Correlates of Left Ventricular Mass in a Population Sample Aged 36 to 37 Years

Focus on Lifestyle and Salt Intake

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Background  Echocardiographically determined left ventricular (LV) mass predicts adverse cardiovascular events in the general population. We have assessed the correlates of LV mass in a population-based study focusing on lifestyle and salt intake.

Methods and Results  A random sample of 120 persons born in 1954 was invited; 93 (42 men) entered the study. The subjects' physical activity and alcohol, tobacco, and coffee consumption were quantified by 2-month diary follow-up, and sodium intake was quantified by 7-day food records. Blood pressure was averaged for casual cuff measurements made 2 months apart. LV mass was determined by M-mode echocardiography, and stroke volume was determined by Doppler. Hematocrit and serum insulin were measured. In multiple linear regression analysis, LV mass was related positively and independently (P<.05) to body mass, systolic blood pressure, stroke volume, sodium intake, hematocrit, and energy expenditure in leisure-time physical activity. Additional analyses showed that the relation of LV mass to daily sodium intake depended on blood pressure (P<.001 for the interaction); the multiple regression coefficient (±SE) was 0.41±0.11 g·mEq⁻¹·d⁻¹ (P=.001) in subjects with systolic blood pressure above the population median but statistically nonsignificant (−0.15±0.10 g·mEq⁻¹·d⁻¹) in those with lower blood pressure. LV mass was clearly elevated only in persons with both blood pressure and sodium intake above the population medians.

Conclusions  Body weight, blood pressure, stroke volume, sodium intake, physical activity, and hematocrit are independent predictors of LV mass among unselected persons aged 36 to 37 years. The synergistic interaction of dietary salt with blood pressure suggests that high sodium intake may sensitize the heart to the hypertrophic stimulus of pressure load. Prospective studies are needed to confirm these cross-sectional associations. (Circulation. 1994;89:1041-1050.)

Key Words  • left ventricle  • lifestyle  • blood pressure  • sodium

Echocardiographically measured left ventricular (LV) mass is an important predictor of adverse cardiovascular events in the general population. Knowledge of its determinants could help design individual and population strategies to prevent or reverse LV hypertrophy. The Framingham Heart Study has shown that age, sex, body size, blood pressure, obesity, and valvular or coronary heart disease have the most influence on the variation of LV mass across the population. Although leisure-time physical activity, alcohol consumption, smoking, and diabetes also had some effect, their role was less consistent and depended on sex or on both sex and age. Other echocardiographic studies have suggested that sodium intake, LV stroke volume and contractility, serum insulin, and blood viscosity may also contribute to the variation of LV mass. However, these studies involved clearly more selected groups of hypertensive and normotensive persons, and their results are of less universal applicability. Potentially important as it is, the association of LV mass with dietary salt has never been evaluated in any general population. We have studied a fully random sample of people born in 1954 to assess further the factors associating with the echocardiographic LV mass in univariate and multivariate analyses. Additional distinctive features of our study are that we focused on the role of such factors as salt intake, physical activity, smoking, and alcohol consumption and looked systematically for interactions between the different explanatory variables.

Methods

Subjects  All persons living in Helsinki and born in 1954 (3730 men and 4250 women) were eligible for our study. Of them, the Central Population Registry took a random sample of 120 individuals (55 men and 65 women) whom we invited by a letter explaining the aims and course of our work. If necessary, a second letter was mailed 2 to 3 weeks later. A total of 112 persons could be contacted, and 95 were willing to participate. Of those declining, 7 did not specify any reason, 5 were busy at work, 3 had medical examinations under way elsewhere, and 2 were pregnant. Each potential participant had a personal appointment with a research nurse who explained the study procedures in detail and recorded the subject's medical history, use of drugs, and presence of hypertension in next-of-kin. Details of the subject's daily work also were recorded, and the occupational physical activity graded as minimal, light, moderate, or heavy. Ninety-three persons (51 women and 42 men, 78% of the original sample) decided to enter the study. Two of them had chronic schizophrenia, and 1 had myasthenia. Seven persons had mild allergic diseases or asthma, but none used sympathomimetics or steroids regularly. Several subjects had been in surveillance for high blood pressure, but none received drugs for it. No subject had a known heart disease. One man reported effort-related chest pain, but his exercise ECG (performed by us) showed no myocardial ischemia.
Study Design

The study started with a prospective collection of lifestyle data. Each participant was given a pocket diary for recording daily activity and consumption of alcohol, tobacco, and coffee. Another diary was given for a complete 7-day food record. The subjects were asked not to change their lifestyle because of participation. After 2 months, they returned the diaries and underwent blood tests; measurement of height and weight; physical examination; 12-lead ECG; complete two-dimensional, M-mode, and Doppler echocardiographic studies; and tests for blood pressure variability. The data were subjected to statistical analyses targeted at identifying independent correlates of echocardiographic LV mass in the study population. The protocol was accepted by the local ethics committee.

