is as yet no data providing the independent and quantitative effect of the syndrome on subsequent cardiac outcomes. We applied the five-year experience of the West of Scot- tland Coronary Prevention Study (WOSCP) to further quantify the prognostic impact of METS. Methods: The study population comprised 6,447 men enrolled in the WOSCP trial aged 45-64 years, with LDL-C 156-255 mg/dl. Diabetics and subjects with fasting glucose >126 mg/dl were excluded. We defined the presence of METS as any three of the following: body mass index >30 kg/m2, HDL-C less than 40 mg/dl, triglycerides >150 mg/dl, fasting glucose >110 -125 mg/dl and systolic blood pressure >130 mmHg or diastolic >85 mmHg or treated for hypertension. Cardiac events were defined as fatal or non-fatal CHD, or revascularization (CABG or PTCA). Cox-regression was used to estimate the independent contribution of METS to events, with age, LDL-C, current smoking, and pravastatin treatment as covariates. Results: The overall prevalence of the metabolic syndrome was 23.8%. Cardiac event rates were 12.6% and 7.3% for subjects with and without METS respectively (p<0.001). The hazard ratio describing the independent association of METS with events was 1.89 (95% CI: 1.52-2.0, p<0.001), and was comparable to age (per 10 years): 1.89 (95% CI: 1.52-2.0, p<0.001), and greater than smoking: 1.5 (95% CI: 1.3-1.7) and HDL-C: 1.4 (95% CI: 1.1-1.7, p<0.001). Conclusions: This is the first reported quantification of the independent association of METS with CHD in a longitudinal cohort of males. The prognostic impact of METS is similar to other traditional risk factors such as LDL-C, age, and smoking. Therapies which target METS risk factors in combination should confer clinical benefit to METS patients.

11:45 a.m.

845-4 Differential Effects of Statins on Hypercholesterolemic Patients With Metabolic Syndrome

Donald B. Hunninghake, Christie M. Ballantyne, Darie L. Maccubbin, Anvid K. Shah, Barry Gumber, Yale B. Mitchell, Heart Disease Prevention Clinic, Minneapolis, MN, Merck Research Laboratories, Rahway, NJ.

Background: Hypercholesterolemic (HC) patients with metabolic syndrome (MS) are at high risk for coronary heart disease (CHD) due to elevated LDL-C and triglycerides (TG), and low HDL-C, an independent precursors of C-HDL. We compared the lipid-modifying efficacy of simvastatin (S) and atorvastatin (A) in HC patients with MS.

Methods: This placebo-controlled withdrawal study was performed on random samples of 37 patients, a double blind dose titration study designed to evaluate the efficacy of S (40-80 mg) and A (20-40 mg) on HDL-C in HC patients (LDL-C>=160 mg/dl). Per NCEP ATP II, patients were classified as having MS if they met 3 or more of the following criteria: TG>=150 mg/dl; HDL-C<40 (men) or<50 (women) mg/dl; type 2 diabetes and/or fasting serum glucose 2>=110 mg/dl; hypertension and/or blood pressure Ll30/85 mmHg; and body mass index 30 (surrogate for waist circumference).

Results: Of 892 evaluable patients, 212 (26%) had MS at baseline, with 99 and 113 in the S and A groups, respectively. At comparable LDL-C and non-HDL-C-lowering doses, both drugs produced large reductions in TG with A producing greater decreases in 2 of 3 dose comparisons. In contrast, the increases in HDL-C with S were 1.5 to 3-fold those observed with A at every dose (table). After 56 weeks, 60% of the MS patients in both treatment groups converted to non-MS status.

Conclusion: Both simvastatin and atorvastatin effectively modified LDL-C, TG and non-HDL-C in HC patients with MS, however, simvastatin provided greater increases in HDL-C.

% change (95% CI)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>S (mg/dl)</th>
<th>A (mg/dl)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>42 (44)</td>
<td>46 (47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-C</td>
<td>10 (8.2)</td>
<td>6 (4.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>TG</td>
<td>-30 (-34)</td>
<td>-24 (-29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>-36 (-42)</td>
<td>-42 (-45)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

11:30 a.m.

845-5 Elevated C-Reactive Protein in High-Risk Asymptomatic Individuals is Strongly Associated With The Metabolic Syndrome

Saman Mours, Roger S. Blumenthal, Lisa R. Yanek, Taryn F. Moy, Lewis C. Becker, Diane M. Becker, Johns Hopkins Medical Institutions, Baltimore, MD.

Background: Chronic inflammation has been associated with certain components of the metabolic syndrome. We evaluated plasma CRP index and serum lipids, but it is unclear if it inflammation should be consdered part of the syndrome.

Methods: We investigated whether high-sensitivity C-reactive protein (hs-CRP) is independently associated with the clustering of metabolic abnormalities in 388 apparently healthy individuals (mean age 57.1 years, 80% white males, 48% HDL-C, 45% men, 51% female, 43% African-American). MS components were defined using ATP III guidelines for abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure, and high glucose.

