were taken for full lipid profile, glucose and insulin. **Results:** Subjects' BMI and fasting lipids were in the normal range and did not differ significantly between trained and untrained men. Whole-group analysis revealed that fasting HDL-C correlated inversely with waist-to-hip ratio ($r = -0.7$, $p < 0.01$). High-fat meal caused triglycerides (TAG) to increase and FMD to decrease (0.8 ± 0.6 mmol/l and 3.0 ± 1.7% respectively, $p < 0.001$) but the TAG increase was significantly less in trained men. Postprandial TAG rise correlated positively with WHR and inversely with physical activity and aerobic fitness. In contrast, postprandial FMD correlated inversely with WHR and positively with aerobic fitness and HDL-C (all $r = \pm 0.5$, all $p < 0.05$) **Conclusions:** Our results suggest that abdominal adiposity adversely affects postprandial lipid metabolism and endothelial function whereas physical activity, aerobic fitness and HDL-C are protective. Endothelial protection in the pro-atherogenic milieu of postprandial lipaemia may be novel mechanisms by which exercise and HDL-C lower cardiovascular risk.

4:24 p.m.

1130MP-170 Noninvasive Ultrasonic Evaluated Endothelial Dysfunction Predicts Future Hypertensive Evolution

Tatsuaki Murakami, Sumio Mizuno, Fukui Cardiovascular Center, Fukui, Japan

Background: Hypertension has great impact to develop cardiovascular diseases, but evolutional mechanism of hypertension remains partially clarified. On the other hand, endothelial dysfunction is thought to affect atherogenic processes, but there has been little clinical evidence for the relationship. This study assessed hypothesis that endothelial dysfunction accelerates hypertensive evolution (HTE). **Methods:** Endothelial dysfunction was graded by noninvasively measured reactive changes in lumen diameter of right brachial artery following transient forearm occlusion for 5minutes (FMD; flow-mediated endothelium-dependent vasodilation) in consecutive 518 ambulatory patients who were suspected coronary artery disease using high resolution ultrasonography. The enrolled patients were categorized into 3 groups according to the values of FMD, and their blood pressure was followed-up for 36 months or more. We prospectively followed up HTE, which was defined as more than two stage upgrade of hypertension proposed by world health organization or new administration of an antihypertensive agent. **Results:** For a mean follow-up period of 57 months with 100% follow-up (range; 36 to 85), the patients with severe endothelial dysfunction (FMD<4%; Group-L, n=174), more frequently manifested HTE [Group-L versus Group-M with mild endothelial dysfunction (4%≤FMD<8%, n=171) plus Group-H with preserved endothelial function (FMD 8% or more, n=173): 44 (25.2%) versus 17 (9.9%) plus 9(5.2%), p<0.001, by Kaplan-Meier analysis]. Systolic and diastolic blood pressure significantly elevated in Group-L (p=0.001 and 0.006, respectively) but not in Group-M or Group-H. Cox proportional hazard model analysis including clinical variables showed that severe endothelial dysfunction was an independent and strong predictor for future HTE (odds ratio=2.87, 95%confidential interval; 1.73-4.77, p<0.001). **Conclusion:** In conclusion, endothelial dysfunction accelerates hypertensive evolution and noninvasive ultrasonic evaluated endothelial dysfunction is a practical predictor for future hypertensive evolution.

4:36 p.m.

1130MP-171 Upregulation of Arginase Mediates Endothelial Dysfunction in Aging Blood Vessels

Anthony R. White, Dan E. Berkowitz, Dechun Li, Hunter C. Champion, Soonyul Kim, Sean Burke, Artin Shoukas, Daniel Nyhan, Joshua M. Hare, Johns Hopkins Medical School, Baltimore, MD

Although abnormal nitric oxide signaling is implicated in endothelial dysfunction of the aging cardiovascular system, the precise biochemical mechanism remains controversial. L-arginine, the NOS substrate, is also metabolized by arginase. We tested the hypotheses that arginase reciprocally regulates NOS by modulating L-arginine bioavailability, and that arginase is upregulated in aging vasculature, contributing to endothelial dysfunction. We exposed isolated PE (10^{-6}M) preconstricted aortic rings to the selective arginase inhibitors, BEC((S)-(2-Boronoethyl)-L-cystein, HCl)) and nor-NOHA (N-Hydroxy-nor-L-arginine). BEC caused a dose-dependent relaxation of rings obtained from young adult rats (n=6, 4 to 5 months), with a maximal vasodilation of (46.4 +/- 9.4 %) at 10^{-5}M. The endothelium and cGMP dependence of this vasorelaxation was confirmed in de-endothelialized rings or pre-treatment with the sGC inhibitor ODQ (P<0.05). Arginase mRNA and protein abundance were increased in rings from old (n=5, 21.7 +/- 0.62 months) rats (7 fold increase in mRNA expression in old aortas compared to young aortas by qPCR). Finally, we determined the effect of arginase inhibition on L-arginine induced vasorelaxation. L-Arginine (10^{-4}M) relaxed young adult rings by 25 +/- 9.1 % but did not affect those from old adult rats (4.7 +/- 5.1 %). In marked contrast, pretreatment of old rings with arginase inhibitors BEC (10^{-5}M) or nor-NOHA (10^{-5}M) enhanced the vasodilatory response to L-arginine (33.7 +/- 6.6 % and 26.8 +/- 7.5 %, respectively), restoring it to the level observed in young rings. Together, these findings demonstrate the critical role for vascular arginase in modulating NOS activity, likely by regulating intracellular L-arginine availability. Arginase upregulation contributes to endothelial dysfunction of aging, a finding with implications for other states characterized by impaired vasodilation.

