Determinants of Left Ventricular Mass in Early Hypertension

One hundred seventy-six unmedicated mildly hypertensive subjects (113 men, 63 women) underwent M-mode echocardiography to determine left ventricular mass (LVM) and relative wall thickness (RWT), 24-h ambulatory blood pressure monitoring, and completed standardized questionnaires measuring marital and job stress. Subjects were aged 46 ± 9 years old; 45.4% had daytime diastolic blood pressure < 90 mm Hg; 96.1% of LVM results were in the normal range. We found that neither marital distress nor job strain was a determinant of LVM. However, a segmental regression approach revealed inflection points of 131 mm Hg systolic daytime blood pressure and 83 and 87 mm Hg nighttime diastolic blood pressure in the relation between LVM and RWT, respectively, and ambulatory BP. In addition, we found that the variability of LVM was best explained by indexing LVM by height, rather than body surface area. Am J Hypertens 1998;11:1248 –1251 © 1998 American Journal of Hypertension, Ltd.

KEY WORDS: Mild hypertension, blood pressure, left ventricular mass, echocardiography, stress, body surface area, height.

The determinants of left ventricular mass (LVM) are incompletely understood and together explain only a portion of the variability in this key predictor of future cardiovascular events.1–4 Other determinants clearly contribute to this variability.5,21 Psychosocial stress may be one such determinant. In one study, employed men experiencing high job strain had a higher prevalence of sustained hypertension, and greater left ventricular mass index, than men without job strain.6 To extend this observation we set out to investigate whether, in a group of untreated mildly hypertensive men and women without coronary disease, another major psychosocial factor, marital stress, played an independent role in determining left ventricular mass when other established determinants, including job strain, were considered.

METHODS

Study Population Using a cross-sectional observational study design we examined a group of men and women aged between 20 and 65 years old who had a sitting diastolic blood pressure (BP) of between 90 and 105 mm Hg on three separate occasions over a minimum of 6 weeks and not exceeding 6 months, cohabiting significant other, and one continuous job (both for a minimum of 6 months), and a technically adequate echocardiogram. Exclusion criteria were evidence of coronary artery or valvular heart disease by history, electrocardiogram, or echocardiography, social or geographic factors making study participation impossible, problems completing the questionnaires
because of language or disability, a refusal to give informed consent, and the use of any hypotensive or hypertensive medications during the previous 6 months. Subjects were recruited from family practitioners, local businesses, and in response to newspaper advertisements. Two hundred and five subjects were enrolled in the study. Of these, 176 had technically adequate M-mode echocardiograms and form the basis of this report. All subjects gave informed consent after reviewing written and oral information and discussing the protocol with study personnel. The study was approved by the Human Subjects Review Committee of the University of Toronto.

Blood Pressure Measurement Sitting diastolic BP was measured by auscultation using a sphygmomanometer and the phase V Korotkoff sound. In addition, all subjects underwent 24-h ambulatory blood pressure monitoring (ABPM) (Spacelabs Model 90207, Redmond, WA) during a normal working day. Blood pressure was measured at 15 min intervals during the day and hourly intervals from 11 pm to 7 am. Correct calibration of the ambulatory monitor was ensured by comparing three to five successive systolic and diastolic BP readings from the monitor with simultaneous BP readings made by an experienced observer using a mercury manometer connected to the monitor via a T-tube. To be deemed acceptable, three successive readings had to agree by ±5 mm Hg.

Left Ventricular Mass LVM was measured by M-mode echocardiography using a widely accepted imaging technique and measurement formula. The echographer was blinded to marital strain score and blood pressure results. In brief, patients were imaged supine in the left lateral position either at end-expiration or during quiet normal respiration. Under two-dimensional guidance, the M-mode cursor was positioned perpendicular to the septum and posterior wall at the chordal level. M-Mode images were considered adequate for measurement when they satisfied previously published criteria. Images were recorded onto ¾ in. videotape at a sweep speed of 100 mm/sec. Left ventricular measurements were made in triplicate off-line using hand-held calipers and the modified American Society of Echocardiography (ASE) convention. LVM was calculated from the mean of these measurements using the corrected ASE formula and was indexed for both body surface area and for height. Left ventricular relative wall thickness was calculated as previously described.

