assessing body composition and LVM, we examined the gender difference of LVM adjusted for LBM in older persons with mild hypertension.
Method: Fifty-two subjects (22 men and 30 women) with untreated mild hypertension, aged 55 to 75 years, and otherwise healthy, were examined. Resting BP was obtained at 4 or 5 visits at least 1 week apart and averaged. Body composition was assessed using dual energy X-ray absorptiometry. LVM was determined from MRI and was indexed by BSA, height, height$^{2.7}$ and LBM.
Results: There were no gender differences in age, SBP and BMI. Men had higher mean BP, unindexed LVM, and LBM than women. Fat mass and percent body fat were higher in women compared to men. Unlike the LVM indexed by other measures, LVM indexed by LBM was greater in women than men, as shown in table. In a multiple regression model, gender was a predictor of LVM after adjustment for LBM, mean BP, percent body fat and LBM - gender interaction (adjusted means, female vs. male, 135 ± 8 g vs. 109 ± 12 g, $p < 0.05$)
Conclusion: In this population of older persons with mild hypertension, women had a higher LVM relative to their lean body size, suggesting that women may be more susceptible to LVH than men.

Table * $p < 0.01$, ** $p < 0.05$, male vs. female

LVM indexed by	BSA**	Height*	Height$^{2.7}$	LBM**
Male	73 ± 16 g/m^2	89 ± 21 g/m	33 ± 7 g/m$^{2.7}$	2.68 ± 0.52 g/kg
Female	64 ± 13 g/m^2	75 ± 13 g/m	33 ± 6 g/ m$^{2.7}$	3.07 ± 0.60 g/kg

1108-96 **Arterial Stiffness and Left Ventricular Geometry and Function in Hypertensive Patients With Electrocardiographic Left Ventricular Hypertrophy: The LIFE Study**

Vittorio Palmieri, Jonathan N. Bella, Mary J. Roman, Eva Gerdts, Vasilios Papademetriou, Kristian Wachtell, Markku S. Nieminen, Björn Dahlöf, Richard B. Devereux, *Weill Medical College of Cornell University, New York, New York.*

Background: Arterial stiffness can be assessed by the ratio pulse pressure (PP) over echocardiographic stroke volume (SV). We evaluated relations of arterial stiffness to left ventricular (LV) geometry and function in hypertensive patients with electrocardiographic (ECG) LV hypertrophy (H).
Methods: Of participants in the echo-substudy of the Losartan Intervention For Endpoint (LIFE) reduction in hypertension study, selected to have ECG-LVH by Cornell voltage-duration product or Sokolow-Lyon voltage criteria, no heart failure or severe aortic stenosis, we identified 858 subjects (88%, 66±7 yrs/old) with PP/SV available. The study sample was divided in tertiles of PP/SV (cutpoints: 0.86 and 1.11 mm Hg/ml). M-mode and Doppler SV were averaged.
Results: With higher PP/SV, age, proportions of women and diabetics, and systolic blood pressure (BP) were higher (all $p<0.01$); diastolic BP, body height and weight, and SV were lower (all $p<0.01$). Mean BP, total/HDL cholesterol, urinary albumin/creatinine and proportion of wall motion abnormalities were similar in tertiles of PP/SV. After adjusting for age, gender and body surface area, LV mass and LV internal diameter were lower while relative wall thickness (RWT=LV concentricity) was higher with higher PP/SV (all $p<0.01$); ejection fraction was similar across tertiles ($p>0.5$) while stress-corrected midwall shortening (scMWS) was lower with higher PP/SV ($p<0.01$). After adjustment for age and gender, LV filling parameters and heart rate were similar in tertiles of PP/SV (all $p>0.1$). In multivariate models, independent correlates of PP/SV were older age, lower body weight, female-gender and diabetes ($R=0.48$, $p<0.001$); higher RWT was related to higher PP/SV independent of age, gender, and mean BP ($R=0.30$, $p<0.001$); higher LV mass was independently predicted by higher SV, male-gender, higher body weight, older age and higher mean BP, but not PP ($R=0.64$, $p<0.001$); PP/SV was not related to scMWS independent of RWT.
Conclusions: In elderly hypertensives with ECG-LVH, higher arterial stiffness is related to concentric LV geometry, which may offset afterload and preserve LV chamber function, but is associated with impaired myocardial function.

FEATURED ORAL PRESENTATION

825FO Featured Oral Session...Current Topics on Hormonal Replacement Therapy

Monday, March 18, 2002, 2:00 p.m.-3:30 p.m.
Georgia World Congress Center, Room 160W

2:15 p.m.

825FO-2 **Addition of Statin Attenuates the Increase in C-Reactive Protein During Estrogen Replacement Therapy in Postmenopausal Women**

Kwang K. Koh, Gyorgy Csako, William Schenke, Richard O. Cannon, III, *NHLBI, Bethesda, Maryland.*

