Cardiovascular Health Status and Incidence of Heart Failure in the Framingham Offspring Study

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Background—The American Heart Association Cardiovascular Health (CVH) score is inversely associated with cardiovascular disease, but its relations to cardiac remodeling traits and heart failure (HF) incidence have not been examined.

Methods and Results—A 14-point score was constructed for each participant based on the presence of poor, intermediate, or ideal status on each of the 7 CVH metrics (ideal score=14). We related the CVH score to echocardiographic traits cross-sectionally and to HF incidence prospectively in the Framingham Offspring Study. In age- and sex-adjusted models, a higher CVH score was associated with lower left ventricular (LV) mass, LV wall thickness, LV diastolic dimension, and left atrial dimension (P<0.01 for all; n=2392; mean age, 58 years; 56% women), and with a 12% to 15% lower odds of prevalent LV concentric remodeling and concentric hypertrophy, respectively (P<0.0001 for both). On follow-up (mean, 12.3 years), 188 incident HF events were observed in 3201 participants (mean age, 59 years; 53% women). In age- and sex-adjusted Cox proportional hazard models, the CVH score was inversely associated with HF incidence (hazard ratio per 1-point higher CVH score, 0.77; 95% confidence interval, 0.72–0.83). This association was partially attenuated upon adjustment for LV mass and inter myocardial infarction (hazard ratio, 0.84; 95% confidence interval, 0.76–0.93), and it was consistent for HF with preserved and reduced ejection fractions.

Conclusions—In our community-based sample, comprised predominantly of middle-aged white individuals of European descent, better CVH was associated with lower HF incidence, in part due to a lower prevalence of adverse cardiac remodeling. (Circ Heart Fail. 2016;9:e002416. DOI: 10.1161/CIRCHEARTFAILURE.115.002416.)

Key Words: American Heart Association ■ cardiac remodelling ■ diastole ■ heart failure ■ life style ■ myocardial infarction

It is estimated that almost 6 million Americans are currently living with heart failure (HF), a number that is projected to exceed 8 million by 2030.1 As a result of the high prevalence and substantial morbidity and mortality associated with HF, the financial burden to the healthcare system is enormous, with an estimated annual cost of $31 billion in the United States.1

Accordingly, preventing HF is integral to improving population health and reducing financial costs, which is reflected by the emphasis on prevention in recent HF practice guidelines.2,3

See Clinical Perspective

The primary modifiable risk factors for HF include high blood pressure (BP), diabetes mellitus, obesity, and smoking.4,5 Recently, investigators from the Physicians Health Study I and Women’s Health Initiative have also demonstrated associations of lifestyle factors, including healthy diet, physical activity, and moderate alcohol intake with a reduced incidence of HF in the community.6,7 Cardiovascular risk factors and unhealthy behaviors have been theorized to contribute to HF pathogenesis by promoting atherosclerotic vascular disease, myocardial infarction (MI), and adverse structural remodeling. These changes in cardiac structure and function, corresponding to stage B of the American Heart Association (AHA)/American College of Cardiology HF Stages, are best characterized by increases in left ventricular (LV) mass (LVM), left atrial dimension (LAD), and LV geometric patterns indicative of adverse remodeling (ie, concentric remodeling, concentric and eccentric hypertrophy).

Each of the aforementioned echocardiographic traits and LV geometry patterns has been related to incident HF in community-based cohorts.8–11

In 2010, the AHA announced the goals of improving cardiovascular health (CVH) by 20%, and reducing deaths from cardiovascular disease (CVD) and stroke by 20% by the year 2020.12 To achieve these objectives, the AHA has promoted a set of 7 behaviors and risk factor values (Life’s Simple 7),
including abstinence from smoking, ideal body mass index (BMI), regular physical activity, healthy diet, low untreated serum total cholesterol concentrations, optimal BP, and absence of diabetes mellitus. Together, these components comprise CVH, which is inversely associated with the risk of CVD and overall mortality in multiple reports. However, the relationship between CVH and HF has not been systematically assessed. We therefore hypothesized that CVH is inversely associated with the risk of incident HF, and that this association is partly attributable to the inverse association of CVH with the prevalence of adverse cardiac remodeling.

Methods

Study Sample
The descriptions of the history, design, and methodology of the Framingham Offspring Study (FOS) have been reported elsewhere. For this investigation, 3532 FOS participants attending the sixth examination cycle (1995–1998) were considered for inclusion, and 2 distinct samples were evaluated for analysis of echocardiographic traits and incidence of HF, respectively, as detailed below. At the sixth examination cycle (referred to as baseline for the present investigation), all attendees underwent a medical history, anthropometry, a cardiovascular-targeted physical examination, electrocardiography, echocardiography, and phlebometry for measurement of standard cardiovascular risk factors at the Framingham Heart Study (FHS) clinic. Of 3532 attendees, we initially excluded participants for serum creatinine concentration ≥2 mg/dL (n=15), BMI <18.5 kg/m² (n=62), missing components of the CVH score (n=219), or outlier laboratory values (n=1), yielding a base sample of 3255 participants. To evaluate the association between CVH and echocardiographic indices of cardiac remodeling, additional exclusions were made from the base sample for missing echocardiographic measurements (n=843), resulting in a sample of 2392 participants (sample 1). For evaluating the association between CVH and incident HF, we excluded from the base sample people with prevalent HF (n=30) and nonavailable follow-up time (n=4), resulting in a sample of 3201 participants (sample 2); this sample was larger because availability of echocardiographic measurements was not required for relating CVH score to incident HF. The Boston University Medical Center Institutional Review Board approved all study protocols. Written informed consent was provided by all participants.

