The Metabolic Syndrome: Is It A Valid Concept?

YES

Congress on Diabetes and Cardiometabolic Health
Boston, MA
April 23, 2013

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The Dual Epidemic: Obesity and Diabetes

- 65% of adult Americans are overweight (BMI >25) and 32% are obese (BMI >30).
- 34% have the Metabolic Syndrome (ATP III criteria).
- There are now an estimated 25.8 million people with DM in the USA (11.3% of adults) and 79 million with prediabetes (IFG/IGT).
- The lifetime risk of developing DM for people born in 2000 is 33% for men and 39% for women.
- In this population CVD is the major cause of mortality.

Obesity Is the Primary Risk Factor for Type 2 Diabetes

Age-adjusted relative risk of type 2 diabetes

Age-Adjusted Percentage of U.S. Adults with Obesity or Diagnosed Diabetes

Global Projections for the Diabetes Epidemic: 2011–2030

Mortality in People With Diabetes: Causes of Death

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**Diabetes and CVD Risk in Framingham Cohort Age 35–64 Years: 30-Year Follow-up**

- CHD: 0
- Stroke: 2
- Intermittent Claudication: 4
- Cardiac Failure: 6
- CVD Total: 10

Risk Ratio

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Intermittent Claudication</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac Failure</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>CVD Total</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>


**Factors Implicated in Macrovascular Disease in Type 2 Diabetes**

- Dyslipidemia
- Hypertension
- Nephropathy
- Obesity/sedentary lifestyle
- Altered coagulation, platelet function, and fibrinolysis
- Hyperinsulinemia/hyperproinsulinemia/insulin resistance
- Cigarette smoking
- Hyperglycemia
- Inflammation


**MRFIT: Cholesterol and CVD Mortality in Men With Type 2 Diabetes**

- Controls: 14
- Type 2 diabetes: 62
- 200–220: 85
- 240–260: 29
- ≥280: 46


**Glycemia in Relation to Microvascular Disease and MI**

*UKPDS 35. BMJ 2000;321:405–12*

**DECODE: Mortality Rate Increases With Increasing 2-Hour Glucose**

- Fasting glucose: 3.9–6.1: 11.7%
- 6.2: 12.3%
- 7.0: 13.4%
- ≥7.8: 15.0%


**What is a Syndrome?**

1. A group of signs and symptoms that occur together and characterize a particular abnormality.
2. A set of concurrent things that usually form an identifiable pattern


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How do we identify people clinically who have insulin resistance and increased CVD risk?

**Metabolic Syndrome ATP III (3 of 5)**

- **Obesity (esp. Abdominal Obesity)**
- **Waist Circumference**
  - Men: ≥ 102 cm (40 in)
  - Women: ≥ 88 cm (35 in)
- **Atherogenic Dyslipidemia**
  - **TG ≥ 150 mg/dL**
- **HDL-C**
  - < 40 mg/dL (M)
  - < 50 mg/dL (F)
- **Elevated BP**
  - **BP ≥ 130/85 mm Hg ≥ 100 mg/dL** *(modified)

**IDF Criteria: Obesity + 2 Others**

- **Obesity (esp. Abdominal Obesity)**
- **Waist Circumference**
  - Men: ≥ 94 cm (37 in)
  - Women: ≥ 80 cm (31.5 in) *(Population Specific)*
- **Atherogenic Dyslipidemia**
  - **TG ≥ 150 mg/dL**
- **HDL-C**
  - < 40 mg/dL (M)
  - < 50 mg/dL (F)
- **Elevated BP**
  - **BP ≥ 130/85 mmHg ≥ 100 mg/dL**

**Metabolic Syndrome as a Precursor of CVD and DM2: The Framingham Offspring Study**

- 1163 men and 1386 women, age 22-81, with no CVD or DM2 at baseline exam (1989-1993), f/u @ 4 & 8 yrs.
- Age-adjusted Prevalence of Metabolic Syndrome (modified ATP III criteria: FBG 100-125mg/dl)
  - Men: Baseline 21.4% 8 Yr f/u 33.9% 56% increase
  - Women: 12.5% 23.6% 47% increase
- Compared to those without Met Synd, those with Met Synd also had higher total and LDL Cholesterol and women had a higher rate of cigarette smoking

