OBESITY
THE GROWING EPIDEMIC
IMPACT ON
CARDIOVASCULAR DISEASE

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OVERVIEW

• Definition
• Prevalence and trends – global and regional, adult and children
• Etiology and pathophysiology
• Consequences and impact on CVD
• Measurement of obesity
• Interventional strategies
DEFINITION

• Condition of increased adipose tissue mass
• Increase in body weight beyond the limits of physical requirement as a result of an excessive accumulation of triacylglycerol (fat)
• Other energy storage (carbohydrate, glycogen or protein in liver and muscle) does not have potential to exceed limits of requirement
• Subtypes – visceral and subcutaneous
GLOBAL TREND IN OBESITY PREVALENCE

International Association for the Study of Obesity 2012
GLOBAL TREND IN OVERWEIGHT CHILDREN

International Association for the Study of Obesity 2012
COMPLEX INTERACTIONS OF FACTORS

Stress
Sleep Deficit
Sedentary Lifestyle
Food Environment
Cultural beliefs
Industrial pollutants
Genetic
Psychological
Behavioral
Environmental
Sociocultural
Metabolic
Physiological
Hormonal

Suzanne et al. Abdominal Imaging 2012
# ETIOLOGY

## Acquired
- Cushing’s syndrome
- Hypothyroidism
- Insulinoma
- Medications
  - Steroids
  - Contraceptives
  - Beta blockers
  - Anti-psychotics
  - Anti-epileptics
  - Anti-diabetics

## Genetic
- Genetic syndromes
  - Prader-Willi
  - Angelman
  - Wilson-Turner
- Twin studies – up to 75% genetic contribution
- Multiple loci of susceptibility genes

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CLINICAL MANIFESTATION OF OBESITY

Pulmonary disease
- Asthma, hypoxemia
- Obstructive sleep apnea
- Hypoventilation syndrome

Nonalcoholic fatty liver disease
- Steatosis
- Steatohepatitis
- GERD

Gall bladder disease

Gynecologic abnormalities
- Abnormal menses
- Infertility
- Polycystic ovarian syndrome

Osteoarthritis

Skin

Gout

Idiopathic intracranial hypertension

Stroke

Psychological and social

Coronary heart disease
- Diabetes, insulin resistance
- Dyslipidemia
- Hypertension
- Metabolic syndrome

Severe pancreatitis

Cancer
- Breast, uterus, cervix
- Colon, esophagus, pancreas
- Kidney, prostate, small intestines, rectum, liver, gallbladder, leukemia, multiple myeloma, lymphoma

Phlebitis
- Venous stasis/thromboembolism

PATHOPHYSIOLOGY OF OBESITY

RELATIONSHIP BETWEEN BMI AND THE RELATIVE RISK OF COMORBID CONDITIONS

Willett WC et al. NEJM 1999
Metabolic Syndrome

Diagnosis is established when ≥3 of these risk factors are present.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
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<tbody>
<tr>
<td>Abdominal obesity</td>
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<tr>
<td>(Waist circumference)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 in)</td>
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<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td>TG</td>
<td>≥150 mg/dL (1.7mmol/L)</td>
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<tr>
<td>HDL-C</td>
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</tr>
<tr>
<td>Men</td>
<td>&lt;40 mg/dL (1.0mmol/L)</td>
</tr>
<tr>
<td>Women</td>
<td>&lt;50 mg/dL (1.3mmol/L)</td>
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<tr>
<td>Blood pressure</td>
<td>≥130/≥85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>≥110 mg/dL (6.1mmol/L)</td>
</tr>
</tbody>
</table>

CARDIOVASCULAR MORTALITY ASSOCIATED WITH METABOLIC SYNDROME

Diabetes Care 2001; 24:683
INCREASE IN HEALTHCARE COSTS AMONG OBESE COMPARED WITH LEAN (BMI <25 KG/M2) PATIENTS

- **BMI 30-34 kg/m²**
  - Healthcare visits: 25% increase in healthcare cost
  - Pharmacy: 44% increase in healthcare cost
  - All outpatient services
  - All inpatient services
  - Total healthcare

- **BMI >35 kg/m²**
  - Healthcare visits: 25% increase in healthcare cost
  - Pharmacy: 44% increase in healthcare cost
  - All outpatient services
  - All inpatient services
  - Total healthcare

*HMO Setting: Northern California Kaiser Permanente.