AHA CVH Score
A CVH score was constructed for each participant by assigning a score of 0 (poor status), 1 (intermediate status), or 2 (ideal status) for each of the 7 metrics of CVH (Table I in the Data Supplement). The CVH score was obtained by summing these values and it can thus vary from a minimum of 0 (consistent with poor CVH) to a maximum of 14 (indicating ideal CVH). Resting BP, BMI, cholesterol, fasting blood glucose, and self-reported smoking status were measured at the FHS clinic. The physical activity index was calculated as the sum of a 24-hour period as previously described. The highest quartile of this index was used to define ideal physical activity, and values higher than the median but less than the top quartile were used to define intermediate status. Dietary quality was assessed using a food frequency questionnaire (Table I in the Data Supplement). In agreement with previous investigations, a score of ≥2 was considered to be ideal status, 1 was considered intermediate status, and 0 was considered poor status.

Echocardiographic Measurements
All attendees at the sixth FOS examination cycle (1995–1998) underwent comprehensive 2-dimensional (2D) transthoracic echocardiography with Doppler color flow imaging as described previously. Echocardiograms were read by a sonographer or a cardiologist who was blinded to clinical information. M-mode measurements, averaged over ≥3 cardiac cycles, were obtained from digitized images using the leading edge-to-leading edge technique for LAD, end-diastolic LV septal wall thickness, posterior wall thickness, and LV diameter at the end of diastole (LVDD) and LV diameter at the end of systole. Fractional shortening (FS) was calculated as: \(\text{FS} = \frac{(\text{LVDD} - \text{LV diameter at the end of systole}) \times 100}{\text{LVDD}}\). LV wall thickness was calculated by summing LV septal wall thickness and posterior wall thickness in end-diastole, and relative wall thickness (RWT) was obtained by dividing LV wall thickness by LVDD. We calculated LVM using the formula: \(\text{LVM} = 0.8 \times (\text{LVDD} + \text{posterior wall thickness} + \text{septal wall thickness})^\frac{1}{3} - \frac{1}{3} \times \text{LVDD}^\frac{1}{3}\). LV hypertrophy was determined by indexing the LVM to body surface area, and values >115 g/m² for men and >95 g/m² for women were considered abnormal. LV systolic dysfunction (LVSD) was defined by FS <29% or <20% for women. We examined the relations of CVH score with the incidence of CVD events including HF, which was defined using the FHS criteria. In brief, ascertainment of HF requires the presence of 2 major or 1 major and 2 minor criteria: major criteria include paroxysmal nocturnal dyspnea or orthopnea, increased venous pressure, distended neck veins, rales, cardiomegaly by radiograph, pulmonary edema, a third heart sound, hepatopulmonary reflex, and weight loss on diuretic therapy. The presence of ankle edema, nocturnal cough, hepatomegaly, dyspnea on exertion, pleural effusion, decrease in vital capacity, and tachycardia comprise the minor criteria. Medical records were obtained for all physician visits and hospitalizations related to CVD, and events were adjudicated by a review committee of 3 FHS physicians. The date of onset of HF was determined by the earliest onset of symptoms, or the date of hospitalization or clinic visit. In secondary analyses, we assessed the associations between CVH score and HF subtype after categorizing HF events as HF with reduced ejection fraction (HFrEF) if the ejection fraction was <45% and HF with preserved ejection fraction (HFpEF) if the ejection fraction was ≥45% based on echocardiographic reports from the index hospitalization.

Statistical Analysis
In both samples, the predictor of interest was the CVH score, which was modeled as a continuous variable in all primary analyses. Using sample 1, we examined the cross-sectional relations of the CVH score with (1) the following echocardiographic indices: LVM, LVDD, LV wall thickness, LAD, and FS in age- and sex-adjusted linear regression models; (2) the presence of LVSD and LV hypertrophy in age- and sex-adjusted logistic regression models (both binary variables); and (3) the presence of 4 LV geometric patterns (normal geometry, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy) in age- and sex-adjusted multinomial logistic regression models using generalized logits treating those with normal geometry as the referent group. Using sample 2, we evaluated the prospective association between the CVH score and HF incidence using age- and sex-adjusted Cox proportional hazard regression models, after confirming that the assumption of proportionality of hazards was met. In secondary analyses, we examined the relations of CVH score with the incidence of HFpEF and HFrEF (separate analyses for each). Fine-Gray proportional hazard models were used to account for competing risks, including the HF subtype not modeled, and indeterminate HF events (ie, HF with unavailable EF). We examined penalized cubic splines to
assess for potential nonlinearity of the associations of the CVH score with HF, and with each of the HF subtypes.