Lifestyle Diary and Data Analysis

Physical Activity

Each day, the subjects recorded the type of physical activity they had practiced (e.g., walking, jogging, swimming, gardening, and so on) and its exact duration. Only leisure-time activities were noted. The energy expended was calculated as suggested by Wilson et al. by multiplying the metabolic equivalent value (MET; 1 MET = the energy expended by a person at rest, ie, 3.5 kcal · kg⁻¹ · h⁻¹) of each activity by the time (hours) spent in it. The MET values of different activities were adopted from published tables. The average energy expenditure per day of follow-up was used as a physical activity index. Supporting its usefulness, the physical activity index (MET · h/d) correlated inversely with body mass index (r = -.27, P = .010) and resting heart rate (r = -.23, P = .039) and directly with the average daily energy intake calculated from the food records (see below) (r = .24, P = .028).

Alcohol, Tobacco, and Coffee Consumption

The subjects entered into the diary the types and exact amounts of alcoholic beverages, the number of cigarettes, and the number of standard-size cups of coffee they consumed each day. The alcoholic drinks were converted to grams of absolute ethanol. The average use of ethanol, tobacco, and coffee was determined by dividing the respective total consumption by the number of follow-up days. Supporting the representativeness of the data, the calculated average daily ethanol consumption correlated directly with serum γ-glutamyltransferase measured at the end of the diary follow-up period (r = .40, P = .001).

Diet Records and Data Analysis

The data on diet were collected by means of a 7-day food record. The days were selected by the investigators and distributed evenly over the 2-month follow-up period. Each day of the week was covered once, but holidays were skipped. In addition to blank forms for recording, the subjects had model forms and written and illustrated instructions prepared by a nutritionist to ensure accurate completion of the records. The subjects returned the records to the nutritionist, who checked the food consumption entries for adequacy and asked supplemental questions if necessary. The records were analyzed for energy, nutrient, and mineral intake using commercial software (UNILEVER DIETARY ANALYSIS PROGRAM, Unilever Inc) and a database on the nutrient and mineral composition of Finnish foods. The average daily intake of sodium (mEq) was calculated for the analyses of the present work.

Laboratory Tests

Venous blood was sampled after the subjects fasted overnight. Peripheral blood count, hematocrit, blood glucose, serum electrolytes, serum creatinine, and liver enzymes were determined immediately, and the remaining serum was stored at −20°C. The serum insulin concentration was measured later using a commercial radioimmunoassay kit (Pharmacia).

Blood Pressure Measurements

The brachial artery blood pressure (Korotkoff phases I and V) was measured after a 15- to 30-minute rest using a sphygmomanometer with the subject in a sitting position. The measurement was made on the subject’s first visit to our unit and repeated twice at the echocardiographic study about 2 months later. The means of all three measurements of systolic and diastolic blood pressure were used in the analyses.

Continuous noninvasive finger arterial pressure recordings were made using an Ommeda 2300 Finapres device and commercial software (CAPS, Medikro Inc). The aim was to quantify the variability and reactivity of blood pressure in addition to its level at rest. Continuous finger arterial pressure signal was loaded into a computer first during 5 to 10 minutes of controlled respirations (15 min⁻¹) at supine rest and then during a standardized Valsalva maneuver (+40 mm Hg for 15 seconds). For our purposes, the following indexes of systolic finger blood pressure were computed: 5-minute average at rest, peak value in the overshoot phase of the Valsalva test, and the total spectral power over frequencies from 0 to 0.5 Hz (representing the beat-to-beat blood pressure variance). The details and validation of our recording technique and power spectral analyses are available elsewhere.

Echocardiography

All echocardiographic studies were made with a commercially available ultrasonograph (Aloka SSD 830) equipped with a 2.5-MHz phased-array transducer and a strip-chart recorder. The subjects were in a postabsorptive state and rested supine for 10 to 15 minutes before the recordings. Throughout the ultrasound study, they were lying in an individual left lateral position.

Determination of LV Mass

Two-dimensional imaging and color Doppler examinations were made first to look for valve diseases and segmental abnormalities of LV function. A standard M-mode LV study was recorded thereafter as detailed elsewhere. The recordings were taken at a speed of 50 mm/s together with an ECG and a phonocardiogram. The tracings were analyzed later on an xy digitizer to determine the LV cavity dimension and wall thicknesses at end diastole. All measurements were made by the leading edge–to–leading edge technique and averaged over five cycles. The analyzer had no knowledge of the subject’s other data. The LV mass was calculated using the cube formula and the correction equation of Devereux et al. The LV mass data were also normalized to body area and body height, but all correlative and regression analyses were made using the uncorrected LV mass.

