Conclusions—Our investigation of a 2-generational community-based sample demonstrates familial aggregation of LV remodeling in HF.3–5

Background—Data regarding the familial aggregation of left ventricular (LV) geometry and its relations to parental heart failure (HF) are limited.

Methods and Results—We evaluated concordance of LV geometry within 1093 nuclear families in 5758 participants of the original (parents) (n=2351) and offspring (n=3407) cohorts of the Framingham Heart Study undergoing routine echocardiography in mid- to late adulthood. LV geometry was categorized based on cohort- and sex-specific 80th percentile cutoffs of LV mass and relative wall thickness (RWT) into normal (both <80th percentile), concentric remodeling (LV mass <80th percentile; RWT >80th percentile), concentric hypertrophy (both >80th percentile), and eccentric hypertrophy (LV mass >80th percentile; RWT <80th percentile). Within nuclear families, LV geometry was concordant among related pairs (parent-child, sibling-sibling) (P=0.0015) but not among unrelated spousal pairs (P=0.60), a finding that remained unchanged after adjusting for clinical covariates known to influence LV remodeling (age, systolic blood pressure, body mass index), excluding individuals with prevalent HF and myocardial infarction, and varying the thresholds for defining LV geometry. The prevalence of abnormal LV geometry was higher in family members of affected individuals, with recurrence risks of 1.4 for concentric remodeling (95% CI, 1.2 to 1.7) and eccentric hypertrophy (95% CI, 1.1 to 1.8) and 3.9 (95% CI, 3.2 to 4.6) for concentric hypertrophy. In a subset of 1497 offspring, we observed an association between parental HF (n=458) and eccentric hypertrophy in offspring (P<0.0001).

Conclusions—Our investigation of a 2-generational community-based sample demonstrates familial aggregation of LV geometry, with the greatest recurrence risk for concentric LV geometry, and establishes an association between eccentric LV geometry and parental HF. (Circ Cardiovasc Genet. 2010;3:492-498.)

Key Words: echocardiography ■ remodeling ■ risk factors

Background

Change in left ventricular (LV) geometry, or LV remodeling, is increasingly recognized as a key determinant of heart failure (HF) incidence and is associated with increased cardiovascular morbidity and mortality.1 In overt HF, LV remodeling is thought to contribute independently to disease progression beyond neurohormonal mechanisms,2 thus supporting therapeutic efforts aimed at preventing or reversing LV remodeling in HF.3–5

Clinical Perspective on p 498

In acknowledgment of the importance of LV remodeling in the evolution of HF, research efforts have focused on defining the factors that influence remodeling patterns and the resultant LV geometry in individuals. Overt diastolic and systolic HF are thought to represent different ends of a disease spectrum that may vary with regard to their underlying patterns of LV remodeling.6,7 According to this paradigm, some individuals are predisposed to develop concentric hypertrophy and diastolic HF, whereas others preferentially develop eccentric hypertrophy and systolic HF. Clinical determinants of LV remodeling, such as age, sex, blood pressure, or body size, are well defined but only partially explain the interindividual variability of LV geometry in the population. To investigate whether genetic factors also may contribute, studies have been performed in twins12–14 and...
siblings, providing evidence of familial predisposition to LV hypertrophy or increased LV mass. Of note, LV mass is only 1 of 2 principal components characterizing LV geometry. The other component is relative wall thickness (RWT), which also varies independently within the population and together with LV mass defines the 4 distinct types of LV geometric patterns: normal, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy. Each of these components (LV mass and RWT) was assessed in the Monitoring of Trends and Determinants in Cardiovascular Disease study in which “exposure” to an affected sibling with LV hypertrophy was associated with increased wall thickness and LV mass index compared to “unexposed” members of the population. However, “exposure” of concentric remodeling (without LV hypertrophy) was not assessed, parental geometry was not investigated, and individual components of LV mass and RWT were analyzed separately without determination of their conjoint effect on overall LV geometry.

Accordingly, the objectives of the present community-based investigation were to evaluate whether LV geometric patterns aggregate within nuclear families of the Framingham Heart Study and to estimate the recurrence risk of abnormal LV geometry in family members. To determine the clinical significance of any familial aggregation of LV geometry, we also examined the association between parental HF and presence of abnormal LV geometry in the offspring. We hypothesized that select LV geometric patterns would cluster within families and that such familial aggregation would be independent of age, sex, body size, or blood pressure, thereby providing evidence for a potential genetic contribution to LV remodeling in the community. We further hypothesized that offspring of parents with overt HF would have a higher prevalence of abnormal LV geometric patterns than individuals without parental HF.

