A 4-Tiered Classification of Left Ventricular Hypertrophy Based on Left Ventricular Geometry

The Dallas Heart Study
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Background—Left ventricular hypertrophy (LVH) is traditionally classified as concentric or eccentric, based on the ratio of LV wall thickness to chamber dimension. We propose a 4-tiered LVH classification based on LV concentricity (mass/end-diastolic volume) and indexed LV end-diastolic volume (EDV).

Methods and Results—Cardiac MRI was performed in 2803 subjects and LVH (n=895) was defined by increased LV mass/height and indexed EDV were defined at the 97.5th percentile of a healthy subpopulation. Four geometric patterns resulted: increased concentricity without increased EDV (“thick hypertrophy,” n=361); increased EDV without increased concentricity (“dilated hypertrophy,” n=53); increased concentricity with increased EDV (“both thick and dilated hypertrophy,” n=13); and neither increased concentricity nor increased EDV (“indeterminate hypertrophy,” n=468). Compared with subjects with isolated thick hypertrophy, those with both thick and dilated hypertrophy had a lower LV ejection fraction and higher NT-pro-BNP and BNP levels (P<0.001 for all). Subjects with dilated hypertrophy had a lower LV ejection fraction and higher troponin T, NT-pro-BNP, and BNP levels versus those with indeterminate hypertrophy (P<0.001 for all). Subjects with indeterminate LVH versus those without LVH had increased LV mass (by definition) but also a higher LV ejection fraction and no increase in troponin or natriuretic peptide levels.

Conclusions—Concentric or eccentric LVH can each be subclassified into 2 subgroups, yielding 4 distinct geometric patterns. Many subjects currently classified with eccentric LVH can be reclassified into an indeterminate subgroup that has better LV function and comparable levels of biomarkers reflecting cardiac stress as compared with those without LVH. (Circ Cardiovasc Imaging. 2010;3:164-171.)

Key Words: heart failure ■ hypertrophy ■ MRI ■ remodeling ■ cardiac volume

Left ventricular hypertrophy (LVH), as defined by increased ventricular mass, can occur either through ventricular dilation or wall thickening. To discriminate these patterns of hypertrophy, LVH has been subclassified based on the relative wall thickness (RWT), which is the relative thickness of the LV wall in proportion to the diameter of the ventricular chamber.1 When this ratio is increased, the hypertrophy is termed “concentric”; when this ratio is not increased, the hypertrophy is termed “eccentric.” Although this 2-tiered classification has been widely used, its ability to add prognostic information beyond simple measure of LV mass is uncertain.2–8

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In considering this issue, we noted that there are 2 potential limitations with the present 2-tiered classification of LVH. First, it does not isolate independent changes in ventricular dilation and wall thickening but rather depends on their ratio. Second, RWT relies on measurement of the LV diastolic dimension, a linear parameter, to reflect the LV volume. In part, this reflects that M-mode and 2D echocardiography are the imaging modalities used most often to assess LVH, and these modalities are better suited to measuring LV diastolic dimension than LV end-diastolic volume (EDV).

To address these limitations, we have developed a new classification of LVH based on whether or not LV concentricity (to reflect wall thickness) and LVEDV are increased. This approach leads to a 4-tiered classification of LVH: (1) increased concentricity without increased LVEDV (“thick hypertrophy”); (2) increased LVEDV without increased concentricity (“dilated hypertrophy”); (3) increased concentricity with increased LVEDV (“both thick and dilated hypertrophy”); and (4) neither increased concentricity nor increased LVEDV (“indeterminate hypertrophy”); because such subjects did not meet criteria either for significant LV dilation or increased wall thickness it could not be determined which pattern of hypertrophy predominated). Our hypothesis was that this approach would provide a more refined assessment of the geometric patterns of increased LV mass. The Dallas Heart Study (DHS) provided an ideal oppor-
tunity to address this question because subjects underwent cardiac MRI, a modality with significant advantages over 2D echocardiography in estimating LV mass\textsuperscript{10} and volumes.\textsuperscript{11} Further, because of the extensive phenotyping of DHS subjects, we were able to compare clinical characteristics and surrogate markers of risk among these 4 profiles and among those without LVH. We were specifically interested in determining whether subclassifying the present 2-tiered system would yield 4 distinct phenotypes.

