Pharmacotherapy Options for Obesity and Cardio metabolic Risk: Helpful or Harmful.

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Disclosure

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Introduction

The increasing prevalence of obesity has led to the emergence of multiple serious obesity-related comorbidities including the cardio metabolic syndrome which require optimal treatment to prevent or delay the onset of type 2 diabetes mellitus and coronary artery disease. Obese subjects are at high risk for multiple comorbidities, which must be optimally treated.

Objectives

A New Understanding Of Obesity and its frequently associated comorbidities ie the M.S. which must be optimally treated

“Genetics loads the gun—the environment pulls the trigger.”

George Bray, 1996
Quiz#1

Prevalence of overweight and obesity in the USA?

A. 20 million
B. 50 million
C. 80 million
D. over 100 million

Question #2

• Perivascular/ Epicardial fat increase in Obesity,
• A. True
• B. False
Question #3

• Excess Epicardial fat is a risk factor:
  • A. True
  • B. False

Planed Discussion
1. Prevalence
2. Etiology
3. Pathophysiologic link between Obesity and cardio metabolic syndrome
4. Guidelines for Diagnosis
5. Risk Assessment in Obesity utilizing novel Tools
6. Obesity associated comorbidities, with emphasis on cardio metabolic syndrome
7. Current Management
8. Novel publications on Obesity and Metabolic from our center
9. Conclusions and take home messages
1. Prevalence

How Prevalent is Obesity?

Obesity epidemic is sweeping the world and there is no evidence that this phenomenon will plateau in the near future.

2 out of 3 US adults are overweight or obese. “Obesity can truly be called America's newest and fastest-growing epidemic.”
Cardio metabolic risk of obesity

• Individuals with obesity are at an increased risk of, insulin resistance, hyperinsulinemia, prediabetes, T2DM. Hypertension and Atherogenic Dyslipidemia

• Why???

Pathophysiologic link between Obesity and the cardio metabolic syndrome & Cardiovascular Disease

Reversible risk factors

Irreversible risk factors

Sub clinical atherosclerosis

Changes in
A Glucose
B Hypertension and
C Lipid metabolism

Disease progression

Disease and CV Events
- Diabetes
- Stroke
- MI

Death

Metabolic Syndrome

Obesity
Secret Excess Atherogenic Adipokines
Assessing overweight & Obesity?

• BMI

• *Waist circumference*

• Waist / Hip Ratio >0.9

2. NIH National Heart, Lung, and Blood Institute. *Obes Res*. 1998;6(suppl 2):S1S.
What are the current Guidelines for the Diagnosis of Obesity?

<table>
<thead>
<tr>
<th>GUIDE LINES</th>
<th>Defining Level</th>
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<tbody>
<tr>
<td>NCEP. ATP III</td>
<td>Waist circumference</td>
</tr>
<tr>
<td>Men</td>
<td>&gt;40 in (102 cm)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;35 in (88 cm)</td>
</tr>
<tr>
<td>W.H.O BMI &gt;30 kg/m2 and or</td>
<td>Waist to Hip ratio</td>
</tr>
<tr>
<td>Men</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td>Women</td>
<td>0.85</td>
</tr>
<tr>
<td>AHA/NHLBI</td>
<td>≥ 40 inches in men</td>
</tr>
<tr>
<td></td>
<td>≥ 35 inches in women</td>
</tr>
<tr>
<td>International Diabetes Federation</td>
<td>waist ≥ 94 cm males and &gt;80 cm females</td>
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OBESITY associated COMORBIDITIES

Obesity is associated with comorbidities affecting almost every system in the body including, but not limited to:

- Cardiovascular
- Pulmonary
- Gastrointestinal
- The endocrine
- Musculoskeletal systems
- Dermatologic and much more.
- The severity of these comorbidities typically increases with the duration and severity of obesity.
OBESE Patients must undergo Optimal Global risk assessment for CVD and future Cardiovascular Events to determine treatment strategy.

Is the Patient Low, Intermediate or High Risk???

