**Debate: What's the Best Way to Treat Obesity in Type 2 Diabetes?**

Lee M. Kaplan, MD, PhD
Osama Hamdy, MD, PhD
Sunday, February 19, 2017
8:00 a.m. – 9:00 a.m.

**Lee M. Kaplan, MD, PhD**

Despite multiple, concerted public health, behavioral and medical initiatives, effective prevention and durable control of obesity have proven elusive. Indeed, rates of obesity continue to rise worldwide, and no country or region has seen a significant, sustained reduction in either obesity prevalence or severity during the past several decades. Given its serious, pleiotropic effects on health, new strategies for prevention and treatment of obesity are needed. This is particularly true for patients with type 2 diabetes. In these patients, where obesity reduction is strongly beneficial for controlling the diabetes, most anti-obesity therapies are even less effective than in patients with normal glucose and lipid metabolism. One potential explanation for the limited effectiveness of most anti-obesity therapies is the heterogeneity of obesity itself. With several thousand genes and several hundred biological pathways contributing to the normal regulation of fat mass and body weight, it stands to reason that different defects in these regulatory systems may produce different subtypes of obesity. These different subtypes are manifest by distinct phenotypes, including differences in age of onset, body fat distribution, response to specific obesogenic environmental factors, associated comorbidities, and response to individual therapies. Optimizing outcomes in obesity treatment requires identifying the therapy or therapies that are most effective for an individual patient. With respect to diet-based treatments, many patients respond to a diet with fewer processed foods. For some, a low-carbohydrate or low-glycemic index diet is most effective, and for others, a fat-restricted diet yields better results. Similarly variable responses are seen to other lifestyle-based, pharmacological and surgical therapies for obesity. The key to optimizing clinical success comes in learning to apply each available therapeutic modality effectively, safely and confidently. Doing so will give each patient the greatest opportunity to receive the treatment that most closely matches their clinical need.

**Osama Hamdy, MD, PhD**

Weight reduction through lifestyle modifications remains the cornerstone in preventing and managing type 2 diabetes among overweight and obese individuals. For a long time, physicians have been skeptical about the long-term maintenance of weight reduction—claiming that nonsurgical weight reduction is always temporary and is frequently followed by gradual weight regain to the starting baseline. Over the last 2 years, this view has been gradually changing. Recent clinical trials and novel clinical practice models showed that long-term maintenance of weight loss is not only possible but is also associated with significant long-term improvement in many of the metabolic and cardiovascular abnormalities seen in patients with type 2 diabetes. Over the past 5 years, the introduction of several diabetes medications that induce satiety and reduce food intake (eg, glucagon-like peptide 1 analogues, SGLT-2 inhibitors and amylin analogues) gave clinicians several additional tools that allow them to help their patients in achieving better diabetes control without compromising their body weight. Use of these medications in proper combinations can help patients with type 2 diabetes not only to lose weight but also to maintain the weight loss. The Why WAIT (Weight Achievement and Intensive Treatment) program showed that it is possible for patients with obesity and diabetes to maintain weight reduction for up to 5 years in real-world clinical practice. On contrary, data from bariatric surgery mainly came from poorly designed studies with a smaller number of participants and for
relatively shorter duration. Variable definition of diabetes remission as shown in surgical intervention studies falsely augmented their results and misled physicians and patients. Cost-effectiveness and safety of bariatric surgeries for obesity management in diabetes are questionable.

References:

64th ADA Postgraduate Course

Treatment of Type 2 Diabetes Mellitus: Medical and Surgical Options

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February 19, 2017

Fernando Botero, 1932-

Relationship between Obesity and Type 2 Diabetes


Weight Loss Varies Widely Among Patients

Diet (Low-carbohydrate) Drug (Liraglutide)

Device (Duodenal Liner) Surgery (Gastric Bypass)

Considerable Variation in Response Within Diets

Atkins Diet Zone Diet

LEARN Program Ornish Diet

Pounds Lost 2

Pounds Lost FGF21 - 1
Long-term Weight Loss after Bariatric Surgery

STAMPEDE Trial


Schauer PR et al., NEJM 2017

Long-term Improved Glycated Hemoglobin

STAMPEDE Trial

Schauer PR et al., NEJM 2017

Anti-Diabetes Medication Use after Bariatric Surgery

STAMPEDE Trial

Schauer PR et al., NEJM 2017

Benefits of Bariatric Surgery are Not BMI Dependent

STAMPEDE Trial

Schauer PR et al., NEJM 2017
Surgery for the Treatment of Type 2 Diabetes

**Recommendations of DSS-II (2016)**

Surgery is recommended for:
- BMI ≥ 40 regardless of glycemic control
- BMI ≥ with inadequately controlled hyperglycemia

