should be considered for BMI 29 – 35 when DM poorly controlled
  - Asians: may reduce BMI threshold to 25
Conclusions

- Bariatric surgery results in complete and durable remission of T2DM in carefully selected patients with BMI 25 – 35
  - Best outcomes for:
    - Short duration of DM (<5yrs)
    - Insulin independent
    - Young
    - Evidence of adequate beta cell mass (C-peptide > 3 ng/ml)
- Will need better long term data
- Surgery, as compared to standard of care, is a safe and cost-effective treatment modality.
Thank You