Novel optimal Method for CV Risk Assessment

Screening Tests for Early Detection of Cardiovascular Disease risk \{EDCVDRS\}
And
Determination of Cardiovascular Risk Category Also known as

RASMUSSEN Risk scores [RRS]
Screening Tests for Early Detection and Determination of Cardiovascular Risk Category

Include Tests for:

1. Vascular Evaluation
2. Cardiac Evaluation
3. Modifiable Disease Contributors

Earl Cardiovascular Disease Risk Score Consists of:

- 10 Non-Invasive tests
  - Large Artery Elasticity (C1)
  - Small Artery Elasticity (C2)
  - Resting BP, BP post-exercise
  - Carotid Intima Media Thickening
  - Retinography
  - Abdominal aorta ultrasound
  - Micro albumin
  - ECG
  - Left Ventricular Ultrasound
  - Pro-BNP
  - Hs-CRP
  - Fasting Lipid Panel
  - Fasting Blood Sugar
Publications on Obesity from our Center

Novel abnormal cardiovascular findings and data on obesity without comorbidities published* from our cardiovascular disease assessment center since 2011

Utilizing ECVDRS

* Presented at the annual meetings of many national and international CV societies since 2011 including AHA, ACC, ESC, SCCT, ASH, HFSA, ESHF and much more

Obesity and CVD: An Association or a Cause and Effect Relationship
Novel data on Obesity study done at CVD Assessment Center, Sarasota, Florida Utilizing ECVDRS

Studies on obesity published from our center:


Studies on obesity published from our center…cont.


6. **Abnormal Carotid Intima-Media Thickness is a Predictor of Coronary Artery Disease in Asymptomatic Obese Subjects Regardless of Sex,** - SCCT 2012

Studies on obesity published from our center…cont.

7. **Novel approaches for risk stratification and management of asymptomatic Metabolic Syndrome subjects : is Metabolic Syndrome a marker of Coronary Artery disease in all ?** - *presented at the Fifth Annual Scientific Meeting of the Society for Cardiovascular Computed Tomography [SCCT] July 15-18, 2010;*

8. **Is metabolic syndrome cardiovascular disease (CVD) risk equivalent?** - *presented at the European Society of Cardiology (ESC) Euro PRevent Annual Meeting, Geneva, Switzerland, April 2011*
Studies on obesity from our center to be presented at next congress of the European Society of Cardiology/EuroPrevent on April 6-8, 2017 in Malaga Spain

Decades of obesity even without comorbidities in asymptomatic subjects is associated with significant cardiovascular structural and functional abnormalities

To be presented at the annual meeting of the European Congress of Cardiology/Europrevent on April 6/2017 Malaga/ Spain
Epicardial adiposity, regardless of visceral adiposity, is associated with significant cardiovascular abnormalities in untreated and asymptomatic subjects, as measured by the calcium score

To be presented at the annual meeting of the European congress of cardiology/Euro prevent
On April 8/2017 Malaga/ Spain

Your abstract has been selected for its outstanding quality and will be presented as a Rapid-Fire presentation during an oral session chaired by two experts in the topics presented

Eight abstracts will be presented during the session

7. Current Management
The clinical evaluation of obese individuals is directed at identifying:

A. The cause of obesity and
B. Obesity-related comorbidities

Management of obesity and cardio metabolic syndrome

Nonpharmacologic: Lifestyle modifications including dietary changes aimed at decreasing total caloric intake, increasing physical activity and decreasing sedentary time are crucial for management. Pharmacologic: Drugs have a role in the treatment of obesity,
Bariatric surgery [Metabolic surgery]

Surgery: Bariatric surgery is effective in achieving weight loss and improving comorbidities in individuals with severe obesity.

Goals for Managing Obesity is to prevent or delay the development of:

* working definition

Gelfand EV et al, 2006; Vasudevan AR et al, 2005
None pharmacologic approach

Therapeutic lifestyle changes/ TLC
REMEMBER:

APETITE IS OUR WORST ENEMY

Self Control
Pharmacologic approach for obesity management beyond TLC

Appropriate use of obesity Drugs and diagnosis and global management of all obesity associated Comorbidities
[optimal control control of ABC and other comorbidities]
Which overweight or obese patients should be considered for obesity drug use?

Published clinical practice guidelines recommend that adjunctive drug treatment be considered in:

- patients with a body mass index $\geq 30$
- or 27-29.9 with medically complicated obesity who have failed achieving optimal weight with therapeutic life style changes [TLC]
Potential Strategies for Anti-Obesity Drug Action

- **Reducing food intake.** Either amplify effects of signals/factors that inhibit food intake or block signals/factors that augment food intake.
- **Blocking nutrient absorption** (especially fat or carbohydrates) in the intestine.
- **Increasing thermogenesis.** Either increase metabolism and dissipate food energy as heat or increase energy expenditure through the enhancement of physical activity.
- **Modulating fat metabolism/storage.** Regulate fat synthesis/breakdown by making appropriate adjustments to food intake or energy expenditure.
- **Modulating the central regulation of body weight.** Either alter the internal set point or modulate the signals.

