Left Ventricular Mass and Cardiovascular Reactivity in Young Men

Morten Rostrup, Gunnar Smith, Hans Bjørnstad, Arne Westheim, Olav Stokland, Ivar Eide

Abstract The relation between left ventricular wall thickness and mass, arterial plasma catecholamines, and blood pressure at rest and during a mental arithmetic challenge and a cold pressor test was examined in 69 healthy men 19 years of age. The subjects were recruited from the 1st (n=21), 50th (n=26), and 99th (n=22) percentiles in mean blood pressure. All underwent echocardiography to determine mean wall thickness and left ventricular mass. Continuous intra-arterial blood pressure, electrocardiogram, and arterial sampling of plasma catecholamines were performed after 30 minutes of supine rest, during a 5-minute mental arithmetic challenge, and during a 1-minute cold pressor test. Stepwise multiple regression analyses considering mean wall thickness and left ventricular mass as the dependent variables were applied.

Left ventricular hypertrophy (LVH) is a major cardiovascular risk factor and is often considered a blood pressure-induced structural adaptation in essential hypertension. However, the pathogenesis of LVH is still unclear. Genetic factors, salt intake, and hormonal factors have all been suggested to induce LVH. Increased sympathetic activity may also be associated with the development of LVH.

We have previously demonstrated that cardiovascular hyperreactivity to mental stress seems to be associated with catecholamine-dependent coronary risk factors such as resting diastolic blood pressure and the ratio of high-density lipoprotein cholesterol to total cholesterol in young men without any elevation in baseline blood pressure. In the present study, we examined possible associations between left ventricular wall thickness and mass and cardiovascular reactivity to stress, blood pressure, and arterial plasma catecholamines in healthy 19-year-old men.

Methods

Subjects

Sixty-nine 19-year-old men were selected from the 1st (group 1, n=21), 50th (group 50, n=26), and 99th (group 99, n=22) percentiles of mean blood pressure. All subjects were examined by the same physicians, and only one subject was examined each day. The physicians were unaware of which group the subject belonged to. The examination started at 8 AM after an 8-hour fast and at least 8 hours of abstention from nicotine and caffeine and 24 hours of abstention from alcohol. A short PTFE catheter (Venflon, 19G, Viggo AB, Halsingborg, Sweden) was introduced with subjects under local anesthesia without epinephrine (Xylocain, Astra, Södertälje, Sweden) into the left brachial artery for blood sampling and intra-arterial pressure monitoring as previously described.

The subjects rested supine for 30 minutes in the presence of the examining physician only. Intra-arterial blood pressure and ECG were recorded continuously. At the end of this 30-minute period, a 5-minute mental arithmetic challenge test was announced. The subjects were told to mentally subtract the number 13, starting with 1079, continuously for 5 minutes. A metronome making noise at a frequency of 2 Hz was used to distract the subjects. Thereafter, the subjects rested for 30 minutes before a 1-minute cold pressor test was announced. The right hand was completely immersed in ice water (0°C) for 1 minute. In half the subjects of each percentile, the sequence of the two tests was reversed.

Arterial blood for catecholamine assay was collected into polypropylene syringes after 30 minutes of supine rest three times during the challenge (after 1, 3, and 5 minutes), two times during the cold pressor test (after 30 seconds and 1 minute), and three times during the recovery periods. Blood samples were immediately mixed with glutathione and EGTA, placed on ice, and

Intra-arterial systolic blood pressure (r=.54, P<.0001) and arterial plasma epinephrine (r=.31, P=.009) after 30 minutes of supine rest were the only independent explanatory variables of mean wall thickness (multiple R²=.33, P<.0001). Blood pressure at screening and during mental stress and cold pressor tests were not independent explanatory variables. The present study suggests that resting arterial blood pressure and plasma epinephrine may be of importance for development of left ventricular hypertrophy. (Hypertension. 1994;23[suppl I]: I-168-I-171.)