Marital and Job Factors On completion of the ABPM measurements, three questionnaires were completed by the patient under the supervision of a research assistant, who also recorded basic demographic data. Marital adjustment was assessed by the Dyadic Adjustment Scale (DAS). This is a 32-item measure with high internal consistency and test-retest reliability. It has been used on over a thousand published studies and is an excellent discriminator of marital distress. Desire for marital change was evaluated by the Areas of Change Questionnaire (ACQ). To assess spouses perception of marital strengths and weaknesses, couples indicated which of 34 behavioral issues required change in them or in their partners. The ACQ has high internal consistency and concurrent validity. Both subject and spouse completed the ACQ. Distressed couples have been found to want more change and to see that more change is desired of them.

Job strain was measured by the Job Content Questionnaire (JCQ) developed by Karasek et al. The JCQ has been used extensively in cardiovascular populations. The construct of job strain, consisting of increased job demands and limited job latitude, was derived from this questionnaire. An association between job strain and cardiovascular disease has been previously noted using this questionnaire. The completed questionnaires were electronically scanned into a correlative database (Microsoft Access, Redmond, WA) and were subsequently managed using dBase IV software (Inprise Inc., Scotts Valley, CA).

Statistical Methods Forward stepwise regression, with P = .05 for a prognostic covariate to enter, was used to select the final model for each expression of the left ventricular morphology. The proportion of total variance in the dependent measure explained by a prognostic covariate, in addition to the significance of the coefficient, was also tested. When necessary, significant deviations from a normal (Gaussian) distribution of the dependent measure were subjected to normalizing transformation. A “knee” or inflection point in blood pressure, where the slope of the blood pressure covariate changed direction, was investigated through testing the differences in the slopes before and after the inflection point. For all statistical analyses, a P = .05 was used to reject the null hypothesis and assert statistical significance.

All models drew from the following pool of prognostic covariates: age, sex, height, weight, years of education, income, race, family hypertension history, history of antihypertensive drug use, alcohol intake, smoking and exercise status, systolic daytime and nighttime ambulatory BP, diastolic daytime and nighttime ambulatory BP, job strain, job demands, job latitude, Dyadic Adjustment Scale total score, and Areas of Change total score.

RESULTS

Demographic data and clinical variables on the 176 included subjects are shown in Table 1. The sample
TABLE 1. POPULATION DEMOGRAPHICS (N = 176)

<table>
<thead>
<tr>
<th>Gender (male/female, %)</th>
<th>64.4/35.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ± SD)</td>
<td>46 ± 9</td>
</tr>
<tr>
<td>LVMI (g/m²), mean (range)</td>
<td>103 (50.1–162.2)</td>
</tr>
<tr>
<td>Systolic BP (daytime mean, mm Hg)</td>
<td>139.3</td>
</tr>
<tr>
<td>Diastolic BP (daytime mean, mm Hg)</td>
<td>89.9</td>
</tr>
<tr>
<td>Systolic BP (nighttime mean, mm Hg)</td>
<td>129.3</td>
</tr>
<tr>
<td>Diastolic BP (nighttime mean, mm Hg)</td>
<td>80.5</td>
</tr>
<tr>
<td>Percent white coat hypertension</td>
<td>45.4</td>
</tr>
<tr>
<td>BMI (mean ± SD)</td>
<td>27.08 ± 4.19</td>
</tr>
<tr>
<td>Current alcohol users (%)</td>
<td>16.1</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>13.2</td>
</tr>
<tr>
<td>Post high school education (%)</td>
<td>70.1</td>
</tr>
<tr>
<td>Medical diagnosis for hypertension (%)</td>
<td>18.4</td>
</tr>
<tr>
<td>Family history of hypertension (%)</td>
<td>64.4</td>
</tr>
</tbody>
</table>

LVMI, left ventricular mass index; BP, blood pressure; BMI, body mass index.

was predominantly male, most of whom had never received antihypertensive treatment. A total of 96.1% of our subjects had normal LVM and almost half (45.4%) had white coat hypertension (based on daytime diastolic BP < 90 mm Hg by ABPM).

Natural log transformation normalized the measure of RWT. LVM indexed by body mass (LVMIbody mass) and by height (LVMIheight) also warranted normalizing transformations. Stepwise multiple regression was executed on only those subjects with complete data on all covariates, ie, 169 individuals.

In the final model for LVMIbody mass, maleness (P = .0001, partial $R^2 = 0.1191$) and systolic daytime ABP (P = .0005, partial $R^2 = 0.0618$) were found to be significantly and positively correlated to the cardiac dependent measure.