Prescription Medications for Weight Loss: FDA approved medications

- Orlistat ............................................. Xenical
- Lorcaserin.................................Belvique
- Phentermine/Topiramate..........Qsymia
- Natrexone/Buprione..............Contrave
- Liraglutise.............................Saxenda
Mechanisms of action of anti-obesity drugs

With the exception of orlistat, medications indicated for obesity target appetite mechanisms.

The medications available for obesity treatment work primarily in the arcuate nucleus to stimulate the POMC neurons, which promote satiety. Some of the medications are:

- serotonergic,
- dopaminergic, or
- norepinephrine-releasing agents/reuptake inhibitors

Antiobesity agents and their mechanism of action.

- Another class of medications is associated with weight loss without an effect on appetite.
- This class is the SGLT-2 inhibitors for T2DM, which promote weight loss by preventing the reabsorption of glucose as well as water in the renal tubules
Anti obesity agents and their mechanism of action.

**Phentermine** is primarily a noradrenergic and possibly dopaminergic sympathomimetic amine.

**Lorcaserin** is a serotonin agent specifically stimulating the serotonin receptor 2c receptor.

The combination of phentermine and topiramate, which is a neurostabilizer and anti seizure medication, seems to be additive; however, it is unclear how topiramate enhances appetite suppression.

Reuptake inhibitor , which stimulates POMC neurons. In combination with Naltrexone, bupropion enhances efficacy due to the release of feedback inhibition of POMC neurons that naltrexone potentiates.

GLP-1 agonists also affect the POMC neurons and cause satiety.

**Orlistat** blocks absorption of25 to 30% of fat calories and is not appreciably absorbed systemically.

Another class of medications is associated with weight loss without an effect on appetite. This class is the SGLT-2 inhibitors for T2DM, which promote weight loss by preventing the reabsorption of glucose as well as water in the renal tubules.

Surgical Intervention: Metabolic Surgery

**NHLBI Recommendations**

- Clinically severe obesity (BMI ≥40, or ≥35 with comorbid conditions)
- Less-invasive methods have failed
- Patients suffering from complications of obesity
- Well-informed, well-motivated patients

Facts on Treatment of Obesity

- **Medical treatment** is an ineffective method of sustaining weight loss for individuals with a BMI >35.

- **Bariatric surgery** is the only effective method of sustaining weight loss for individuals with a BMI >35 (1991 NIH consensus).

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**Body Mass Index (BMI)**

NICE Indications for Bariatric Surgery

- BMI > 40
- BMI > 35 + co-morbidity eg DM, high BP
- Failure to achieve/maintain adequate weight loss after non-surgical intervention
- Receiving specialist obesity service treatment
- Commitment to long-term follow-up
- Fit for anaesthetic/procedure
- First line treatment if BMI > 50

Indications for Surgery

- 18-70 years of age
- BMI > 40
- BMI 35 - 39 with associated medical conditions such as:
  - Diabetes
  - Hypertension
  - Hyperlipidemia
  - Cardiac disease
  - Respiratory disease
  - Arthritis
  - Depression
Bariatric Surgery Options

- Laparoscopic Adjustable Gastric Band
- Laparoscopic Roux-en-Y Gastric Bypass
- Laparoscopic Biliopancreatic Diversion with Duodenal Switch (BPD/DS)
- Laparoscopic Vertical Sleeve Gastrectomy (VSG)
- Laparoscopic Gastric imbrication

How does these operations work?

- **Restriction**: restricts the volume of food consumed during each meal
- **Malabsorption**: decreases your ability to absorb ingested foods
- **Lifestyle changes**: helps you develop new eating habits and encourages lifestyle changes
- **Manipulation of gut hormones/ metabolic surgery**
Adjustable Gastric Band

- Restrictive procedure
- Minimally invasive
- Good results in Europe and Australia
- Bioenterics Lap Band™
  FDA approved

Roux-en-Y Gastric Bypass

- Restrictive and mal-absorptive procedure
- Most frequently performed bariatric procedure in the US
- First done in 1967
- Laparoscopic since 1993
- 75% EWL in 18-24 months
- 50% EWL is still maintained at a 14yr follow-up
Biliopancreatic Diversion with Duodenal Switch (BPD/DS)

- Restrictive and mal-absorptive procedure
- Lesser degree of nutrient absorption
- 75-80% EWL
- 77% EWL at 5yr follow-up

Scopinaro 1998

Vertical Sleeve Gastrectomy (VSG)

- Restrictive procedure
- First done in US in 2001
- Removing 60-85% stomach
- 30-50% EWL
Mortality Rate

- Adjustable Gastric Band 0.1%
- Gastric Bypass 0.5%
- BPD/DS 1.1%
- Vertical Sleeve gastrectomy 0.25%

