1107-139 Metabolic Syndrome Is Highly Prevalent in Patients With Coronary Artery Disease

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Background: Recent Adult Treatment Panel III (ATP III) guidelines have emphasized the significance of metabolic syndrome (MS) as an important risk factor for coronary artery disease (CAD). However, the prevalence of MS in CAD patients is not known. Accordingly, we evaluated the prevalence of MS among patients with established diagnosis of CAD at our Medical Center.

Method: A random group of 668 patients with established diagnosis of CAD was selected from computer records of VACCHCS, Fresno. Patients' age, HR, BP, height, weight, body mass index, FBS, and total, LDL and HDL cholesterols were recorded. History of treatment for diabetes, hypertension, or dyslipidemia was also recorded. Diagnosis of MS was based on ATP III guidelines. Statistical analyses were done using the Chi-Square test for categorical variables and the t-test, for continuous variables.

Results: The study population consisted of 668 men with CAD (mean age 69 yrs). Of these, 570 were found to have MS, giving a prevalence of 75% (CI 72%-78%, p value < .001). Of the MS patients, 77% and 87% were found to have dyslipidemia and hypertension, respectively (p value < .0001 for both). The table below shows the mean values of important variables in patients with (+) and without (-) MS.

Conclusion: These data suggest that MS is highly prevalent among patients with CAD. Future prospective studies should evaluate the risk of CAD in patients with MS.

Variable	Metabolic Syndrome +	Metabolic Syndrome -	P-value
Age (years)	69	71	0.014
Pulse (bpm)	69	70	0.307
Systolic (mm Hg)	141	130	0.015
Diastolic (mm Hg)	72	69	0.004
BMI (kg/m^2)	31	26	0.0001
T. Cholesterol (mg/dl)	179	174	0.198
LDL (mg/dl)	99	106	0.07
HDL (mg/dl)	43	46	0.158
FBS (mg/dl)	133	103	0.0001

1107-140 The Impact of Moderate Elevations of Blood Pressure and Low-Density Lipoprotein Chlosterol on Coronary Heart Disease Risk

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The effects of moderately elevated lipid levels and blood pressure on coronary heart disease (CHD) risk were examined in Framingham Heart Study participants 30-74 years of age at baseline. Risk factors assessed included systolic blood pressure (SBP), LDL cholesterol (LDL-C), age, sex, diabetes status, and history of cigarette smoking. SBP categories (<140, 140-159, ≥160 mm Hg) and LDL-C levels (<100, 100-129, 130-159, ≥160 mg/dl) were key components in the analyses. Men and women contributed 3952 and 4489 person-exams of experience respectively and were followed 12 years for the onset of new CHD (angina pectoris, myocardial infarction or coronary death). Analyses used age-adjusted Cox models and persons with highly elevated SBP, highly elevated LDL-C, or moderate elevations of both factors experienced greater CHD risk in comparisons with a referent group that had SBP <140 mm Hg and LDL-C < 100 mg/dl (see table, where * denotes P<0.01 vs referent after age adjustment). Furthermore, moderately elevated LDL-C and SBP frequently coexist and the CHD risk related to this combination did not differ from that for the highly elevated LDL-C or highly elevated SBP groups. These results emphasize the need for awareness, diagnosis and treatment of persons with moderately increased blood pressure and lipid levels.

BP, LDL-C and CHD Risk

Group	Group Criteria (units mm Hg and mg/dl)	Frequency Men / Women	10 yr CHD risk Men / Women
Referent	SBP <140 and LDL-C <100	11%/17%	5%/0.7%
Mod Elev SBP and LDL-C	SBP (140-259) and LDL-C (100-159)	11%/ 8%	17%*/12%*
Highly Elev LDL-C	LDL-C>160	25%/25%	19%*/12%*
Highly Elev SBP	SBP >160	7%/7%	24%*/14/%*

1107-141 Decreased Activities of Paraoxonase and High-Density-Lipoprotein Associated Platelet Activating Factor Acetylhydrolase in Hemodialysis Patients

