Treatment and Management of Obesity as a Chronic Disease

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The Obesity Medicine Association’s Definition of Obesity

“Obesity is defined as a chronic, relapsing, multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences.”

Disclosures

• Novo Nordisk advisory council

Obesity as a Chronic Disease

• Long term problem, not likely to improve without treatment
• Treatable and manageable, not thought of as “curable”
• Stopping treatment leads to recurrence or relapse
• Strategies are Long Term!
• Multidisciplinary care continuum approach

CLINICAL LEADERS IN OBESITY MEDICINE

OMA members are physicians and health care professionals who work to advance the prevention, treatment, and reversal of the disease of obesity.

Chronic Disease Examples
How is Obesity Linked to Diabetes?

- The answer is based on adipose tissue structure and function
- Adipose tissue is metabolically very active

Metabolic Syndrome

- AKA Dysmetabolic Syndrome
- AKA Syndrome X
- AKA "Insulin Resistance"
- ICD 10 code E88.9
- "Syndrome" of combination abnormalities:
  - Blood pressure
  - Lipids
  - Glucose
  - Increased abdominal girth
  - +/- microalbuminuria
- Metabolic Syndrome leads to **Cardiometabolic Risk**

Cytokines and Inflammation

- **Inflammatory Cytokines**
  - TNF-α
  - Interleukin-1
  - IL-6
  - IL-8
  - Resistin
  - Monocyte Chemotactic Protein (MCP)
  - Adipsin
  - Plasminogen Activator Inhibitor-1 (PAI-1)
  - Angiotensinogen

- **"Downstream" Effects**
  - Inflammation
  - CRP
  - Thrombosis
  - Atherosclerosis
  - Dyslipidemia
  - Type 2 Diabetes
  - Hypertension
  - Metabolic Syndrome
  - Cardio-Metabolic Da
  - Androgen Deficiency

Factors Contributing to Cardiometabolic Risk

- Metabolic Syndrome
  - Lipids, BP, Glucose

- Obesity

- Age, Race, Gender, Family History
- Hypertension
- Smoking, Physical Inactivity

Brunzell, et al. JACC 2008; 51:1512-1524
Natural History of Type 2 Diabetes

Years from Diagnosis

Insulin Resistance and Beta cell dropout begin years before diagnosed diabetes.

-15 -10 -5 0 +5 +10 +15

Diagnosed Diabetes

Cardiovascular Complications

Impaired Glucose Tolerance

Insulin Resistance


Diet – Nutritional Composition

Macronutrients

- Low Fat
  - AHA, Ornish, Pritikin
- High Fat
  - Atkins
- Low Carb
  - Atkins
- High Protein

Names associated with diets are examples only

Diet – Caloric Composition

- 0-400
  - Starvation or near starvation, never recommended
- 400-800
  - Very Low Calorie Diet (VLCD)
- 800-1500
  - Low Calorie Diet (LCD)
- Above 1500
  - Balanced Deficit Diet (BDD)
    - Reduction of 500-1000 cal/day from DMR

Diet – Type or Brand

- Atkins
- Protein Power
- ZONE
- LEARN (balanced deficit)
- ADA (diabetic)
- South Beach
- Weight Watchers
- Jenny Craig
- Nutrisystems
- Optifast
- HCG
- Mediterranean
- Body for Life
- DASH
- AHA
- Pritikin
- Ornish
- “Whole Food, Plant Based”
- Vegan
- Vegetarian
- Kosher
- Halal

Diet – Is there a “Best” diet?

- Diet should be individualized
- All diets can be described in terms of caloric content and macronutrient content
- Many different diets have strong adherents
- All diets can be effective in weight loss
- Most obesity medicine specialists use some version of a reduced carbohydrate approach
  - All calories are not created equal

Obesity Treatment Strategies

- Diet
- Surgery
- Behavior and Lifestyle Modification
- Medication Management
- Exercise

Diet – Is there a “Best” diet?
Glucose AUC was lowest for the low-carbohydrate diet (p=0.001). Insulin AUC was different for each diet (p=0.001).


Behavior and Lifestyle Modification

- Goal is to help patient learn behaviors and patterns of thinking that support weight loss and weight maintenance
- Varied counseling approaches are useful
  - Motivational Interviewing
  - Cognitive Behavioral Therapy
  - Relational/Interpersonal Therapy
- 5 A's approach currently used by Centers for Medicare and Medicaid Services (CMS)

Carbohydrate Metabolism

- Glucose
- Insulin
- Fat Storage
- Inhibition of Fat Burning

Five Major Steps to Intervention – The 5 A’s

1. Ask
2. Assess
3. Agree
4. Advise
5. Assist

Diet

Behavior and Lifestyle Modification

Surgery

Medication Management

Exercise
Exercise and Activity

- Part of a comprehensive plan
- More important for weight maintenance than weight loss
- Many benefits other than weight control
- Exercise Prescription

Exercise and Activity – How much does it contribute to weight loss?

