Body Composition and Prevalence of Left Ventricular Hypertrophy

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Background—Fat-free mass (FFM) has been proposed as an optimal normalization of left ventricular (LV) mass to body size. We sought to evaluate the novel FFM-based criteria of LV hypertrophy (LVH).

Methods and Results—A population sample of 1371 men and women aged 25 to 74 years was examined by echocardiography and bioelectrical impedance analysis. Internal partition values for LVH were generated in a healthy population subgroup on the basis of LV mass divided by FFM and by the traditional indexations to body height, height2.7, and body surface area. In contrast to the sex-specific criteria required by traditional indexations, the value of LV mass/FFM that divided individuals with and without LVH was identical for men and women (4.1 g/kg). Estimates of LVH prevalence varied significantly by type of indexation used, internally or externally derived cut points, and by population subgroups. Differences were pronounced among hypertensives and the obese. Thus, the application of LV mass/FFM more than halved the risk of LVH in obese versus nonobese women (odds ratio, 2.5; 95% confidence interval, 1.6 to 4.0) compared with criteria based on LV mass/height2.7 (odds ratio, 5.5; 95% confidence interval, 3.6 to 8.3). Implications among hypertensives were less marked.

Conclusions—Indexation of LV mass to FFM eliminates sex-specific LVH criteria. The proportion of individuals defined as having LVH using the new criteria deviate markedly from traditional indexations. Prospective investigations will be needed to identify the prognostic implications of different indexations, especially in subgroups such as the obese.

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Key Words: hypertrophy ■ fat-free mass ■ obesity ■ epidemiology

Clinical studies in patient groups1–5 and population-based epidemiological studies6–9 provide evidence that increased left ventricular (LV) mass is an independent risk factor for cardiovascular morbidity and mortality. The risk increases continuously as LV mass rises,4,7 with no indication of a threshold to clearly separate normal from abnormal LV mass dimensions. When defining the range of normal LV mass, individual body size and composition must be taken into consideration because metabolic demand and perfusion needs vary with stature and determine the physiological adaptation of heart size. However, the most appropriate method of adjusting LV mass for body size remains uncertain. In early reports, LV mass was commonly indexed to body surface area (BSA).5,10 To preclude a tendency to misclassify the degree of hypertrophy in the presence of obesity,11–13 indexes to body height and to exponentials of body height (named allometric signals) have been invoked to better account for the nonlinear associations of body size with LV mass.5,12–15 More recent investigations have suggested that the normalization of LV mass to fat-free mass (FFM) is theoretically an even more promising option.12,14–19 However, the assessment of FFM in larger studies has long been hampered by technical impediments. The advent of bioelectrical impedance analysis (BIA) now provides a validated20–23 and easily applicable method of measuring FFM.18,19 In the present investigation, we used BIA to compute individual FFM values, and we derived criteria for LV hypertrophy (LVH) on the basis of the values of the ratio of LV mass/FFM. We evaluated how these novel criteria compared with traditional indexation methods and how they affected the estimation of LVH prevalences in a large population sample.

Methods

Study Population
The third survey of the Monitoring of Trends and Determinants of Cardiovascular Disease (MONICA) Augsburg Project took place from October 1994 to June 1995. The Augsburg Project is part of the international collaborative World Health Organization MONICA Study.24 The study design, sampling frame, and data collection have been described in detail elsewhere.24–28 Briefly, 6640 individuals aged 25 to 74 years were randomly sampled by a 2-stage, age-
sex-stratified cluster sampling from the population registry. A total of 4856 men and women (response rate, 74.9%) participated in the study. For logistic reasons, only 2376 participants residing within or close to the city of Augsburg were offered an additional echocardiographic examination. The 826 men and 852 women who agreed to be examined had the same sex distribution as the nonresponders, but they differed in the following ways: they were younger (on average, by 3.2 years), their body-mass index (BMI) was lower (by 0.7 kg/m²), and their systolic blood pressure was lower (by 3.0 mm Hg) ($P<0.001$).