Key Words • blood pressure • vascular resistance • epinephrine • hypertension, essential • hypertrophy, left ventricular • stress • sympathetic nervous system
Assays

The intraobserver correlation and methodologic error have been reported previously.13

Echocardiographic Evaluation

An Irex III B echocardiograph with a 2.5-MHz transducer was used for echocardiographic evaluation, with measurements of the left ventricle being recorded as guided by a two-dimensional picture in the parasternal long- and short-axis positions. In each case, a two-dimensional picture with the M-mode line depicted was recorded to avoid including trabeculae and papillary muscles in the measurements of septal and posterior wall thicknesses. Recordings were made at end expiration with the examiner blinded, and three beats were assessed, the reading being made according to the leading-edge principle10 at a paper speed of 50 mm/s. The following measurements were made: left ventricular diastolic internal diameter, interventricular septum, and left ventricular posterior wall. Diastolic dimensions were measured at the start of the QRS complex. Left ventricular mass (LVM) was calculated according to the Penn Cube LVM formula.11 LVM was divided by height to index (LVMI) for body size as suggested by Nidorf et al.11

Statistics

Data were analyzed by use of the statistical package srs-pc+ (SPSS-PC+ Inc, Chicago, Ill). Analysis of variance (ANOVA) was applied for comparing the three groups. Subsequent univariate analyses were performed with individual t tests. Four categories of potential LVH correlates were studied: resting blood pressure and heart rate, blood pressure and heart rate during the laboratory stress tests, plasma catecholamines at rest and during the stress tests, and body weight. Multiple stepwise regression analyses considering MWT, LVM, and LVMI as dependent variables were performed.

The data are presented as mean±SEM. The null hypothesis was tested by two-tailed tests. Based on previous studies, we expected an increased left ventricular wall thickness and mass in the group with the highest resting blood pressure. The null hypothesis of no difference among the three groups in MWT, LVM, and LVMI was thus tested by a one-tailed test. The level of significance was set at a value of P<.05.

Results

Baseline

As can be seen from the Table, the three groups differed significantly in intra-arterial systolic (P<.001) and diastolic (P<.001) blood pressures after 30 minutes of supine rest. MWT, LVM, and LVMI differed among the three groups (P<.05, ANOVA) and were significantly higher in group 99 than group 50 (P<.05 for all three variables, t test). There were no differences in resting heart rates or plasma catecholamines.

Responses to Stress Tests

Group 99 revealed significantly larger heart rate and blood pressure responses to mental arithmetic challenge (Table) compared with the two other groups, which responded equally. There were no differences in

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n=21)</th>
<th>Group 50 (n=26)</th>
<th>Group 99 (n=22)</th>
<th>P, ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>68±16</td>
<td>67±20</td>
<td>71±17</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>115±1</td>
<td>126±2</td>
<td>134±3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>60±1</td>
<td>66±1</td>
<td>70±2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>21.4±1.7</td>
<td>23.4±3.2</td>
<td>23.0±2.9</td>
<td>.040</td>
</tr>
<tr>
<td>Plasma epinephrine, nmol/L</td>
<td>0.20±0.02</td>
<td>0.25±0.03</td>
<td>0.28±0.04</td>
<td>NS</td>
</tr>
<tr>
<td>Plasma norepinephrine, nmol/L</td>
<td>0.63±0.05</td>
<td>0.62±0.05</td>
<td>0.69±0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Mean wall thickness, cm</td>
<td>0.94±0.02</td>
<td>0.92±0.02</td>
<td>1.00±0.03</td>
<td>.013</td>
</tr>
<tr>
<td>Left ventricular mass, g</td>
<td>191±7</td>
<td>197±6</td>
<td>221±13</td>
<td>.020</td>
</tr>
<tr>
<td>Left ventricular mass index, g/cm</td>
<td>107±4</td>
<td>110±4</td>
<td>122±7</td>
<td>.029</td>
</tr>
</tbody>
</table>

Responses to mental stress*

Systolic blood pressure, %              | 19±2          | 20±2           | 30±3          | <.001   |
| Diastolic blood pressure, %            | 24±2          | 23±2           | 34±3          | .007    |
| Heart rate, %                         | 33±4          | 36±4           | 61±5          | <.001   |

Responses to cold pressor test*

Systolic blood pressure, %              | 24±2          | 21±1           | 23±2          | NS      |
| Diastolic blood pressure, %            | 30±3          | 33±2           | 32±4          | NS      |
| Heart rate, %                         | 24±4          | 21±3           | 17±3          | NS      |

bpm indicates beats per minute. Values are mean±SEM.

*Maximal percent increase from baseline to peak.
the percentage changes of plasma catecholamines among the three groups. The cardiovascular responses to the cold pressor test did not differ among the three groups (Table).

