

ORAL CONTRIBUTIONS

882 Beyond Low-Density Lipoprotein Cholesterol for Assessment of Coronary Artery Disease Risk

Wednesday, March 20, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 255W

8:30 a.m.

882-1 Association of Trp64Arg β 3-Adrenergic Receptor Gene Polymorphism With LDL Particle Size in Japanese Population

Kenji Okumura, Hideo Matsui, Hajime Imai, Tomofumi Mizuno, Akiko Imamura, Yasuhiro Ogawa, Hiroki Kamiya, Nagoya University Graduate School of Medicine, Nagoya, Japan.

People with a predominance of small, dense low-density lipoprotein (LDL) particle appear to be at increased risk for coronary disease, independent of the presence of other risk factors. The Trp64Arg mutation of the β ₃-adrenergic receptor gene has been reported to be associated with abdominal obesity and resistance to insulin. Therefore, we investigated whether the β ₃-adrenergic receptor gene polymorphism contributes to the variance in LDL particle size in 136 Japanese subjects, aged 33-59 years, who visited for a routine annual check up. None of these subjects were taking medications. The diameter of LDL particle was determined in fresh plasma samples by nondenaturing 2-16 % polyacrylamide gradient gels. The genotype frequencies were: Trp/Trp, 71.3%; Trp/Arg, 22.1%; Arg/Arg, 6.6%; with allelic frequencies of 0.82 for the Trp64 allele and 0.27 for the Arg64 allele. There was no significant correlation between β ₃-adrenergic receptor genotypes and age, blood pressure, total cholesterol or HDL cholesterol. However, the subjects with the Trp/Trp genotype showed significantly higher levels of fasting plasma insulin and triglycerides, and smaller LDL particle size than the subjects with the Trp/Arg genotype. Diabetes mellitus and obesity are significantly more frequent in the subjects with the Arg64 allele. The number of the allele for Arg64 is significantly related with fasting insulin ($P=0.005$), BMI ($P=0.02$), triglycerides ($P=0.02$), HDL-C ($P=0.03$) and fasting glucose ($P=0.04$), and conversely related with LDL particle size ($P=0.008$). These findings indicate that the Trp64Arg polymorphism in the β ₃-adrenergic receptor gene is attributed to a variation in LDL particle size, probably via a variation in insulin resistance.

8:45 a.m.

882-2 LDL Particle Concentration and Insulin Level Predict Carotid Atherosclerosis in High Risk Patients

Wendy S. Post, Roger S. Blumenthal, Lisa R. Yanek, Taryn F. Moy, Lewis C. Becker, Diane M. Becker, Johns Hopkins University, Baltimore, Maryland.

Carotid intima media thickness (IMT) is a measure of subclinical atherosclerosis and a potent predictor of cardiovascular events. The purpose of this study was to evaluate novel risk factors (RF) as predictors of carotid IMT in asymptomatic African-American siblings (SIBS) of patients with premature coronary artery disease, a population at increased risk for manifest cardiovascular disease. We measured the far wall IMT of the distal 1 cm of the common carotid artery using a validated edge detection system in 216 SIBS, mean age 48 +/- 7 yrs, 69% female. LDL cholesterol (LDL-C) was calculated by the Friedewald equation. LDL particle concentration (CONC) and size were measured by NMR spectroscopy (LipoMed). IMT was increased (> 0.7 mm) in 46%. The following nontraditional RFs were associated with increased carotid IMT on univariate analyses- pulse pressure, waist circumference, LDL particle CONC (all $p < 0.005$), insulin, waist-hip ratio, serum creatinine, LDL particle size and apoB (all $p < 0.05$). There were no significant associations with Lp(a), fibrinogen or homocysteine. Stepwise multivariate logistic regression was performed including both traditional and non-traditional RFs for atherosclerosis. LDL particle CONC ($p=0.008$) and insulin level ($p=0.03$) were the only nontraditional RFs which significantly predicted increased carotid IMT after adjusting for age ($p=0.004$), male gender ($p=0.01$) and systolic blood pressure (SBP) ($p < 0.001$). In order to evaluate the independent contribution of related lipid variables which tend to be correlated, in predicting carotid IMT, three separate multivariate logistic regression models were performed with LDL-C, apoB and LDL particle size. There were trends for LDL-C ($p=0.06$), and apoB ($p=0.08$) predicting IMT, after controlling for age, gender, SBP and insulin level. LDL particle size was not an independent predictor of increased carotid IMT ($p=0.3$). RFs may differ in the strength of their associations with atherosclerosis in different vascular beds and ethnic groups; however, we found that LDL particle CONC, which is a measure of the number of LDL particles, and insulin level are both independent predictors of increased carotid IMT in African-American SIBS.

9:00 a.m.

882-3 Prevalence of Atherogenic LDL Pattern B in Asymptomatic Middle Aged African Americans With a Family History of Premature Coronary Heart Diseases

Khurram Nasir, Diane M. Becker, Lisa R. Yanek, Taryn F. Moy, Lewis C. Becker, Roger S. Blumenthal, Johns Hopkins Medical Institutions, Baltimore, Maryland.