- Not as much as we might think
- Example:
  - 45 yo female patient with DMR of 2200 cal/day.
  - 1100 Low Calorie Diet => diet deficit of ~1100 cal/day
  - Calories burned with 1 hour of walking ~300

Exercise and Activity

- Mood
- Cardiovascular fitness
- Pain
- Glucose control
- Dyslipidemia
- Strength
- Balance/Coordination
- ADLs (Activities of Daily Living)
- Lowers risk of some cancers

Medications

- Medications used to treat weight
- Medications that affect weight

Medications Used to Treat Weight

- Sympathomimetics
  - Phentermine
  - Phendimetrazine
  - Diethylpropion
  - Metformin – Off label
  - Topiramate – Off label
  - Gastric Lipase Inhibitor
    - Orlistat (Alli®, Xenical® – RX)
- “New” Drugs
  - GLP-1 analogues
    - Liraglutide (Saxenda®)
  - Combination
    - Phentermine/Topiramate (Qsymia®)
    - Bupropion/Naltrexone (Contrave®)
  - Serotonergic (5HT-2CR)
    - Lorcaserin (Belviq®)
Medications Used to Treat Weight
Relative Advantages

- Sympathomimetics
  - Years of experience
  - Predictable
  - Inexpensive

- Newer Agents
  - Approved for extended use
  - Offer variety
  - Different mechanisms

Medications That Affect Weight

Weight Positive (Gain)
- Corticosteroids
- Antihistamines
- Cyproheptadine(Periactin®)
- Many Antidepressants
  - Tofepride, TCA, most SSRI (e.g. paroxetine)
- Opioids
- Atypical Antipsychotics
  - risperidone, olanzapine, aripiprazole, ziprasidone
- Most Antihistamine drugs
- Many Antidepressants
- Beta Blockers

Weight Negative (Lose)
- Metformin
- Nefazodone (Serzone®)
- Bupropion (Wellbutrin®)
- Fluoxetine (Prozac®)
- Incretins
  - Exenatide (Byetta®, Bydureon®)
  - Liraglutide (Victoza®, Saxenda®)

Weight Neutral
- Venlafaxine (Effexor®)
- Citalopram (Celexa®)
- Sertraline (Zoloft®)

Diabetic Medications Effects on Weight

Weight Positive (gain)
- Insulins
- Thiazolidinediones (TZDs)
  - pioglitazone (Actos®)
  - rosiglitazone (Avandia®)
- Sulfonylureas
  - glibizide (Glucotrol®)
  - glyburide (Micronase®, DiaBeta®)
- Meglitinides
  - nateglinide (Starlix®)
  - repaglinide (Prandin®)

Weight Negative (lose)
- Metformin
- GLP-1 analogues
  - exenatide (Byetta®, Bydureon®)
- DPP-4 Inhibitors
  - sitagliptin (Januvia®)
- GLP-1 Inhibitors
  - canagliflozin (Invokana®)
  - dapagliflozin (Farxiga®)
  - empagliflozin (Jardiance®)

“The new guidelines recognize for the first time surgery as a legitimate diabetes treatment and should inform physicians and policymakers about the appropriate selection of patients for surgical treatment. Both practically and conceptually it is one of the greatest innovations in diabetes care in recent times.”

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Algorithm for the treatment of T2D, as recommended by DSS-III voting delegates.

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**Weight Maintenance after Bariatric Surgery**

- **Long Term Mortality after Gastric Bypass**
  - 7.1 years follow-up
  - Overall deaths dropped **40%** with Surgery
  - Heart Disease Deaths dropped **56%**
  - **Diabetes deaths dropped 92%**
  - Cancer deaths dropped **60%**

**Newer Technologies**

**Intragastric Balloons**

- Placed endoscopically
- Early balloons (1980's) had high rates of gastric ulcers and erosions (14-26%)
- Current balloons soft, smooth, spherical, and filled with saline
- Approved for 6 months duration
- Nausea and vomiting very common (75-85%) but typically resolve within 1-2 weeks
- About 10% weight loss at 6 months (7.5% at 12 months)
- To be used in conjunction with diet and behavior modification program
Summary

• Obesity is a chronic condition amenable to long term strategies
• Insulin resistance is central to many downstream metabolic diseases of obesity
• Carbohydrate metabolism is central to obesity and associated morbidities
• The concept of a “care continuum” is very useful and allows for combined approaches

Thank You!

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