Determinants of Sensitivity and Specificity of Electrocardiographic Criteria for Left Ventricular Hypertrophy

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Numerous electrocardiographic criteria, which are largely dependent on fixed voltage thresholds, have been proposed for the diagnosis of left ventricular hypertrophy (LVH). Electrocardiographic criteria for LVH were examined in 4,684 subjects of the Framingham Heart Study who underwent echocardiographic study for LVH. Echocardiographic LVH was detected in 290 men (14.2%) and 465 women (17.6%). Electrocardiographic features of LVH were present in 2.9% of men (60/2,042) and 1.5% of women (39/2,642). The overall sensitivity of the electrocardiographic diagnosis of LVH was 6.9%, whereas specificity was 98.8%. Sensitivity of the electrocardiogram (ECG) for LVH was marginally lower in women than in men (5.6% vs. 9.0%, \( p = 0.075 \)). Obesity was inversely associated with sensitivity (\( p < 0.05 \), both sexes combined, sex-adjusted). Smoking was also inversely related to sensitivity (\( p = 0.001 \), both sexes combined, sex-adjusted). In contrast, sensitivity of the ECG increased with age (\( p < 0.001 \), both sexes combined, sex-adjusted). These findings suggest that electrocardiographic detection of LVH can be improved by incorporating information about noncardiac factors that impact on electrocardiographic sensitivity for LVH, presumably by attenuating QRS voltage.

New strategies that take into consideration sex, age, smoking status, and obesity might improve the sensitivity of the ECG without diminishing specificity. (Circulation 1990;81:815–820)

Electrocardiographic evidence of left ventricular hypertrophy (LVH) is a major marker of cardiovascular morbidity and mortality.\(^1\)\(^-\)\(^5\) Several criteria for the electrocardiographic diagnosis of LVH have been proposed.\(^6\)\(^-\)\(^9\) Though the specificities of these criteria are typically high (>90%), the sensitivities are lower and in the range of 20–60%.\(^10\)\(^-\)\(^11\) The advent of echocardiography has provided a noninvasive means of estimating left ventricular mass with close correlation to autopsy values (\( r > 0.90 \)).\(^12\)\(^-\)\(^15\) Emerging data suggest that echocardiographically defined LVH is also predictive of cardiovascular disease risk.\(^16\)\(^-\)\(^19\)

Studies that have examined the performance of the electrocardiogram (ECG) for the detection of LVH have largely been limited to select groups of patients, and are subject to selection bias. An inherent limitation of the ECG in detecting LVH is its dependence on fixed voltage criteria, which can be substantially altered by extracardiac factors such as gender, age, weight, and chest wall configuration.\(^20\) The purpose of this study is to examine the sensitivity and specificity of the ECG as a tool for detecting electrocardiographically defined LVH in a population-based sample. Second, this setting offers an opportunity to examine the impact of a variety of factors that attenuate the sensitivity and specificity of the ECG for the detection of LVH. It is hoped that identifying these factors and taking them into consideration in new diagnostic strategies will lead to improvement of the sensitivity of the ECG for LVH, without compromising specificity.

Methods

Study Population

In 1948, residents of Framingham, Massachusetts, between the ages of 28 and 62 years old, were invited to participate in a prospective epidemiologic study. Offspring of these subjects (and spouses of offspring) were entered into prospective study in 1971.
Echocardiographic Methods

Echocardiographic methods used at the Framingham Study have been previously reported.23 Subjects were studied using M-mode echocardiography. Measurements were made according to the recommendations of the American Society of Echocardiography with a leading-edge-to-leading-edge convention.24 The left ventricular internal dimension, ventricular septum, and left ventricular posterior wall were measured at end diastole as defined by the onset of the QRS complex. Left ventricular mass (in grams) was calculated from the simplified cubed formula, as follows: left ventricular mass=1.05[(LVID+VST+PWT)3−(LVID)3], where LVID is left ventricular internal diameter, VST is ventricular septal thickness, and PWT is posterior wall thickness. Measurements (mass in grams) were also made in accordance with “Penn” criteria and formula of Devereux and Reichek,12 as follows: left ventricular mass=1.04[(LVID+VST+PWT)3−(LVID)3]–13.6. This approach has been found to correlate more closely with autopsy-derived left ventricular mass.13

Criteria for LVH were derived from an apparently healthy reference population of 347 men and 517 women.23 Values for LVH corresponding to two standard deviations above the mean for calculated left ventricular mass/height (American Society of Echocardiography methods and cubed formula) are 163 g/m in men and 121 g/m in women.23 Corresponding values for LVH, based on “Penn” methods and formula,12 are 143 g/m in men and 102 g/m in women.