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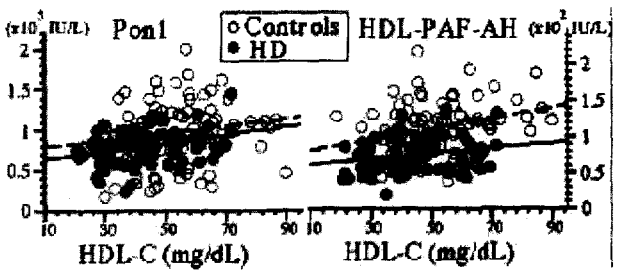
Background: HDL is antiatherogenic partly because of its antioxidative and antin-flammatory properties, in which paraoxonase (Pon1), which protects LDL from oxidation, and HDL-associated PAF acetylhydrolase (PAF-AH), which degrades PAF and oxidizes phosphatidylcholine, play an important role. Since patients with chronic renal failure have an increased cardiovascular risk and reduced HDL-C levels, we examined whether patients on hemodialysis (HD) have altered activities of Pon1 and HDL-associated PAF-AH (HDL-PAF-AH).

Methods: Eighty-seven male non-diabetic HD patients and 73 normal male subjects were measured with regard to serum lipids, lipoproteins, Pon1 activity with paraoxon as substrate, and plasma PAF-AH activity and HDL-PAF-AH activity with a specific substrate (Azwell Inc.).

Results: Pon1 and HDL-PAF-AH were correlated with HDL-C levels (r=0.30 and 0.38, p<0.01) in all of the subjects. HD patients had lower (p<0.05) levels of TC, TG, HDL-C, and plasma PAF-AH (391 ± 155 vs. 453 ± 145 IU/L) than controls. Activities of Pon1 (770 ± 242 vs. 1014 ± 379 IU/L) and HDL-PAF-AH (75 ± 26 vs. 117 ± 36 IU/L) were also lower (p<0.05) in HD patients than in controls. Similar results were obtained after adjusting for HDL-C (Figure) by a General Linear Model, suggesting that Pon1 and HDL-PAF-AH were associated with chronic renal failure independent of serum HDL-C levels.

Conclusion: The reduced Pon1 and HDL-associated PAF-AH may contribute to cardiovascular risk independent of HDL-C levels in HD patients.



1107-142 Comparative Value of Carotid Ultrasound, High Sensitivity C-Reactive Protein, and Low-Density Lipoprotein Particle Size in Predicting Coronary Artery Disease in Young Adults

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Background: Preventing premature coronary artery disease (CAD) has been difficult. We have previously reported that many young adults suffering myocardial infarctions do not have high cholesterol and that the National Cholesterol Education Program guidelines (NCEP III) fail to appreciate disease risk. Our objective was to evaluate high sensitivity C-reactive protein (Hs-CRP), low dense lipoprotein (LDL) particle size, and carotid ultrasound (CU) for the ability to predict angiographic CAD in a group of young adults scheduled for coronary angiography.

Method: Subjects scheduled for elective cardiac catheterization were recruited. Subjects underwent CU and had blood drawn for Hs-CRP, LDL particle size, and lipoprotein analysis (LPA). Subjects were excluded for age (women >65 and men >55 years), statin therapy, or known CAD or equivalent. Any coronary stenosis was considered evidence of angiographic disease and ≥50% stenosis was considered severe disease. Criteria for abnormal CU included intima media thickness >1.0 cm, focal plaque or calcium deposits. Risk score for a ten-year probability of cardiac event was calculated for each patient as per the NCEP III guidelines.

Results: 147 subjects (73 women, mean age 54 and 74 men, mean age 47) completed all tests. LPA was as follows: total 209 +/- 46 mg/dL, LDL 131 +/- 38 mg/dL, HDL 48 +/- 15 mg/dL, and triglyceride 159 +/- 87 mg/dL. 20% of subjects had LDL cholesterol < 100 mg/dL and only 17% had ≥160 mg/dL. 58 subjects had normal CU and 87 were abnormal. 75 subjects had normal angiograms and 70 had disease. The sensitivity for CU compared to angiogram was 70%, with a negative predictive value of 78% (p = 0.013). The odds ratio (OR) for abnormal CU in predicting angiographic disease was 2.3 (CI: 1.5 - 4.5). The sensitivity for small dense LDL was 44%, specificity 56% (OR: 1.5; CI: 0.78 - 2.9, p = ns). The OR for CRP was 1.3 (p = 0.5, CI: 0.65 - 2.5). Multiple regression revealed that only CU abnormalities independently predicted coronary angiographic disease. LDL particle size and Hs-CRP had no additional benefit.