Surgery should be considered for:
- BMI 30-35 with inadequately controlled hyperglycemia
- Asians with BMI 27.5-35 with inadequately controlled hyperglycemia

Conclusions

**Pharmacotherapy**

- On average, anti-diabetes medications are highly effective in the treatment of diabetes, far more effective than lifestyle therapy alone
- Some medications, however, can exacerbate underlying obesity
- Some medications may accelerate the progression of underlying beta cell failure

**Conclusions**

**Lifestyle-based Therapies**

- Diet and exercise are critical components of lifestyle-based therapies; they are not the only components, however
- All anti-diabetes therapies exhibit substantial patient-to-patient variation in effect
- There are genetic and other biological factors that determine which diets are most effective in individual patients
- Even for lifestyle therapies, one size doesn’t fit all

**Conclusions**

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**Surgical Therapy**

- Metabolic surgery provides substantial, long-term improvement in type 2 diabetes
- While risk and cost of surgery preclude its use as first-line therapy, it is likely underused as “rescue” therapy
- The optimal use of surgery in the pathway of care for type 2 diabetes remains to be determined

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Coordinated Care

- Lifestyle, medical and surgical care for both obesity and type 2 diabetes should be viewed as cooperative, not competitive, approaches
- New patient care models that promote integrated pathways and shared medical and surgical responsibility for care within those pathways (including post-operative care) should be encouraged
- Use and optimization of combination therapies that employ all available approaches need to be supported and further evaluated

Clinical Data Evaluation – A Serial Approach

- Statistical significance
- Effect size
- Number needed to treat
- Durability of effect
- Risk-benefit profile
- Cost-benefit profile

64th ADA Postgraduate Course

Treatment of Type 2 Diabetes Mellitus: Medical and Surgical Options

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February 19, 2017
The Best Management of Obesity in Type 2 Diabetes

Osama Hamdy, MD, PhD, FACE
Medical Director, Obesity Clinical Program, Director of Inpatient Diabetes Management, Joslin Diabetes Center
Harvard Medical School
Boston, USA

Evolution of History

After Weight-Loss Surgery, a Year of Joys and Disappointments
Even as the pounds fell away and their health improved, two patients contended with the feeling that life hadn't changed as much as they'd hoped.

Before You Spend $26,000 on Weight-Loss Surgery, Do This
The old-fashioned way to treat diabetes. It is cheaper than weight-loss surgery. And probably more effective

We are in agreement
1. Anti-obesity medications are effective for weight reduction
2. Bariatric surgeries are indicated for patients with very high BMI (Class III obesity)
3. Gastroscopic procedures are promising

Results of Bariatric Surgery

Is this true?
**What is the Reality without Bariatric Surgery Propaganda?**

6 Claims:
1. Diabetes remission is well-documented in high quality and long-term studies
2. Diabetes resolution (complete remission) occurs in around 80% of cases
3. Weight loss after bariatric surgery is huge and sustainable
4. Bariatric surgery is far more superior than intensive lifestyle intervention
5. Bariatric surgeries are safe
6. Bariatric surgeries are cost-effective

**Bariatric Surgery Versus Intensive Lifestyle Intervention**

To Answer this Question you Need:
1. RCT
2. Good sample size
3. ISS versus ILI
4. Long duration of intervention

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**Major Bariatric Surgery Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Design</th>
<th>Intervention</th>
<th>Sample Size</th>
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<td>Courcoulas et al.</td>
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<td>Courcoulas et al.</td>
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**Definition of Remission from T2DM**

* Partial Remission: FPG <100 mg/dl without medications
* Complete Remission: FPG <60 mg/dl without medications
* Very Poor Remission: FPG >200 mg/dl

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**Who Had the Surgery? and How Much Weight Loss?**

Average Weight Loss in 3-10 years is 20-24 kg
Any Remission from T2DM at 3-5 Years

Partial and Complete Remission from T2DM at 3 Years

Impact of Bariatric Surgery on Healthcare Utilization & Costs in Patients with DM over 6 Years