In further secondary analyses, the CVH score was modeled in categories with grouping of 0 to 7, 8 to 9, and 10 to 14 (to provide approximate tertiles), treating the lower CVH tertile (scores, 0–7) as the referent. We also analyzed the CVH score as a 7-point score with each of the 7 AHA metrics considered as a binary variable. Sensitivity analyses were performed after removing the hypertension metric from the CVH score, thus constructing a score with a maximum value of 12 points. Statistical significance was assessed based on a 2-sided P value of <0.05. The SAS Software version 9.3 (Cary, NC) was used for all analyses. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the article as written.

Results

The baseline characteristics of the larger sample (sample 2) are shown in Table 1. Participants were mostly middle-aged and overweight with a high prevalence of hypertension. Ideal CVH was present in a small proportion of participants (Figure 1). Characteristics were similar in sample 1 (Table III and Figure I in the Data Supplement).

Association Between CVH Score and Echocardiographic Traits

In cross-sectional analyses, statistically significant associations between the CVH score and several echocardiographic measures were observed (Table 2). LVM was inversely associated with CVH score, in concordance with its 2 primary components: LV wall thickness and LVDD. LAD also demonstrated an inverse association with the CVH score. No statistically significant associations were observed between the CVH score and FS, LVSD, or LV hypertrophy.

Association Between CVH Score and Geometric Patterns of Cardiac Remodeling

Normal LV geometry was present in 1283 participants (54%), concentric remodeling in 486 (20%), eccentric hypertrophy in 352 (15%), and concentric hypertrophy in 271 (11%). Each 1-point higher CVH score was associated with a 12% and 15% lower odds of concentric remodeling and concentric hypertrophy, respectively, compared with the normal geometric pattern. When the CVH score was analyzed according to categories, the higher CVH category (score, 10–14) had 42% and 54% lower odds of concentric remodeling and concentric hypertrophy, respectively, compared with the lower CVH category (score, 0–7; P<0.01 for both), Table IV in the Data Supplement. We did not observe a statistically significant association between the CVH score (continuous or categorical) and the odds of eccentric hypertrophy.

Association Between CVH Score and HF Incidence

A total of 3201 participants were followed for ≤16 years (mean, 12.3 years) and 188 individuals developed HF (5.9%). The CVH score was inversely associated with incident HF (Figure 2). For each 1-point higher CVH score, we observed a 23% lower risk of HF, adjusting for age and sex (Table 4). When the CVH score was modeled as a categorical variable, the HF hazard ratio for CVH scores of 8 to 9 and 10 to 14 was 45% and 66% lower, respectively, when compared with scores of 0 to 7 (Table V in the Data Supplement). The effect of CVH score on incident HF was partially attenuated when further adjusted for LVM and interim myocardial infarction (Table 4 models 2–4), which occurred in 250 participants (7.8%). This partial attenuation is reflected by a 35% change in the parameter estimate corresponding to the CVH score (β=−0.26 in the model adjusted for age and sex as compared with β=−0.17 in the model adjusted for age, sex, interim MI, and LVM). Further adjustments for B-type natriuretic peptide and urine albumin/creatinine ratio did not result in additional attenuation (Table 4, model 5).

Association Between CVH Score and HF Subtype

Of the 188 participants with incident HF, 85 (45.2%) developed HFPEF; 89 (47.3%) developed HFREF, and in 14 (7.5%) subjects the HF subtype was indeterminate because of an unavailable EF. Using Fine-Gray Proportional Hazard models to adjust for competing risks, the relations of the CVH score with incident HF did not vary significantly by HF subtype (Table 5; Figure II in the Data Supplement). When adjusted for interim MI, the relation between the CVH score and the HFPEF remained essentially unchanged (β=−0.22 for model adjusted for age and sex as compared with β=−0.23 in the model adjusted for age, sex, and interim MI), whereas the association of CVH score and incident HFREF was mildly attenuated (β=−0.27 for model adjusted for age and sex as compared with β=−0.21 in the model adjusted for age, sex, and interim MI).

In secondary analyses, the CVH score was modeled in categories and as a 7-point score without notable differences.