Determination of Stroke Volume and Peripheral Arterial Resistance

LV stroke volume was determined as the product of the cross-sectional area and the velocity-time integral in the LV outflow tract. The diameter of the outflow tract was determined in parasternal two-dimensional views as the average of three measurements; the area was calculated by circular geometry. Pulsed wave Doppler was used to record the systolic velocities at three adjacent sites in the outflow tract as detailed elsewhere. The modal velocities were traced on the xy digitizer, and the velocity-time integral was averaged over all measured cycles (five cycles per measurement site). Peripheral arterial resistance was calculated as 10⁴ · MBP/HR · SV, where MBP is the computed 5-minute average of finger arterial mean pressure at echocardiography (mm Hg), HR is heart rate (beats per minute), and SV is stroke volume (mL).
Reproducibility

The reproducibility of our M-mode echocardiographic technique has been validated earlier. To confirm the reproducibility of the key measurements in this work, the ultrasound study was repeated 3 weeks later in six subjects. The standard deviations of the differences between the paired data were 23.5 g for the LV mass and 7.5 mL for stroke volume. The absolute difference as percentage of the mean of the two measurements was 10.8±5.3% for the LV mass and 12.7±8.7% for the stroke volume.

Statistical Analysis

Group mean values were compared by Student’s t test, ANOVA, or Mann-Whitney U test. Associations between the studied variables were tested by calculating bivariate Pearson’s product-moment or Spearman’s rank correlation coefficients. To find out the independent correlates of LV mass, multiple linear regression analyses were made. Before the analyses, all continuous variables were tested for normal distribution by Kolmogorov-Smirnov one-sample test. If the distribution was nonnormal, the data were transformed to their natural logarithms or square roots, whichever method moved the distribution closer to normality. A basic multiple regression model was first constructed for the prediction of LV mass in the total study population and in men and women separately; the variables included in these analyses are listed in “Results.” Additional analyses were performed thereafter in the total population by substituting related variables of body size or blood pressure in the basic equation. Interactions between any two explanatory variables were assessed by correlating their product term with the residuals of the model. Because an interaction of systolic blood pressure and sodium intake was found, the LV mass data were analyzed also after stratification by the median values of blood pressure and sodium intake. When necessary, the LV mass data were adjusted for factors other than sodium intake and blood pressure using the multiple regression coefficients of the basic model. The group data are given as mean±SD or as median (range), and the associations are reported as bivariate correlation coefficients, partial correlation coefficients, and multivariate regression coefficients (b) ±SE. Squared multiple correlation coefficients (R²) were also calculated. Values of P<.05 were considered statistically significant. All analyses were performed on a microcomputer using commercially available statistical software (SYSTAT Version 5.2, Systat Inc).

Results

Of the 93 participants, all except two women completed the study. The mean diary follow-up time was 64 days (range, 13 to 74 days). High-quality echocardiographic recordings were obtained in 89 subjects (42 men), and the diet records were sufficiently exact for calculation of salt intake in 85 subjects (40 men).

Study Population Characteristics

Clinical, Hemodynamic, and Echocardiographic Data

All subjects were aged 36 to 37 years. Their anthropometric characteristics are shown in Table 1. The body mass index was <20 kg/m² in 11 subjects, 20 to 25 kg/m² in 49, 25 to 30 kg/m² in 25, and >30 kg/m² in 6 subjects. Twenty-two participants (12 men) had a family history of hypertension. Clinical examination did not suggest heart disease in any subject. None had signs of significant mitral or aortic valve disease at echocardiography, but incipient dilated cardiomyopathy was considered possible in one man.

The hemodynamic and echocardiographic data are shown in Table 2. All LV measurements were different in men and women, including ratios of mass to height and mass to body area. After adjustment for height and weight in a linear regression model, sex (male, 0; female, 1) had significant influence on stroke volume (b = -6.1±2.9 mL, P = .042), sepal thickness (b = -1.4±0.4 mm, P = .001), and free wall thickness (b = 1.1±0.5 mm, P = .025) but not on end-diastolic diameter or peripheral arterial resistance.

Lifestyle Characteristics and Laboratory Data

Fifty subjects (22 men) were nonsmokers, 24 (10 men) consumed 1 to 10 cigarettes per day, and 17 (10 men) smoked more than 10 cigarettes per day (P = .21 for the sex difference). Occupational physical workload was graded minimal in 42 persons, light in 21, moderate in 22, and heavy in 3; 3 persons were not in active work. The other lifestyle data and the key laboratory measurements are summarized in Table 3. Men drank more alcohol and had higher physical activity and higher hematocrit than women. Their salt intake was also higher, but the difference was not statistically significant when the intake was calculated per body weight. All subjects had normal peripheral blood counts, serum electrolytes, creatinine, and fasting blood glucose (data not shown).

