1108-70 Is the Relationship Between Left Ventricular Mass and Endothelium-Dependent Vasodilatory Function Independent of Blood Pressure?

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Background: Recent studies reported that increased left ventricular mass (LVM) is associated with impaired endothelium-dependent vasodilatory function (EDF). It is unclear, however, whether this relationship is independent of blood pressure (BP) in hypertensives and normotensives. Methods: We therefore evaluated the effects of BP on the relationship between echocardiographic LVM and EDF in 59 African American (AA) hypertensives (49±12 yrs) and 42 AA normotensives (40±11 yrs). LVM was calculated (Devereux formula) and indexed to body surface area (LVMI) to define the presence of LV hypertrophy (LVH) (LVMI >134/110 g/m² for men/women). EDF was assessed as flow-mediated dilation (FMD) of the brachial artery during reactive hyperemia, using high-resolution ultrasound. Results: Compared to normotensives, hypertensives had higher LVMI (105±32 vs. 81±24 g/m², P<0.001) and lower FMD (9±6 vs. 16±6%, P<0.0001). In addition, patients with LVH had a significantly lower FMD than patients without LVH (7±6 vs. 13±7, P<0.001). FMD inversely correlated with LVMI (r =-0.53, P<0.0001), systolic BP (r =-0.45, P<0.0001) and diastolic BP (r =-0.43, P<0.0001). Regression coefficients revealed a negative relation between LVMI and FMD in univariate model (beta= -0.10, P<0.0001) and after adjusting for age, gender, systolic and diastolic BP (beta= -0.05, P<0.05). Conclusion: Impairment of FMD is inversely related to LVM, and this relationship appears to persist but likely attenuated after accounting for the well-known influences of blood pressure.

1108-91 Exercise Blood Pressure Threshold for Left Ventricular Hypertrophy in Normotensive and Hypertensive Middle-Aged Men

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Background: An abnormal rise in systolic blood pressure (SBP) during exercise is associated with increased risk for hypertension (HTN) and left ventricular hypertrophy (LVH). However, the magnitude of change in exercise SBP associated with LVH is not well defined.
Methods: We assessed left ventricular structure (echocardiography) and exercise blood pressure (BP) in middle-aged (52±5 yrs) normotensive (n=133) and hypertensive (n=121) men free from heart disease, smoking, and antigypertensive medication, to determine the association between left ventricular structure and exercise BP.
Results: Multiple regression analysis (stepwise) revealed that SBP at 6 minutes of exercise was the strongest predictor of left ventricular mass index (LVMI) for normotensive (R^2= 0.49) and hypertensive men (R^2=0.41). Since LVH was defined as LVMI>116 g/m², we regressed the 6-minute exercise SBP against LVMI for each group. The model revealed that a SBP≥167 mm Hg for normotensive and ≥160 mm Hg for hypertensive men were the minimum SBP levels to yield LVMI values >116 g/m². LVH was present in 71% of normotensive and 90% of the hypertensive men whose SBP met the respective level at 6 minutes of exercise. Furthermore, these men were 6 times more likely to have LVH (Odds Ratio: 6.0; CI:3.6-9.8; p<0.000). Comparisons between those who met or exceeded the respective level of SBP at 6 minutes of exercise and those who did not, revealed higher LVMI values (129±22 g/m² vs 101±14 g/m² ; p=0.000) for normotensive and (144±21 g/m² vs 106±6 g/m²; p=0.000) for hypertensive men respectively.
Conclusions: 1) SBP at 6 minutes of exercise is the strongest predictor of LVH for normotensive and hypertensive middle-aged men; 2) The exercise BP threshold for LVH appears to be a SBP≥167 mm Hg for normotensive and ≥160 mm Hg for hypertensive men achieved at a workload of approximately 7 METs.

1108-92 Electrocardiographic Markers of Cardiac Hypertrophy Show Greater Heritability Than Echocardiographic Left Ventricular Mass: A Family Study

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Background: Electrocardiographic and echocardiographic measures of cardiac hypertrophy are independent predictors of cardiovascular morbidity and mortality. There is increasing evidence to show that echocardiographic left ventricular mass is genetically determined, but little is known about the magnitude of genetic determination of electrocardiographic measures of cardiac hypertrophy. We set out to assess the heritability of continuous measures of left ventricular hypertrophy determined by electrocardiography and echocardiography.
Methods: We studied 955 members of 229 Caucasian extended families, ascertained through a hypertensive proband. Electrocardiographic measurements were performed manually on normal resting 12-lead electrocardiograms, and echocardiographic parameters were determined on M-mode images. Sex-specific residuals for left ventricular phenotypes were calculated, adjusted for age, systolic blood pressure, weight, height, waist-hip ratio, and presence of diabetes. Heritability was estimated from familial correlations with adjustment for spouse resemblance, and by using variance components methods with ascertainment correction for proband status.
Results: The heritability estimates (range) were higher for Sokolow-Lyon voltage (39-41%) and RaVL voltage (30-31%) than for echocardiographic left ventricular mass (23-29%). Cornell voltage, Cornell product, and electrocardiographic left ventricular mass had heritability estimates of 19-25%, 28-32%, and 12-18%, respectively.
Conclusions: The greater heritability of Sokolow Lyon voltage and RaVL voltage suggests that electrocardiographic phenotypes may be particularly important for the molecular investigation of the genetic susceptibility to cardiac hypertrophy. Finding genes that influence the electrocardiographic markers could help unravel the pathophysiology of cardiac hypertrophy and lead to improvements in prevention, diagnosis, and treatment of at-risk populations.

