POSTER SESSION

1202 Vascular and Endothelial Physiology

Tuesday, April 01, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 4:00 p.m.-5:00 p.m.

1202-146 Impact of Insulin Resistance and Hyperinsulin Response on Arterial Stiffness

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Background-Cardiovascular disease is the most common cause of disability and death among subjects with type 2 diabetes mellitus (DM). Measurement of pulse wave velocity (PWV) is a non-invasive method to estimate arterial stiffness. In order to determine the effect of diabetes on arterial stiffness, we conducted a large scale and cross-sectional study in single center.
Methods- A total of 11,802 subjects were performed 75g-oral glucose tolerance test (OGTT), blood chemistry and PWV measurement, and were enrolled in the present study (mean age 64.5+/-8.9 years, 14% hypertension, 56% dyslipidaemia, 37% current smoker). We diagnosed, 5,593 were normal, 641 impaired fasting glucose (IFG), 3,360 impaired glucose tolerance (IGT), and 2,238 Type 2 DM.
RESULTS-Compared with normal group, abnormal groups (IFG, IGT and type 2 DM) had significantly increased PWV(8.4 versus 8.7, 8.9 and 9.1m/sec ,p<0.001). Multivariate analysis showed that age, gender male, systolic blood pressure, serum triglycerides, 2 hour plasma glucose, and sigma-IRI (sum of insulin value in OGTT) were positively correlated with PWV, and lower serum HDL-cholesterol was inversely correlated (all P<0.001). Linear relationship was appreciated between sigma-IRI and PWV(r=0.986, p=0.014).
CONCLUSION-These results suggest that, in addition to age, sex, systolic blood pressure and triglycerides, hyper-insulin response as assessed by OGTT is independently associated with early atherosclerosis in newly diagnosed type 2 DM.

1202-147 Persistence of Impaired Vascular Function Despite an Improved Metabolic Profile Following Three Months of Significant Weight Loss

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Background: Obesity impairs endothelial function and arterial compliance. We therefore sought to determine if weight loss significantly improves vascular health.
Methods: 43 adults (BMI $\geq$ 27 kg/m^2) without other risk factors underwent a 3 month trial of diet + orlistat (120 mg PO QAC). Endothelial-dependent and independent vasomotion were determined by brachial flow-mediated dilatation (FMD) and nitroglycerin-mediated dilatation (NMD). Large (LVC) and small (SVC) vessel compliance was determined by computerized arterial pulse waveform analysis. Metabolic parameters, C-reactive protein (CRP), and asymmetric dimethyl arginine (ADMA) were also assessed.
Results: Body weight was reduced by an average of 6.6 % after 3 months. BMI (34.9 ± 4.8 to 32.7 ± 4.8 kg/m^2, p<0.001) and waist circumference (107.5 ± 10.7 to 102.2 ± 15.4 cm, p=0.001) significantly decreased. LDL-C (114 ± 27 to 104 ± 25 mg/dl, p=0.005), LDL particle concentration (1339 ± 359 to 1222 ± 325 mmol/l, p=0.009), insulin (8.8 ± 4.1 to 7.4 ± 2.7 UU/ml, p=0.002), and glucose (88.3 ± 6.8 to 85.5 ± 9.2 mg/dl, p=0.069) improved. Vascular function, CRP, and ADMA were not altered (Table).
Conclusion: Despite reduced adiposity and a significant improvement in the metabolic profile, 3 months of weight reduction did not alter endothelial function or vascular compliance. These results are important because they demonstrate that a greater amount, or a more prolonged time period, of weight loss may be required to restore vascular health in overweight adults.

	Baseline	Post weight loss	P
FMD (%)	3.86 ± 3.54	3.74 ± 3.78	0.86
NMD (%)	17.18 ± 5.89	18.87 ± 7.11	0.13
SVC ((ml/mm Hg) x 100)	10.2 ± 3.8	10.5 ± 5.7	0.74
LVC ((ml/mm Hg) x 100)	18.6 ± 6.3	17.7 ± 6.8	0.51
ADMA (μM)	0.95 ±0.13	0.95 ± 0.15	0.75
CRP (mg/dL)	0.47 ± 0.41	0.40 ± 0.45	0.23

1202-148 C-Type Natriuretic Peptide and Adrenomedullin Levels in Patients With Obstructive Sleep Apnea

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BACKGROUND. Obstructive sleep apnea (OSA) has been related to an increased incidence of hypertension, atherosclerosis, arterial thrombosis and other cardiovascular diseases. C-type natriuretic peptide (CNP) is a novel endothelium-derived mediator with vasodilatory, anti-atherogenic and anti-thrombotic properties. We hypothesized that OSA might be associated with reduced plasma CNP concentration. METHODS. Plasma CNP levels were measured during the night (at 9:30 p.m., 2 a.m., 6 a.m.) in 15 healthy male OSA patients and in 10 matched controls. RESULTS. Baseline CNP levels before sleep were significantly lower in the OSA than in the control group (21.3±2.3 vs. 32.9±4.0 pg/ml, respectively, p=0.013). During the night, there was a gradual decrease in CNP levels in the control group (from 32.9±4.0 to 21.0±3.1 pg/ml, p=0.012). However, in the OSA group, CNP levels increased during the period of untreated sleep apnea, and subsequently decreased in response to CPAP therapy. In contrast to CNP, plasma levels of another endothelium-derived vasodilator, adrenomedullin, were not affected by OSA (either chronically or acutely). CONCLUSION. OSA exerts a twofold effect on CNP regulation. Baseline CNP production is markedly reduced, whereas acute episodes of sleep apnea during the night cause a modest, but significant increase in plasma CNP levels.