Methods

Dallas Heart Study

The DHS is a population-based, multiethnic, probability sample of residents of Dallas County, designed to study subclinical cardiovascular disease. Self-reported blacks were intentionally oversampled to ensure that 50% of the final sample included this ethnic group. Details of the study design and cohort have been reported elsewhere.\textsuperscript{9} The study was approved by the University of Texas Southwestern Medical Center Institutional Review Board, and all subjects provided written informed consent. The study involved 3 separate visits. The initial in-home visit included 6101 participants and consisted of demographic and medical history data collection as well as objective measurements (including blood pressure). Participants largely in the 30- to 65-year age group were invited for a second in-home visit for collection of fasting blood and urine samples. Participants completing the second visit had a third visit, at which time ECG, cardiac MRI, electron beam CT,\textsuperscript{12} and dual-energy x-ray absorptiometry scanning studies were performed. In the early phases of DHS, 96 subjects ages 18 to 29 years were invited to participate and completed all 3 visits including the cardiac MRI and are included in this analysis. Overall, a total of 3557 and 3072 subjects completed the second and third visits, respectively. Of these, 2832 participants underwent cardiac MRI.

Cardiac MRI

Cardiac MRI was performed using 2 comparable 1.5-T MRI systems (Phillips Medical Systems, Best, The Netherlands) as described.\textsuperscript{13} Briefly, short-axis breath-hold ECG-gated cine MRI were obtained from the LV apex to base using the following parameters: 6-mm slice; 4-mm gap; field of view of 36 to 40 cm; acquired pixel size at 36-cm field of view, 1.29×2.58; and temporal resolution of 40 ms. MASS software (Medis Medical Imaging Systems, Leiden, The Netherlands) was used to analyze data. End-diastolic and end-systolic endocardial and epicardial borders were traced manually to measure LV cavity and wall volume in each slice. Myocardial mass was estimated by multiplying the myocardial wall volume at end-diastole by the specific gravity of muscle (1.05 g/mL). The papillary muscles were included in the myocardial mass and excluded from the LV volume. Measurements from each slice were summed using the method of disks. Mean LV wall thickness was determined by averaging the wall thickness of each short-axis slice (excluding the apical slice).\textsuperscript{14} LV ejection fraction (LVEF) was calculated in standard fashion from the endocardial volumes: $LVEF = \frac{100 \times (EDV - end-systolic volume)/EDV}{\text{Interobserver and intraobserver difference and interclass variability have been described.}^{15}$

Biomarker Assays

Cardiac troponin T (cTnT) (Roche Diagnostics, Inc, Indianapolis, Ind), B-type natriuretic peptide (BNP) (Biosite, Inc, San Diego, Calif) and N-terminal-pro-BNP (NT-pro-BNP) (Roche Diagnostics, Inc) were measured from thawed frozen plasma samples as reported previously.\textsuperscript{16,17}

Definition of Variables

Sex, ethnicity, and age were self-reported. Body surface area (BSA) was calculated with the use of sex-specific equations derived by Tikuisis et al.\textsuperscript{18} Diabetes mellitus was defined by a fasting serum glucose ≥126 mg/dL (≥7 mmol/L), nonfasting serum glucose ≥200 mg/dL (≥11.1 mmol/L), or self-reported diabetes with use of an antihyperglycemic medication. Hypertension was defined as a mean systolic blood pressure (SBP) from the 3 visits of ≥140 mm Hg, mean diastolic blood pressure (DBP) ≥90 mm Hg, or use of antihypertensive medication. Obesity was defined as body mass index (BMI) ≥30 kg/m\textsuperscript{2}. Coronary artery calcium was considered present when the average Agatston score was >10.\textsuperscript{12} Sex-specific threshold values for low LVEF were defined as <0.61 (women) and <0.55 (men).\textsuperscript{14} History of myocardial infarction\textsuperscript{15} and chronic heart failure or cardiomyopathy\textsuperscript{19} were defined as before.