Correlates of LV Mass in Univariate Analyses and After Adjustment for Sex and Body Size

Participants with a family history of hypertension had an LV mass of 186±60 g compared with 162±42 g in the remaining population (P = .050 for sex-adjusted difference). Table 4 shows the correlation of LV mass with the anthropometric and lifestyle characteristics, and Table 5 shows the correlation with the hemodynamic and laboratory measurements. The partial correlations given in Tables 4 and 5 represent the residual association of LV mass with the studied variables after adjustment for sex, weight, and height, alone or in combinations. Table 4 shows that LV mass was related more closely to weight than to height or body mass index. Sodium intake, stroke volume, hematocrit, brachial artery systolic pressure, and peak systolic finger arterial pressure at the Valsalva test correlated statistically significantly with the LV mass even when the variation related to sex and body size was taken out (Tables 4 and 5). The association of LV mass with physical activity was significant only after adjustment for weight (Table 4). By contrast, LV mass was related to serum insulin in univariate analysis but not after adjustment for weight (Table 5).
### Table 2. Hemodynamic and Echocardiographic Measurements in Study Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Subjects (n=91)</th>
<th>Men (n=42)</th>
<th>Women (n=49)†</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>67±10</td>
<td>65±11</td>
<td>68±8</td>
<td>.093</td>
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<tr>
<td>Brachial artery blood pressure, mm Hg</td>
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<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>125±14</td>
<td>129±14</td>
<td>121±14</td>
<td>.011</td>
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<tr>
<td>Diastolic</td>
<td>80±9</td>
<td>81±9</td>
<td>79±10</td>
<td>.309</td>
</tr>
<tr>
<td>Finger arterial systolic pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-Min average</td>
<td>137±18</td>
<td>141±16</td>
<td>134±18</td>
<td>.080</td>
</tr>
<tr>
<td>Square-root total power</td>
<td>4.4±1.2</td>
<td>4.4±1.2</td>
<td>4.4±1.3</td>
<td>.830</td>
</tr>
<tr>
<td>Peak value at Valsalva test</td>
<td>179±32</td>
<td>184±35</td>
<td>174±29</td>
<td>.135</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>56±11</td>
<td>63±12</td>
<td>51±7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Peripheral arterial resistance, mm Hg · L⁻¹ · min⁻¹</td>
<td>26±6</td>
<td>24±5</td>
<td>28±6</td>
<td>.001</td>
</tr>
<tr>
<td>Left ventricular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic diameter, mm</td>
<td>49.5±4.1</td>
<td>51.2±4.6</td>
<td>48.1±3.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Septal thickness, mm</td>
<td>9.1±1.7</td>
<td>10.0±1.8</td>
<td>8.4±1.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Posterior wall thickness, mm</td>
<td>9.6±1.8</td>
<td>10.5±1.8</td>
<td>8.9±1.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mass, g</td>
<td>168±48</td>
<td>197±45</td>
<td>142±33</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mass/height, g/m²</td>
<td>97±25</td>
<td>110±25</td>
<td>86±19</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mass/body area, g/m²§</td>
<td>92±20</td>
<td>101±21</td>
<td>84±16</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

bpm indicates beats per minute. Values are mean±SD.
*P values for the sex difference.
†n=47 for the echocardiographic left ventricular measurements.
‡Left ventricular mass/height³ exceeded 102 g/m in 7 women and 143 g/m in 4 men.
§Left ventricular mass/body area² exceeded 110 g/m² in 3 women and 134 g/m² in 3 men.

### Multiple Regression Analyses

**Basic Model**

To find out the independent correlates of LV mass, multiple linear regression analyses were performed with the following variables: sex (male, 0; female, 1), height, weight, body mass index category (<20 kg/m², −1; 20 to 25 kg/m², 0; 25 to 30 kg/m², 1; >30 kg/m², 2), family history of hypertension (negative, 0; positive, 1), square-root physical activity index, occupational physical workload (minimal, 0; light, 1; moderate, 2; heavy, 3), smoking (non-smoker, 0; 1 to 10 cigarettes per day, 1; >10 cigarettes per day, 2), square-root daily ethanol consumption, daily coffee consumption, daily sodium intake, systolic brachial artery pressure, stroke volume, peripheral arterial resistance, hematocrit, and log serum insulin. The analyses were made both in all subjects and separately in men and women. The statistically significant correlates of LV mass are shown in Table 6. It is noteworthy that sex was not an independent predictor of LV mass. The factors included in the model (Table 6, all subjects) were also tested for sex interactions, but none were found, suggesting that the regression slopes were not statistically significantly different between men and women.

**Substitutes for Weight and Systolic Blood Pressure**

To study further the association of LV mass with obesity, height and body mass index were substituted