Methods

Participants

As detailed previously, the Framingham Heart Study began in 1948 with the enrollment of the original cohort who undergo biennial examinations. In 1971, the Framingham Offspring Study was initiated with the recruitment of children of the original cohort as well as their spouses who are examined approximately every 4 to 8 years. Participants of both cohorts are under continuous surveillance for the development of cardiovascular disease events, including HF. All HF events are adjudicated by a panel of 3 physicians according to the Framingham HF criteria. Accordingly, the objectives of the present community-based investigation were to evaluate whether LV geometric patterns aggregate within nuclear families of the Framingham Heart Study and to estimate the recurrence risk of abnormal LV geometry in family members. To determine the clinical significance of any familial aggregation of LV geometry, we also examined the association between parental HF and presence of abnormal LV geometry in the offspring. We hypothesized that select LV geometric patterns would cluster within families and that such familial aggregation would be independent of age, sex, body size, or blood pressure, thereby providing evidence for a potential genetic contribution to LV remodeling in the community. We further hypothesized that offspring of parents with overt HF would have a higher prevalence of abnormal LV geometric patterns than individuals without parental HF.

was identified at examination cycle 6. This was a subset of offspring with both parents in the original cohort, thus ensuring that complete information regarding both parents’ HF status was available from continuous surveillance. We have previously reported an association between parental HF and LV systolic dysfunction in this subset, but the association between parental HF and abnormal LV geometry has not been previously investigated.

All participants provided written informed consent. The study protocols were approved by the Boston University Medical Center Institutional Review Board.

Characterization of LV Geometry

All participants underwent transthoracic echocardiography using standardized techniques. M-mode measurements of LV internal dimensions and LV wall thickness were made by the leading edge-to-leading edge method, with excellent reproducibility demonstrated within examination cycles. LV mass was calculated using the following formula: LV mass (g) = 0.8[(1.04(LVEDD + SWT + PWT) - (LVEDD)^2)] + 0.6, where LVEDD is the LV end-diastolic diameter, SWT is diastolic septal wall thickness, and PWT is diastolic posterior wall thickness. RWT was derived as (SWT/LVEDD).

To define LV geometry, we empirically used the sex-specific 80th percentile cutoffs for LV mass and RWT. These cutoffs were defined for each cohort separately to account for possible measurement differences because of changes in echocardiographic instrumentation from 1979 (original cohort examination 16) to 1995 (offspring cohort examination 6), temporal trends in LV mass and RWT, and other birth cohort effects. Further recognizing the known differences between sexes in heart size, sex-specific cutoffs were used as previously detailed. Thus, increased LV mass (ie, LV hypertrophy) was defined as LV mass equal to or above the sex- and cohort-specific 80th percentile of LV mass and increased RWT as RWT equal to or above the sex- and cohort-specific 80th percentile of RWT, whereas values below the respective sex- and cohort-specific 80th percentiles were regarded as normal. LV geometry was then defined as follows:

1. normal geometry (normal LV mass, normal RWT);
2. concentric remodeling (normal LV mass, increased RWT);
3. concentric hypertrophy (increased LV mass, increased RWT); and
4. eccentric hypertrophy (increased LV mass, normal RWT).

Abnormal LV geometry referred to any type of geometry other than normal geometry and therefore included concentric remodeling, concentric hypertrophy, or eccentric hypertrophy.

Statistical Analyses

Testing for Concordance in LV Geometric Pattern

In primary analyses, concordance of traits was assessed within nuclear families. The binary traits of normal and increased LV mass and normal and increased RWT were first tested individually, followed by the polychotomous trait of LV geometry (normal, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy). Concordant pairs, defined as both individuals having the same abnormal type of LV geometric pattern, were counted among parent-child relationships and among siblings. Spousal pair concordance was evaluated in a separate analysis assessing the effects of shared environmental factors. Based on the null hypothesis of no familial aggregation, testing was performed using the permutation method. For each permutation, we randomly permuted phenotypes of all individuals regardless of their family membership and computed the number of concordance pairs within nuclear families. The number of concordant pairs from all permutations then formed the null distribution. We used 10^5 permutations in each analysis to assess the probability that the observed number of concordant pairs was greater than that expected under the null hypothesis of a random
assortment of LV geometric patterns across nuclear families. To account for covariates known to influence LV geometry (age, blood pressure, and body size), we regressed age, systolic blood pressure, and body mass index in each sex and cohort stratum on LV mass or RWT and used the sex- and cohort-specific residuals to categorize LV geometry. Sensitivity analyses were performed to evaluate the effect of using different percentile cutoffs (80th, 75th, 50th percentiles) as well as recommended cutoffs by the American Society of Echocardiography17 to define each trait in concordance testing.