Defining LV Geometry

Sex-specific values of LVH were defined as previously: LV mass/height\textsuperscript{2.7} ≥39 g/m\textsuperscript{2.7} (women) and ≥48 g/m\textsuperscript{2.7} (men).\textsuperscript{13} To identify wall thickening, we used a modified formula to calculate concentricity. In considering how the ratio of LV mass to volume would reflect wall thickness, we noted in a simple geometric assumption that volume = 4/3πr\textsuperscript{3}, and mass = density×surface area×thickness = density×(4πr\textsuperscript{2} thickness). Eliminating radius from these 2 equations leads to: thickness = k mass/volume\textsuperscript{2/3}, where k is a constant. In preliminary analyses, the ratio of LV mass/vol\textsuperscript{1.67} (herein termed concentricity\textsuperscript{0.67}) was more highly correlated with both LV wall thickness (sex-adjusted r\textsuperscript{2}=0.89) and systolic blood pressure (r\textsuperscript{2}=0.42) than was the standard definition of concentricity (LV mass/LVEDV) (r\textsuperscript{2}=0.69 and 0.22, respectively), and thus concentricity\textsuperscript{0.67} was used for all analyses. We defined sex-specific values for increased LVEDV/BSA and for concentricity\textsuperscript{0.67} as ≥97.5th percentile of the previously described healthy subpopulation used to define LVH\textsuperscript{10} yielding values of LVEDV/BSA: ≥68 mL/m\textsuperscript{2} (women) and ≥74 mL/m\textsuperscript{2} (men) and concentricity\textsuperscript{0.67}: ≥8.1 g/mL\textsuperscript{0.67} (women) and ≥9.1 g/mL\textsuperscript{0.67} (men). A 4-tiered classification of LVH was developed based on whether concentricity\textsuperscript{0.67} and LVEDV/BSA were increased or not using the above threshold values. To recapitulate the standard 2-tiered classification, given that we do not have the 2D measurements necessary for RWT, we classified concentric hypertrophy when concentricity\textsuperscript{0.67} was greater or equal to the above sex-specific thresholds and eccentric hypertrophy when below those values. In 3 different sensitivity analyses, we defined LVH based on LV mass/BSA using previously published values\textsuperscript{13} and defined increased indexed LVEDV using ≥97.5th percentile of the previously described healthy subpopulation for LVEDV/height (≥70.4 mL/m for women and ≥79 mL/m for men) or LVEDV/BSA\textsuperscript{1.5} [≥53.3 mL/m\textsuperscript{1.5} for women and ≥55.5 mL/m\textsuperscript{1.5} for men].

Statistical Analysis

All statistical analyses were performed with the use of SAS version 9.1 (SAS Institute, Inc, Cary, NC) statistical software. Continuous variables are expressed as mean±SD, except for BNP and NT-pro-BNP levels, which are expressed as median and interquartile ranges. Categorical variables are expressed as percentages within the geometric group. For continuous variables, statistical comparisons of variables among the LV geometric categories were tested by 1-way ANOVA except for comparisons with BNP and NT-pro-BNP, which were tested with the Kruskal-Wallis test. Differences in categorical variables among the geometric patterns were evaluated using Pearson\textsuperscript{2} χ\textsuperscript{2} test. Multiple comparisons were assessed for those variables that were statistically different across the geometric patterns by the Tukey method for continuous variables and a resampling, bootstrapping technique for categorical variables. For all statistical testing, a probability value <0.05 was considered statistically significant.