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Metabolic Syndrome Increases Risk for CHD and Type 2 Diabetes

Metabolic Syndrome

- High LDL-C
- Metabolic Syndrome
- Type 2 Diabetes
- Coronary Heart Disease

Prevalence of Metabolic Syndrome in IGT & Diabetes

IGT:
- 53% at baseline in the Diabetes Prevention Program

Type 2 Diabetes:
- 65-85% in various studies

Multifactorial Intervention and Treatment Goals in Type 2 Diabetes: Steno-2

Intensive therapy vs. Conventional therapy

Multifactorial Intervention and CV Events in Type 2 Diabetes: Steno-2

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What can we learn from the Diabetes Prevention Program?

About the prevalence and prevention of the Metabolic Syndrome in people with IGT?

About the effect of the DPP interventions on the reduction of CVD risk?

Prevalence of Metabolic Syndrome at Randomization

- 1711 (53%) of the 3234 participants had the syndrome at randomization
- Prevalence of the syndrome did not vary by gender or age group (<45, 45–64, 65+ years)
- Prevalence did vary by ethnicity, being lowest in Asians (41%) and highest in Caucasians (57%)
- Prevalence of the individual components did vary by ethnicity and by age group

Cumulative Incidence of Metabolic Syndrome by Treatment Group

Risk reduction: 17%* by Metformin 41%* by Lifestyle vs Metformin 29%* by Placebo

Other Key Findings

- HTN was present in 30% of subjects at baseline; over 3 years it increased in the placebo and metformin groups, but significantly decreased in the ILS group
- TG decreased in all groups, but fell significantly more in ILS group
- ILS significantly increased HDL-C and decreased LDL Phenotype B
- After 3 yrs the use of medications to achieve targets for HTN was 27–28% less and for dyslipidemia was 25% less in the ILS group

3-Year Incidence (%) of Components by Treatment Group

<table>
<thead>
<tr>
<th>Component</th>
<th>Placebo</th>
<th>Metformin</th>
<th>Lifestyle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist Circ.</td>
<td>33</td>
<td>15*</td>
<td>8*</td>
</tr>
<tr>
<td>Low HDL-C</td>
<td>70</td>
<td>67</td>
<td>68</td>
</tr>
<tr>
<td>High Trig.</td>
<td>27</td>
<td>30</td>
<td>18*</td>
</tr>
<tr>
<td>High FPG</td>
<td>40</td>
<td>28*</td>
<td>28*</td>
</tr>
<tr>
<td>High BP</td>
<td>41</td>
<td>44</td>
<td>35*</td>
</tr>
</tbody>
</table>

Effects of DPP Interventions on Reversal of the Metabolic Syndrome

- Placebo: reversal at 3.2 yrs 18%
- Metformin: " 23%
- Lifestyle: " 38%

Overall prevalence of MS at 3.2 yrs

- Placebo: 61% +6% from baseline
- Metformin: 55% +2% " "
- Lifestyle: 42% -9% " "

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Other Key Findings

- Mean baseline hsCRP (5.9 mg/L) was increased in all groups and was higher in women than in men (median 4.9 vs 1.9 mg/L).
- Baseline hsCRP correlated with BMI, waist circumference, FPG, and HOMA-IR.
- After 1 year the median change was:
  - men: Placebo +5%, Met -7%, ILS -33%
  - women: 0% -14% -29%
- The changes correlated mainly with weight loss and not with physical activity

Summary

- There is an epidemic of diabetes that is associated with lifestyle changes and obesity.
- The metabolic syndrome and IGT are more prevalent than diabetes.
- The metabolic syndrome and IGT are known risk factors for both type 2 diabetes and cardiovascular disease.
- Both lifestyle modification and medications are effective in preventing, delaying and treating type 2 DM and in reducing CVD risk factors.

My Conclusions

- YES-The Metabolic Syndrome is a useful clinical tool to identify people at high risk for type 2 diabetes and CVD
- The presence of one or more of the individual components of the Metabolic Syndrome should alert the clinician to check for and treat other related CVD risk factors
- A Global Approach to the treatment of diabetes must be the standard of care.

THANK YOU