Conclusion: In the evaluation of premature CAD in young adults with low cholesterol, CU predicts angiographic disease and is superior to LDL particle size and Hs-CRP.

1107-143 Which Lipid/Lipoprotein Ratio Best Predicts Angiographic Coronary Artery Disease?

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Background: Various lipid or lipoprotein (LP) ratios have been proposed as a single, composite lipid-related risk factor (i.e., total cholesterol [TC]/high density lipoprotein cholesterol [HDL], low density lipoprotein-C [LDL]/HDL, non-HDL/HDL, and triglycerides [TG]/HDL). These derived measures have not, however, been assessed and compared as predictors of angiographic coronary artery disease (CAD).

Methods: We evaluated the predictive value for angiographic CAD of TC/HDL, LDL/HDL, non-HDL/HDL, and TG/HDL ratios, and individual LP fractions in a consecutive series of consenting, prospectively assessed patients. Acute MI at presentation was excluded. Fasting LPs were measured at the time of angiography after an overnight fast and assayed by colorimetry (Vitros 950). Angiography was performed prior to LP and LP ratio determinations. Analysis used logistic regression.

Results: Patients (N=4,724) averaged 63±13 years of age; 66% were male. Significant CAD (≥70% stenosis) was found in 54%, mild/moderate CAD in 11%, and no CAD

(<10% stenosis) in 35%. All 4 LP ratios univariately predicted significant (compared to no) CAD, in the order of: LDL/HDL (Wald chi-square 108, odds ratio [OR]=1.30, 95% CI 1.24-1.36), TC/HDL (chi-square 105, OR=1.21, CI 1.17-1.26), NonHDL/HDL (chi-square 105, OR=1.21, CI 1.17-1.26), TG/HDL (chi-square 33, OR=1.06, CI 1.04-1.08) (each p<0.001). Individually, HDL, LDL, nonHDL-C, and TC (trend), but not TG, predicted CAD. In multivariable (MV), stepwise modeling considering the 4 LP ratios and 4 LP fractions, HDL and LDL were selected as LP-related CAD predictors. In further MV modeling considering 6 traditional risk factors, with analysis restricted to younger patients (men <55 years, women <65 years), age, HDL, LDL, hypertension, smoking, and diabetes were selected as independent predictors of CAD.

Conclusions: Of 4 advocated risk-associated LP ratios, we found 3 to be roughly equivalent (LDL/HDL, nonHDL/HDL, and TC/HDL) for predicting angiographic CAD and TG/HDL to be less predictive. However, both in models including lipid measures only and in those also including traditional risk factors, none of the ratios was superior to HDL and LDL (considered separately).

1107-144 Preventing Coronary Events by Control of Lipids and Blood Pressure in Persons With the Metabolic Syndrome

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Background The metabolic syndrome (MetS) is associated with significant risk for coronary heart disease (CHD). We estimated CHD events preventable by treatment of lipids and blood pressure in persons with MetS.

Methods Among persons aged 30-74 years (without diabetes or CHD) in the United States, MetS was defined by the National Cholesterol Education Program criteria. Expected CHD events over 10 years were estimated by Framingham algorithms. Incremental benefit was estimated in terms of CHD events that could be potentially prevented by statistically "controlling' blood pressure, LDL-C, and HDL-C to either "normal' (120-129 mmHg systolic (SBP) / 80-84 mmHg diastolic blood pressure (DBP), HDL-C 45-49 mg/dl in males and 50-59 mg/dl in females, and LDL-C to 100-129 mg/dl) or "optimal' (<120 mmHg SBP / <80 mmHg DBP, HDL-C to $\geq$ 60 mg/dl, and LDL-C to <100 mg/dl) levels. Population attributable risks (PARs) for the proportion of CHD events that could be prevented were calculated.