Results

Four-Tiered Classification of LVH

The resulting 4 patterns of LVH are graphically depicted and compared with the prior 2-tiered classification and with subjects without increased LV mass (Figure 1). The newly proposed 4-tiered classification subclassifies eccentric hypertrophy into...
dilated hypertrophy or indeterminate hypertrophy and subclassifies concentric hypertrophy into thick hypertrophy or both thick and dilated hypertrophy. Using this classification, there were 468 subjects with indeterminate hypertrophy, 53 with dilated hypertrophy, 361 with thick hypertrophy, and 13 with both thick and dilated hypertrophy. In a 2-tiered classification (defining concentric LVH by increased concentricity$^{0.67}$), the latter 2 groups would be classified as concentric LVH (n = 374) and the former 2 groups as eccentric hypertrophy (n = 521). Representative cardiac MRIs from subjects with each LVH pattern and from a subject without LVH are shown (Figure 2). Among those without LVH (n = 1908), 188 (9.9%) had increased concentricity$^{0.67}$ as defined, and these subjects would be analogous to those with concentric remodeling in the previous classification system.\(^1\)

### Association of LVH Pattern With Baseline Characteristics and Cardiac Structure and Function

Baseline characteristics and measures of cardiac structure and function are shown stratified by presence and type of LVH (Table). Systolic blood pressure was higher, and hypertension was more prevalent among those with thick hypertrophy (with or without LV dilation) as compared with those without thick hypertrophy. Participants with thick hypertrophy, as defined by increased concentricity$^{0.67}$ (with or without LV dilation) versus those without thick hypertrophy had a larger LV wall thickness. Participants with dilated hypertrophy (with or without thick hypertrophy) versus those without dilated hypertrophy had lower LVEF. In comparing subjects with indeterminate LVH with the other subjects with LVH, the former had a significantly lower LV mass (irrespective of indexation) and higher LVEF.

### Comparison of the 2 Newly Proposed Subgroups of Subjects With Concentric LVH and of Subjects With Eccentric LVH

To determine whether the newly created subgroups of concentric hypertrophy (thick hypertrophy versus both thick and dilated hypertrophy) or eccentric hypertrophy (indeterminate hypertrophy versus dilated hypertrophy) identified distinct phenotypes, we compared their association with various markers of cardiac stress. Subjects with both thick and dilated hypertrophy as compared with those with isolated thick hypertrophy had higher prevalence of reduced LVEF (Figure 3A). The differences in elevated troponin T levels in this comparison did not reach statistical significance ($P = 0.1$, Figure 3B), but those with both thick and dilated hypertrophy did have higher NT-pro-BNP (Figure 4A) and BNP levels (Figure 4B). Those with dilated hypertrophy as compared with those with indeterminate hypertrophy were more likely to have a reduced LVEF (Figure 3A) or elevated troponin T (Figure 3B) and had higher NT-pro-BNP (Figure 4A) and BNP levels (Figure 4B).
In comparing them with those without LVH, although the prevalence for concentricity and LVEDV/BSA, respectively, but did not meet criteria for thick or dilated hypertrophy (ie, they were not hypertrophic). Among those with indeterminate LVH, there was a higher prevalence of reduced LVEF and elevated troponin as well as higher BNP and NT-pro-BNP levels compared to those without LVH (Table and Figures 3 and 4). Further, those with indeterminate LVH versus those without LVH had an increased LVEF.

**Comparison of Subjects With Indeterminate Hypertrophy to Those Without LVH**

By definition, subjects with indeterminate LVH had increased indexed LV mass (>97.5th percentile of the healthy subpopulation) but did not meet criteria for thick or dilated hypertrophy (ie, they were not hypertrophic). Among those with indeterminate LVH, there was a higher prevalence of reduced LVEF and elevated troponin as well as higher BNP and NT-pro-BNP levels (P<0.05 for troponin; all other P<0.005).