### Table 3. Lifestyle Characteristics and Laboratory Data in Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Subjects (n=91)</th>
<th>Men (n=42)</th>
<th>Women (n=49)†</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity index, MET · h/d</td>
<td>2.2 (0-14)</td>
<td>2.4 (0.2-14)</td>
<td>1.7 (0-8.8)</td>
<td>.025</td>
</tr>
<tr>
<td>Ethanol consumption, g/d</td>
<td>14.6 (0-84)</td>
<td>29.6 (0-84)</td>
<td>7.5 (0-65)</td>
<td>.005</td>
</tr>
<tr>
<td>Ethanol consumption/weight, g · kg⁻¹ · d⁻¹</td>
<td>0.21 (0-1.2)</td>
<td>0.35 (0-1.2)</td>
<td>0.13 (0-1.0)</td>
<td>.037</td>
</tr>
<tr>
<td>Coffee consumption, cups per day</td>
<td>3.5 (0-11.9)</td>
<td>3.6 (0-11.9)</td>
<td>3.4 (0-11)</td>
<td>.584</td>
</tr>
<tr>
<td>Sodium intake, mEq†</td>
<td>158±50</td>
<td>182±51</td>
<td>134±38</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sodium intake/weight, mEq · kg⁻¹ · d⁻¹</td>
<td>2.3±0.6</td>
<td>2.4±0.6</td>
<td>2.2±0.6</td>
<td>.093</td>
</tr>
<tr>
<td>Blood hematocrit, %</td>
<td>42±4</td>
<td>44±3</td>
<td>39±3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Serum insulin, mU/L</td>
<td>4.7 (1.5-30.4)</td>
<td>5.4 (1.5-30.4)</td>
<td>4.2 (1.6-19.4)</td>
<td>.159</td>
</tr>
</tbody>
</table>

MET indicates metabolic equivalent (≈1 kcal · kg⁻¹ · h⁻¹).
Values are median (range) of normally distributed data and mean±SD of normally distributed data.
*P value for the sex difference.
†Sodium intake could be estimated in 85 subjects (40 men).
TABLE 4. Correlation of Left Ventricular Mass With Anthropometric and Lifestyle Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bivariate Correlation Coefficient</th>
<th>Sex</th>
<th>Height</th>
<th>Weight</th>
<th>Sex and Height</th>
<th>Sex and Height and Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>-.59†</td>
<td>-.36†</td>
<td>-.41‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>.52†</td>
<td>.19</td>
<td></td>
<td>.24*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>.66†</td>
<td>.55†</td>
<td>.53‡</td>
<td></td>
<td>.53‡</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>.43†</td>
<td>.48†</td>
<td>.51‡</td>
<td>-.28*</td>
<td>.50‡</td>
<td>-.22*</td>
</tr>
<tr>
<td>Physical activity index§</td>
<td>.17</td>
<td>.06</td>
<td>.02</td>
<td>.33†</td>
<td>.03</td>
<td>.27*</td>
</tr>
<tr>
<td>Occupational physical workload</td>
<td>.11</td>
<td>.05</td>
<td>-.01</td>
<td>.18</td>
<td>.01</td>
<td>.14</td>
</tr>
<tr>
<td>Smoking</td>
<td>.07</td>
<td>.03</td>
<td>.06</td>
<td>.09</td>
<td>.04</td>
<td>.06</td>
</tr>
<tr>
<td>Ethanol consumption§</td>
<td>.20</td>
<td>.06</td>
<td>.17</td>
<td>.15</td>
<td>.08</td>
<td>.05</td>
</tr>
<tr>
<td>Coffee consumption</td>
<td>.01</td>
<td>.09</td>
<td>-.01</td>
<td>-.02</td>
<td>.06</td>
<td>.05</td>
</tr>
<tr>
<td>Sodium intake</td>
<td>.59†</td>
<td>.43†</td>
<td>.45‡</td>
<td>.43‡</td>
<td>.41‡</td>
<td>.35†</td>
</tr>
</tbody>
</table>

Results are based on data in 89 subjects (42 men) regarding all other variables except sodium intake, which was available in 83 subjects (40 men). The bivariate correlation coefficients are Pearson's product-moment coefficients (continuous variables) or Spearman's rank correlation coefficients (categorical variables).

*P<.05, †P<.01, ‡P<.001.
§Square-root transformed data.
Values assigned to categorical variables—sex: male, 0; female, 1; smoking: nonsmoker, 0; 1 to 10 cigarettes per day, 1; ➤10 cigarettes per day, 2; occupational physical workload: minimal, 0; light, 1; moderate, 2; heavy, 3.

TABLE 5. Correlation of Left Ventricular Mass With Hemodynamic and Laboratory Measurements