Table 1. Clinical Characteristics of Study Sample 2

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Women (n=1703)</th>
<th>Men (n=1498)</th>
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</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>58±9.6</td>
<td>59±9.6</td>
</tr>
<tr>
<td>Follow-up time, y</td>
<td>12±3</td>
<td>12±3</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>27±5.7</td>
<td>28±4.4</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>212±38</td>
<td>198±36</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>57±16</td>
<td>43±11</td>
</tr>
<tr>
<td>Lipid-lowering medication, %</td>
<td>10</td>
<td>16.3</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>100±26</td>
<td>107±28</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>7.6</td>
<td>11.9</td>
</tr>
<tr>
<td>Diabetes mellitus medication, %</td>
<td>3.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>127±20</td>
<td>129±17</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>73±9</td>
<td>77±9</td>
</tr>
<tr>
<td>Hypertensive, %</td>
<td>66.8</td>
<td>77.4</td>
</tr>
<tr>
<td>Antihypertensive medication, %</td>
<td>25.0</td>
<td>30.6</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>14.9</td>
<td>14.2</td>
</tr>
<tr>
<td>Diet score</td>
<td>1.7±0.9</td>
<td>1.4±0.9</td>
</tr>
<tr>
<td>Physical activity score</td>
<td>33.8±5.1</td>
<td>36±7.3</td>
</tr>
<tr>
<td>Biomarkers,* median (Q1–Q3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B-type natriuretic peptide, pg/mL</td>
<td>9.8 (4.0–19.6)</td>
<td>6.3 (4.0–15.9)</td>
</tr>
<tr>
<td>Urine albumin/creatinine ratio, μg/mg</td>
<td>8.5 (3.5–17.3)</td>
<td>4.8 (2.0–10.6)</td>
</tr>
<tr>
<td>CVH score (mean±SD)</td>
<td>8.7±2.2</td>
<td>8.4±2.0</td>
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</tbody>
</table>

CVH indicates cardiovascular health; HDL high-density lipoprotein; Q1, quartile 1; and Q3, quartile 3.

*Sample size for the biomarker evaluation was 2046.
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from these findings (data not shown). In addition, we performed a sensitivity analyses after removing the hypertension metric from the CVH score (thus creating a 12-point CVH score), and the results were essentially unchanged (Tables VI–IX in the Data Supplement).

Discussion

Principal Findings

The principal findings of our report are 2-fold. First, CVH was inversely associated with the prevalence of several echocardiographic traits and with concentric forms of LV geometric patterns cross-sectionally. Second, CVH was inversely associated with HF incidence prospectively, a relation that was consistent among the HF subtypes of HFPEF and HFREF, and it was partly attributable to the inverse association of CVH with the presence of adverse LV remodeling.

Comparison With Previous Studies

Ideal CVH was rare in our sample, consistent with findings from other community-based cohorts. Previous reports have demonstrated associations between CVH and a reduced incidence of cardiovascular outcomes, including stroke, cardiovascular death, and the composite of CVD. Several studies have demonstrated the beneficial effects of a healthy lifestyle on reducing HF incidence. However, these investigations focused primarily on 4 of the 7 components of the CVH score, namely: abstinence from smoking, BMI ≤25 kg/m², physical activity, and healthy diet, with 1 study also including alcohol consumption. In each of these previous reports, there was a graded and stepwise association between the positive behavior or risk factor value achieved and a reduced risk of HF. Similarly, in our study we found that each point achieved in the CVH score was associated with a lower incidence of HF. Furthermore, we observed that this association was true for both HFPEF and HFREF; previous reports did not examine the association of CVH with HF subtypes.

Mechanisms Underlying the Association of CVH With a Reduction in HF Incidence

There are several plausible pathomechanisms responsible for the increased risk of HF in those with poor CVH. First, poor CVH is known to promote atherosclerotic vascular disease and, therefore, may lead to clinical HF via reductions in the overall cardiac output. Second, poor CVH is associated with adverse LV remodeling, which may exacerbate the risk of HF. Third, poor CVH is associated with an increased risk of atrial fibrillation, which is a major risk factor for HF. Fourth, poor CVH is associated with an increased risk of stroke, which is a major cause of HF. Finally, poor CVH is associated with an increased risk of diabetes, which is a major risk factor for HF. Therefore, poor CVH is associated with an increased risk of HF via multiple mechanisms.

Table 2. Age- and Sex-Adjusted Associations Between CVH Score and Echocardiographic Measurements

<table>
<thead>
<tr>
<th>Echocardiographic Measurement</th>
<th>β Coefficient (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass, g</td>
<td>−3.88 (−4.59 to −3.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV wall thickness, mm</td>
<td>−0.27 (−0.31 to −0.23)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV diastolic dimension, mm</td>
<td>−0.15 (−0.23 to −0.06)</td>
<td>0.001</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>−0.40 (−0.49 to −0.30)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>0.00 (0.00 to 0.00)</td>
<td>0.56</td>
</tr>
<tr>
<td>LV systolic dysfunction</td>
<td>0.94 (0.86 to 1.03)</td>
<td>0.16</td>
</tr>
<tr>
<td>LV hypertrophy</td>
<td>0.96 (0.92 to 1.00)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

β coefficient values represent the mean change in echocardiographic measurement per 1-point higher CVH score. Odds ratios represent the odds of having the echocardiographic trait for each 1-point higher CVH score versus not having the trait. CVH indicates cardiovascular health; and LV, left ventricular.
in ventricular systolic and diastolic function as a result of MI. Although this sequence of events is frequently encountered in clinical practice, the association between the CVH score and HF incidence was only mildly affected by adjusting for interim MI in our study. However, when HF incidence was assessed according to HF subtype, we did observe that the magnitude of association between the CVH score and HFREF was slightly attenuated after adjusting for interim MI, whereas the association between CVH score and HFPEF was unchanged. This is consistent with previous observations that ischemic heart disease is more closely related to incident HFREF than HFPEF. Certainly, subclinical ischemic heart disease resulting in reduced cardiac function without overt MI is another possible mechanism linking incident HF with poor CVH that was not assessed by this study.