**Table. Baseline Characteristics Stratified by Presence of LVH and 4-Tiered Geometric Pattern of LVH**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No LVH</th>
<th>Eccentric</th>
<th>Dilated</th>
<th>Thick</th>
<th>Both Thick and Dilated</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1908</td>
<td>468</td>
<td>53</td>
<td>361</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>44±10</td>
<td>44±9</td>
<td>44±10</td>
<td>48±10†∥</td>
<td>51±8‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, %</td>
<td>53†</td>
<td>14</td>
<td>47†</td>
<td>43†</td>
<td>77†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black race, %</td>
<td>41†</td>
<td>54</td>
<td>66</td>
<td>79†</td>
<td>85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>122±13†</td>
<td>128±16</td>
<td>130±20</td>
<td>145±20§</td>
<td>149±16†</td>
<td></td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>24†</td>
<td>38</td>
<td>42</td>
<td>73§</td>
<td>92‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anthypertension, % therapy</td>
<td>15‡</td>
<td>21</td>
<td>31</td>
<td>44†</td>
<td>73‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28±6†</td>
<td>36±7</td>
<td>31±8†</td>
<td>36±9§</td>
<td>34±7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obese, %</td>
<td>30†</td>
<td>78</td>
<td>47†</td>
<td>73§</td>
<td>62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Very obese (BMI ≥35), %</td>
<td>11†</td>
<td>49</td>
<td>23†</td>
<td>45∥</td>
<td>31</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>8†</td>
<td>13</td>
<td>11</td>
<td>25†</td>
<td>38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior myocardial infarction, %</td>
<td>2</td>
<td>1</td>
<td>9‡</td>
<td>6†</td>
<td>8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic heart failure/ cardiomyopathy, %</td>
<td>1†∥</td>
<td>3</td>
<td>19†</td>
<td>8‡</td>
<td>46**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery calcium present, %</td>
<td>19</td>
<td>15</td>
<td>37‡</td>
<td>37†</td>
<td>25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wall thickness, mm</td>
<td>11.2±1.6‡</td>
<td>11.4±1</td>
<td>12±1.5‡</td>
<td>14.4±2‡</td>
<td>15.2±1‡∥</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV volume, mL</td>
<td>98±22‡</td>
<td>106±21</td>
<td>176±56†</td>
<td>102±27§</td>
<td>205±59†∥</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV volume/BSA, mL/m²</td>
<td>51±10</td>
<td>54±8</td>
<td>90±27</td>
<td>49±11</td>
<td>92±23</td>
<td>By definition</td>
</tr>
<tr>
<td>LV mass/height².⁷</td>
<td>36±6</td>
<td>45±5.4</td>
<td>56±11</td>
<td>54±13</td>
<td>72±12</td>
<td>By definition</td>
</tr>
<tr>
<td>LV mass/BSA, g/m²</td>
<td>79±14†∥</td>
<td>81±12</td>
<td>115±25†</td>
<td>104±25∥</td>
<td>150±29§∥</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass/fat free mass, g/kg</td>
<td>2.8±0.3†∥</td>
<td>3.1±0.3</td>
<td>3.9±0.9†</td>
<td>3.6±0.8∥</td>
<td>4.8±0.9§∥</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Concentricity².⁷, (g/mL¹.⁶⁷)</td>
<td>7.2±1.3</td>
<td>7.2±0.8</td>
<td>7.2±1</td>
<td>10±2</td>
<td>9.6±0.7</td>
<td>By definition</td>
</tr>
<tr>
<td>Concentricity, g/mL</td>
<td>1.6±0.3</td>
<td>1.5±0.2</td>
<td>1.3±0.2</td>
<td>2.2±0.5</td>
<td>1.7±0.2</td>
<td>By definition</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>70±16†</td>
<td>79±16</td>
<td>101±27†</td>
<td>72±19‡∥</td>
<td>96±25‡∥</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>72±7†</td>
<td>75±6</td>
<td>61±18†</td>
<td>71±9§</td>
<td>51±19†∥</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LVH defined by indexation height².⁷.