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bivariate Correlation Coefficient</th>
<th>Sex</th>
<th>Height</th>
<th>Weight</th>
<th>Sex and Height</th>
<th>Sex and Height and Weight</th>
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</thead>
<tbody>
<tr>
<td>Systolic brachial artery blood pressure</td>
<td>.40†</td>
<td>.33†</td>
<td>.44‡</td>
<td>.26*</td>
<td>.38†</td>
<td>.25*</td>
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<tr>
<td>Diastolic brachial artery blood pressure</td>
<td>.33†</td>
<td>.33†</td>
<td>.39‡</td>
<td>.19</td>
<td>.37†</td>
<td>.23*</td>
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<tr>
<td>Finger arterial systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-Min average</td>
<td>.26*</td>
<td>.22*</td>
<td>.30†</td>
<td>.24*</td>
<td>.24*</td>
<td>.21</td>
</tr>
<tr>
<td>Total power§</td>
<td>-.12</td>
<td>-.01</td>
<td>-.15</td>
<td>-.12</td>
<td>-.06</td>
<td>-.04</td>
</tr>
<tr>
<td>Peak value at the Valsalva test</td>
<td>.28†</td>
<td>.29*</td>
<td>.40‡</td>
<td>.31†</td>
<td>.34†</td>
<td>.29*</td>
</tr>
<tr>
<td>Stroke volume</td>
<td>.60†</td>
<td>.42‡</td>
<td>.44‡</td>
<td>.39‡</td>
<td>.38†</td>
<td>.31†</td>
</tr>
<tr>
<td>Peripheral arterial resistance</td>
<td>-.28†</td>
<td>-.11</td>
<td>-.09</td>
<td>-.02</td>
<td>-.07</td>
<td>-.01</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>.56†</td>
<td>.30†</td>
<td>.42‡</td>
<td>.36†</td>
<td>.29†</td>
<td>.22*</td>
</tr>
<tr>
<td>Serum insulin§</td>
<td>.28†</td>
<td>.24*</td>
<td>.26*</td>
<td>.01</td>
<td>.24*</td>
<td>.04</td>
</tr>
</tbody>
</table>

Results are based on measurements in 89 subjects. Bivariate correlation coefficients are Pearson's product-moment coefficients.

*P<.05, †P<.01, ‡P<.001.
§Square-root transformed data.
||Log-transformed data.
coefficients of sodium intake and systolic blood pressure, which now have a negative sign, cannot be used in isolation from their product term to predict LV mass. The explanatory power of the model increased from 69% to 75%.

For further analyses, the subjects were divided into groups of “low” and “high” systolic blood pressure at the population median of 121 mm Hg. Table 8 summarizes the regressions of LV mass on weight, systolic blood pressure, stroke volume, sodium intake, physical activity, and hematocrit in these groups, and Fig 1 highlights the group difference in the association of LV mass with sodium intake. Although there appeared to be differences in the regressions of LV mass on other factors, too—weight and physical activity in particular (see Table 8)—the standard errors of the coefficients were large, and these differences were not statistically significant. The subgroups by blood pressure were divided further into groups of low and high sodium intake at the population median of 148 mEq/d. Fig 2 compares the mean values of LV mass (adjusted for weight, stroke volume, physical activity, and hematocrit) across the four subgroups. Persons with both systolic blood pressure and sodium intake below the median had an LV mass of 161±20 g compared with 153±18 g in subjects with high blood pressure alone (P=.425), 165±29 g in persons with high sodium intake alone (P=.685), and 186±42 g in subjects with both high systolic blood pressure and high sodium intake (P=.004).

**Discussion**

Our study showed that as much as 75% of the cross-sectional variation in LV mass can be attributed to weight, blood pressure, stroke volume, leisure-time physical activity, sodium intake, and hematocrit in unselected persons aged 36 to 37 years. The contributions of stroke volume, sodium intake, and hematocrit were demonstrated for the first time in a population-based study. However, the most outstanding finding was the synergistic interaction of blood pressure and salt intake; LV mass was particularly high in persons whose blood pressure and salt intake were both in the upper half for the study population.

**Methodological Considerations**

Our study group was a fully random sample of people living in our area and born in 1954. The sample can be considered representative of the target population because the participation rate was close to 80%. The age criterion was used to recruit an age-homogeneous cohort with a low prevalence of heart diseases; we wanted to reduce the number of confounding factors in the statistical analyses.

The quantification of the lifestyle variables was made with 2-month prospective daily recording instead of retrospective questioning, which has been relied on in earlier studies. We aimed at obtaining as accurate lifestyle information as possible for the last 6 to 8 weeks preceding the ultrasound study because the LV mass can change within days to a few weeks of changes in physical activity or salt intake. The physical activity index that we used is similar in principle to previously described instruments, except the activity data were collected prospectively in the present study.
TABLE 8. Regression of Left Ventricular Mass on Body Weight, Systolic Blood Pressure, Stroke Volume, Sodium Intake, Physical Activity, and Hematocrit in Subjects With Systolic Brachial Artery Blood Pressure Below or Above Population Median (121 mm Hg)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Systolic Blood Pressure &lt;121 mm Hg (n=42)</th>
<th>Systolic Blood Pressure ≥121 mm Hg (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>SE</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>1.41</td>
<td>0.49</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>1.17</td>
<td>0.72</td>
</tr>
<tr>
<td>Sodium intake, mEq/d</td>
<td>-0.15</td>
<td>0.10</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>1.07</td>
<td>0.51</td>
</tr>
<tr>
<td>Physical activity index, MET·h/d</td>
<td>20.8</td>
<td>5.8</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>2.55</td>
<td>1.21</td>
</tr>
<tr>
<td>Constant, g</td>
<td>-243</td>
<td></td>
</tr>
<tr>
<td>R²</td>
<td>0.724</td>
<td></td>
</tr>
</tbody>
</table>

b indicates multiple linear regression coefficient; MET, metabolic equivalent (=1 kcal·kg⁻¹·h⁻¹); P, statistical significance of the coefficient; R², squared multiple correlation coefficient; and SE, standard error of the coefficient.