After a detailed interview, body height and weight were measured in light clothing. BMI was computed as weight divided by height squared (kg/m²). Obesity was defined according to the National Institutes of Health Consensus Development Panel criteria as a BMI ≥27.3 kg/m² in men and ≥27.8 kg/m² in women. Resting blood pressure was measured in a sitting position and after a rest of 30 minutes using a Hawksley random zero sphygmomanometer. Blood pressure was recorded 3 times in the right arm under standardized conditions, and the mean of the second and third measurement was used for this study. Hypertension was defined as a systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg or use of antihypertensive medications.

**BIA**

Fat-free mass was determined by measuring bioelectrical impedance with a Body Composition Analyzer TVI-10 (Danziger Medical Technology). Measurements were performed under highly standardized conditions with all subjects in a supine position. All measurements were performed using an alternating current with a frequency of 50 kHz and an amplitude of 800 mA. A tetrapolar placement of electrodes was used. This method has been validated in previous studies against a variety of other, more laborious techniques. Studies in children and adults have shown that BIA can be validly applied to assess body composition in epidemiological studies if proper consideration is given to population-specific characteristics. As reported previously, we used a formula derived by Heitmann. Analysis of the intraobserver and interobserver variability of BIA measurements indicated a high reliability, with coefficients of variation consistently below 1%. Body fat was calculated by subtracting FFM from total body weight (in kilograms).

**Echocardiographic Measurements**

Two-dimensional guided M-mode echocardiograms were obtained by 2 expert sonographers using the Sonos 1500 (Hewlett Packard Inc). M-mode tracings were recorded on strip-chart paper at 50 mm/s. All M-mode tracings were analyzed by a single cardiologist who was blinded regarding clinical data. All measurements were made according to the Penn convention, and left ventricular mass was calculated by the formula described by Devereux and Reichek. The rank correlation for 144 duplicate measurements of the 2 sonographers was 0.91, and there was a mean difference (systematic bias) between both observers of 0.9 g, with a SD of 10.8 g.

**Healthy Reference Group**

Using procedures analogous to a previous report from the Framingham Heart Study, a healthy reference population was defined to generate partition values for LVH. Only M-mode tracings with optimal visualization of left ventricular inferences were allowed for this study. For the 825 men and 850 women with a complete examination, the echocardiographic recordings of 161 men and 110 women were considered technically not adequate. Appropriate BIA measurements could not be obtained in 19 men and 30 women. Further exclusion criteria were as follows: (1) evidence of cardiopulmonary disease by history, physical examination, and ECG or echocardiographic evidence of valve disease (except mitral valve prolapse) (356 men and 420 women); (2) arterial blood pressure ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic (368 men and 289 women); (3) taking medications for cardiopulmonary disease (156 men and 171 women); and (4) obesity, which was defined according to the criteria described above (326 men and 334 women). A healthy reference group of 213 men and 291 women, with none of the exclusion criteria, was eventually identified.

**Statistical Methods**

There were 653 men and 718 women with a complete set of data for echocardiography, BIA measurements, and the other variables. BSA was determined according to the Dubois formula. Indexations of LV mass were obtained by computing the ratios of LV mass/height, LV mass/height², LV mass/height³, LV mass/BSA, and LV mass/FFM. Because results for LV mass/height³ were not qualitatively different from those for LV mass/height, they were not included in this report. Results for continuous variables are presented as means and SDs. Because all 4 indexed LV mass values showed an approximately normal distribution, we derived the partition values for LVH in the healthy reference group using the sex-specific mean value plus 2×SD (internal criteria). The prevalence of LVH was first estimated in the total study population by applying the internal MONICA Augsburg partition values. For comparison, prevalences were additionally computed using LVH partition values from the literature (external criteria). Sex differences were assessed by χ² tests. Prevalence estimates were further evaluated by 10-year age groups, in normotensives versus hypertensives, and in those with normal weight versus the obese. Agreement of prevalence estimates was evaluated by McNemar's test. Age-adjusted logistic regression analyses were used to determine how different indexations and criteria impacted the odds ratios for LVH in hypertension and obesity. All analysis were performed with the SAS System for Windows, release 6.11.