In the final model for RWT, diastolic nighttime ambulatory BP (ABP) (P = .0031, partial $R^2 = 0.0511$) and body mass index (BMI) (P = .0003, partial $R^2 = 0.0718$) were found to be significantly and positively correlated to the cardiac dependent variable of RWT. In the final model for LVMIheight, maleness (P = .0001, partial $R^2 = 0.2196$), BMI (P = .0002, partial $R^2 = 0.0636$), and systolic daytime ABP (P = .0012, partial $R^2 = 0.0445$) were found to be significantly and positively correlated to this cardiac dependent measure.

At no point in any of the above analyses did job or marital strain emerge in a significant relationship with any of the cardiac morphology measures.

Only one inflection point was detected for the relationship of LVMIheight to systolic daytime ABP corrected for maleness and BMI. Scrutiny of the slope segments before and after the 131 mm Hg inflection point suggests that there is a statistically significant change (P = .0437) of slope from −0.94 to +0.43. The slope of the positive segment based on a sample size of 131 is identical to the overall slope of the blood pressure covariate of the complete sample size of 169. Although statistically different, due to the change of direction, the before-inflection point slope was not significantly different from 0.

Two inflection points were detected for the relationship of RWT to diastolic nighttime ABP corrected for BMI. Scrutiny of the slope segments before and after the 83 mm Hg inflection point suggest that there is a statistically significant (P = .0437) change of slope from 0.0045 to 0.0110. The slope of the preinflection segment was based on a sample size 119 rounds to be identical to the overall slope of the blood pressure covariate of the complete sample size of 169. Although the study detected more than a doubling of slope after the inflection point of 83 mm Hg, only the segment before the inflection point with the larger sample size was significantly different from zero. Another inflection point at 87 mm Hg was found (P = .0322), representing a quadrupling of the presecond inflection slope (0.0041 to 0.0162).

DISCUSSION

There were three principal findings in our study: first, we found no relationship between either marital distress or job strain and left ventricular mass or relative wall thickness; second, we found thresholds in the relationships between systolic daytime blood pressure and left ventricular mass and between diastolic nighttime blood pressure and relative wall thickness; finally, we found that indexing left ventricular mass by height, rather than by body surface area, led to the most complete understanding of the variables determining left ventricular mass.

The lack of relationship between job strain and both left ventricular mass and relative wall thickness found in our study differs from a previous study that found that increased job strain was associated with a small increase in LVM in men aged between 30 and 40 years.6 However, the populations studied were different. All of our subjects had mild systemic hypertension by office BP measurement and over a third were women. In contrast, Schnall et al studied a group of 151 male patients, 76% of whom had a diastolic BP < 85 mm Hg.6 Our negative findings suggest that the adverse effect of job strain on LVM may only be evident at a diastolic BP level within the normal range and only in male patients, possibly in a limited age range.

We also found that there was no relationship between the marital variables measured and either left ventricular mass or relative wall thickness. Our study is limited in that the measurement of marital factors in relation to LVM may not be appropriately determined by the self-report scales used. The DAS and ACQ are able to discriminate well those with marital distress, but evaluation of marital factors that affect LVM may...
well require the measurement of other dimensions as well as the use of objective methods to evaluate marital interaction.

Some studies have suggested a link between target organ and BP reactivity to mental stress; however, caution has been advised in the interpretation of such results, and the link has not always been confirmed. The nonlinear relationship between average systolic daytime blood pressure and left ventricular mass, and between relative wall thickness and daytime diastolic blood pressure, suggests that the adverse effects of systemic hypertension on cardiac structure only become evident above certain threshold values. Our cutoff values of 131 mm Hg (daytime ambulatory systolic BP) and 87 mm Hg (nighttime diastolic BP) are similar to the values previously proposed by Verdecchia et al in their study of the relationship between left ventricular mass and ambulatory blood pressure. Patients whose ambulatory blood pressure levels are below these cutoffs might safely have antihypertensive therapy withheld, although this would have to be validated by prospective outcome studies.

We found that the determinants of LVM were more completely identified when LVM was indexed by height rather than by body surface area. Epidemiologic studies have shown that body surface area is a major determinant of LVM, the two being directly related. Thus, indexing LVM by body surface area may spuriously normalize a pathologic increase in left ventricular weight caused by the excess body surface area. To avoid this inappropriate normalization, recent studies have indexed ventricular mass by height. Our finding that the variability in LVM is more fully explicable when indexed by height rather than by body surface area supports indexing by height.

REFERENCES