Results Of an estimated 7.5 million men and 8.9 million women with MetS, approximately 1.5 million men and 0.45 million women, if risk factors were left uncontrolled, would suffer CHD events in 10 years. In men and women, BP control to normal levels "prevented' 28.1% and 12.5% of CHD events (p<0.01), respectively, while optimal BP control resulted in PARs of 28.2% and 45.2%, respectively (p<0.01). Control of HDL-C to normal levels resulted in PARs of 25.3% in men and 27.3% in women, while control to optimal levels gave PARs of 51.2% and 50.6%, respectively. Control of LDL-C to normal levels prevented only 9.3% of events in men and 9.8% of events in women, but optimal control prevented 46.2% and 38.1% of events (p<0.05), respectively. Control of all three risk factors to normal levels resulted in PARs of 51.3% for men and 42.6% for women, whereas control to optimal levels resulted in PARs of 80.5% and 82.1%, respectively.

Conclusion Up to half of CHD events in persons with MetS may be preventable with control of lipids and blood pressure to normal levels, and four-fifths of events may be preventable with optimal control. Whether hypothetical control of risk factors as projected is similar to actual risk reduction requires further investigation.

1107-145 Using Carotid Atherosclerosis as a Replacement for Age: Effect on National Cholesterol Education Program Risk Classification

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Introduction: The National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) recommends Framingham global risk assessment to classify risk of future coronary events. Framingham risk estimates are influenced strongly by chronological age (CA), however atherosclerotic burdens of individuals of the same CA may differ substantially. We investigated the impact of carotid intima-media thickness (CIMT) measurement, an ultrasound measure of current atherosclerotic burden, on individual risk prediction and classification using the NCEP ATP III guidelines.

Methods: CIMT was measured in 82 consecutive subjects who were free of coronary heart disease. Far wall thicknesses of three carotid arterial segments were measured on each side and averaged to define a composite CIMT. Vascular age (VA) was determined by linear regression models of nomograms from the Atherosclerosis Risk in Communities Study. VA was substituted for CA in the Framingham risk model for hard coronary events, resulting in modified 10-year hard coronary risk estimates. Odds ratios (OR) were determined for prediction of re-classification of coronary risk.

Results: Although the mean CA was 55.8±9.0 years, the mean VA using CIMT values was 65.4±18.9 years (p<0.001). The mean risk estimate for coronary events was 6.5±4.4%. Substituting VA for CA increased the mean risk estimate to 8.0±6.8% (p<0.001). Use of modified risk estimates re-classified 12 (15%) subjects into higher risk and 3 (3.8%) subjects into lower risk groups. Of 14 subjects initially at intermediate risk, 5 (35.7%) were re-classified as higher and 2 (14.3%) were re-classified as lower risk. Significant predictors (p<0.05) of re-classification were tobacco use (OR 19.83), high-density lipoprotein cholesterol (OR 0.81), systolic blood pressure (OR 1.09), and low-density lipoprotein cholesterol (OR 1.02) (chi-square goodness of fit = 38.2, p=0.999).

Conclusions: Vascular age, determined by CIMT, altered NCEP ATP III risk classification in 50% of intermediate-risk subjects. Assessment of current atherosclerotic burden using CIMT may help clinicians tailor primary prevention strategies to an individual patient's risk of a first coronary event.

POSTER SESSION

1130MP Moderated Poster Session...Endothelial Function

Monday, March 31, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A

3:00 p.m.

1130MP-163 Effects of Insulin Resistance on Flow: Mediated Dilation of Conduit Vessels

Umberto Campia, Gail Sullivan, Melissa B. Bryant, Michael J. Quon, Julio A. Panza, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD

Background: Insulin resistance is a major link between metabolic risk factors and atherosclerotic vascular disease. Whether insulin resistance affects conduit vessel endothelial function is unknown. This investigation aimed to assess the effects of insulin resistance on flow-mediated dilation in normotensive, normoglycemic subjects with a spectrum of lipid profile.