Electrocardiographic Methods

Standard 12-lead ECGs were obtained on all subjects, and interpretation was performed by the examining physician using previously reported methods for the electrocardiographic diagnosis of LVH.1–2 The diagnosis of LVH was made on the basis of fulfillment of at least one of the following voltage criteria: R wave greater than 1.1 mV in AVL, R wave at least 2.5 mV in left precordial leads, S wave at least 2.5 mV in right precordium, sum of precordial SV1 or SV2 plus RV5 or RV6 at least 3.5 mV, sum of limb lead RI plus SIII at least 2.5 mV. For the purposes of the present study, patients with electrocardiographic evidence of LVH by voltage with concomitant “strain pattern” (definite LVH) and those with less pronounced repolarization changes (borderline LVH) were combined. Subjects with complete bundle branch block, electrocardiographic evidence of myocardial infarction, and Wolf-Parkinson-White Syndrome were excluded from analysis because these abnormalities interfere with the detection of LVH.

<table>
<thead>
<tr>
<th>Table 1. Summary of Criteria for Eligibility</th>
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<tr>
<td>Entered study*</td>
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<tr>
<td>Dead previous to index exam†</td>
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<tr>
<td>Attended index exam</td>
</tr>
<tr>
<td>Adequate electrocardiogram</td>
</tr>
<tr>
<td>Evaluable electrocardiogram‡</td>
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</tbody>
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*Cohort subjects plus offspring subjects, †Cohort exam 16 and offspring exam 2, ‡Bundle branch block, Q wave infarction, and WPW were excluded.

Statistical Methods

The χ² test was used to test for differences between sexes in the sensitivity and specificity of the ECG for echocardiographically defined LVH. The Cochran-Mantel-Haenszel statistic was used to adjust for sex and test the association between cigarette smoking (current smoker, 1 vs. nonsmoker, 0) and sensitivity and specificity of the ECG. Bivariate logistic regression was used to adjust for sex and test the sensitivity and specificity trends with increasing age, obesity, and left ventricular mass/height.

Results

Criteria for eligibility in this study are summarized in Table 1. A total of 4,977 subjects had echocardiograms of adequate quality to assess left ventricular mass. The 293 subjects with electrocardiographic findings that would interfere with the electrocardiographic detection of LVH were excluded from analysis. Of the remaining 4,684 subjects eligible for this study, echocardiographic criteria for LVH were fulfilled in 290 men (14.2%) and 465 women (17.6%). Electrocardiographic LVH was detected in 60 men (2.9%) and 39 women (1.5%). The overall sensitivity of the ECG for detection of echocardiographically determined LVH was 6.9%, and overall specificity was 98.8%. (Table 2).

Influence of Sex

Although prevalence of echocardiographic LVH is higher in women than in men, sensitivity of the ECG was marginally lower in women (5.6% vs. 9.0%, p=0.075). Specificity was high in both sexes (99.4% in women and 98.1% in men).

<table>
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<tr>
<th>Table 2. Cross-Classification of Electrocardiogram and Echocardiographic Left Ventricular Hypertrophy Status According to Sex</th>
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<tbody>
<tr>
<td>ECG LVH</td>
</tr>
<tr>
<td>Women No Yes Men No Yes</td>
</tr>
<tr>
<td>Ecchocardiographic LVH</td>
</tr>
<tr>
<td>No 2,164 13 1,718 34</td>
</tr>
<tr>
<td>Yes 439 26 264 26</td>
</tr>
</tbody>
</table>

ECG sensitivity and specificity percentages are 5.6% and 99.4%, and 9.0% and 98.1%, for women and men, respectively.

ECG, electrocardiographic; LVH, left ventricular hypertrophy.
Influence of Age

The prevalence of echocardiographic LVH increases steadily with advancing age in both sexes and is accompanied by a trend toward increasing sensitivity of the ECG (Figure 1). The overall trend for sensitivity to increase with advancing age was significant (p<0.0001, both sexes combined, sex-adjusted). There was a concomitant trend toward declining specificity with advancing age, largely because of a decrease after the eighth decade (p<0.0001, both sexes combined, sex-adjusted).

Influence of Obesity

Subjects were classified into four quartiles according to increasing degrees of obesity as determined by body mass index (weight [kg]/height [m²]). Sensitivity was inversely related to increasing body mass index (p<0.05 for trend, both sexes combined, sex-adjusted) (Figure 2), whereas no significant differences in specificity were observed.

Influence of Smoking

Sensitivity of the ECG in detecting LVH was lower among cigarette smokers as compared with nonsmokers (5.7% vs. 10.9% in men, and 1.6% vs. 8.0% in women; p=0.001, both sexes combined, sex-adjusted). Corresponding specificities were 98.2% and 99.5% in smoking men and women versus 97.9% and 99.4% in nonsmoking men and women (differences were not statistically significant).