The assessment of salt intake was based on diet records designed, accepted, and analyzed by an expert nutritionist. The calculated sodium intake included not only the sodium in the natural and commercial processed foods but also the average sodium added during cooking with standard Finnish recipes. In the previous studies on salt and LV mass, sodium intake was estimated by 8 to 24-hour urine collections. We did not measure urinary sodium, but earlier research has shown that sodium intake by food records correlates well with 24-hour urinary sodium and can be used to estimate salt intake.

The key echocardiographic measurements of this study have been validated previously by other researchers. We showed, however, that the reproducibility of these methods in our hands was sufficient and comparable with the experience of other echocardiographers. Regarding the statistical methods, all main results and conclusions were derived from multivariate analyses combining men and women. Although the sex-specific regression equations were not identical (Table 6), the lack of sex interactions in the model for both sexes suggests that the regression slopes were not statistically significantly different in men and women. Admittedly, the relatively small total sample size may have limited the power of our statistical analyses (particularly in the subgroups) to identify true associations or interactions.

Correlates of LV Mass

Body Size and Obesity

Of the variables characterizing body habitus, weight predicted the LV mass better than height or body mass index. Regarding the quantitative association of LV mass with weight, the data in Tables 6 and 7 suggest that...
may reflect differences in the study groups and in the assessment of physical activity. Contrary to our prospective method, the other works estimated leisure-time activity for a 1-year period with retrospective recalls.4,26 Furthermore, the temporal relation of the ultrasound study to the period covered by the recall was not specified in either study.

**Stroke Volume**

Previous work by Ganau et al12 has suggested that stroke volume is an essential determinant of LV mass along with systolic blood pressure and contractility. Other studies, by contrast, have found no independent relation of LV mass to stroke volume in hypertensives8 or in selected hypertensive and normotensive persons.11 In our study, stroke volume predicted LV mass even after adjustment for blood pressure and several other variables, including weight as a measure of body size (see Tables 6 through 8).

**Blood Pressure and Sodium Intake**

Our data are consistent with the well-known association of LV mass with blood pressure.3,12,23 Ambulatory or exercise blood pressure may8,36 predict the LV mass better than casual readings, but such measurements could not be evaluated in this study. Instead, we used continuous finger arterial pressure monitoring to quantify the beat-to-beat variation of systolic blood pressure and its behavior in the Valsalva test. The overshoot of blood pressure after the release of strain in the Valsalva maneuver results from a sudden increase of cardiac output at a time of peripheral vasoconstriction.37 We reasoned that the resulting peak of systolic blood pressure could reflect the reactivity of blood pressure and serve as a useful predictor of the LV mass. However, the peak blood pressure at the Valsalva test was no better predictor of LV mass than the average of three casual brachial cuff measurements. The LV mass was fully unrelated to the beat-to-beat variation of the resting systolic blood pressure.

The relation of LV mass to sodium intake has been shown previously in experimental animals38 and in selected people with8,10,28 or without9 hypertension. The mechanism of this association is unknown, but direct effects of sodium on the myocyte, modulation of neurohormonal systems, and effects on the intravascular volume state have been proposed. As a novel finding, our study uncovered a synergistic interaction of sodium intake with blood pressure regarding association with LV mass. Importantly, neither blood pressure nor salt intake alone above the population median predicted an increased LV mass (Fig 2), but when both were high, the LV mass was clearly elevated. Experiments in animals have shown that a sodium-deficient diet reduces heart weight in hypertension but has no effect in normotension,38 which supports the possibility of a salt-blood pressure interaction. On the other hand, DuCaillie et al19 reported that LV mass was positively related to sodium excretion both in normotensive subjects and in hypertension. Their work was not a population-based study, however.

The mechanisms underlying the sodium-blood pressure interaction cannot be deduced from our data. However, because dietary sodium can modulate the signals for synthesis of myocardial proteins,38 we spec-

Fig 2. Bar graph of left ventricular mass in the subgroups of the activity data adjusted for sodium (Na) intake and systolic blood pressure (SBP). Group means are, from left to right, 161 g, 153 g, 165 g, and 186 g. Bars indicate standard errors. Overall statistical differences across the groups are shown. In separate comparisons, people with both Na intake and SBP above the population median (right) differed from each of the other groups (P ≤ .004), but differences across the three groups with Na intake, SBP, or both below the median were not statistically significant. Left ventricular mass data are adjusted for the effects of weight, stroke volume, physical activity, and hematocrit using the regression coefficients in Table 6 (all subjects).