Methods: 25 normoglycemic, normotensive subjects participated in the study. Endothelium-dependent (flow-mediated dilation, FMD) and -independent (nitroglycerin-mediated dilation, NMD) responses of the brachial artery were studied by high-resolution ultrasound, and insulin sensitivity (SI_{Clamp}) was measured by euglycemic clamp. To evaluate the effects of lipid profile on insulin sensitivity and FMD, participants were divided in 2 subgroups (normal cholesterol, NC; and high cholesterol, HC) based on their total cholesterol levels, with a cutoff of 200 mg/dL.

Results: In the whole group, FMD was directly correlated with SI_{Clamp} (r=0.512, P=0.01) and inversely correlated with total cholesterol levels (r=-0.57, P=0.005). No correlation was observed between NMD and SI_{Clamp} (r=0.11, P=0.625). SI_{Clamp} was significantly lower in the HC compared to the NC participants (7±1 vs 12.3±1.7; P=0.02, respectively). FMD was lower in the HC compared to the NC subjects (4.4±0.7% vs 8±0.7%, respectively; P=0.002). In the HC subjects, FMD was significantly correlated with SI_{Clamp} (r=0.715, P=0.006), but not with total cholesterol levels (r=0.123, P=0.675), whereas no significant relationship was noted between FMD and SI_{Clamp} (r=-0.219, P=0.57), and between FMD and total cholesterol levels (r=-0.227, P=0.50) in the NC subjects.

Conclusion: In normotensive, normoglycemic subjects, conduit vessel endothelial function directly correlates with insulin sensitivity, suggesting a potential mechanism by which insulin resistance might predispose to vascular damage.

3:12 p.m.

1130MP-164 Endothelial Function and Inflammatory Process in Young Patients With Beta-Thalassemia Major

Constadina Aggeli, Christine Chrysohoou, Spyros Lambrou, Alexadra Frogoudaki, Charis Antoniadis, Dimitrios Tousoulis, Markisia Karageorga, Dimitrios Ladis, Christos Pitsavos, Christodoulos Stefanadis, Pavlos Toutouzas, Hippokration Hospital of Athens, Athens, Greece

Background: Endothelium plays an important role in the modulation of vascular tone and structure while its dysfunction may be representative of vascular inflammation. The aim of this study was to identify the endothelial function and to determine the inflammatory factors in transfusion-dependent patients with beta-thalassemia.

Methods: Twenty young transfusion-dependent patients (pts) with beta-thalassemia (age 27±5 years, 15 male, serum ferritin 2180±1150 ng/ml) and 20 matched by sex and age controls, without any evidence of cardiac disease or diabetes mellitus were included in the study. In all subjects, we evaluated the endothelial function as well as serum inflammatory markers level, 1-2 days before the scheduled transfusion in the case of pts. Endothelium dependent flow mediated vasodilation (FMD) was expressed as the % change from baseline to post reactive hyperemia blood flow. Endothelium independent flow (NTG%) was expressed as the % change from baseline to post sublingual administration flow. Serum sVCAM-1, sICAM-1, TNF-a, and IL-1beta were measured.

Results: FMD (%) was significantly lower in pts compared to controls (55.8±4 vs. 110±16, p<0.05). NTG% and sICAM-1 (ng/ml) were not different between pts and controls. The levels of sVCAM-1 (ng/ml), TNF-a (pg/ml), and IL-1beta (pg/ml) in the serum of pts were higher than those of the controls (931.8±180 vs. 295.1±28, 6.65±2.1 vs. 1.28±0.15, 5.48±1.6 vs. 0.118±0.013, p<0.05, respectively). No correlation was found between FMD and serum ferritin levels. All the results were adjusted for the smoking status of the subjects enrolled

Conclusion: Transfusion-dependent pts with beta-thalassemia are associated with endothelial dysfunction. sVCAM-1, TNF-a, and IL-1beta serum levels are elevated in this group of pts. These findings expand our understanding in vascular function and increased incidence of cardiovascular events in beta-thalassemia pts possible related to a vascular inflammatory process.