*P for comparison among the 4 patterns of LVH.
†P<0.001 versus indeterminate.
‡P<0.05 versus indeterminate.
§P<0.001 versus thick.
∥P<0.05 versus thick.
¶P<0.001 versus dilated.
††LV mass/BSA and LV mass/FFM in individuals without LVH were significantly lower than those with indeterminate.

(Figure 4B). After excluding subjects with self-reported history of myocardial infarction and chronic heart failure or cardiomyopathy, those with dilated hypertrophy (n=43) versus those with indeterminate hypertrophy (n=445) still had a higher prevalence of reduced LVEF and elevated troponin as well as higher BNP and NT-pro-BNP levels (P<0.05 for troponin; all other P<0.005).

**Sensitivity Analyses to Account for Method of Indexation When Defining LVH or Increased LV Volume**

We performed 3 sensitivity analyses to verify that our findings persisted irrespective of indexation method. First, we defined LVH based on LV mass indexed to BSA rather than height².⁷. There were 2489 subjects without LVH, 44 with dilated hypertrophy, 209 with thick hypertrophy, 55 with indeterminate hypertrophy, and 13 with both thick and dilated hypertrophy with this approach. The majority of the key findings noted above with LVH defined by indexation to height².⁷ persisted.
indeterminate hypertrophy (P<0.005 for all), and those with both thick and dilated hypertrophy had higher NT-pro-BNP levels (P=0.05) and lower LVEF (P<0.001) than those with isolated thick hypertrophy. An elevated troponin T was present in 0.3% of the subjects with indeterminate hypertrophy, which was significantly lower than among the other 3 patterns (3% thick, 2% dilated, 5% both thick and dilated, P=0.005). In comparing those with indeterminate hypertrophy versus those without LVH, there was no significant difference in NT-pro-BNP (P=0.3) levels, and the former had a higher LVEF (P<0.001) than the latter.

Third, we defined increased LVEDV based on indexation to BSA1–5 rather than BSA.20 Among those subjects with LVH (defined by height2,7), there were 36 with dilated hypertrophy, 366 with thick hypertrophy, 485 with indeterminate hypertrophy, and 8 with both thick and dilated hypertrophy using this approach. Again, key findings from the primary analysis persisted including that subjects with dilated hypertrophy had higher natriuretic peptide levels, a lower LVEF, and more often had elevated troponin levels compared with those with indeterminate hypertrophy (P<0.005 for all).

Discussion

The Dallas Heart Study afforded the opportunity to refine the currently accepted 2-tiered classification of LV geometric patterns because cardiac MRI, a modality known to offer significant advantages over 2D echocardiography in estimating LV mass and volume,10,21 was performed on a large, population-based cohort. Herein we demonstrate that the present classification of LVH as concentric or eccentric can be refined into a 4-tiered classification. This refinement is based on the assessment of ventricular dilation and increased LV concentricity rather than the current practice of using the RWT. We found that subjects with eccentric LVH can be subclassified into 2 distinct groups: 1 with dilated hypertrophy and a much larger group without either thick or dilated hypertrophy (indeterminate group). Similarly, subjects with concentric LVH can be subclassified into those with thick hypertrophy and those with both thick and dilated hypertrophy. The potential utility of these subclassifications was demonstrated by finding significant differences in biomarkers reflecting pathological cardiac stress between the new subgroups, both in those presently classified as eccentric or concentric LVH. Further, these conclusions were insensitive to the method of indexation of LV mass or LVEDV.