Alternatively, our findings support a second plausible pathomechanism that poor CVH promotes a program of adverse cardiac remodeling that begins as subclinical changes in cardiac structure and function (AHA/American College of Cardiology stage B HF) and eventually progresses to clinical HF (AHA/American College of Cardiology stage C HF). In our study, a lower CVH score was associated with higher LVM and LAD, and higher odds of having concentric remodeling or concentric hypertrophy. These abnormalities are associated with incident HF and may suggest a mechanistic link between the CVH score and HF incidence. This notion is further supported by the attenuation of the association between CVH score and incident HF when adjusted for LVM, suggesting that increased LVM partially attenuates the relation.

Traditional cardiovascular risk factors leading to clinical HF via subclinical remodeling is biologically plausible and,
Concentric geometric patterns of LV remodeling seem to be more related to the presence of hypertension and diabetes mellitus, whereas eccentric patterns may correlate more strongly with preserved ejection fraction (HFPEF) and heart failure with reduced ejection fraction (HFREF). This notion is supported by data from the Multiethnic Study of Atherosclerosis (MESA) cohort, in which Heckbert et al reported that ejection fraction increased with higher systolic BP until a critical point (≥180 mm Hg) after which it demonstrated an inverse relationship. Diastolic BP, in contrast, was inversely associated with ejection fraction throughout its range of values. The CVH score does not take into account this level of complexity. For example, 2 individuals would both be assigned 0 points for the BP metric even if 1 had a BP of 140/90 mm Hg and the other had a BP of 190/120 mm Hg. In addition, we used relatively crude measures of LV pump function and not more sophisticated measures of myocardial performance (such as strain rate imaging, diastolic function, torsion, and synchronicity, all of which may contribute to HF risk and may be potentially related to the CVH score).

### Strengths and Limitations

This study was performed in a large community-based sample under continuous surveillance for clinical outcomes (including HF) during a long period of follow-up. Our findings are consistent with previous reports of the relation between traditional cardiovascular risk factors and HF incidence and extend this knowledge by specifically evaluating the impact of the CVH score on HF incidence, by analyzing the HF subtypes (HFPEF and HFREF) separately, and by examining a wide range of echocardiographic measures of cardiac remodeling.

However, several limitations also merit consideration. Our sample included predominantly white, middle-aged participants of European ancestry with a high prevalence of hypertension, potentially limiting the generalizability of our findings to other age groups and ethnicities with differing risk factor distributions. In addition, the exposure (CVH score) was assessed at a single examination and, therefore, changes in the score over time could not be assessed. Similarly, the cross-sectional nature of the echocardiographic measurements limits our ability to track changes in the indices over time and may lead to a regression dilution bias, which would be expected to result in an underestimation of the true underlying associations of CVH with HF incidence are also possible and warrant further investigation. These and other novel mechanisms linking CVH with HF incidence are also possible and warrant further investigation in future reports.

Given the powerful effect of CVH score on incident HF, it is perhaps intriguing that relations were not observed between CVH score and FS, LVSD or eccentric hypertrophy. One potential explanation is that ischemic heart disease, which is more likely to lead to changes in ventricular function, LVSD, and eccentric remodeling was relatively uncommon in our middle-aged sample. In addition, the biological mechanisms underlying the associations of the CVH score with LV systolic function might be more complex than the mechanisms linking the CVH score with concentric hypertrophy. This knowledge is supported by data from the Multiethnic Study of Atherosclerosis (MESA) cohort, in which Heckbert et al reported that ejection fraction increased with higher systolic BP until a critical point (≥180 mm Hg) after which it demonstrated an inverse relationship. Diastolic BP, in contrast, was inversely associated with ejection fraction throughout its range of values. The CVH score does not take into account this level of complexity. For example, 2 individuals would both be assigned 0 points for the BP metric even if 1 had a BP of 140/90 mm Hg and the other had a BP of 190/120 mm Hg. In addition, we used relatively crude measures of LV pump function and not more sophisticated measures of myocardial performance (such as strain rate imaging, diastolic function, torsion, and synchronicity, all of which may contribute to HF risk and may be potentially related to the CVH score).

