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.

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

cardiogram (ECG), routine blood tests, and urinalysis. None were on medical treatment or abused drugs or alcohol, as evaluated by thorough history and liver enzymes. All the subjects were sedentary. None took part in any rigorous endurance or isometric training.

Body mass index, baseline heart rate, and intra-arterial blood pressure after 30 minutes of supine rest in our laboratory are listed in the Table.

Protocol
The study was approved by the Ethics Committee of Ullevål Hospital, and informed consent was obtained from each subject. 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 abstinence from nicotine and caffeine and 24 hours of abstinence from alcohol. A short PTFE catheter (Venflon, 19G, Viggo AB, Helsingborg, 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

From the Department of Cardiology, Ullevål Hospital, University of Oslo (Norway).
Reprint requests to Morten Rostrup, MD, Department of Cardiology, Ullevål Hospital, University of Oslo, N-0407 Oslo, Norway.
Heart Rate, Blood Pressure, Body Mass Index, Plasma Catecholamines, Mean Wall Thickness, and Left Ventricular Mass in the Study Groups

<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>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<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**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=21)</th>
<th>Group 50 (n=26)</th>
<th>Group 99 (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, %</td>
<td>19±2</td>
<td>20±2</td>
<td>30±3</td>
</tr>
<tr>
<td>Diastolic blood pressure, %</td>
<td>24±2</td>
<td>23±2</td>
<td>34±3</td>
</tr>
<tr>
<td>Heart rate, %</td>
<td>33±4</td>
<td>36±4</td>
<td>61±5</td>
</tr>
</tbody>
</table>

**Responses to cold pressor test**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=21)</th>
<th>Group 50 (n=26)</th>
<th>Group 99 (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, %</td>
<td>24±2</td>
<td>21±1</td>
<td>23±2</td>
</tr>
<tr>
<td>Diastolic blood pressure, %</td>
<td>36±3</td>
<td>33±2</td>
<td>32±4</td>
</tr>
<tr>
<td>Heart rate, %</td>
<td>24±4</td>
<td>21±3</td>
<td>17±3</td>
</tr>
</tbody>
</table>

bpm indicates beats per minute. Values are mean±SEM. *Maximal percent increase from baseline to peak.

**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 principle 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. LVM was divided by height to index (LVMI) for body size as suggested by Nidorf et al. Mean wall thickness (MWT) was calculated as (interventricular septum+left ventricular posterior wall)/2. The interpretation was carried out examiner-blind by one investigator (G.S.). The intraobserver correlation and methodological error have been reported previously.

**Assays**

Plasma catecholamines were measured by a radioenzymatic technique as previously reported. On all samples, the assay was performed examiner-blind by the same technician.

**Statistics**

Data were analyzed by use of the statistical package spss-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.

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
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 ($r=0.0038 \times$ systolic blood pressure [mm Hg]+0.11 $\times$ epinephrine [nmol/L]+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 hypertreactivity 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 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 finding 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. 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. No subjects in our population took part in regular weight-lifting exercise. Thus, such factors cannot explain the differences we observed among the three groups.

The cardiovascular responses reported in the present study may seem larger than expected, but they are in accordance with a previous report from our laboratory. The large responses are probably due to the experimental design, which included an intra-arterial cannula, a metronome, and repeated sampling of blood during the arithmetic challenge. Because blood pressure and 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 LVH. Blood pressure during short-term mental stress and a cold pressor test does not contribute independently.

Acknowledgments

This study was supported by grants from the Norwegian Council on Cardiovascular Diseases, the Family Blix' Foundation, and Nanki and Sigvald Bergesen d.y. Research Foundation. We would like to thank Ruth Amundsen, Medical Department, Ulleval Hospital, for her expert assay of plasma catecholamines, and Joint Norwegian Medical Services, Headquarters Defence Command, Norway, for their generous cooperation.

References

Left ventricular mass and cardiovascular reactivity in young men.
M Rostrup, G Smith, H Bjørnstad, A Westheim, O Stokland and I Eide

_Hypertension_. 1994;23:I168
doi: 10.1161/01.HYP.23.1_Suppl.I168

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1994 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/23/1_Suppl/I168

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Hypertension_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Hypertension_ is online at:
http://hyper.ahajournals.org//subscriptions/