**Results**

Quite expectedly, the healthy reference group was substantially younger, taller, and less heavy than the total sample. The reference group had lower systolic and diastolic blood pressures, less body fat, and less LV mass. However, the values for FFM were only slightly lower in the healthy subgroup (Table 1).

The criteria for the distinction of individuals with and without LVH differed considerably by sex and type of indexation. Generally, partition values based on indexations to height, height², and BSA were higher for men than for women. In contrast, using LV mass/FFM produced a partition value of 4.1 g/kg, which was identical in men and women. We further noted that the internally derived Augsburg partition values deviated, in part substantially, from the external criteria that have been reported in other populations (Table 2).

Consequently, different indexations and criteria had a considerable impact on the estimation of LVH prevalences in the total sample. When using internal MONICA Augsburg criteria, the prevalences ranged from 16.2% to 21.6% in men and from 17.0% to 23.7% in women (Table 3). Using external cut points, prevalence estimates varied more drastically, from 12.4% to 28.6% in men and from 7.0% to 29.1% in women. Except for the external FFM criteria, all indexations estimated LVH prevalence as higher in women than in men. We noted, however, that sex differences were not statistically significant for any of the internal criteria but that LVH prevalences were significantly higher in women when using external criteria for LV mass/height and LV mass/BSA ($P<0.001$).

Internal LVH criteria were applied in all further analyses. In each age group, indexation to height or height² produced higher LVH prevalences than LV mass/FFM (Figure 1). The disagreement over all age groups was highly significant.
The present study demonstrates that varying indexations of LV mass exert a prominent influence on the proportion of subjects identified as having LVH. Indexations to FFM largely reduced sex differences in LV mass and, in this study, resulted in identical partition values for men and women with hypertrophy. Differences between indexations were present across all age groups, but they were more pronounced among the obese and in women.

We recently suggested indexing LV mass to FFM (or lean body mass) to account for variations in body size and composition. Techniques to determine FFM have improved over the years, and FFM can now be easily determined by BIA. 18 –20,30 –32

Indexation to FFM eliminates sex differences in the measurement of LV mass in children and adolescents.16,36 Thus, sex differences in cardiac size in adults may also mostly reflect differences in the hemodynamics and metabolic demands of sex. Indexations to FFM can now be easily determined by BIA.18 –20,30 –32

Table 2 summarizes the partition values for LVH using different indexations. The table shows that LVH prevalences among hypertensives were similar but less pronounced in men and women. In hypertensives and the obese, odds ratios obtained with FFM-based criteria were similar to those obtained with BIA. By contrast, prevalence estimates differed significantly among individuals with hypertension and obesity when height- and height 2.7-based LVH was compared with estimates obtained with either FFM or BSA criteria (Figure 2). In multivariate analyses including age, hypertension, and obesity as covariates, the odds of LVH using height- and height 2.7-based indexations were raised 3.5-fold in men and 5.5-fold in women when comparing obese and normal-weight individuals (Table 4). Applying FFM-based criteria, the odds ratios were reduced to 2.1 in men and 2.5 in women. The results for hypertensives were similar but less pronounced. In hypertensives and the obese, odds ratios obtained with indexations to BSA tended to be close to those obtained with FFM.

**Discussion**

The present study demonstrates that varying indexations of LV mass exert a prominent influence on the proportion of LVH.