Background: The majority of coronary heart disease (CHD) events occur in individuals with LDL-Cholesterol (LDL-C) levels <160mg/dl. Other atherogenic lipoprotein patterns such as LDL pattern B (LDL-C particle diameter <20.5 nm) may increase for CHD risk in normal-borderline LDL-C. The purpose of the study is to determine the prevalence of atherogenic LDL pattern B across a spectrum of LDL-C, non-HDL and triglycerides (TG) levels in apparently asymptomatic but high-risk African Americans (AA) population.

Methods: Study population consisted of 333 asymptomatic AA siblings of persons with documented CHD < 60 years of age. Lipid levels and TG were determined by standard chemistry methods, LDL-C estimated by Friedewald formula, and LDL particle size using NMR spectroscopy.

Results: Mean age was 47 years; 35% were males. Overall, 28% had LDL pattern B and the prevalence was similar across increasing LDL-C and non HDL-C classifications. Individuals with pattern B had significantly higher TG ($p<0.0001$), non-HDL-C ($p=0.04$), IDL ($p=0.02$) and Apo lipoprotein B ($p=0.01$). TG >200 mg/dl were strongly associated with the presence of LDL pattern B (78%).

Conclusions: Increasing LDL-C levels did not predict the presence of LDL pattern B. Increasing levels of TG was strongly related to presence of LDL pattern B, while a TG <100 mg/dl was uncommonly associated with this atherogenic lipoprotein in this population. This suggests that clinician should try to achieve normal TG along with LDL-C in high risk asymptomatic AA.

LDL-C levels	<130 mg/dl	130-159 mg/dl	160-189 mg/dl	>190 mg/dl
LDL pattern B	28%	29%	23%	29%
non-HDL-C levels	<160 mg/dl	160-189 mg/dl	190-219 mg/dl	>220 mg/dl
LDL pattern B	23%	28%	50%	78%
TG levels	<100 mg/dl	101-150 mg/dl	150-200 mg/dl	>200 mg/dl
LDL pattern B	11%	28%	50%	78%

9:15 a.m.

882-4 Yellow Coronary Plaques Observed With Angioscopy Are Closely Related to Increased Plasma Levels of Triglyceride-Rich Remnant Lipoproteins

Nobuhiko Kondo, Yasunori Ueda, Toshiya Kurotobi, Masahiko Shimizu, Tomohito Otani, Atsushi Hirayama, Kazuhisa Kodama, Osaka Police Hospital, Osaka, Japan.

Background: Coronary atherosclerotic plaques are angiographically observed as yellow plaques (YPs), which are histologically lipid-rich and considered unstable plaques, or as white plaques (WPs), which are histologically fibrous and considered stable plaques. The purpose of this study was to determine whether atherogenic triglyceride-rich remnant lipoproteins predict yellow coronary plaques observed with angioscopy. **Methods:** We observed coronary plaque color of symptom-related lesions with angioscopy in 30 patients with symptomatic coronary artery disease receiving no lipid-lowering therapies. We measured fasting plasma levels of remnant like particle cholesterol (RLP-C), index for triglyceride-rich remnant lipoproteins, one or two days before angiographic observation. We also measured fasting plasma levels of total cholesterol, triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol, apolipoprotein (apo) AI, apo B, and apo E. **Results:** The study patients were divided into two groups according to findings of angioscopy: 15 patients with YPs (group Y) and 15 patients with WPs (group W). Mean plasma triglycerides and RLP-C levels in group Y were significantly higher than those in group W (200 ± 105 mg/dl vs. 121 ± 67 , $p=0.0196$, 8.0 ± 4.6 vs. 3.8 ± 1.4 mg/dl, $p=0.0022$, respectively) whereas other lipid fractions did not differ between two groups. On multiple stepwise regression analysis, only RLP-C was selected as a lipid fraction independently related to YPs (standard partial regression coefficient: 0.538, $p=0.0022$). **Conclusions:** Our results show that triglyceride-rich remnant lipoproteins predict unstable yellow coronary plaques observed with angioscopy in patients with symptomatic coronary artery disease. High blood remnant lipoproteins may increase risk for acute coronary syndrome.

9:30 a.m.

882-5 Extremely High Levels of Lipoprotein(a) [Lp(a)] Are Associated With Peripheral Endothelial Dysfunction in a Multiethnic Cohort

Henry D. Wu, Lars Berglund, Clarito Dimayuga, Jeffery Jones, Robert Sciacca, Marco R. Di Tullio, Shunichi Homma, Columbia College of Physicians and Surgeons, New York, New York.

Elevated lipoprotein(a) levels have been shown to be associated with increased cardiovascular risk in Caucasians. Although African Americans (B) and Hispanics (H) tend to have higher Lp(a) levels than Caucasians (W), the pathogenic role of Lp(a) in these two ethnic groups remains unclear. Thus, we studied the relationship of Lp(a) levels to endothelial dysfunction, an early and critical event in atherogenesis, in a multiethnic cohort (35 W, 27 B, 19 H). Endothelium-dependent, flow-mediated dilation (FMD) and endothelium-independent, nitrate-induced dilation (NTG) were measured by high resolution ultrasound imaging of the brachial artery in 81 healthy subjects without cardiac risk factors (aged 43 ± 11 years, 45 men, 36 women). Lp(a) levels were measured by an ELISA technique. In this cohort, Lp(a) levels ranged from 1 to 195 mg/dL (mean = 38.7 ± 46.4 mg/dL) and were found to be inversely correlated with FMD (Spearman's correlation $r = -0.32$, $p < 0.005$).