Influence of Severity of Left Ventricular Hypertrophy

When subjects with LVH were stratified according to quartile of left ventricular mass/height, a statistically significant trend toward increasing sensitivity of the ECG with increasing severity of LVH was observed in both sexes (Figure 3) (p=0.0006 in men and p<0.0001 in women).

Impact of Other Echocardiographic Criteria for Left Ventricular Hypertrophy

We considered the impact of two additional sex-specific echocardiographic criteria for LVH on the performance of the ECG—criteria based on unindexed left ventricular mass and criteria based on body surface area correction of left ventricular mass. The overall sensitivity of the ECG remained under 10% in both cases. The relations of age, sex, smoking, and left ventricular mass/body surface area to ECG sensitivity were all statistically significant (p<0.05, both sexes combined, sex adjusted). Of interest, the relation of obesity to prevalence of LVH is attenuated when left ventricular mass is divided by body surface area (compared with uncorrected left ventricular mass or height correction). Because obesity is a determinant of body surface area, dividing left ventricular mass by body surface area permits...
obese individuals to attain higher levels of left ventricular mass before achieving threshold levels for LVH. As a result, obesity was not significantly related to declining sensitivity of the ECG when left ventricular mass/body surface area criteria for echocardiographic LVH are used (see page 819).

Discussion

Electrocardiographically detected LVH is associated with increased risk for cardiovascular disease morbidity and mortality. Recently, echocardiographically detected LVH has also been shown to carry a poor prognosis. Subjects with echocardiographic LVH are at increased risk for several forms of cardiovascular disease including coronary heart disease, congestive heart failure, stroke, total cardiovascular disease, and ventricular arrhythmias. An inexpensive method of detecting anatomical LVH would have great clinical value. This study reveals that the ECG is a poor screening test for echocardiographic LVH, identifying a surprisingly small fraction of persons with echocardiographic hypertrophy.

A variety of electrocardiographic criteria for detection of LVH have emerged over the years, including the Sokolow-Lyon and Romhilt-Estes strategies, which are predicated on fixed QRS voltage criteria, which apply identical voltage cut points to the young and elderly, to men and women, and to lean and obese individuals. Though the specificities of these approaches are high (>90%), the sensitivities have been in the range of 20–60%. In contrast, the present study found that the overall sensitivity of the ECG for electrocardiographically defined LVH is only 6.9%, whereas its specificity is in excess of 98%.

We found that the sensitivity of the ECG for echocardiographic LVH is marginally lower in women than in men, possibly because of attenuation of QRS voltage by the greater spatial separation of myocardium from precordial electrodes because of breast tissue in women. Consistent with this is the finding that precordial QRS voltage is lower in women than in men. Similarly, mastectomy results in increased QRS amplitude. Diminished electrocardiographic sensitivity in women might also be, in part, a result of less voltage generated by the female heart, which contains approximately 25% less wall mass than the male heart. The findings of this study suggest that the voltage threshold for defining LVH should be lower in women than in men. Recent sex-specific strategies for the electrocardiographic diagnosis of LVH have reported increased sensitivity.

A major limitation of commonly used criteria for electrocardiographic detection of LVH is their reliance on the same voltage thresholds for young and old subjects, alike. The development of age-specific electrocardiographic LVH criteria would seem indicated both on the basis of these results and knowledge of the substantial differences in normal R and S wave voltage, according to age. Despite the previously described attenuation of QRS voltage with advancing age in a healthy subset of this population, there was a trend toward increasing sensitivity of the ECG for LVH with advancing age. This apparent paradox might be a consequence of increasing prevalence of echocardiographic LVH with advancing age and a shift toward more severe extremes of LVH in the elderly. Consistent with this hypothesis is the finding of increased electrocardiographic sensitivity with increasing severity of LVH (Figure 3).

An inverse association of obesity with sensitivity was observed in both sexes (Figure 2). This is especially significant in view of the association of obesity with LVH. Obesity masks the detection of LVH because, although it is positively correlated with left ventricular mass and prevalence of LVH, it attenuates precordial voltage and reduces sensitivity of the ECG.

The discrepancies in reported prevalence of ECG and echocardiographic LVH reflect the technical differences between these modalities. Echocardiography provides precise anatomical measurements, whereas electrocardiography records cardiac electrical events from surface leads. Attenuation of voltage can result from extracardiac features including advancing age, adipose tissue, lung tissue, and pericardial fluid, which can mask the electrocardiographic clues to the presence of hypertrophy. The variables selected for study in this report were chosen because of the suspicion that they might confound the electrocardiographic detection of LVH.