4:48 p.m.

1130MP-172 Progression of Coronary Artery Disease, Vascular Remodeling, and In-Stent Restenosis in Humans as a Function of Endothelial Shear Stress: An *In-Vivo* Six-Month Follow-Up Study

Peter H. Stone, Yerem Yeghiazarians, Ahmet U. Coskun, Scott Kinlay, Maureen E. Clark, Milan Sonka, Andreas Wahle, Olusegun J. Ilegbusi, Jeffrey J. Popma, John Orav, Richard E. Kuntz, Charles L. Feldman, Brigham & Women's Hospital, Boston, MA, University of Iowa, Iowa City, IA

Background: Endothelial shear stress (ESS) is critical to vascular behavior: low ESS is pro-atherosclerotic, physiologic ESS is vasculoprotective, high ESS promotes vascular remodeling. The effect of ESS on instent restenosis is unclear. The purpose of this study was to determine if vascular behavior both in native coronary arteries and in stented coronary arteries could be predicted *in-vivo* based on ESS. **Methods:** 12 arteries in 8 patients were studied at baseline and at 6 mo (6 native arteries with luminal obstruction < 50% and 6 stented arteries). 3-D anatomy of the arterial segments was determined using intracoronary ultrasound, biplane coronary angiography, and coronary flow measurements. Lumen, external elastic membrane (EEM) and the plaque thickness (EEM minus the lumen) were recreated in accurate 3-D space. Local ESS was calculated using computational fluid dynamics. Endothelial regions were grouped into 6 categories of cumulative percentiles of ESS values, from 1-55 dynes/cm^2 . Measurements made at baseline were then compared to those made at 6-mo followup, matching the regions using anatomic landmarks. Changes in regions were assessed by repeated measures linear regression, adjusted for within-patient correlation. **Results:** There were 81 regions of similar baseline ESS in native segments and 29 regions in stented segments (mean size 24 mm^2, range 1-137 mm^2). In native arteries, regions of abnormally low baseline ESS exhibited a significant increase in plaque thickness, as well as enlargement of the outer vessel wall, such that lumen radius remained unchanged (Glagov outward remodeling); regions of physiologic baseline ESS showed little change; regions with increased baseline ESS exhibited outward remodeling with normalization of ESS. In stented arteries, there was evidence of restenosis (increased in intima-medial thickness, a decrease in lumen radius, and increase in ESS) at all levels of baseline ESS. **Conclusion:** Different areas within the coronary artery rapidly change in response to different environments. Coronary vascular behavior, including progressive atherosclerosis and outward remodeling, can be predicted from ESS. ESS may have a limited role in in-stent restenosis.

POSTER SESSION

1131 Platelets, Endothelium, and Thrombosis II

Monday, March 31, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 4:00 p.m.-5:00 p.m.

1131-134 Is Coronary Endothelial Function Impaired Both at the Level of Resistance Vessels and at That of Conduit Vessels in Women With Atypical Chest Pain?

Hiroki Teragawa, Keiji Matsuda, Kentaro Ueda, Masashi Kimura, Fumiharu Miura, Hidekazu Hirao, Kazuaki Chayama, Masao Yoshizumi, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan

Background: Atypical chest pain (ACP) is frequently observed in women. While impaired vasoreactivity of the coronary arteries at the level of resistance vessels has been considered a possible factor contributing to the genesis of ACP, its precise mechanisms remain to be elucidated. It also remains to be clarified whether women with ACP present coronary endothelial dysfunction at the level of conduit vessels. Methods: Thirty-three women (mean age 64 yrs) with ACP and normal coronary angiograms (Group I) and eleven women with normal coronary angiograms without any chest symptom, who were evaluated for arrhythmia (Group II), were enrolled for the study. Acetylcholine (Ach, 3 μg/min and 30 μg/min) was infused into the left coronary ostium over 2 min. Patients with vasospastic angina were excluded from the study. The diameter at the proximal and distal segments of epicardial coronary arteries was quantitatively measured and coronary blood flow (CBF) was calculated by quantitative angiography and Doppler flow velocity measurements. The change in coronary diameter and CBF in response to each drug was expressed as the percent change from baseline values. Coronary flow reserve (CFR) was also calculated as the ratio of coronary flow velocity after an injection of 20μg of adenosine triphosphate relative to the baseline value. Results: Age, body mass index, and the frequency of individual coronary risk factors did not differ between the two groups. The hemodynamics, coronary diameter, and CBF at baseline were also similar between the two groups. The percent change in coronary diameter at the proximal and distal segments and CBF in response to Ach were impaired in Group I, compared with Group II ($p = 0.0441$, $p = 0.0001$, and $p = 0.0315$, respectively). Nitroglycerin-induced dilation and CFR were similar between the two groups. Conclusion: These findings suggest that coronary endothelial function is impaired both at the level of resistance vessels and at that of conduit vessels in women with ACP. This impairment may contribute to the genesis of ACP.