1202-149 Interactive Effects of the ACE DD Polymorphism With the NOS III Homozygous G849T (Glu298-Asp) Variant in Determining Endothelial Function in Coronary Artery Disease

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Background: The products of Nitric Oxide Synthase (NOS) and Angiotensin Converting Enzyme (ACE) play a critical role in determining vessel wall structure and function. Polymorphisms in both genes have been independently demonstrated to influence propensity to cardiovascular events. We wished to determine the influence of the homozygous G849T(Glu^{298} $\rightarrow$ Asp) polymorphism in NOS III on peripheral conduit artery endothelial function and to elucidate the modifier role, if any, of a common ACE polymorphism.
Methods: 397 consecutive subjects presenting to the cardiac catheterization laboratory of the University of Michigan over a period of 18 months were recruited. DNA was extracted and PCR analysis for ACE and NOS polymorphisms performed. Patients with homozygosity for G849T at both loci (TT) who belong to DD and II ACE genotype (groups 1 and 2) and those who are negative for this polymorphism (GG) and belong to either DD or II genotype (groups 3 and 4) were identified. The four groups then underwent determination of conduit endothelial function. Heterozygosity Glu^{298} -Asp or the ID variant of the ACE were not studied.
Results: Median FMD value in the TT-DD group was 0.20 (-3.17, 2.01) compared to 2.23% (-0.29, 4.17) in the GG-II group. Median values in the TT-II and the GG-DD groups were 3.04(-1.16, 6.61) and 2.46% (-1.83, 6.52) respectively. These values were not statistically significant (p>0.05 by one way ANOVA). Median nitroglycerin mediated dilation in the four groups did not differ between the four groups (p=NS by ANOVA). Atherosclerosis burden as assessed by angiography were not different across the groups.
Conclusions: The homozygous NOS III variant (GG) status does not seem to interact additively with the ACE homozygous DD genotype, in determining flow mediated vasodilation in individuals with established atherosclerosis and pre-existent endothelial dysfunction.

1202-150 Effect of a Severe Coronary Stenosis and Percutaneous Cornary Intervention on the Coronary Microcirculation

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Background Classically, epicardial stenoses are thought to exert their clinical effect by limitation of the maximal flow capacity. In animal studies, artificial coronary stenoses have been shown to decrease the microvascular resistance (MR) to compensate for the epicardial obstruction. In human studies, data on the effect of atherosclerotic epicardial stenoses on the MR are conflicting. A constrictor response of the microcirculation (MC), supplied by a severely narrowed epicardial coronary, was found to pacing induced tachycardia.
Methods We simultaneously measured mean flow velocity (APV) and distal coronary pressure (Pd) distal to a coronary stenosis, at baseline and maximal hyperemia, induced by adenosine. The MR was defined as the hyperemic ratio of Pd by APV. Data were acquired in 23 normal coronaries (group A), in 54 arteries with an intermediate stenosis without ischemia (group B), and in 29 stenoses with evidence of ischemia, detected by non-invasive tests (group C), and in 14 arteries (group D) immediately after PCI.
Results A significant difference was found between the MR of the different groups. The MR in group C was statistically higher (*p<0.05) compared to the other groups and the MR after PCI was significantly (*p<0.05) lower.
Conclusion We found that the MR in areas perfused by severe coronary stenoses is elevated, suggesting that the MC can aggravate the effect of a severe coronary stenosis. Immediately post PCI the MR was significantly lower compared to normal arteries.

	group A	group B	group C	group D
APV(cm/sec)	50±11	46±14	33±15	56±17
Pd (mm Hg)	92±15	85±14	64±15	80±12
MR (mmHg.sec/cm)	2.0±0.5	2.1±0.7	2.6±1.4*	1.7±0.6*

1202-151 Direct Vasodilatory Effects of the Antidepressant Sertraline in the Human Internal Mammary Artery

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Background: Depression is associated with a significantly increased risk of cardiac events in patients who had coronary artery bypass graft (CABG) surgery. It is unknown whether antidepressive medication can improve cardiac prognosis in these patients. Because Selective Serotonin Re-uptake Inhibitors (SSRIs) are frequently prescribed antidepressants, we studied the vasoactive response of human Internal Mammary Artery (IMA) preparations to sertraline, which is one of the SSRIs.
Methods: IMAs (n=22) were harvested during CABG surgery and cut into rings. In