In secondary analyses, concordance of LV geometric pattern was assessed within sibships alone. The binary traits of increased LV mass and increased RWT were first tested individually, followed by the polychotomous trait of LV geometry. Pairs of siblings that were concordant for LV geometric pattern pairs were counted among sibships, and permutation resampling was conducted to test the null hypothesis of no familial aggregation among siblings.

Recurrence Risk Estimates

Recurrence risk ratios for abnormal LV geometry were estimated within nuclear families and sibships and defined as the risk of having an abnormal LV geometric pattern given an affected family member (with that pattern) compared to the prevalence of that geometric pattern in the general population. For the polychotomous trait of LV geometry, recurrence risk ratios were calculated using 2 definitions of the trait: (1) any abnormal LV geometry (concentric remodeling, eccentric hypertrophy, or concentric hypertrophy) and (2) each specific type of LV geometric pattern.

Table 1. Baseline Characteristics at Index Examination

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Men (Original Cohort)</th>
<th>Women (Original Cohort)</th>
<th>Men (Offspring Cohort)</th>
<th>Women (Offspring Cohort)</th>
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<tbody>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age, y</td>
<td>70±7</td>
<td>71±7</td>
<td>59±10</td>
<td>59±10</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>26.9±3.8</td>
<td>26.4±4.8</td>
<td>28.5±4.3</td>
<td>27.3±5.6</td>
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<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>139±19</td>
<td>141±21</td>
<td>130±17</td>
<td>127±20</td>
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<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>79±10</td>
<td>76±10</td>
<td>77±9</td>
<td>74±9</td>
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<td>Antihypertensive medication, %</td>
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<td>42.1</td>
<td>31.5</td>
<td>25.1</td>
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<tr>
<td>Diabetes mellitus, %</td>
<td>10.1</td>
<td>12.7</td>
<td>14.1</td>
<td>9.5</td>
</tr>
<tr>
<td>Myocardial infarction, %</td>
<td>13.8</td>
<td>4.6</td>
<td>7.4</td>
<td>1.5</td>
</tr>
<tr>
<td>HF, %</td>
<td>1.1</td>
<td>2.4</td>
<td>0.8</td>
<td>0.5</td>
</tr>
</tbody>
</table>

| Echocardiographic        |                       |                         |                        |                          |
| LV mass, g               | 202±67                | 149±46                  | 193±43                 | 140±31                   |
| RWT                      | 0.42±0.09             | 0.44±0.10               | 0.40±0.07              | 0.40±0.06                |
| LV geometry*             |                       |                         |                        |                          |
| Normal                   | 630 (67.5)            | 967 (68.2)              | 1050 (65.0)            | 1158 (64.6)              |
| Concentric remodeling    | 115 (12.3)            | 167 (11.8)              | 242 (15.0)             | 276 (15.4)               |
| Concentric hypertrophy   | 74 (7.9)              | 116 (8.2)               | 81 (5.0)               | 82 (4.6)                 |
| Eccentric hypertrophy    | 115 (12.3)            | 167 (11.8)              | 242 (15.0)             | 276 (15.4)               |

Data are presented as mean±SD or no. (%), unless otherwise indicated.

*Using the following cohort- and sex-specific 80th percentile cutoffs: original cohort LV mass, 240 g (men) and 170 g (women); original cohort RWT, 0.45 (men) and 0.51 (women); offspring cohort LV mass, 217 g (men) and 175 g (women); offspring cohort RWT 0.43 (men) and 0.42 (women).