### Table 5. Associations Between CVH Score and HFPEF and HFREF

<table>
<thead>
<tr>
<th>Model</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Adjusted for age and sex</td>
<td>0.80 (0.72–0.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted for age, sex, and interim MI</td>
<td>0.80 (0.71–0.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted for age and sex</td>
<td>0.77 (0.69–0.85)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted for age, sex, and interim MI</td>
<td>0.81 (0.73–0.90)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values represent HRs for each 1-point higher CVH score. CI indicates confidence interval; CVH, cardiovascular health; HFPEF, heart failure with preserved ejection fraction; HFREF, heart failure with reduced ejection fraction; HR, hazard ratio; and MI, myocardial infarction.
with echocardiographic traits and with HF. We used M-mode echocardiography rather than 2D measurements and determined left atrial size by diameter rather than volume, both of which are potential limitations. Finally, the definitions used for diet and physical activity were extrapolated from data available from questionnaires completed at the clinical examinations and differ slightly from the AHA metrics.16

Conclusions and Future Directions
Better CVH was associated with a lower risk of HF incidence in our large community-based sample. This association was probably at least partially attributable to a lower prevalence of adverse cardiac remodeling in those with a high CVH score. Further studies are warranted to evaluate the biological mechanisms underlying the associations between CVH and adverse cardiac remodeling, as well as to assess the role for potential interventions (behavioral and pharmacological) that might assist in preventing or delaying HF events in higher risk populations. Although observational, our findings provide evidence that targeting strategies to improve CVH in the community (using the CVH score as a metric) may potentially reduce the prevalence of subclinical HF stages (stage B) and perhaps overt HF as well.

Sources of Funding
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Disclosures
None.

References


CVH might be related, in part, to a lower prevalence of adverse cardiac remodeling. HF incidence with a 23% lower hazard of HF observed per 1-point higher CVH score. The association was consistent among 3201 participants. The CVH score was inversely associated with 188 incident HF events (85 [45.2%] with preserved ejection fraction, 89 [47.3%] with reduced ejection fraction, and 14 [7.5%] with unknown ejection fraction) were observed in 3201 participants. The CVH score was inversely associated with a higher (better) CVH score was associated with lower left ventricular mass, left ventricular wall thickness, and HF incidence in the community. In this well-characterized sample of predominantly middle-aged white individuals of European descent, a higher (better) CVH score was associated with lower left ventricular mass, left ventricular wall thickness, and HF incidence. In the Framingham Heart Study, the Framingham Offspring Study. Circulation. 2010;121:667–674. doi: 10.1161/CIRCULATIONAHA.109.885806.

Heart failure (HF) is an important public health problem, and evidence regarding appropriate tools to promote HF prevention is currently limited. In 2010, the American Heart Association articulated 7 metrics of cardiovascular health (CVH) with the goal of improving CVH by 20% and as a result reducing CVD mortality by 20% by the year 2020. Using data from the Framingham Heart Study, we evaluated whether a score consisting of these 7 metrics is associated with cardiac remodeling and HF incidence in the community. In this well-characterized sample of predominantly middle-aged white individuals of European descent, a higher (better) CVH score was associated with lower left ventricular mass, left ventricular wall thickness, left ventricular diastolic dimension, and left atrial dimension, and with lower odds of concentric remodeling patterns in cross-sectional analyses (among 2392 participants with echocardiographic imaging). Over a mean follow-up of 12 years, 188 incident HF events (85 [45.2%] with preserved ejection fraction, 89 [47.3%] with reduced ejection fraction, and 14 [7.5%] with unknown ejection fraction) were observed in 3201 participants. The CVH score was inversely associated with HF incidence with a 23% lower hazard of HF observed per 1-point higher CVH score. The association was consistent among the HF subtypes of preserved versus reduced ejection fractions. These findings suggest that the American Heart Association CVH score might be a valuable tool for public health efforts to promote HF prevention, and that the benefits of improved CVH might be related, in part, to a lower prevalence of adverse cardiac remodeling.
Cardiovascular Health Status and Incidence of Heart Failure in the Framingham Offspring Study
Matthew Nayor, Danielle M. Enserro, Ramachandran S. Vasan and Vanessa Xanthakis

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http://circheartfailure.ahajournals.org/content/suppl/2015/12/23/CIRCHEARTFAILURE.115.002416.DC1

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SUPPLEMENTAL MATERIAL

Supplementary Table 1. Derivation of 14-point CVH score

Supplementary Table 2. Geometric patterns of left ventricular remodeling.

Supplementary Table 3. Clinical characteristics of study sample 1.

Supplementary Table 4. Age- and sex- adjusted associations between CVH score categories and LV geometric patterns.

Supplementary Table 5. Age- and sex- adjusted associations between CVH score categories and incident heart failure.

Supplementary Table 6. Age- and sex- adjusted associations between 12-point CVH score and echocardiographic measurements.

Supplementary Table 7. Age- and sex- adjusted associations between 12-point CVH score and LV geometric patterns.

Supplementary Table 8. Multivariable associations between 12-point CVH score and incident HF.

Supplementary Table 9. Associations between 12-point CVH score and HFPEF and HFrEF.

Supplementary Figure 1. Distribution of CVH scores in sample 1.

Supplementary Figure 2a. Age- and sex- adjusted associations between CVH score and HFpEF.

