

Doris D. Disposati, PA-SIII
University of South Dakota
Physician Assistant Studies Program
PAST 788 Masters Project
2009

METABOLIC SYNDROME

QUESTION

Is the use of statins alone or statins plus diet and exercise enough to treat metabolic syndrome thereby preventing T2DM?

DEFINITION OF METABOLIC SYNDROME

A term used to describe abnormal levels of lipids and lipoproteins in the blood of which are present in both T1 and T2DM and include elevated triglycerides, LDL-C, TC and decreased HDL-C.

Elevated triglycerides and TC are main lipids of interest for their role in CVD.

CRITERIA FOR METABOLIC SYNDROME

- ✘ A. Increased low-density lipoprotein-cholesterol (LDL-C) with decreased high-density lipoprotein-cholesterol (HDL-C)
- ✘ B. Increased Triglycerides (TG)
 - >200 mg/dL
- ✘ C. Hypertension
 - >130mmHg/>80mmHg
- ✘ D. Central Obesity - waist circumference, BMI, or waist-to-hip ratio
- ✘ E. Intolerance to Glucose – fasting plasma glucose \geq 110 mg/dL

The Metabolic Syndrome

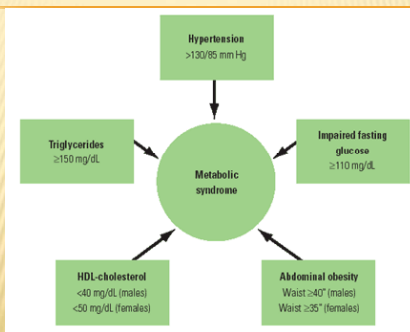


FOR MEN:

- Waist Circumference \geq 40 Inches
- Triglycerides \geq 150 mg/dL
- HDL Cholesterol $<$ 40 mg/dL
- Blood Pressure \geq 130/85 mm Hg
- Fasting Glucose \geq 100 mg/dL

FOR WOMEN:

- Waist Circumference $>$ 35 Inches
- Triglycerides $>$ 150 mg/dL
- HDL Cholesterol $<$ 50 mg/dL
- Blood Pressure $>$ 130/85 mm Hg
- Fasting Glucose $>$ 100 mg/dL

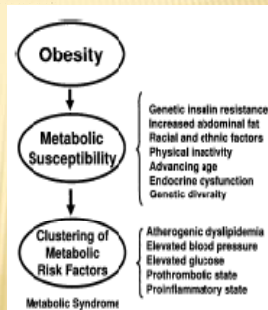


INCIDENCE/PREVALENCE

- * Individuals with T2DM commonly have dyslipidemia
- * >70% have LDL-C greater than US recommendation of <100mg/dL
- * 1/2 of men and 2/3 of women have HDL-C lower than US recommendation of >50 mg/dL
- * Over half of men and women have ↑d triglycerides
- * 28.2% w/T2DM on lipid-lowering drug
- * 3% controlled targets for all lipids

ETIOLOGY/RISK FACTORS

- * Obesity that is visceral or central → increased amount of FFA's released into portal circulation
- * Impaired insulin action → loss of suppression of lipolysis
- * Increased release of FFA's into portal circulation → increased FFA's delivered to liver
- * Increased production of triglycerides by liver → decreased HDL-C
- * Impaired clearance of triglycerides alters enzymatic activity and formation of LDL particles



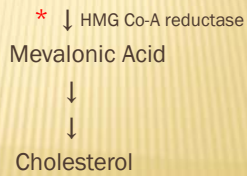
KEY EVIDENCE

- * Statin Use
 - Atorvastatin (Lipitor)
 - Rosuvastatin (Crestor)
 - Simvastatin (Zocor)
- * Diet
 - decrease energy-dense diets
- * Physical Activity/TLM's
 - moderate-intensity
 - vigorous-intensity
 - maximal treadmill

STATINS

* HMG Co-A reductase inhibitors *

Acetyl-CoA → 3-hydroxy-3-methylglutaryl-CoA



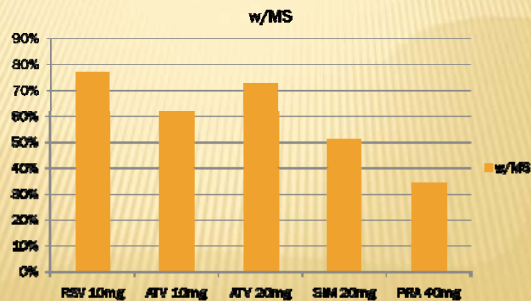
COMPARING STATINS

* Rosuvastatin (Crestor)

- + 10mg more efficacious at helping patients reach ATP III goals compared to other statins and doses; both w/MS and w/o MS
- + Greater reductions in LDL-C, TC, non-HDL-C
- + Similar or greater reductions in TG's, increases in HDL-C
- + Non-HDL-C is secondary target of therapy, goal is 30 mg/dL above goal for LDL-C and a better predictor of CVD
- + Non-HDL-C = total cholesterol - HDL-C
- + Non-HDL-C consists of LDL-C, VLDL-C, IDL-C, Lp

Stender S, Schuster H, Barter P, Watkins C, Kallend D. Comparison of rosuvastatin with atorvastatin, simvastatin, and pravastatin in achieving cholesterol goals and improving plasma lipids in hypercholesterolemic patients with or without the metabolic syndrome in the Mercury I trial. *Diabetes, Obesity and Metabolism* 2005;7:430-438.