Table 2. Concordance Within Nuclear Families

<table>
<thead>
<tr>
<th>Trait*</th>
<th>Observed/Expected Concordance Pairs</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted analyses in entire sample</td>
<td>Increased LV mass 86/64</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>Increased RWT 101/63</td>
<td>0.00001</td>
</tr>
<tr>
<td></td>
<td>Abnormal LV geometry 90/64</td>
<td>0.002</td>
</tr>
<tr>
<td>Adjusted analyses in entire sample†</td>
<td>Increased LV mass 92/64</td>
<td>0.0008</td>
</tr>
<tr>
<td></td>
<td>Increased RWT 97/65</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>Abnormal LV geometry 112/75</td>
<td>0.00005</td>
</tr>
<tr>
<td>Analyses excluding prevalent myocardial infarction and HF‡</td>
<td>Increased LV mass 77/54</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Increased RWT 88/58</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>Abnormal LV geometry 97/65</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*Traits defined using cohort- and sex-specific 80th percentile cutoffs. †Adjusting for age, body mass index, and systolic blood pressure. ‡Excluding 96, 43, and 117 for analyses using the traits increased LV mass, increased RWT, and abnormal LV geometry, respectively.

Concordance of LV Geometry

LV geometry was concordant within nuclear families, whether LV geometry was assessed as separate binary traits (normal/increased LV mass and normal/increased RWT) or as a combined polychotomous trait (Table 2). The familial concordance of LV geometry remained significant in analyses adjusting for key covariates, in analyses that excluded those with prevalent myocardial infarction and HF, and when

Association With Parental HF

In a subset analysis of 1497 offspring with known parental HF status, multivariable logistic regression was performed, where the dependent variable was parental HF and independent variables were offspring LV geometry (modeled as a categorical variable), age, sex, and body size. The authors had full access to the data and take responsibility for their integrity. All authors have read and agreed to the manuscript as written.

Results

Baseline Characteristics

The study sample included a total of 5758 participants (original cohort, 2351; offspring cohort, 3407) who attended the index examinations and provided echocardiographic data for the determination of the LV mass and RWT cohort- and sex-specific 80th percentile cutoffs. Baseline characteristics by cohort are presented in Table 1. Both parents (original cohort) and adult children (offspring cohort) were examined in mid- to late adulthood. Compared to the original cohort, offspring had larger body size and lower systolic blood pressure at index examination, likely reflecting temporal trends in these variables.27,28 In both cohorts, women had lower LV mass but similar RWT compared to men.
we evaluated sibling pairs alone (Table 3). In contrast, there was no concordance of LV geometry among spousal pairs in both cohorts (P=0.60). Familial concordance of LV geometry was maintained in analyses using different percentile cutoffs as well as cutoffs recommended by the American Society of Echocardiography to define abnormal LV mass and RWT (online-only Data Supplement).

### Recurrence Risk Ratios

The prevalence of any abnormal LV geometry (concentric remodeling, concentric hypertrophy, eccentric hypertrophy) as well as of each specific type of LV geometric pattern was higher in related family members of affected individuals than in the study population (Figure 1A). Accordingly, the recurrence risk within nuclear families was 1.2 (95% CI, 1.1 to 1.3) for any abnormal LV geometry and varied from 1.4 (95% CI, 1.1 to 1.8) for eccentric hypertrophy to 1.4 (95% CI, 1.2 to 1.7) for concentric remodeling to 3.9 (95% CI, 3.2 to 4.6) for concentric hypertrophy (Figure 1B). Similar results were seen among sibling pairs alone.

### Association With Parental HF

In the subset of 1497 offspring (mean age, 57 years; 55% women) with known parental HF status during continuous surveillance (both parents in the original cohort), the distribution of LV geometry was 990 (66%) with normal geometry, 207 (14%) with concentric remodeling, 206 (14%) with eccentric hypertrophy, and 94 (6%) with concentric hypertrophy. There was a positive association between the presence of parental HF (n=458) and any abnormal LV geometry in offspring, even after adjusting for age, sex, and height (P<0.0006). Compared to normal geometry, the odds of parental HF was significantly increased in offspring with eccentric hypertrophy, adjusting for age, sex, and height (adjusted odds ratio, 1.9; 95% CI, 1.4 to 2.7; P<0.0001) (Figure 2). The association of parental HF in offspring with concentric hypertrophy (adjusted odds ratio, 1.4; 95% CI, 0.9 to 2.2) or concentric remodeling (adjusted odds ratio, 1.1; 95% CI, 0.8 to 1.5) did not reach statistical significance. Adjusting for age, sex, body mass index, and systolic blood pressure yielded similar results (adjusted odds ratio for eccentric hypertrophy, 1.5; 95% CI, 1.1 to 2.1; P=0.011).