Bariatric surgery and cardiovascular risk factors

- A. Diabetes
- B. Systemic hypertension
- C. Hyperlipidemia
- Cardiac function
Medical Co-Morbidities Resolved

Type 2 Diabetes 95%
Hypertension 92%
Cardiac Function Improvement 95%
Osteoarthritis 82%
Sleep Apnea 75%
Cholesterol 97%
GERD 98%
Stress Incontinence 87%


Continue: Treatments for Cardio metabolic syndromes Beyond Lifestyle Modification and obesity

• A1C < 6.5%
• Blood pressure targets according to JNC 7 recommendations 130/80
• Cholesterol: LDL targets as per NCEP ATP 3 and recently ACC?AHA November 2013
• [low to intermediate risk, 100 and high risk <70mg%]
Conclusions and Take home Messages on Obesity and Cardio metabolic Syndrome
Visceral and/or perivascular adiposity are “a modern disease” frequently associated with several cardio-metabolic syndrome, markers and CVD events.

- Silent sub clinical atherosclerosis is prevalent in asymptomatic obese individuals particularly those with associated cardio metabolic syndrome components which is a risk for future stroke and heart attack.
- Accordingly it is time to focus on early detection and prevention of subclinical atherosclerosis in individuals with metabolic risk. Early Detect to Protect.
Obesity and Cardiometabolic Syndrome with evidence for early CVD

Still:

- Under Diagnosed
- Under Treated
- Under Controlled

TAKE HOME MESSAGES

Unless Obese patients change their lifestyle, existing cardiovascular and metabolic risk factors will worsen or new risk factors will develop.
TAKE HOME MESSAGES

• The Goals for Managing Obesity and or cardio metabolic syndrome Is to prevent or delay the development of T2DM and CVD
• Physician Dx of Overweight/besity Status Predicts Successful Weight Loss
• Whether we like it or not, it seems that we matter in the battle against obesity

So, don’t sweep it under the rug.
Talk to your patients about their weight.


TAKE HOME MESSAGE

Medical management must shift its emphasis from treatment of advanced disease to early detection and prevention of disease progression

Time to focus on early Cardiovascular Disease prevention

One Ounce of Early CVD/Stroke Prevention is Better Than One Pound of Late Cure
Clinical Pearls

- Far from being incidental to chronic illness, Obesity is at the very heart for the Cardio metabolic Syndrome
- There are 2 simple practical gold standard measurements to carefully monitor obesity: waist circumference and BMI
- A 5% to 10% weight loss is achievable in today's medical world and has a profound positive impact on common co morbidities such as the cardio metabolic syndrome

Continue Clinical Pearls

A. The root causes of metabolic syndromes associated with overweight & obesity are reversible,

B. The comorbidities frequently associated with Obesity i.e. hyperglycemia, Hypertension and Dyslipidemia are modifiable,

C. Hence The Recognition of obesity as a Disease provides an opportunity for risk reduction in this high risk group of patients.
Final departing Recommendation

Don't ever forget that:

One Ounce of Early
Cardiovascular Disease
Prevention is Better Than

Pounds of Late Cure

Cardiologists, Internists, Family Practitioners, PA, and ARNP are better fitted to screen and treat cardiovascular Risk factors associated with Obesity with the hope to prevent or delay the onset of Cardiovascular complications and its devastating sequels.
Final Advice

Optimizing the use of evidence based and personalized Medicine in early diagnosis and management of Obesity and associated comorbidities i.e. the metabolic syndrome would reduce or delay the onset of Diabetes and other comorbidities thus resulting in decrease of CV Disease and would Save Lives.

Also keeping in mind that TLC (nutrition, exercise, cessation of smoking and weight reduction) are of paramount importance.

No Cardiovascular Disease
Despite Risk Factors

Wall Street Journal, 2001
Preparing for a Cesarean

Wrap Up

• Obesity increases risk of developing cardiovascular risk factors
• Obesity increases long-term risk for cardiovascular disease

“Don’t step on it... it makes you cry.”
Guiding principles to be a priority

Treatment of all risk factors rather than the disease: a new approach to world health

Philip A Poole-Wilson, 2003

What to Do in 2017?

Treatment of all risk factors rather than the disease: PLUS

Utilize accurate and cutting edge tools to assess evidence for early CVD i.e. Subclinical Atherosclerosis, which must be treated aggressively to avert or delay morbid cardiovascular events. This must be

The new approach to world health in the 21st Century

MAHFOUZ EL SHAHAWY, MD 2017
We are ALL Preventive Health care Providers
Thank You

Improvement Never Ends . .

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