1108-93 Is Urinary Albumin Excretion an Independent Predictor of Cardiovascular Mortality in Patients With Electrocardiographic Left Ventricular Hypertrophy? The LIFE Study

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Background: Recently, we found that increased urine albumin/creatinine ratio (UACR) as well as electrocardiographic (ECG) left ventricular hypertrophy (LVH) were related to high blood pressure (BP) in hypertensive patients independent of age, smoking, prevalence of diabetes, suggesting parallel BP-induced cardiac hypertrophy and renal glomerular permeabilty. However, it is not clear whether this predicts an independent effect on mortality.
Methods: ECG and morning spot urine were obtained in 8,165 patients with stage I-III hypertension and ECG LVH (Cornell voltage-duration or Sokolow-Lyon voltage criteria) after 14 days placebo treatment. Renal glomerular permeability was evaluated by UACR and was defined as micro- or macroalbuminuria if >3.5 or 35 mg/mol, respectively.
Results: During 68 [95% CI 67-69] months 592 (6%) deaths occurred. Of these 317 (3.9%) were cardiovascular (CV) deaths, which plus non-fatal myocardial infarction and stroke compressed the composite primary CV end-point (n=888, 10.9%). Patients with either micro- or macroalbuminuria had on average 1.7 or 4.3-fold higher CV mortality rate, respectively, compared to normoalbuminuric patients. Similar micro- or macroalbuminuria groups had 1.8 or 2.6-fold higher rates of composite end-point compared to normoalbuminuric patients. CV mortality rate and composite CV end-point rate increased 8- and 9-fold in patients with macroalbuminuria and LVH by both criteria as compared to normoalbuminuric patients without LVH by either criterion (all p<0.001). When divided into quartiles a striking increase in CV end-points was seen in the 3rd quartile with UACR-values between 1.3-3.9 g/mmol. Cox regression analysis showed that UACR predicts CV mortality and composite CV end points independent of LVH, systolic BP, age, sex, diabetes and smoking.
Conclusion: UACR is an independent predictor of CV morbidity and mortality, even after taking into account baseline ECG LVH and other CV risk factors. The presence of cardiac end-organ damage and albuminuria potentiates the risk of overall mortality. Furthermore, the threshold-limit for microalbuminuria in patients with hypertension and LVH should be reduced to no more than 1.0 mg/mmol.

1108-94 Increased Expression of Type-2A and Type-2B Protein Phosphatases During the Development of Left Ventricular Hypertrophy

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Background: Type-2B protein phosphatase (PP2B) is implicated in the development of LV hypertrophy (LVH). The role of type-2A protein phosphatase (PP2A) in LVH, however, is not known. We tested the hypothesis that both PP2A and PP2B are involved in the LVH.
Methods: Expression of the catalytic subunit of PP2A (PP2Ac) and PP2B (PP2Bc) was examined by Western blots in SDS-extract of LV myocardium obtained from Lewis rats (n=18) in which LVH was produced using one kidney-one clip (1K1C) and in sham-operated rats (n=18). Six rats from each group were sacrificed at 1, 4, and 8 weeks thereafter. LV weight to body weight (LVW/BW) ratio was used to index of LVH. Western blots were quantified in densitometric units and the data expressed as percent change from sham values.
Results: 1K1C rats developed LVH as early as week 1 post-operatively and the extent of LVH increased progressively thereafter. In LVH rats, PP2Bc but not PP2Ac expression increased at week 1. Expression of both PP2Ac and PP2Bc, however, increased significantly at 4 weeks and 8 weeks compared to sham. Both PP2Ac and PP2Bc were lower at week 8 compared to week 4 (data in table).
Conclusions: The results suggest that increased expression of PP2Bc is associated with initiation and progression of LVH. Increased expression of PP2Ac follows at a later stage of LVH and may play a role in its progression. These temporal differences in the expression of PP2Ac and PP2Bc represent therapeutic opportunities to interfere with the LVH process at different stages of its evolution.

	LVW/BW (%)	PP2Ac (%)	PP2Bc(%)
Week 1	117 ± 4	100 ± 7	253 ± 18
Week 4	135 ± 5	255 ± 26*	314 ± 11*
Week 8	186 ± 6*^	142 ± 15*^	183 ± 8*^

*=P<0.05 vs Week 1; ^=P<0.05 vs. Week 4

1108-95 Older Women With Mild Hypertension Have Higher Left Ventricular Mass Than Men After Adjustment for Lean Body Mass

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Background: When left ventricular mass (LVM) is indexed by measures of body size, such as body surface area (BSA) and height, gender difference persist with men having a higher LVM index. Recent studies suggest that LVM indexed by lean body mass (LBM) may eliminate the gender difference seen in general populations. With the novel techniques for