Effective Non-Surgical Alternatives to $$$ Procedures

“Let thy food be thy medicine, and let thy medicine be thy food.”
Hippocrates, father of medicine
Effective Non-Surgical Alternatives to $$$ Procedures

1. Structured Multidisciplinary lifestyle intervention
2. Very low calorie diet
3. Very low carbohydrates diet
4. Anti-obesity medications
5. Diabetes medications with weight loss action

Why WAIT

Program Look AHEAD

Structure of Look AHEAD Versus Why WAIT

Structured Meal Plan

Calorie Distribution
- 40-45% from carbohydrates
- 30-35% from fat
- <10% from saturated fat

Diabetes-Specific Nutrition Formula
- 1-3 times/day to replace equivalent calories
- 1-1.5 g/kg of body weight from protein
- 14 g fiber/1000 Kcal

Dinner Menus
17 choices with detailed ingredients, cooking instructions and nutrition facts

Snack Lists
Includes 100 and 200 calorie snacks

Balanced Exercise Model

Strength exercise is particularly important during weight reduction

Diabetes Medications and Body Weight

<table>
<thead>
<tr>
<th>List A</th>
<th>List B</th>
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<tbody>
<tr>
<td>1. Identify</td>
<td>Weight Gain</td>
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<tr>
<td>2. Plan</td>
<td>Metformin</td>
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<tr>
<td>Flexibility</td>
<td>Pioglitazone</td>
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<tr>
<td>Aerobic</td>
<td>SUs</td>
</tr>
<tr>
<td>Strenght</td>
<td>Glyburide</td>
</tr>
<tr>
<td>Strectching</td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>Yag</td>
<td>Metformin</td>
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</table>

Medications:
- SUs
- Glimepiride
- Glipizide
- Insulin NPH
- Glargine
- Regular Aspart
- Lispro
- Glulisine
- Pioglitazone
- DPP-4 Inhibitors
- Metformin
- SGLT2 Inhibitors
- Sitagliptin
- Saxagliptin
- Linagliptin
- Alogliptin
- Acarbose
- Miglitol
- Colesevelam
- Bromocriptine
- GLP-1 Analoges
- Exenatide
- Liraglutide
- Dulaglutide
- Albiglutide
- Pramlintide
- Prometride
- SU12-Inhibitor
- DPP-4 Inhibitors
- GLP-1 Analoges
- Exenatide
- Liraglutide
- Dulaglutide
- Albiglutide
- Pramlintide
- Prometride
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- DPP-4 Inhibitors
- GLP-1 Analoges
- Exenatide
- Liraglutide
- Dulaglutide
- Albiglutide
- Pramlintide
- Prometride
- SU12-Inhibitor

Stop, Reduce or Switch | Continue | Add
Effective Non-Surgical Alternatives to $$$ Procedures

1. Structured Multidisciplinary lifestyle intervention
2. Very low calorie diet
3. Very low carbohydrates diet
4. Anti-obesity medications
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### Relationship Between Insulin Sensitivity and Insulin Secretion Before and After Interventions

![Graph showingRelationship Between Insulin Sensitivity and Insulin Secretion Before and After Interventions](image)

- Pre-RYGB
- Post-RYGB
- Pre-VLCD
- Post-VLCD

### History of Diabetes Nutrition

<table>
<thead>
<tr>
<th>Date</th>
<th>Carbs</th>
<th>Protein</th>
<th>Fat</th>
<th>Calories</th>
<th>Description</th>
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<tbody>
<tr>
<td>1940</td>
<td>38%</td>
<td>17%</td>
<td>45%</td>
<td></td>
<td></td>
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<tr>
<td>1950</td>
<td>43%</td>
<td>10%</td>
<td>37%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1971</td>
<td>45% or more</td>
<td>5%</td>
<td>39%</td>
<td></td>
<td>American Diabetes Association</td>
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</table>

### National Recommendations and Principles for Individuals with Diabetes Mellitus

- **1979**, the Committee on Food and Nutrition of the American Diabetes Association published a special report titled "Principles of Nutrition and Dietary Recommendations for Individuals With Diabetes Mellitus."
- **2001**, the American Diabetes Association released a report on the management of diabetes and its complications, including dietary recommendations.
- **2006**, the latest report includes new and emerging information regarding effects of diet on blood glucose concentrations, in diabetes, and information relating alternatives to blood lipid levels, particularly cholesterol, with differences in the general population. Since 1979, much new information has emerged on the link between nutrition and diabetes, including the role of the glycemic index and its relation to the exchange system, and the value of its properties as a factor in the weight loss process. The 1979 report also included a transformation in the approach to the nutrition education. Health care should be provided by a team of professionals, with each member playing an important role in the overall care of the patient.