| TABLE 1. Characteristics of the Total Study Sample and of the Healthy Reference Group |
|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|
|                                    | **Total Study Sample**                  | **Healthy Reference Group**                   |
|                                    | **Men (n=653)**                        | **Women (n=718)**                             | **Men (n=213)**                              | **Women (n=291)**                             |
| Age, y                              | 49.6±13.9                             | 49.3±13.6                                    | 41.7±11.9                                   | 41.6±11.6                                    |
| Height, cm                          | 175.0±6.2                             | 161.8±6.5                                    | 176.4±6.3                                   | 163.7±6.3                                    |
| Weight, kg                          | 82.1±10.7                             | 68.5±11.8                                    | 76.4±8.1                                    | 61.6±7.3                                     |
| BMI, kg/m²                          | 26.8±3.3                              | 26.3±4.7                                     | 24.6±2.1                                    | 23.0±2.4                                     |
| BSA, m²                             | 1.97±0.14                             | 1.72±0.14                                    | 1.93±0.12                                   | 1.67±0.11                                    |
| FFM, kg                             | 59.9±5.5                              | 43.8±4.4                                     | 58.9±4.8                                    | 43.2±3.9                                     |
| Body fat mass, kg                   | 22.1±6.8                              | 24.7±9.0                                     | 17.4±4.8                                    | 18.4±5.0                                     |
| Systolic BP, mm Hg                  | 135.9±18.6                            | 129.7±20.3                                   | 123.6±9.3                                   | 116.0±10.7                                   |
| Diastolic BP, mm Hg                 | 82.7±11.5                             | 78.1±11.1                                    | 76.7±7.4                                    | 71.3±8.1                                     |
| LV mass/height, g/m                 | 115.1±35.2                            | 88.6±29.5                                    | 97.0±20.9                                   | 71.3±18.3                                    |
| LV mass/height², g/m²               | 44.7±14.4                             | 39.4±14.0                                    | 37.0±8.0                                    | 30.9±8.3                                     |
| LV mass/BSA, g/m²                   | 101.9±28.8                            | 82.7±24.3                                    | 88.7±17.9                                   | 69.9±16.9                                    |
| LV mass/FFM, g/kg                   | 3.36±0.99                             | 3.27±1.03                                    | 2.91±0.59                                   | 2.71±0.70                                    |

Values are mean±SD. BP indicates blood pressure.

| TABLE 2. Internal and External Partition Values for LVH |
|----------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
|                                        | **Internal**                          | **External**                          | **Internal**                          | **External**                          |
|                                        | **Men**                               | **Women**                             | **Men**                               | **Women**                             |
| LV mass/height, g/m                   | 97.0±108                              | 71±104                                | 73±102                                | 102±100                               |
| LV mass/BSA, g/m²                     | 89.0±104                              | 70±104                                | 72±104                                | 100±104                               |
| LV mass/height², g/m²                 | 37.0±50†                              | 31±48†                                | 32±47†                                | 47±47†                                 |
| LV mass/FFM, g/kg                     | 2.9±4.1                               | 2.7±4.1                               | 2.7±4.1                               | 3.6±4.9‡                               |

Internal partition values were determined using the MONICA Augsburg healthy reference group; external values were from previously published reports and are provided for comparison.

*See reference 34 for details.
†See reference 12 for details.
‡See reference 19 for details; mean values were not reported.
tion. Recently, the Strong Heart Study in American Indians, which also used FFM-indexed LV mass, reported LVH criteria identical to ours.19 It must be noted, however, that this value of 4.1 g/kg was an averaged estimate derived from an LVH criterion of 4.9 g/kg in women and 3.6 g/kg in men. Thus, contrary to all previous reports, LVH criteria in the Strong Heart Study were substantially higher for women than for men. The lower body height and higher body fat content of American Indians, particularly women, may account for these striking discrepancies with our Caucasian sample.

Irrespective of age and sex, FFM indexation assigned significantly less individuals to the group with LVH than the height- and height2.7-based criteria. BSA-based estimates were closer to FFM results, but they were significantly higher with young age and significantly lower with older age. Interestingly, the frequency of LVH was similar in normotensive and normal weight subjects, irrespective of the type of indexation applied. Significant differences occurred among hypertensives and, more markedly, among the obese, especially in women. Allometric signals and indexations to height have been introduced in the past to eliminate a “forgiveness for obesity” that is supposedly associated with indexations for BSA.11,12,14,34 Our suggestion to use FFM indexations might be similarly reproached. Clearly, using a measure of adult height for indexation implicitly denies that body composition is a relevant determinant of LV mass because it ignores that weight differences in subjects of the same height can either result from a more athletic or from a more adipose body habitus. Thus, although adaptive LV mass increments in the former may be considered appropriate, they should be rated as potentially adverse in the latter instance. We contend here that only FFM indexation permits the distinction between gains of fat-free mass and those of fat mass and, thus, it can attribute changes in LV mass accordingly.