Supplementary Figure 2b. Age- and sex- adjusted associations between CVH score and HFrEF.
**Supplementary Table 1. Derivation of 14-point CVH score.**

<table>
<thead>
<tr>
<th>Goal/Metric</th>
<th>Poor Status</th>
<th>Intermediate Status</th>
<th>Ideal Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status</td>
<td>Current smoker</td>
<td>Quit ≤ 12 months ago</td>
<td>Never smoker or quit &gt;12 months ago</td>
</tr>
<tr>
<td>Body mass index</td>
<td>≥ 30 kg/m²</td>
<td>25-29.9 kg/m²</td>
<td>&lt;25 kg/m²</td>
</tr>
<tr>
<td>Physical activity score*</td>
<td>&lt; Median value</td>
<td>Median value-top quartile</td>
<td>Top quartile</td>
</tr>
<tr>
<td>Healthy diet score†</td>
<td>0 components</td>
<td>1 component</td>
<td>≥ 2 components</td>
</tr>
<tr>
<td>Serum total cholesterol</td>
<td>≥ 240 mg/dL</td>
<td>200-239 mg/dL</td>
<td>&lt; 200 mg/dL and not untreated or treated to goal or on cholesterol lowering treatment</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>SBP ≥ 140 mmHg</td>
<td>SBP 120-139 mmHg</td>
<td>SBP &lt; 120 and DBP &lt;80 mmHg and not on treatment for hypertension</td>
</tr>
<tr>
<td></td>
<td>or DBP ≥ 90 mmHg</td>
<td>or DBP 80-89 mmHg</td>
<td>or treated to goal</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>≥ 126 mg/dL</td>
<td>100-125 mg/dL or treated to goal</td>
<td>&lt;100 mg/dL and not on treatment for diabetes</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

*Median=33.4, 75th percentile=37.1

Physical activity score was calculated using the formula:

1*sleep hrs/day + 1.1*sedentary hrs/day + 1.5*slight activity hrs/day + 2.4*moderate activity hrs/day + 5*heavy activity hrs/day.

This definition is qualitatively similar to the AHA physical activity metric.
† Healthy diet score components: ≥ 4.5 cups/day fruits and vegetables, ≥ 2x3.5 oz servings/week of fish, ≥ 3x1 oz servings/day of fiber-rich whole grains, < 1500 mg/d of sodium, and < 36 oz/week of sugar sweet beverages.

In agreement with other community-based investigations, the prevalence of individuals with ≥4 components was very low (<2%) in our sample. We have therefore defined an ideal status as ≥2 components.
### Supplementary Table 2. Geometric patterns of left ventricular remodeling.

<table>
<thead>
<tr>
<th>Normal left ventricular mass*</th>
<th>High left ventricular mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal regional wall thickness†</td>
<td>Normal geometry</td>
</tr>
<tr>
<td>High regional wall thickness</td>
<td>Concentric remodeling</td>
</tr>
</tbody>
</table>

*Normal left ventricular mass: ≤115 g/m² for men and ≤95 g/m² for women.

†Normal regional wall thickness: ≤0.42
**Supplementary Table 3. Clinical characteristics of study sample 1.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Women (N=1351)</th>
<th>Men (N=1041)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58.1±9.5</td>
<td>58.2±9.7</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.8±5.1</td>
<td>28.1±3.9</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>212.0±38.8</td>
<td>198.4±36.2</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>58.5±16.1</td>
<td>43.6±11.3</td>
</tr>
<tr>
<td>Lipid lowering medication (%)</td>
<td>10.1</td>
<td>16.5</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>98.6±25.7</td>
<td>107.1±29.1</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>6.1</td>
<td>11.2</td>
</tr>
<tr>
<td>Diabetes medication (%)</td>
<td>3.2</td>
<td>6.9</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>126.0±20.3</td>
<td>129.2±17.2</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>73.7±9.2</td>
<td>76.9±9.3</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
<td>64.0</td>
<td>74.8</td>
</tr>
<tr>
<td>Antihypertensive medication (%)</td>
<td>21.8</td>
<td>30.0</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>14.2</td>
<td>13.0</td>
</tr>
<tr>
<td>Diet score</td>
<td>1.7±0.9</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>Physical activity score</td>
<td>33.8±5.0</td>
<td>36.4±7.2</td>
</tr>
<tr>
<td>Left ventricular mass (gm)</td>
<td>142.5±31.0</td>
<td>196.8±44.2</td>
</tr>
<tr>
<td>Left ventricular wall thickness (cm)</td>
<td>1.8±0.2</td>
<td>2.0±0.3</td>
</tr>
<tr>
<td>Left ventricular diastolic dimension (cm)</td>
<td>4.6±0.4</td>
<td>5.1±0.5</td>
</tr>
<tr>
<td>Left atrial dimension (cm)</td>
<td>3.7±0.5</td>
<td>4.2±0.5</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>0.38±0.1</td>
<td>0.35±0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Left ventricular hypertrophy (%)</td>
<td>26.3%</td>
<td>34.5%</td>
</tr>
<tr>
<td>Left ventricular systolic dysfunction (%)</td>
<td>2.9%</td>
<td>9.7%</td>
</tr>
<tr>
<td>CVH score (mean ± SD)</td>
<td>3.5±1.4</td>
<td>3.0±1.3</td>
</tr>
</tbody>
</table>

HDL indicates high-density lipoprotein; CVH, cardiovascular health.
**Supplementary Table 4. Age and sex-adjusted associations between CVH score categories and LV geometric patterns.**