### Regression Analyses

Intra-arterial systolic blood pressure after 30 minutes of supine rest ($r=.54$, $P<.0001$; see the Figure), peak systolic blood pressure during mental arithmetic challenge ($r=.34$, $P=.006$) and cold pressor test ($r=.43$, $P<.001$), peak diastolic blood pressure during cold pressor test ($r=.29$, $P=.016$), and resting plasma epinephrine ($r=.31$, $P=.009$; Figure) were the only significant correlates of MWT. By multiple stepwise regression analyses, we found that resting systolic blood pressure and plasma epinephrine were the only independent explanatory variables of MWT ($y=0.0038x_{\text{systolic BP}}+0.44$; multiple $R^2=.33$, $P<.0001$). Blood pressure at screening, body weight, and plasma catecholamines during stress were not significant correlates. Indexing MWT for height did not change the correlations reported (MWT index versus resting systolic blood pressure: $r=.55$, $P<.0001$; MWT index versus resting arterial plasma epinephrine: $r=.32$, $P=.007$).

Resting systolic blood pressure was the only independent explanatory variable of LVM ($r=.46$, $P=.0001$) and LVMI ($r=.47$, $P=.0001$). Plasma epinephrine did not contribute significantly in these multiple-regression analyses.

### Discussion

Both left ventricular MWT and LVM were increased in 19-year-old men in the group with the highest resting intra-arterial blood pressure and cardiovascular hyperreactivity to mental stress. The only independent explanatory variables of left ventricular wall thickness were intra-arterial systolic blood pressure and arterial plasma epinephrine after 30 minutes of supine rest. Blood pressure and plasma catecholamines during mental stress and a cold pressor test and body weight did not contribute independently.

The pathogenesis of LVH is still unclear. An association between systolic blood pressure and cardiac mass was published as early as 1921 in an autopsy study by Evans. In echocardiographic studies, however, the correlations between LVM and casual blood pressure have been poor, in accordance with the present study. LVM seems to be more dependent on 24-hour ambulatory blood pressure, peak systolic blood pressure during exercise, and diastolic blood pressure during physical work. Moreover, certain humoral factors may be important as well, such as plasma norepinephrine and angiotensin. In a preliminary report from Hinderliter et al. on subjects with normal or marginally elevated blood pressure, plasma norepinephrine and LVMI has also been reported. In the present study, however, we found intra-arterial resting systolic blood pressure to be the best correlate of MWT, LVM, and LVMI. To the best of our knowledge, no studies have been published that correlate resting intra-arterial blood pressure to MWT in young, healthy men. Interestingly, Kjeldsen et al. showed that intra-arterial blood pressure after 30 minutes of supine rest correlates better to home blood pressure than to a casual clinic blood pressure. Thus, our findings may be in accordance with studies that relate LVM to daily blood pressure load.

The lack of significant correlation between blood pressure during mental stress and LVM or MWT is in accordance with a study by Schmieder et al. The best correlation they reported was found between resting systolic blood pressure and LVM ($r=.35$). In contrast, a preliminary report from Hinderliter et al. on subjects with normal or marginally elevated blood pressure suggests that systolic blood pressure during forehead cold stimulation and not at rest is the best correlate of LVM. However, it is not clear whether some of the subjects in this study were aware of their blood pressure status. We have previously demonstrated that awareness of hypertension may increase resting systolic blood pressure, thus increasing the variance. This effect may conceal a significant correlation. In the present study, the increase in standard deviation of blood pressure during the stress tests may likewise contribute to the reduced Pearson correlations seen between stress blood pressure and LVM or MWT. A preliminary report from McCaffrey et al. in children seems to support the work of Hinderliter et al.

Plasma epinephrine was the other independent determinant of MWT. Catecholamines have been suggested as trophic factors, which is in accordance with the present study. However, a negative relation between plasma norepinephrine and LVMI has also been reported. We did not find any independent contribution of body weight, which in some studies has been considered an important correlate. Overweight may contribute to development of eccentric hypertrophy, and as overweight and hypertension are closely related, they may...
represent a synergistic burden on the heart.27 The lack of such a correlation in the present study may be due to a narrow distribution of body weight in our population. All subjects had body mass indexes within the normal range.

Isometric exercise such as weight lifting might induce concentric hypertrophy of the left ventricle because of increased afterload. In contrast, endurance training is associated with left ventricular enlargement rather than wall thickening.28-30 No subjects in our population took a cold pressor test does not contribute to increased blood pressure after 30 minutes of supine rest and resting heart rate were recorded continuously, the maximal responses may also be more easily registered than with the cuff method.

The present study suggests that intra-arterial blood pressure after 30 minutes of supine rest and resting plasma epinephrine may be of importance for development of such a correlation in the present study may be due to a narrow distribution of body weight in our population. All subjects had body mass indexes within the normal range.

Acknowledgments

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References


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