Background: Randomized clinical trials have shown that HMG-CoA reductase inhibitor (statin) therapy reduces cardiovascular risk, the mechanism of which may include diminished arterial inflammation as evidenced by reduction in levels of C-reactive protein (CRP) in serum. Because estrogen replacement therapy increases CRP in postmenopausal women, which could have pro-inflammatory consequences and compromise any benefit to cardiovascular risk, we determined whether the addition of statin might modify the estrogenic effect on CRP. **Methods:** In a double blind, 3-period crossover study, we randomly assigned 28 healthy postmenopausal women to conjugated equine estrogens (CEE) 0.625 mg, simvastatin 10 mg, and their combination daily for 6 weeks, with each treatment period separated by 6 weeks off drugs. CRP was measured by high sensitivity immunometric assay (sensitivity 0.01mg/dL) before and after 6 weeks of each treatment. **Results:** CEE increased CRP from 0.37 ± 0.06 to 0.65 ± 0.13 mg/dL, simvastatin decreased CRP from 0.37 ± 0.06 to 0.33 ± 0.05 mg/dL, and the therapies combined increased CRP from 0.38 ± 0.08 to 0.48 ± 0.08 mg/dL (all $P<0.02$ vs. respective baseline values), with significant differences in changes in CRP levels among these therapies ($P<0.05$ by ANOVA). Post-hoc testing showed that the 29 ± 8 % increase in CRP on the combination of CEE with simvastatin was significantly less than the 89 ± 32 % increase in CRP on CEE alone ($P<0.01$). The effect of combination therapy on CRP did not correlate with baseline CRP, or with baseline or treatment-induced changes in levels of LDL cholesterol, HDL cholesterol, interleukin-6, or brachial artery flow-mediated dilation as a measure of nitric oxide bioactivity (all $r<0.32$). **Conclusion:** The combination of statin with estrogen therapy may attenuate the potential proinflammatory effect of estrogen administration to postmenopausal women, and maximize any benefit of hormone replacement therapy to cardiovascular risk.

2:30 p.m.

825FO-3 **The Differential Effects of Hormone Replacement Therapy and Selective Estrogen Receptor Modulator on Endothelial Function Seem Related to an Effect on Plasma Asymmetric Dimethylarginine, an Inhibitor of Nitric Oxide Synthase**

Giuseppe Mercuro, Massimo Fini, Cristiana Vitale, Otavio Gebara, Sandra Zoncu, Mauricio Wajngarten, Antonello Silvestri, Paola Rossini, José Antonio F. Ramires, Giuseppe M. Rosano, *San Raffaele Hospital, Roma, Italy, University of Cagliary, Cagliary, Italy.*

Background: Hormone replacement therapy (HRT) improves endothelial function in postmenopausal women. Although in vitro animal studies suggest that the selective estrogen receptor modulator, raloxifene (R), improves endothelial function, its effect in women has yielded conflicting results. One mechanism by which HRT may reverse endothelial dysfunction and increase NO bioavailability is by lowering asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide (NO) synthase. The aim of this study was to evaluate endothelial function and plasma ADMA with HRT or R.
Methods: Brachial artery diameter, endothelium-dependent flow-mediated vasodilation (FMD) of the brachial artery, and plasma levels of nitrite, nitrate, endothelin-1 and ADMA were measured in 20 postmenopausal women with increased cardiovascular risk, treated with either HRT (0.625 conjugated equine estrogens and 2.5 mg medroxyprogesterone acetate) or R (60 mg) for 4 weeks in a double-blind, single cross-over study.
Results: Baseline brachial artery diameters remained unchanged after each treatment phase. FMD significantly improved with HRT but not with R. ADMA significantly decreased with HRT, while a trend towards increased plasma ADMA levels was noted with R.
Conclusions: HRT improves endothelial function in postmenopausal women at risk of cardiovascular disease, which may be due, at least in part, to a reduction in ADMA. In contrast, R seems to increase plasma ADMA, which may negatively affect endothelial function.

	Baseline	HRT	R
FMD (%)	7.4±0.5	12.4±0.6**	6.1±2.0
ADMA	0.76±0.51	0.68±0.63**	0.80±0.65
Nitrite+nitrate (Nox)	41.1±10.3	47.3±8.4*	38.8±6.8
Endothelin-1 (pg/ml)	3.2±0.6	2.8±0.6*	3.2±0.7

*=p<0.05; **=p<0.01, compared to baseline

2:45 p.m.

825FO-4 **Hormone Replacement Therapy and Risk of Myocardial Infarction in Women With Diabetes**

Apoor S. Gami, R. Scott Wright, Sharonne E. Hayes, Stephen L. Kopecky, *Mayo Clinic, Rochester, Minnesota.*

Background: The effect of hormone replacement therapy (HRT) on coronary heart disease (CHD) in postmenopausal women is controversial. Women with diabetes are at markedly increased risk of CHD, yet data on HRT in this population is scarce. The purpose of this study is to describe the effect of HRT on risk of MI in postmenopausal women with diabetes.
Methods: We conducted a case-control study in which case subjects (n = 99) were consecutive postmenopausal women with diabetes admitted to our institution from 1998 to 2000 with a principal diagnosis of MI. Control subjects (n = 306), matched in a 3:1 ratio by age and admission year, were postmenopausal women with diabetes admitted with principal diagnoses other than MI. Medical records were reviewed for demographics, medical history including diabetes complications, CHD risk factors, laboratory data, and current medications. Differences between case and control groups were assessed by the two-sample T-test for continuous variables and the chi-square test for dichotomous variables. The odds ratio, adjusted for group differences by logistic regression models, was used to estimate the relative risk of incident MI for HRT users.
Results: Case and control subjects were of similar age (73 years), height (157 cm), and weight (77 kg). Case and control groups had similar frequencies of hypertension (73%) and active cigarette use (8%). Frequencies of use of insulin (53%), oral hypoglycemic agents (36%), aspirin (46%), and statins (22%) were similar. Frequencies of diabetic retinopathy (19%), neuropathy (21%), and nephropathy (32%) were similar. Average levels of hemoglobin A1c (8.6%) and creatinine (1.7 mg/dl) were similar. More case subjects had previous MI (29% vs. 17%, p = 0.01) and hypercholesterolemia (52% vs. 39%, p = 0.02). Current users of estrogen (with or without progesterone) comprised 16% of case and 15% of control subjects. The relative risk of incident MI for current HRT users was 0.92 (95% CI 0.44 - 1.94).