Limitations of the Standard 2-Tiered Classification of LVH

Echocardiographic classification of LV geometry as concentric or eccentric has relied on the RWT.1 Some findings using this approach have been unexpected or suboptimal. For example, eccentric hypertrophy was more prevalent than concentric hypertrophy in hypertensive populations,1,22 contrary to the expected finding in a pressure-overloaded state. Additionally, the prognostic utility of LV geometry based on this classification beyond LV mass was uncertain.2–5,7,8 These
data suggest the possibility of a need to refine the present 2-tiered classification of LVH.

Subclassification of Eccentric LVH

When eccentric LVH was classified into 2 subgroups, based on whether LV dilation was present, 2 distinct phenotypes appeared. Subjects with dilated hypertrophy versus those with indeterminate hypertrophy had higher indexed LV mass, lower LVEF, and higher levels of natriuretic peptides, among many other differences. The association between increased LVEDV with a decline in LVEF has been emphasized.23 Where eccentric LVH was considered a lower risk profile versus concentric LVH in the old classification, such findings likely were driven by those with indeterminate hypertrophy and may not be true of those with dilated hypertrophy.

The proposed subclassification of eccentric LVH will also affect the relative frequency of thick and dilated hypertrophy in a population. Using the standard 2-tiered classification that defines eccentricity by the absence of concentricity, ≈60% of the 895 subjects with LVH in the DHS would have eccentric LVH. Other cohorts using the 2-tiered classification similarly reported an increased frequency of eccentric versus concentric hypertrophy, ranging from 1 (men) to 1.5-fold (women) in the Framingham Heart Study4 to 3.9-fold in the Cardiovascular Health Study.24 In contrast, with the newly proposed 4-tiered classification system, thick hypertrophy was 6-fold more common than dilated hypertrophy, whereas indeterminate hypertrophy was the most common geometric pattern observed. These data offer a plausible explanation as to why eccentric LVH has been reported to be more common.
than concentric LVH in prior studies of hypertensive populations.

Indeterminate Hypertrophy and Potential Implications for Defining LVH

More than 50% of subjects with LVH did not have thick or dilated hypertrophy ("indeterminate hypertrophy"). Such individuals had increased LV mass as compared with those subjects without LVH (by definition). They also had increased LV concentricity, wall thickness, and end-diastolic volume than those without LVH but not sufficient to meet the criteria for either thick or dilated hypertrophy. Further, their LV mass was lowest among the 4 LV geometric patterns (Table).

Interestingly, subjects with indeterminate hypertrophy, as compared with those subjects without LVH, were not more likely to have prevalent coronary artery calcium or elevated troponin or NT-pro-BNP or BNP levels and had a higher LVEF (Table). In sensitivity analyses, these data largely persisted regardless of indexation method for LV mass or volume. Whether these data will translate into equivalent cardiovascular risk over time in these 2 groups can only be addressed with longitudinal follow-up. Similarly, it will be important to determine whether individuals with indeterminate hypertrophy progress to develop thick or dilated hypertrophy, and, if so, to identify risk factors for those transitions. Regardless, identification of a subgroup of subjects with increased LV mass that is not associated with detectable markers of cardiac stress touches on the question on how best to define LVH. Specifically, these data raise the question as to whether pathological LVH should only be defined as present when LV mass is increased and there is evidence of thick and/or dilated hypertrophy. If such a standard was implemented in the future, then the 4-tiered classification of LVH proposed herein would be simplified to a 3-tiered classification (thick, dilated, or both thick and dilated).

Thick Hypertrophy

Concentricity $^{0.67}$ was used to define thick hypertrophy in this study. The relationship between concentricity and pressure load has been demonstrated in animals and humans.$^{25}$ In our study, thick hypertrophy was associated with increased prevalent hypertension and SBP (Table). The majority of subjects (n=361) with increased concentricity did not have dilated hypertrophy, whereas 13 subjects did have both thick and dilated hypertrophy. In addition to an increase in LV volume (required by definition), the latter subjects also had a lower LVEF (Table and Figure 3A) and higher NT-pro-BNP and BNP levels (Figure 4A and 4B) than those with isolated thick hypertrophy. It is of interest that fewer than 5% of subjects with increased concentricity also had LV dilation, data consistent with our previous observations suggesting the transition from concentric LVH to reduced systolic dysfunction is uncommon.$^{26,27}$ although we recognize the possibility of survivor bias. Whether thick hypertrophy is a precursor for combined thick and dilated hypertrophy cannot be ascertained from these cross-sectional data.