Differences in electrocardiographic sensitivity and specificity between this and previous studies are in part due to selection bias, with more pathological extremes of LVH encountered in hospital and clinic-based series. Additionally, this study might underestimate the sensitivity of the ECG because it is based on a primarily healthy population from which many cases of LVH were excluded (e.g., bundle branch block, myocardial infarction, and technically suboptimal echocardiograms). It is also possible that the low sensitivity of electrocardiographic LVH criteria reported in this study is a reflection of liberal echocardiographic criteria for LVH and conservative electrocardiographic criteria. The echocardiographic criteria applied are unlike those used elsewhere and are based on correcting left ventricular mass by height. This approach resulted in the detection of more cases of LVH as compared with the widely used method of indexing left ventricular mass according to body surface area. Notably, even when left ventricular mass is indexed according to body surface area, electrocardiographic sensitivity for LVH remains under 10%. Correcting LV mass by body surface area is an approach that allows more obese individuals to attain higher levels of left ventricular mass before achieving threshold levels for LVH, resulting in an attenuation of the relation of obesity to anatomic hypertrophy. The practice of correcting left ventricular mass by body surface area is even more questionable in the present study because of the demonstration that such an approach obscures the tendency
Sensitivity* and Specificity* of Framingham Criteria for ECG LVH, According to Quartiles of Body Mass Index and Echocardiographic Criteria† Used to Define LVH

<table>
<thead>
<tr>
<th>BMI Quartile</th>
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<tbody>
<tr>
<td>Men</td>
<td>(n=510)</td>
<td>(n=512)</td>
<td>(n=508)</td>
</tr>
<tr>
<td>LVM criteria for echo LVH</td>
<td>5.88</td>
<td>8.19</td>
<td>11.02</td>
</tr>
<tr>
<td>LVM/BSA criteria for echo LVH</td>
<td>8.24</td>
<td>9.57</td>
<td>9.25</td>
</tr>
<tr>
<td>LVM/Ht criteria for echo LVH</td>
<td>6.47</td>
<td>9.77</td>
<td>12.40</td>
</tr>
<tr>
<td>Women</td>
<td>(n=661)</td>
<td>(n=659)</td>
<td>(n=663)</td>
</tr>
<tr>
<td>LVM criteria for echo LVH</td>
<td>3.33</td>
<td>8.65</td>
<td>17.35</td>
</tr>
</tbody>
</table>

BMI, body mass index (weight [kg] and height [m²]); LVM, left ventricular mass (g); LVH, left ventricular hypertrophy; ECG, electrocardiography; BSA, body surface area (m²); Ht, height (m).
*Sensitivity, specificity, and prevalence are expressed as a percentage.
†Echocardiographic criteria for LVH are based on Penn measurements of left ventricular mass: a) left ventricular mass ≥259 g in men and 166 g in women; b) left ventricular mass/body surface area ≥131 g/m² in men and 100 g/m² in women; c) left ventricular mass/height ≥143 g/m in men and 102 g/m in women. Corresponding values based on American Society of Echocardiography measurements and cubed formula are: a) left ventricular mass ≥294 g in men and 198 g in women; b) left ventricular mass/body surface area ≥150 g/m² in men and 120 g/m² in women; c) left ventricular mass/height ≥163 g/m in men and 121 g/m in women (details of criteria provided in Reference 23).

Sensitivity and Specificity of Framingham ECG LVH criteria. In women, however, the lower voltage thresholds of Cornell criteria resulted in greatly enhanced sensitivity (22%) at a cost of lower specificity (95%) and no improvement in overall accuracy. Regardless of which echocardiographic or ECG criteria for LVH are used, there are a number of biological factors that impact on the low sensitivity of the ECG for anatomic hypertrophy that transcend methodological differences.

We have identified several extracardiac factors that have an adverse impact on electrocardiographic sensitivity for LVH, presumably by attenuating QRS voltage. These findings underscore limitations of fixed voltage criteria for the electrocardiographic diagnosis of LVH. New strategies might improve overall performance of the ECG for detecting LVH by incorporating factors such as age, sex, obesity, and smoking. Existing computerized electrocardiographic technology makes possible the incorporation of data regarding these factors into algorithms for detecting LVH. Successful identification of LVH using computerized electrocardiographic technology would enhance clinical usefulness of the ECG as an inexpensive screening device for LVH. In the absence of such improvement in electrocardiographic performance, the very low sensitivity of the ECG for detection of LVH among adults in the general population, as documented in the present study, renders the ECG a relatively cost-ineffective method for identification of prognostically significant increases in left ventricular mass.16–19

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