### Discussion

Our investigation of a large 2-generational community-based sample demonstrated familial aggregation of LV geometry. The presence of a family member with abnormal LV geometry was associated with a 20% increased odds of altered LV geometric pattern in the offspring compared to the prevalence in our study population. Specifically, there was a 40% increased odds of eccentric hypertrophy or concentric remodeling and an almost 4-fold increased odds of concentric hypertrophy among family members of individuals with the corresponding abnormal LV geometric pattern. These associations remained significant after accounting for clinical factors known to influence LV geometry, such as age, sex,
and body size. These data extend previous reports of the heritability of LV mass by establishing familial concordance of LV geometry, thus underscoring a potential contribution of familial predisposition to patterns of LV remodeling. The association between parental HF and prevalence of eccentric LV geometry in their offspring further suggests that familial factors may play a role in adverse LV remodeling and HF progression in the community.

Current guidelines strongly emphasize that HF is a progressive disorder that begins with the acquisition of clinical risk factors (stage A), involves adaptive cardiac structural changes in the absence of symptoms (stage B), and eventually leads to cardiac decompensation and the development of overt symptoms (stage C). The structural changes that occur in the heart, collectively referred to as LV remodeling, have been postulated to contribute to the pathophysiology of HF independent of neurohormonal mechanisms, shown to predict worse outcomes in natural history studies of HF, and identified as key therapeutic targets in HF.

The clinical determinants of LV remodeling have been well defined and include age, sex, blood pressure, and body size. However, these factors only partially account for the interindividual variability of LV geometry in the population.

To investigate whether genetic factors may contribute to LV remodeling, previous studies have examined the individual components of LV geometry, namely LV mass and wall thickness. Several studies in twins and in the general population have demonstrated the heritability of LV mass and wall thickness. None, however, have comprehensively examined familial clustering of LV geometric patterns or their associations with parental HF. In the Monitoring of Trends and Determinants in Cardiovascular Disease study, 319 siblings of participants with LV hypertrophy (mean age, 55 years) were compared to 636 age- and sex-matched subjects and found to have increased odds of concentric hypertrophy (odds ratio, 1.98) but not of eccentric hypertrophy. Consistent with this observation, we found the highest sibling recurrence risk with the concentric hypertrophy group. The larger estimated risk in our study (recurrence risk, 3.9) may be related to the inclusion of the full spectrum of LV geometry, older age at the time of study of our participants, differences in sample size, or possible sociogeographic differences between the study samples. Of note, by studying the aggregation of the polychotomous trait of LV geometry in families, we also were able to demonstrate familial clustering of eccentric hypertrophy and concentric remodeling in our sample, although the recurrence risks were smaller than that of concentric hypertrophy.

The relation between the presence of abnormal LV geometry in offspring and increased risk of parental HF deserves comment. We have previously shown that parental HF is associated with increased prevalence of LV systolic dysfunction cross-sectionally and increased risk of HF longitudinally in offspring. The current evidence of abnormal LV geometry in offspring with parental HF is consistent with the notion that abnormal LV remodeling may mediate the association between parental HF and development of LV systolic dysfunction or future HF in the offspring. Accordingly, the pattern of LV remodeling most strongly associated with parental HF was eccentric hypertrophy. Smaller numbers of offspring with concentric hypertrophy (n=94) compared to eccentric hypertrophy (n=206) in the former subset analysis may explain the lack of statistical significance for concentric hypertrophy in these analyses. Differences in the time course of HF progression in eccentric versus concentric remodeling also may explain these observations: concentric remodeling and diastolic HF are recognized as disorders of elderly individuals, whereas familial dilated cardiomyopathy is known to be associated with early onset systolic HF. Offspring were examined at a mean age of 57 years; hence, it is possible that at an older mean age (>75 years), when more concentric remodeling and hypertrophy may be expected, an association between concentric hypertrophy and parental HF may emerge. Similarly, an examination restricted to women (female offspring and their mothers) may be revealing because women are more prone to concentric hypertrophy and diastolic HF than men; however, our limited sample size did not allow adequately powered sex-specific analyses. Finally, the contribution of concomitant coronary heart disease to HF progression in the face of asymptomatic eccentric LV remodeling deserves further study. Overall, our data suggest an important contribution of familial factors to LV remodeling and HF progression in the community.