Results: Mean hs-CRP was 4.4 ± 3.5 mg/L. There was a significant difference in mean hs-CRP in those with MS (≥3 components) compared to those without MS (5.7 versus 4.0, p=0.0001). There was a graded increase in mean hs-CRP levels with increasing number of MS components present, p for trend <0.001 (Table). Using multiple linear regression, each additional component of MS was associated with a 0.9 ± 0.1 mg/L increase in mean hs-CRP level (p<0.001), after adjusting for age, sex, race, and smoking status.

Conclusion: These findings suggest that inflammation is strongly associated with the metabolic syndrome in high-risk individuals who may benefit from further risk-stratification using hs-CRP levels.

11:45 a.m.

845-6 The Association of the Metabolic Syndrome With Myocardial Infarction and Stroke in the National Health and Nutrition Examination Survey III

John K. Ninomiya, Gilbert J. Li, Lietz, Michael H. Grpini, Joanne L. Whyte, Anthony Garnet, Roland S. Chen, University of California, San Diego, School of Medicine Epidemiology, San Diego, CA, Bristol-Myers Squibb, PRB, Princeton, NJ.

Background: The association of the Metabolic Syndrome and its component conditions with self-reported history of myocardial infarction (MI) and stroke was evaluated in a large cross-sectional population survey, the NHANES III, 1988-1994. Methods: Based on NCEP Adult Treatment Panel III (NCEP-ATPIII) guidelines, we evaluated 10,357 subjects for each of the five component conditions of the Metabolic Syndrome: insulin resistance (IR), abdominal obesity based on waist circumference (WC), hypertriglyceridemia, low HDL-cholesterol, and hypertension (HTN), and the overall syndrome defined as presence of 3 or more of the 5 conditions. Logistic regression was used to estimate the association of the syndrome, and each of its 5 component conditions individually, with MI and stroke. Models were adjusted for age, sex, race and smoking history. SUDAAN software was used to weight for the complex sampling frame used in NHANES III. Results: The prevalence of MI was 3.7%, stroke 2.0% and the combined outcome (either or both) 5.2%. The Metabolic Syndrome was significantly related in multivariate analysis to MI (OR = 2.01, 95% CI = 1.53 - 2.64), stroke (OR = 2.16, 95% CI = 1.46 - 3.16) and the combined outcome (OR = 2.05, 95% CI = 1.64 - 2.57). The combined outcome association was observed in both women (OR = 2.20, 95% CI = 1.56 - 3.11) and men (OR = 1.98, 95% CI = 1.34 - 2.97). Among the component conditions, IR (OR = 1.30, 95% CI = 1.03 - 1.66), low HDL (OR = 1.35, 95% CI = 1.05 - 1.74), HTN (OR = 1.44, 95% CI = 1.00, 2.08) and hypertriglyceridemia (OR = 1.86, 95% CI = 1.20 - 2.30) were significantly related to the combined outcome in multivariate analysis; only obesity, as measured by waist circumference, was not independently related to disease (OR = 1.11, 95% CI = 0.88 - 1.42). Conclusions: These results indicate a strong, consistent relationship of the Metabolic Syndrome, as defined in NCEP-ATPIII III, with history of MI and stroke. These results emphasize the importance of the Metabolic Syndrome in the progression of atherosclerotic disease.

10:30 a.m.

O47-1 Lipoasial Type Prostaglandin D Synthase as a Sensitive Biomarker for Coronary Atherosclerosis

Yoi Kato, Yoshiyuki Kijima, Yasuyuki Matsura, Taketomi Yasuda, Yutaka Eguchi, Tenu Insue, Hiroshi Oda, Kousuke Seki, Nanae Tamagushi, Kousuke Aratame, Haruko Kumanogoh, Naomi Eguchi, Yoshihiro Urade, Ishikawa Yao General Hospital, Yao, Japan, Osaka Biosoience Institute, Suita, Japan.

Background: Lipoprotein(a), C-reactive protein (CRP) and lipocaltin-type prostaglandin D synthase (L-PGDS) have been proposed as serum markers for coronary artery disease, but no consensus has yet been reached. Methods: Serum levels of L-PGDS, lipoprotein(a), and CRP were measured in sera from 38 patients with chest symptoms who were investigated by coronary angiography. Immunohistochentical localization and mRNA expression for L-PGDS were determined in autopsy specimens. Results: The acute and various levels of L-PGDS and the veno-arterial difference were increased in patients with single mean (mean±SD; 97.1, 85.2, and 8.1 µg/L respectively), and multiple (68.9, 82.0, and 13.0 µg/L respectively) vessel disease compared with those in the patients with normal coronary angiography or coronary risk factors (48.5, 51.6 and 3.1 µg/L respectively). The acute and various levels in patients with multiple vessel disease were significantly (p<0.0009, 0.048) higher than those of the other 2 groups. The veno-arterial differences were significantly higher in patients with multiple vessel disease than in those with normal coronary angiography (p<0.01). However, neither lipoprotein(a) nor