PATIENTS MEETING ATP III GOALS (%)



DIET

- ✘ Energy-dense diet – amount of energy intake (in kcal) divided by weight of all food consumed (in gm)
 - + Are high in starches, sugars, refined grains, fat
 - + Are inexpensive, palatable, convenient
 - + Lead to increased waist circumference
 - + Give glycemic load>>promotes insulin resistance>>↑ risk T2DM

Mendoza JA, Drewnowski A, Christakis DA. Dietary energy density is associated with obesity and the metabolic syndrome in U.S. adults. Diabetes Care. 2007;30(4):974-979.

HYPOTHESIS

- ✘ Energy-dense diets independently associated with higher BMI and waist circumference
- ✘ Energy-dense diets independently associated with glycemia, insulinemia, and MS

LIMITATIONS

- ✘ Validity of methods used to measure energy, protein, carb, fat have already been confirmed
- ✘ Overweight patients underestimate intake of food more than normal weight
- ✘ Study was cross-sectional
- ✘ Self-reported PA

EXERCISE

- ✦ 3 studies showing benefits of physical activity in reducing MS risk factors
 1. Exercise and weight loss improves insulin sensitivity in patients with MS
 2. Cardiorespiratory fitness improves MS prevalence in racially diverse women
 3. Physical activity reduces MS risk factors

RISK FACTOR IMPROVEMENT

- ✦ Subjects
 - 25 (females, males) with BMI 26-43 kg/m²
 - 135 (AA, NA, CAU) females
 - 146 (AA, NA, CAU) females
- ✦ Participation
 - weight loss program 4-7 months
 - 4 consecutive days x2, one month apart
 - one time assessment
- ✦ Activity
 - supervised moderate activity of walking or jogging 5/7 days w/occasional stationary cycling or elliptical exercise
 - supervised maximal treadmill exercise 2 min stages graded by 1 MET/stage
 - moderate intensity to vigorous intensity including, maximal treadmill

| | Baseline | Post wt. loss | % Change |
|------------------------|----------|---------------|----------|
| TG, mg/dL | 117.4 | 102.4 | -12.8 |
| TC, mg/dL | 189.5 | 174.4 | -8.0 |
| HDL-C, mg/dL | 49.1 | 49.0 | NC |
| LDL-C, mg/dL | 116.8 | 104.9 | -10.2 |
| BMI, kg/m ² | 33.0 | 29.9 | -9.4 |
| QUICKI | 0.33 | 0.35 | +6.0 |

RESULTS

Rector RS et al. Exercise and diet induced weight loss improves measures of oxidative stress and insulin sensitivity in adults with characteristics of the metabolic syndrome. *Am J Physiol Endocrinol Metab* 2007; 293:E500-E506.

TLM'S

- ✘ Therapeutic lifestyle modifications
- ✘ Are the “cornerstone” of preventing and treating Metabolic Syndrome
- ✘ Can reduce subclinical inflammation
 - ↑ CRP + risk factors for MS = Inflammation
- ✘ Higher levels of PA inversely related to MS

Lanone MJ, Answorth BE, Durstine JL. Influence of cardiorespiratory fitness on the association between C-reactive protein and metabolic syndrome prevalence in racially diverse women. *Journal of Women's Health*. 2005;14(5):233-239.

OVERVIEW OF STUDY

- ✘ Statin therapy is essential
- ✘ Physical activity is crucial
- ✘ Diet is important
- ✘ All three are needed together to have greater benefit of reducing risk factors of MS

CLINICAL PEARLS

- ✘ Maintain a healthy diet, more fruits, vegetables, and fiber plus low-fat dairy
- ✘ Get regular physical activity
- ✘ Keep alcohol consumption low
- ✘ Attain and maintain an ideal body weight
 - BMI 18.5 – 24.9 kg/m²
- ✘ Keep a waist circumference of <102cm for men and <88cm for women
- ✘ Reduce sodium intake to <2300 mg/day
- ✘ Maintain a smoke free environment

NEW

Non-HDL-C
Management

- Niacin
- Omega-3 FA's
- Fibrates

Table to "tummy" measurement- better indicator of obesity