The strengths of our study include the large sample size, well-defined pedigrees within 2 generations, prospective community-based design, complete ascertainment of risk factors, and routine echocardiography. Limitations were the exclusively white racial make-up of our sample that limits the generalizability of findings to other ethnicities. Findings in younger or older adults also may differ from that observed in our predominantly middle-aged sample. The contribution of shared environment to familial aggregation of LV geometry
cannot be excluded, although the lack of concordance among unrelated spousal pairs suggests otherwise. Similarly, although we accounted for important factors known to influence LV geometry (age, blood pressure, body size, myocardial infarction, and HF), residual confounding by other factors may still be present. It should be recognized that our results were derived in community-based adults rather than in hospital- or clinic-based patients with HF or myocardial infarction in whom factors affecting remodeling may differ. In conclusion, familial aggregation of LV geometry was demonstrated in the large, 2-generational community-based sample of the Framingham Heart Study. These findings provide support for future studies investigating the genetic mechanisms that underlie LV remodeling and HF progression in the community.

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Disclosures
None.

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**CLINICAL PERSPECTIVE**

Left ventricular (LV) remodeling is a central process in the pathophysiology of heart failure. However, the factors that influence remodeling patterns in individuals remain unclear. Clinical determinants, such as age, sex, blood pressure, and body size, only partially explain the interindividual variability of LV geometry in the population. We investigated the role of familial factors by studying a large, 2-generational community-based sample from the Framingham Heart Study undergoing echocardiography in mid- to late adulthood. We found strong evidence of concordance of LV geometry among related pairs of individuals within nuclear families (parent-child, sibling-sibling) but not among unrelated spousal pairs. The presence of a family member with abnormal LV geometry was associated with a 20% increased odds of altered LV geometric pattern in the offspring compared to the prevalence in our study population. Specifically, there was a 40% increased odds of eccentric hypertrophy or concentric remodeling and an almost 4-fold increased odds of concentric hypertrophy among family members of individuals with the corresponding abnormal LV geometric pattern. These associations remained significant after accounting for clinical factors known to influence LV geometry. Further, there was an association between parental heart failure and prevalence of eccentric LV geometry in their offspring. These data demonstrate a potential contribution of familial predisposition to patterns of LV remodeling and suggest that familial factors may play a role in adverse LV remodeling and heart failure progression in the community.
Familial Aggregation of Left Ventricular Geometry and Association With Parental Heart Failure: The Framingham Heart Study

Carolyn S.P. Lam, Xuan Liu, Qiong Yang, Martin G. Larson, Michael J. Pencina, Jayashri Aragam, Margaret M. Redfield, Emelia J. Benjamin and Ramachandran S. Vasan

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## SUPPLEMENTAL MATERIAL

Results of sensitivity analyses for concordance among nuclear families in the entire sample

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<tr>
<th>Trait</th>
<th>Percentile</th>
<th>Cutoff</th>
<th>Observed/expected concordance pairs</th>
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<td></td>
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<td>Men, Original cohort</td>
<td>Women, Original cohort</td>
<td>Men, Offspring cohort</td>
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<tr>
<td>Increased LV mass</td>
<td>80th</td>
<td>240g</td>
<td>170g &amp; 217g</td>
<td>175g</td>
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<td></td>
<td>75th</td>
<td>226g</td>
<td>148g &amp; 195g</td>
<td>156g</td>
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<td>50th</td>
<td>228g</td>
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<td>75th</td>
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<td>0.54 &amp; 0.41</td>
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<td>50th</td>
<td>0.42</td>
<td>0.41 &amp; 0.38</td>
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<td>ASE</td>
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<td>0.42 &amp; 0.42</td>
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<td>Abnormal LV geometry</td>
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<td>170g (LV mass)</td>
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<td>140g (LV mass)</td>
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<td>ASE</td>
<td>0.42 (RWT)</td>
<td>0.41 (RWT)</td>
<td>0.38 (RWT)</td>
</tr>
</tbody>
</table>

LV, left ventricular; RWT, relative wall thickness; ASE, American Society of Echocardiography

*Adjusting for age, body mass index and blood pressure for analyses using the 80th, 75th and 50th percentile cutoffs within the sample