AMPLIFICATION OF FRAMINGHAM CHD RISK

Kerstyn C et al. Med Clin N Am 2011; 919-37
## INTERHEART STUDY

### EFFECT OF POTENTIALLY MODIFIABLE RISK FACTORS ON MI IN 52 COUNTRIES - CASE CONTROLLED STUDY

**Risk factor** | **Sex** | **Control (%)** | **Case (%)** | **Odds ratio (95% CI)** | **PAR (95% CI)**
--- | --- | --- | --- | --- | ---
Current smoking | F | 93 | 20.1 | 2.86 (2.36–3.48) | 15.8% (12.9–19.3) |
 | M | 33.0 | 53.1 | 3.05 (2.78–3.33) | 44.0% (40.9–47.2) |
Diabetes | F | 7.9 | 7.5 | 4.36 (3.51–5.18) | 19.1% (16.8–21.7) |
 | M | 7.4 | 15.2 | 2.67 (2.36–3.02) | 10.1% (8.9–11.4) |
Hypertension | F | 28.3 | 53.0 | 2.95 (2.57–3.39) | 35.8% (32.1–39.6) |
 | M | 19.7 | 34.6 | 2.32 (2.12–2.53) | 19.5% (17.7–21.5) |
Abdominal obesity | F | 33.3 | 45.6 | 2.26 (1.90–2.68) | 35.9% (28.9–43.6) |
 | M | 33.3 | 46.5 | 2.24 (2.03–2.47) | 32.1% (28.0–36.5) |
Psychosocial index | F | – | – | 3.49 (2.41–5.04) | 40.0% (28.5–52.6) |
 | M | – | – | 2.58 (2.11–3.14) | 25.3% (18.2–34.0) |
Fruits/veg | F | 50.3 | 39.4 | 0.58 (0.48–0.71) | 17.8% (12.3–24.1) |
 | M | 39.5 | 34.7 | 0.74 (0.66–0.83) | 10.3% (6.9–15.2) |
Exercise | F | 16.5 | 9.3 | 0.58 (0.39–0.88) | 37.3% (26.2–50.0) |
 | M | 20.3 | 15.8 | 0.77 (0.69–0.85) | 22.9% (16.9–30.2) |
Alcohol | F | 11.2 | 6.3 | 0.41 (0.32–0.53) | 46.9% (34.5–60.5) |
 | M | 29.1 | 29.6 | 0.88 (0.81–0.96) | 10.5% (5.1–17.5) |
ApoB/ApoA1 ratio | F | 14.1 | 27.0 | 4.42 (3.43–5.70) | 52.1% (44.0–60.2) |
 | M | 21.9 | 35.5 | 3.96 (3.23–4.83) | 53.8% (48.3–59.2) |

Yusof S. Lancet 2005
OBESITY AND RISK OF HEART FAILURE

5881 participants from Framingham Heart Study

After adjustment for established risk factors, the risk of heart failure is 5 percent for men and 7 percent for women for each increment of 1 in BMI

Satish et al. NEJM 2002;347(5):305-13
OBESITY AND ATRIAL FIBRILLATION

Framingham Cohort, 5283 patients without baseline AF

4% (95% CI: 1-7%) AF risk with each unit of BMI increment

Thomas Wang et al. JAMA 2004;292:2471-77
THE OBESITY PARADOX IN CARDIOVASCULAR DISEASE

• ‘Survival paradox’
• Acute coronary events, emergent or elective coronary revascularization procedures

For 2nd Cardiac Rehabilitation Conference 2013

Curtis J P. Arch Int Med 2005;165:55-61
RELATIONSHIP BETWEEN OBESITY AND RISK OF HEART FAILURE

1203 patients with moderate to severe heart failure

Horwich et al. JACC 2001;38:789-95
Should we then accept obesity as desirable?

- Lifestyle intervention, including exercise training with at least mild weight reduction → 60% reduction of DM risk
- Cardiac rehabilitation and exercise training → 37% reduction in metabolic syndrome
- Marked reduction in CRP after cardiac rehabilitation in obese CHD patients
- Weight reduction associated with improvements in CHD risk factors (CRP, lipids, sugar) with a trend towards lower mortality and CHD events
- Weight loss improve LV mass and systolic and diastolic heart function

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Carl J et al. JACC 2009;53:1925-32
ASSESSMENT OF OBESITY

• Several ways of assessment
• Different aspects of obesity – total vs regional
• Anthropometry
  • Body weight and dimension measurements
  • Rapid and cheap
  • Used in studies, clinical setting
• Densitometry
• Imaging