### Effective Non-Surgical Alternatives to $$$ Procedures

1. Structured Multidisciplinary Lifestyle Intervention
2. Very low carbohydrates diet

### Anti-obesity medications

Diabetes medications with weight loss action
The High Fat Era (Michigan Diet) (Use of a High Fat Diet in the Treatment of Diabetes)

Avoid the danger of:
- Inadequate energy
- Excess Carbohydrates
- Excess protein

<table>
<thead>
<tr>
<th>Calories</th>
<th>Fat</th>
<th>Carbohydrates</th>
<th>Protein</th>
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<tbody>
<tr>
<td>900-1000</td>
<td>90 gm</td>
<td>10 gm</td>
<td>14 gm</td>
</tr>
<tr>
<td>1400</td>
<td>170 gm</td>
<td>25-30 gm</td>
<td>30-40 gm</td>
</tr>
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</table>

Further additions up to 2,500 calories may be made to suit individual cases.
Maintain nitrogen balance by 0.66 gm/kg.

73 cases in 1920: 4 died from unrelated reasons
45 cases in 1921: (blood glucose 60-130 mg/dL)

Joslin Diabetes, 1923
Quantity of food required by severe diabetic patient weighing 60 Kg

<table>
<thead>
<tr>
<th>Food</th>
<th>Calories (%)</th>
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<tbody>
<tr>
<td>Protein</td>
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<tr>
<td>Fat</td>
<td>150 g</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>10 g</td>
</tr>
<tr>
<td>Alcohol</td>
<td>15 g</td>
</tr>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

“Strict diet”: Meats, poultry, game, fish, clear soups, gelatin, eggs, butter, olive oil, coffee, tea

Osler W & McCrae T, The Principles and Practice of Medicine, 1923; Westman EC, Perspect Biol Med, 2006

An Online Intervention: Very Low-Carbohydrate Diet Versus a Plate Method Diet in Overweight Individuals with Type 2 Diabetes: A Randomized Controlled Trial

8 Keys to Optimal Lifestyle Intervention for Long-term Weight Reduction

1. Aim for meaningful weight loss goal (5-10%)
2. Gradual, balanced and individualized physical activity
   - Type of exercise
   - Exercise records
3. Structured dietary intervention & modified macronutrient composition
   - Relatively higher protein, LGI & higher fibers
   - Provided menus
   - Food records
4. Medication adjustment and frequent BG monitoring
5. Counseling and cognitive behavioral change
6. Group intervention and frequent participant contact
7. Daily weighing
8. Online and mobile interaction and support

Keys to Optimal Lifestyle Intervention for Long-term Weight Reduction

Joslin Diabetes Center
Economic Impact of Non-Surgical Weight Loss over One Year in Patients With Diabetes

Cost Saving (1% wt loss) Estimated Saving with (7% wt loss)

- $256 (1.4%) - $131 (7.4%)
- $1,046

Take Home Message
- Remission from type 2 diabetes after bariatric surgery is overstated
- Bariatric studies are misleading, poorly designed, of short duration or include very small sample size
- Bariatric surgeries are not cost effective over 6 years
- Diabetes remission occurs with low-calorie diet, low-carbohydrates diet or with structured lifestyle intervention
- Non-surgical intervention improves patients’ quality of life in comparison to bariatric surgeries
- Referring patients with diabetes to bariatric surgery should be limited to severe cases of obesity
- Endocrinologist should not be fooled by bariatric propaganda!

Complications after bariatric surgery
- Gastric erosion (LAGB)
- Postprandial symptoms: heartburn/GERD, dysphagia, epigastric pain
- Surgical complications:
  - Bleeding
  - Anastomosis leakage
  - Obstruction
  - Wound infection
  - Abcess formation
  - Pulmonary complications
  - Incisional hernia
- Nutrient deficiency, biochemical abnormalities
  - Iron
  - Folate
  - Thiamine
  - Vitamin D
  - B12 (gastric bypass)