<table>
<thead>
<tr>
<th>LV geometric pattern</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Concentric remodeling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVH score 0-7</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>CVH score 8-9</td>
<td>0.70 (0.53, 0.92)</td>
<td>0.0099</td>
</tr>
<tr>
<td>CVH score 10-14</td>
<td>0.58 (0.44, 0.77)</td>
<td>0.0002</td>
</tr>
<tr>
<td>b. Concentric hypertrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVH score 0-7</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>CVH score 8-9</td>
<td>0.61 (0.44, 0.84)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CVH score 10-14</td>
<td>0.46 (0.32, 0.65)</td>
<td>0.0023</td>
</tr>
<tr>
<td>c. Eccentric hypertrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVH score 0-7</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>CVH score 8-9</td>
<td>0.79 (0.59, 1.06)</td>
<td>0.2027</td>
</tr>
<tr>
<td>CVH score 10-14</td>
<td>0.83 (0.62, 1.11)</td>
<td>0.1142</td>
</tr>
</tbody>
</table>

OR indicates odds ratio.

Values represent the odds of each geometric pattern for each category compared to the referent category.
**Supplementary Table 5. Age- and sex- adjusted associations between CVH score categories and incident heart failure.**

<table>
<thead>
<tr>
<th>CVH score category</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVH score 0-7</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>CVH score 8-9</td>
<td>0.55 (0.40, 0.75)</td>
<td>0.0002</td>
</tr>
<tr>
<td>CVH score 10-14</td>
<td>0.34 (0.22, 0.51)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

HR represents hazard ratio.

Values represent the difference in hazards for each category compared to the referent.
Supplementary Table 6. Age- and sex- adjusted associations between 12-point CVH score and echocardiographic measurements.

<table>
<thead>
<tr>
<th>Echocardiographic Measurement</th>
<th>Beta Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass, gm</td>
<td>-3.47 (-4.26, -2.67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV wall thickness, mm</td>
<td>-0.25 (-0.30, -0.20)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV diastolic dimension, mm</td>
<td>-0.11 (-0.21, -0.02)</td>
<td>0.02</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>-0.38 (-0.48, -0.28)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Beta coefficient values represent the mean change in echocardiographic measurement per 1-point higher CVH score.
**Supplementary Table 7. Age- and sex- adjusted associations between 12-point CVH score and LV geometric patterns.**

<table>
<thead>
<tr>
<th>LV Geometric Pattern</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentric remodeling</td>
<td>0.89 (0.83, 0.94)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Concentric hypertrophy</td>
<td>0.89 (0.82, 0.96)</td>
<td>0.0019</td>
</tr>
<tr>
<td>Eccentric hypertrophy</td>
<td>1.02 (0.95, 1.08)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

OR indicates odds ratio.

Values represent the odds of having the geometric pattern (compared to the normal geometric pattern) for each 1-point higher CVH score.
Supplementary Table 8. Multivariable associations between 12-point CVH score and incident HF.

<table>
<thead>
<tr>
<th>Model</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adjusted for age and sex</td>
<td>0.76 (0.70, 0.82)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2. Adjusted for age, sex and LVM</td>
<td>0.80 (0.72, 0.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3. Adjusted for age, sex and interim MI</td>
<td>0.78 (0.73, 0.85)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4. Adjusted for age, sex, LVM and interim MI</td>
<td>0.83 (0.75, 0.93)</td>
<td>0.0007</td>
</tr>
<tr>
<td>5. Adjusted for age, sex, LVM, interim MI, log (BNP) and UACR*</td>
<td>0.80 (0.71, 0.91)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio; BNP, B-type natriuretic peptide; LVM, left ventricular mass; UACR, urine albumin-to-creatinine ratio.

Values represent HRs for each 1-point higher CVH score.

*Due to unavailability of biomarker measurements in a number of participants, the sample size for this model included 2046 participants. When tested in this smaller sample, the results for the other models were unchanged.
**Supplementary Table 9. Associations between 12-point CVH score and HFPEF and HFREF.**

<table>
<thead>
<tr>
<th>Model</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HFPEF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Adjusted for age and sex</td>
<td>0.80 (0.71, 0.91)</td>
<td>0.0004</td>
</tr>
<tr>
<td>b. Adjusted for age, sex and interim MI</td>
<td>0.80 (0.70, 0.90)</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>HFREF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Adjusted for age and sex</td>
<td>0.74 (0.67-0.83)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>b. Adjusted for age, sex and interim MI</td>
<td>0.80 (0.71, 0.89)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio; HFPEF, heart failure with preserved ejection fraction; HFREF, heart failure with reduced ejection fraction

Values represent HRs for each 1-point higher CVH score.
**Supplementary Figure Legends**

**Supplementary Figure 1.** Distribution of CVH scores in sample 1.

**Supplementary Figure 2a.** Age- and sex- adjusted associations between CVH score and HFpEF.

**Supplementary Figure 2b.** Age- and sex- adjusted associations between CVH score and HFrEF.
Supplementary Figure 1.
Supplementary Figure 2a.
Supplementary Figure 2b.
Supplementary References