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BMI FOR ASIANS

• Asian population shows higher CV risk factors than Western populations at any given BMI
• Asians have different associations between BMI, % body fat and health risks
• Available data do not clearly indicate a clear cut-off point for Asians to define overweight and obesity
• International Obesity Task Force (IOTF) and WHO propose:

<table>
<thead>
<tr>
<th>BMI</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 – 24.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For 2nd Cardiac Rehabilitation Conference 2013

IOSO and IOTF 2000
Lancet 2004; 363 (9412): 902
For 2nd Cardiac Rehabilitation Conference 2013

ANTHROPOMETRY

- Waist circumference = midway between lower rib margin and iliac crest, horizontal tape at the end of gentle expiration
- Waist to hip ratio
- Good correlation with visceral fat

Han TS. Int J of Obes Relat Metab Discord 1997;21:587-93
# Waist Circumference

For 2nd Cardiac Rehabilitation Conference 2013

Adapted from National Institute of Health
BMJ 2006;333

<table>
<thead>
<tr>
<th>High Risk Group</th>
<th>Caucasian</th>
<th>Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>&gt; 102 cm</td>
<td>&gt; 90 cm</td>
</tr>
<tr>
<td></td>
<td>(40 inches)</td>
<td>(35.5 inches)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt; 88 cm</td>
<td>&gt; 80 cm</td>
</tr>
<tr>
<td></td>
<td>(35 inches)</td>
<td>(31.5 inches)</td>
</tr>
</tbody>
</table>

**Waist Circumference**

<table>
<thead>
<tr>
<th>BMI</th>
<th>Men &lt;102 cm, women &lt;88 cm</th>
<th>Men ≥102 cm, women ≥88 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>18.5</td>
<td>Not increased</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-24.9</td>
<td>Not increased</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
<td>Increased</td>
</tr>
<tr>
<td>Obesity (class I)</td>
<td>30.0-34.9</td>
<td>High</td>
</tr>
<tr>
<td>Obesity (class II)</td>
<td>35.0-39.9</td>
<td>Very high</td>
</tr>
<tr>
<td>Extreme obesity (class III)</td>
<td>≥ 40.0</td>
<td>Extremely high</td>
</tr>
</tbody>
</table>
OTHER METHODS OF OBESITY ASSESSMENT

**Densitometry**
- Underwater weighing facility
- Principle based on different density between fat (0.7g/ml) and fat-free tissue (1g/ml) \(\rightarrow\) fat weighs less underwater

**Imaging**
- CT
- MRI
BENEFITS OF INTENTIONAL WEIGHT REDUCTION ON CARDIOVASCULAR SYSTEM

- Blood volume
- Stroke volume
- Cardiac output
- Pulmonary capillary wedge pressure
- Left ventricular mass
- Improvement of left ventricular diastolic dysfunction
- Improvement of left ventricular systolic dysfunction
- Resting oxygen consumption
- Systemic arterial pressure
- Filling pressures of the right and the left side of the heart
- or no change in systemic arterial resistance
- Resting heart rate
- QTc interval
- HRV

Paul P et al. Circulation 2006;113:898-918
GOALS OF OBESITY THERAPY

• Achieve weight loss
• Maintain lower body weight
• Prevent further weight gain
• Treat co-morbidities/underlying cause
ACHIEVEMENT OF WEIGHT LOSS

- 10% reduction from baseline weight over 6 months
- Calorie deficit of 500-1000 kcal/day with 0.5-1 kg/week weight loss
- Rapid weight reduction may lead to risk of gallstones, electrolyte imbalance, weight regain

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**MAINTAIN LOWER BODY WEIGHT**

- Rate of weight loss often declines after initial 6 months of weight reduction
- Priority being weight maintenance – regain of <3 kg in 2 years + sustained reduction in waist circumference of at least 4 cm
- Diet, physical activity and behavior therapy

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PREVENTION OF FURTHER WEIGHT GAIN

• If significant weight reduction is not achievable
• May be considered as partial therapeutic success for many patients
• Regular consultations for at least 1 year recommended, physician and multidisciplinary team
  • Education of lifestyle modification (diet, physical activity and behavior therapy)
  • Review food and activity log
  • Monitoring exercise regimes
  • Monitoring diet structure and use of portion-controlled foods

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CARDINAL BEHAVIORS OF SUCCESSFUL LONG-TERM WEIGHT MANAGEMENT
NATIONAL WEIGHT CONTROL REGISTRY DATA