Limitations

Several limitations of this study should be noted. First, our study is cross-sectional and does not have outcome data. Therefore, we cannot determine whether the newly proposed geometric patterns convey prognostic information, despite their associations with surrogate markers of risk such as LV ejection fraction, troponin, and natriuretic peptide levels. Similarly, our data cannot address whether subjects with LVH in the absence of thick or dilated hypertrophy have comparable cardiovascular risk as compared with subjects without LVH. Second, we are unable to dissect the relative contributions of LV geometric pattern from LV mass itself. Third, internal LV diameter was not measured from the baseline MRI study and thus RWT could not be determined. As such, a direct comparison of subject allocation in the proposed DHS scheme with the current 2-tiered system of LVH classification by RWT could not be performed. Instead, we used LV concentricity $^{0.67}$ as a surrogate for RWT in such analyses and then defined eccentric LVH by the absence of elevated concentricity. Fourth, midwall shortening was not assessed, and this may have affected our assessment of systolic function in the presence of thick hypertrophy.$^{30}$ Finally, because diastolic function was not measured, we could not analyze its relationship with the proposed 4-tiered LVH classification.

Conclusions

Eccentric and concentric LVH can each be subdivided into 2 further subgroups, based on whether or not LV volume is increased. These new subgroups appear to have distinct phenotypes though longitudinal data are necessary to determine whether they convey independent prognostic information. More than one half of subjects who had increased LV mass did not meet criteria for increased LV concentricity or ventricular dilation, and these individuals did not have elevated markers of cardiac stress as compared with subjects without LVH. These data raise the question whether pathological LVH should be considered present only if LV mass is increased, and there is also evidence of increased wall thickness and/or ventricular dilation.

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New Classification of LV Geometry in LVH

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CLINICAL PERSPECTIVE

Left ventricular hypertrophy (LVH), defined as increased indexed LV mass, is presently classified based on the ratio of the LV wall thickness to chamber dimension. If this ratio is increased, then the LVH is concentric; otherwise the LVH is eccentric. We propose a 4-tiered classification based on whether or not LV concentricity0.67 (LV mass/LV end-diastolic volume0.67 [EDV]) and LVEDV/body surface area are increased. Among 2803 subjects who underwent cardiac MRI, 895 had LVH. Of these, 361 had increased concentricity0.67 but not LVEDV (“thick hypertrophy”), 53 had increased LVEDV but not concentricity0.67 (“dilated hypertrophy”), 13 had both increased concentricity0.67 and LVEDV (“both thick and dilated hypertrophy”), and 468 had neither increased concentricity0.67 nor LVEDV (“indeterminate hypertrophy”). Subjects with both thick and dilated hypertrophy had a lower LV ejection fraction and higher natriuretic peptide levels versus those with isolated thick hypertrophy. Subjects with indeterminate hypertrophy had a higher LV ejection fraction and lower troponin T and natriuretic peptide levels versus those with dilated hypertrophy and no increase in troponin T or natriuretic peptide levels versus those without LVH. We conclude that concentric and eccentric LVH can each be subclassified into 2 distinct subgroups based on the presence of LV dilation. These data question whether LVH should be considered present only if there is increased LV mass and also increased LV wall thickness and/or ventricular dilation. Refinement of the phenotypic characterization of LVH may improve our understanding of its natural history and provide an opportunity for more specific and possibly earlier therapeutic intervention.
A 4-Tiered Classification of Left Ventricular Hypertrophy Based on Left Ventricular Geometry: The Dallas Heart Study
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