Each 1-kg difference in weight could explain an average increment of 1 g in LV mass. To distinguish between the effects of body stature and obesity (weight reflects them both), we constructed an alternative model for LV mass by substituting height and body mass index category for weight. The data suggest that marked obesity (body mass index, >30 kg/m²) could explain an increment of 27 g in LV mass compared with nonobesity (body mass index, 20 to 25 kg/m²). In previous studies of hypertensive10 or mixed normotensive and hypertensive persons,31 a difference of 10 kg/m² in body mass index explained 34-410 to 45-g31 increments in the LV mass by echocardiography. In the Framingham population free of cardiopulmonary disease, the difference in age-adjusted LV mass/height between obese (body mass index, >28 kg/m²) and lean people (body mass index, <24 kg/m²) was 18 g/m² for men and 20 g/m² for women.32 Other reports also support the key role of obesity as a predictor of high LV mass.33,34

**Physical Activity**

The LV mass was associated with leisure-time physical activity more strongly in this study than has been reported previously.5,26 According to the regression coefficients (Tables 6 and 7), an energy expenditure of 2 kcal·kg⁻¹·d⁻¹ (1000 kcal/wk in a 70-kg person) could explain a 17- to 20-g increment in LV mass. The association tended to be more clear in women, although no statistically significant sex interaction was observed. In the Framingham population, a similar activity level explained only a 2.5- to 4.6-g change in LV mass in young men; no association was found in women or in older men.4 Washburn et al26 reported that expenditure of 1000 kcal/wk in leisure-time physical activity explained a 3-g/m² difference in ratio of LV mass to body area, but only men were studied. These varying results

[Graph showing data]
ulate that higher sodium intake might sensitize the heart to the hypertrophic stimulus of pressure load. Ferrara et al. have reported that the percent reduction of LV mass induced by salt depletion in hypertension increases proportionately with initial LV mass. They believed that reduction of dietary sodium might interfere with the mechanisms modifying LV mass in hypertension.

**Hematocrit**

Whole-blood viscosity has also been raised as a factor possibly influencing the LV mass. In normal adults, hematocrit is the main determinant of whole blood viscosity and explains about four fifths of its variation. We used hematocrit as a surrogate of blood viscosity and found that it was an independent although relatively weak predictor of LV mass. Each 1% difference in hematocrit could on average explain a 2.1- to 2.7-g difference in the LV mass. One earlier report on hypertensive subjects found an association of hematocrit with LV wall thickness, but not with LV mass, and another study in children showed a univariate but no multivariate association of LV mass with hematocrit.

**Other Factors**

Many although not all earlier reports have shown that men have higher LV mass than women even after adjustment for body size. We found a similar difference (see Tables 2 and 4), which, however, disappeared when the hemodynamic, lifestyle, and laboratory characteristics were included in the analysis. This suggests that the sex difference in the body size-adjusted LV mass was attributable to differences between men and women in the other independent factors of the multivariate model. It is noteworthy in this respect that systolic blood pressure, hematocrit, and physical activity were higher in men and that the sex difference in stroke volume persisted after adjustment for height and weight.

Trophioc hormonofluences on the myocardium have also been implicated as determinants of LV mass, particularly in hypertension. Evidence for their significance is weak, however. In the study of Schmieder et al., LV mass was unrelated to plasma catecholamines, renin, angiotensin, or aldosterone. Two other studies have found a relation of LV mass to plasma renin in hypertension, but, confusingly, the relation was negative in one and positive in the other. We did not assess these factors, but we showed that serum insulin does not predict LV mass independently of body weight. Finally, LV mass has been associated with smoking and alcohol intake. Our data did not confirm these findings, but we did not estimate the lifetime ethanol consumption, which has been claimed to be superior to current drinking as a predictor of LV mass. We have shown that LV mass increases with chronic alcohol abuse.

**Conclusions and Implications**

Our study shows that up to three fourths of the variation of LV mass in a population sample aged 36 to 37 years can be attributed to body weight, systolic blood pressure, stroke volume, sodium intake, leisure-time physical activity, and hematocrit. Increases of LV mass with higher values of these factors are consistent for each variable apart from sodium intake and blood pressure. The interaction of these two factors makes the relation of LV mass to salt intake critically dependent on the level of blood pressure (and vice versa). The data in Table 8 suggest that a 100-mEq/d difference upward in sodium intake could explain an increment between 19 g and 63 g (95% confidence interval) in the LV mass if the systolic blood pressure is in the upper half for the population, but a change between a 5-g increase and a 35-g decrease (ie, no systematic change) in persons with lower blood pressure. These findings are of potential epidemiological and clinical importance but suffer from the limitations of the cross-sectional design and the relatively small sample size of our study. More firm conclusions must await clinical experiments on how manipulation of dietary sodium influences LV mass in relation to blood pressure and habitual salt intake.

**Acknowledgments**

This work was supported by a grant from the Foundation for Alcohol Studies, Helsinki, Finland. We are grateful to Markku Ventila, MSc, Marjaana Lahti-Koski, MSc, Tuovi Pekuri, RN, and Soili Sirenius, RN, for help and skillful assistance during the study. The technical support of Christian Nissen, Inc, Helsinki, Finland, is also acknowledged.

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*Circulation*. 1994;89:1041-1050
doi: 10.1161/01.CIR.89.3.1041

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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