- **Self-monitoring:**
  - Diet: record food intake daily, limit certain foods or food quantity
  - Weight: check body weight >1 x/wk

- **Low-calorie, low-fat diet:**
  - Total energy intake: 1000-1200 kcal/d *female*
    - 1200-1500 kcal/d *male*
  - Energy intake from fat: 20%-25%

- **Eat breakfast daily**

- **Regular physical activity:** 2500-3000 kcal/wk
  (e.g., walk 4 miles/d)

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<table>
<thead>
<tr>
<th>BMI Range</th>
<th>Lifestyle changes (Diet, Physical activity, Behaviour therapy)</th>
<th>Anti-Obesity Drug</th>
<th>Very-Low-Calorie-Diet (VLCD) (with supervision)</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI 18.5 - 22.9 kg/m² with Increased WC*</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI 23.0 - 24.9 kg/m²</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI 25.0 - 27.4 kg/m² No additional risk Increased WC* / DM/CHD/HT/HL</td>
<td>√</td>
<td>√ (consider in the presence of ≥ 2 risk factors)</td>
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<tr>
<td>BMI 27.5 - 34.9 kg/m²</td>
<td>√</td>
<td>√ (consider in the presence of ≥ 2 risk factors)</td>
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</tr>
<tr>
<td>BMI 35.0 - 39.9 kg/m² No additional risk Increased WC* / DM/CHD/HT/HL</td>
<td>√</td>
<td>√ (consider in the presence of ≥ 2 risk factors)</td>
<td></td>
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</tr>
<tr>
<td>BMI ≥ 40.0 kg/m²</td>
<td>√</td>
<td></td>
<td>√ (consider in the presence of ≥2 risk factors)</td>
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<tr>
<td>Drug</td>
<td>Introduced</td>
<td>Mechanism of action</td>
<td>Status</td>
<td></td>
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<td>------------------------------</td>
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<tr>
<td>Dinitrophenol</td>
<td>1930s</td>
<td>Increases metabolic rate</td>
<td>Withdrawn—risk of neuropathy and cataracts</td>
<td></td>
</tr>
<tr>
<td>Amphetamines:</td>
<td>1936</td>
<td>Appetite suppression</td>
<td>Banned, restricted or discouraged—dependency and abuse potential, cardiovascular adverse effects</td>
<td></td>
</tr>
<tr>
<td>dexamphetamine, methamphetamine</td>
<td></td>
<td></td>
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<tr>
<td>Phentermine, diethylpropion, phenylpropanolamine</td>
<td></td>
<td></td>
<td>Phentermine—available for short-term use (≤12 weeks)</td>
<td></td>
</tr>
<tr>
<td>Aminorex</td>
<td>1965</td>
<td>Appetite suppression</td>
<td>Withdrawn 1968—pulmonary hypertension</td>
<td></td>
</tr>
<tr>
<td>Mazindol</td>
<td>1970s</td>
<td>Appetite suppression</td>
<td>Discontinued 1993—Australia</td>
<td></td>
</tr>
<tr>
<td>Orlistat</td>
<td>1998–Europe and US</td>
<td>Decreased fat absorption</td>
<td>Also available over-the-counter in several countries</td>
<td></td>
</tr>
<tr>
<td>Sibutramine</td>
<td>1997–US; 2001–Europe</td>
<td>Appetite suppression</td>
<td>Temporarily withdrawn 2002 Italy-concerns of raised risk of heart attacks and strokes</td>
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<td></td>
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<td></td>
<td>Increase in contraindications 2010 = US, Australia</td>
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<td></td>
<td>Suspension of market authorization 2010</td>
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<tr>
<td>Rimonabant</td>
<td>2006–Europe</td>
<td></td>
<td>Withdrawn 2009—potential of serious psychiatric disorders</td>
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SURGERY FOR WEIGHT REDUCTION

- Severe and resistant morbid obesity failing other therapy and suffering from serious complications of obesity
- Substantial weight loss – 50 to 100 kg over 6 months to 1 year
- Longest period of sustained weight loss
- Aim – modify GI tract to reduce net food intake
- Liposuction – unsightly local collections of fat
SUMMARY

• Obesity - chronic disease of increased body fat stores
• Growing epidemic worldwide
• Etiology - Biological (genetics), behavioral, social and environmental factors
• Overwhelming evidence of obesity in pathogenesis and progression of CV disease
• Obesity paradox - overweight and obese patients with established CV disease show favorable prognosis
• Constellation of data still supports purposeful weight reduction in the prevention and treatment of CV disease