artery FMD in treated hypertensive heart transplant recipients. Methods: FMD after release of a five minute transient upper arm occlusion (reactive hyperemia) was measured in the brachial artery of 16 stable male heart transplant recipients with chronic post-transplant hypertension (average age 54±0.7 years) taking one or more vasodilators before and 45 minutes after oral administration of sildenafil (50 mg). Arterial internal diameter (mm) was measured at end-diastole from the anterior to the posterior internal images using nrog resonance ultrasound and Piko calipers as the percent increase in diameter from baseline at 50 seconds after release of the occlusion. Also, for comparison baseline measurements of FMD were collected in a healthy age and gender matched control group of 13 normotensive subjects.

Results: Arterial brachial diameter was 4.5±0.4 mm at baseline and did not significantly change with sildenafil administration. Heart transplant recipients had impaired FMD (5.4±0.9%) as compared with the healthy control group (7.1±2.5%, p=0.001). In the heart transplant recipients sildenafil administration increased FMD significantly from 5.4±0.9% to 6.6±0.2% (p=0.01) and was associated with a reduction in systolic from (134±10 to 126±8.9 mm Hg, p=0.01) and pulse (from 74±15 to 43±10 mm Hg, p=0.001) blood pressure. Conclusions: The results from this study demonstrated that a single oral dose of 50 mg sildenafil acutely improves FMD in the brachial artery of treated hypertensive male heart transplant recipients with endothelial dysfunction. These changes were associated with a reduction in peripheral arterial blood pressure.

4:15 p.m.

832-2 Presence of Endothelial Dysfunction is the Major Determinant of Maladaptive Vascular Remodeling in Brachial Arteries of Untreated Hypertensive Patients

Tomoko Furumoto, Satoshi Fuji, Keiko Nishihara, Satoshi Yamada, Hisao Onouchi, Katsuyuki Kohro, Kazutomo Utou, Wu Li, Yasuhiro Itoh, Yutaka Kitasaka, Akira Nishida, Akira Kasahara, Koutaro Hayakawa, Sapporo, Japan

Background: Flow-mediated distal (FMD) of the brachial artery is a useful marker to detect endothelial dysfunction and early atherosclerosis. Although FMD is impaired in patients with hypertension, the relationship between the hypertensive changes in vascular morphology of brachial arteries and endothelial function remains undetermined. The aim of the study was to assess the relative L-NAME as well wall thickness. Methods: Brachial media thickness (IMT) and FMD of brachial arteries were measured in untreated essential hypertensives (56 ± 8 yrs, n = 21) and age-matched normotensives (56 ± 13 yrs, n = 10) using a newly developed arterial linear scanner with very high frequency (1MHz).

Results: IMT was significantly higher in hypertensives (0.63 ± 0.06 mm) as compared with normotensives (0.27 ± 0.05 mm, p = 0.001). L-NAME adversely affected systemic and regional hemodynamics (Table), as evidenced by an increase in MAP and TPR, a decrease in CI, and decreased organ blood flows with increased resistances. Stain therapy markedly improved these changes, with exception of MAP which remained elevated. Cholesterol levels were similar.

4:30 p.m.

832-3 Enhanced Vascular Activity of Endogenous Endothelin-1 in Obese Hypertensive Patients

Carmin Carollo, Micaela Iantomno, Umberto Camillo, Julio A. Panza, Catholic University, Rome, Italy, Washington Hospital Center, Washington, DC

Hypertensive patients (HTs) have increased endothelin (ET-1)-dependent vasoconstrictor tone. The ET-1 system, however, might not be uniformly activated in all forms of hypertension as suggested by studies showing that ET-1 activity is enhanced predominantly in low-renin, salt-sensitive hypertension models. This study sought to determine whether activation of the ET-1 system in hypertension is associated with increased body mass index (BMI). To this aim, forearm blood flow (FBF) responses (strain-gauge plethysmography) to intraarterial infusion of an ET(A) receptor blocker (BQ-123, 100 nmol/min for 60 min) were analyzed in HTs (n=27) and normotensive controls (NTs; n=28) using a newly developed arterial linear scanner with very high frequency (1MHz).

Results: L-NAME adversely affected systemic and regional hemodynamics (Table), as evidenced by an increase in MAP and TPR, a decrease in CI, and decreased organ blood flows with increased resistances. Stain therapy markedly improved these changes, with exception of MAP which remained elevated. Cholesterol levels were similar.

4:45 p.m.

832-4 Pleiotropic Hemodynamic Action of Statins in Rats Resistant Hypertension by Inhibition of Nitric Oxide Synthesis

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Background: Endothelial function and nitric oxide are impaired in hypertension. We examined whether statins may improve hemodynamics in a model with endothelial dysfunction exaggerated by nitric oxide synthesis inhibition.

Methods: Control Wistar-Kyoto rats received no treatment. The 2nd group was given nitric oxide synthetase inhibitor L-NAME (~15mg/kg/d) in drinking water. In addition to L-NAME the third group received rosuvastatin (R) (20mg/kg/d) by gavage. After 6 weeks, indexes of systemic and regional hemodynamics were measured in instrumented conscious rats. The following was measured: mean arterial pressure (MAP), cardiac index (CI), total peripheral resistance (TPR), renal blood flow (RBF) and resistance (RVR), coronary blood flow (CBF) and resistance (CFR), and, after bipyridylamine infusion, minimal coronary vascular resistance (MCVR) and coronary flow reserve (CFR).

Results: L-NAME adversely affected systemic and regional hemodynamics (Table), as evidenced by an increase in MAP and TPR, a decrease in CI, and decreased organ blood flows with increased resistances. Stain therapy markedly improved these changes, with exception of MAP which remained elevated. Cholesterol levels were similar.

5:00 p.m.

832-5 Relationship of Soluble Angiopoietin Receptor Tie-2 to Tissue Factor, Endothelial Dysfunction, and Vascular Endothelial Growth Factor in Hypertension

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Background: We have developed an assay for a novel marker of angiogenesis, soluble angiopoietin receptor Tie-2, and aimed to study its relationship to indices of angiogenesis [vascular endothelial growth factor (VEGF) and its receptor sFlt-1], thrombogenesis [tissue factor (TF)] and endothelial dysfunction (vWF) and flow mediated dilatation (FMD) of the brachial artery] in hypertension. Methods: FMD and plasma vWF, sFlt-1, TF, and vWF (all ELISA) were measured in 40 untreated hypertensive patients (28 male, mean age 56±11.8years, mean blood pressure (BP) 161±19 (mmHg) and compared to 20 healthy controls (13 male, mean age 51±1.1±10years). Plasma Tie-2 levels of TF (0.020) and Tie-2 (0.040) were significantly higher in patients compared to controls, but FMD was lower (0.002). Levels of Tie-2 correlated with VEGF (Spearman, r=0.65, p=0.001), sFlt-1 (r=0.69, p=0.001) and TF (r=0.34, p=0.035). VEGF also correlated with sFlt-1 (r=0.80, p=0.001). TF (r=0.41, p=0.001) and vWF (r=0.32, p=0.044) and FMD (r=0.34, p=0.034). Conclusion: We have shown for the first time raised Tie-2 levels in hypertension, in association with abnormal thrombogenesis and endothelial dysfunction. These processes appear to be closely related and may have implications for the pathophysiology of cardiovascular complications associated with hypertension.