In this context, it must be noted that in obese individuals, fat mass and FFM are raised. Thus, the age-adjusted difference in FFM between obese and nonobese subjects in our study was 5 kg in men and 4.2 kg in women, with contrasting related differences in fat mass of 10 kg and 15 kg, respectively. The mechanisms underlying the rise of fat-free mass in the obese are still poorly understood, and it is not clear whether the increase of FFM in obesity and the subsequent cardiac response is indeed prognostically benign. To obtain conclusive evidence in this regard, the impacts of normalizing LV mass for FFM in obese individuals must be evaluated in prospective studies.

We attempted to replicate as closely as possible the procedures used in the Framingham Heart Study to generate criteria for LVH.34 However, our internal partition values for

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**TABLE 3. Estimated Prevalence of LVH in Total Study Sample According to the Different Partition Values Given in Table 2.**

<table>
<thead>
<tr>
<th>Indexation</th>
<th>Men (n=653)</th>
<th>Women (n=718)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal</td>
<td>External</td>
<td>Internal</td>
</tr>
<tr>
<td>Height</td>
<td>19.8%</td>
<td>17.1%</td>
</tr>
<tr>
<td>BSA</td>
<td>16.2%</td>
<td>12.4%</td>
</tr>
<tr>
<td>Height2.7</td>
<td>21.6%</td>
<td>25.0%</td>
</tr>
<tr>
<td>FFM</td>
<td>17.5%</td>
<td>28.6%</td>
</tr>
</tbody>
</table>

*P<0.001 compared with men using external criteria.

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Figure 1. Age-specific prevalence of LVH based on internal MONICA-Augsburg partition values for 4 different indexations of LV mass in men and women aged 25 to 74 years.

Figure 2. Crude prevalence of LVH based on internal MONICA-Augsburg partition values for 4 different indexations of LV mass among normotensive and hypertensive (>140/90 mm Hg or drugs) and normal weight and obese (men, ≥27.3 kg/m²; women, ≥27.8 kg/m²) men and women aged 25 to 74 years.
LV mass/BSA and LV mass/height differed notably from their cut points (Table 2). Using Framingham criteria, LVH was estimated to be significantly more frequent in women than in men. However, such a marked excess of LVH in Augsburg women does not seem very likely because hypertension and obesity, the major determinants of LVH, have been consistently more prevalent in men than in women for at least a decade.37 The internal partition values for LV mass/height22 also differed from the external criteria, especially in men. This can perhaps be explained by the fact that the external criteria were derived in a multiethnic population, of which ≈36% were African-Americans.12,14 Finally, the application of the FFM-based criteria of the Strong Heart Study led to prevalence estimates for the Augsburg sample that were highly inconsistent with all other estimates (Table 3). Our analyses suggest that the indiscriminate adoption of external criteria for LVH may be grossly misleading, and we propose using internally derived partition values whenever possible.

There are limitations to this study. In particular, technically adequate echocardiography and BIA requirements caused some selection.18 The impact of this selection is difficult to assess, but it is reassuring to note that our healthy reference group was, for most characteristics, similar to that selected in an analogous way from the Framingham Heart Study.34 We conclude that FFM seems physiologically appropriate for LV mass indexation. Its use results in significantly lower proportions of individuals with LVH in the population, in particular among hypertensives and the obese. We propose that FFM-indexed partition values of LVH be derived in other populations and that the diagnostic significance of these values, including that in subgroups such as the obese, be evaluated in prospective studies.

Acknowledgment

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2. Koren MJ, Devereux RB, Casale PN, et al. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. Ann Intern Med. 1991;114:345–352.