Relation of Echocardiographic Left Ventricular Mass and Hypertrophy to Persistent Electrocardiographic Left Ventricular Hypertropy in Hypertensive Patients: The LIFE Study

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Background: The Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) trial used left ventricular hypertrophy (LVH) on a screening ECG to identify patients at high risk for morbid events. Because of regression to the mean, not all patients who met screening criteria had persistent ECG LVH on the ECG performed at study baseline.

Methods: The relationship of echocardiographic LV mass and LVH to persistence or loss of ECG LVH between screening and baseline evaluation was examined in 906 hypertensive patients in the LIFE study, who had echocardiograms and additional ECG performed at study baseline. Patients were categorized according to the presence or absence of ECG LVH by Cornell voltage–duration product criteria or Sokolow-Lyon voltage criteria; echocardiographic LVH was defined by LV mass index (LVMI) > 104 g/m² in women and > 116 g/m² in men.

Results: A total of 678 patients (75%) had persistent ECG LVH at baseline evaluation. Compared with the 228 patients without ECG LVH on the second ECG by either criterion, the 106 patients with LVH by both Cornell product and Sokolow-Lyon voltage criteria had significantly higher LVMI (140 ± 31 vs 114 ± 21 g/m², P < .001) and a higher prevalence of echocardiographic LVH (86% vs 55%, P < .001). Patients with ECG LVH on the baseline ECG by either Cornell product criteria (n = 410) or Sokolow-Lyon voltage criteria (n = 162) had intermediate values of LVMI (125 ± 25 and 121 ± 21 g/m²) and prevalences of echocardiographic LVH (78% and 62%). After controlling for possible effects of age, sex, ethnicity, systolic blood pressure, and body mass index, persistence of ECG LVH on the baseline ECG was associated with an increased risk of echocardiographic LVH: compared with patients with neither ECG criteria for LVH, patients with only Sokolow-Lyon voltage criteria had a 1.2-fold increased risk of echocardiographic LVH, those with only Cornell product criteria had a 2.7-fold increased risk, and patients with both ECG criteria had a 4.1-fold increased risk of echocardiographic LVH (P < .001).

Conclusions: Persistent ECG LVH between screening and LIFE study baseline identified patients with greater LV mass and a higher prevalence of echocardiographic LVH, suggesting that these patients may be at higher risk for subsequent morbid and mortal events. Am J Hypertens 2001;14:775–782 © 2001 American Journal of Hypertension, Ltd.

Key Words: Electrocardiogram, hypertension, hypertrophy.
remained stable or increased. However, these studies and most therapeutic trials aimed at regression of LVH have had several limitations, including relatively small sample size, incomplete knowledge of blood pressure (BP) and cardioactive medication use during treatment, short duration of follow-up, high subject drop-out rate, or the absence of overt LVH before therapy.8–11 As a result, further analysis of the prognostic value of regression and progression of LVH remains an important clinical goal.8

Recently, the Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) trial was initiated,12,13 in which hypertensive patients with ECG LVH by either Cornell voltage-duration product14,15 or Sokolow-Lyon voltage criteria16 on a screening ECG were enrolled in a prospective, double-blind study that is large enough (n = 9194) to determine whether appreciable reduction in mortality and morbidity events is associated with either use of losartan as opposed to atenolol, or with regression as opposed to persistence or progression of ECG LVH.12 However, even in the absence of definitive data on the prognostic value of serial changes in ECG LVH criteria, little is known regarding the relation of echocardiographic LV mass and LVH to short-term changes in ECG LVH criteria. Furthermore, due to both the phenomenon of regression to the mean and to inherent test variability, one would anticipate that a proportion of patients who meet study entry criteria requiring values above specified thresholds for measures of ECG LVH on a screening ECG would not have persistent LVH on a subsequent ECG at study baseline. The availability of separate screening and baseline ECG and the undertaking of an echocardiographic substudy involving >10% of LIFE participants offers a unique opportunity to assess the relationship of echocardiographic LV mass and prevalence of LVH to persistence or loss of ECG LVH by Cornell product and Sokolow-Lyon voltage criteria between screening and baseline study entry in LIFE.

Methods
Subjects

Eligible patients for LIFE were men and women aged 55 to 80 years with previously untreated or treated essential hypertension with mean seated BP in the range 160 to 200/95 to 115 mm Hg after both 1 and 2 weeks on placebo. Patients were required to fulfill Cornell voltage-duration product or Sokolow-Lyon voltage criteria for ECG LVH, as described below, on a pre-enrollment screening ECG. All study inclusion and exclusion criteria have been previously published.12,13 A representative sample of the whole LIFE study, totaling 964 patients, underwent baseline echocardiograms, of which 906 had measurable echocardiographic LV mass and complete baseline ECG measurements. There were 377 women and 529 men whose mean age was 66 ± 7 years.

Electrocardiography

The presence of LVH on a screening ECG read at a central core laboratory was required for entry into LIFE to use a cost-effective means of identifying patients at high risk for morbid events due to the important target organ manifestations of LVH. Patients enrolled into LIFE had an additional baseline ECG performed at study enrollment, performed a median of 23 days (interquartile range, 14 to 33 days) after screening, before beginning treatment. Based on previous evidence that the product of QRS voltage and duration, as an approximation of the time–voltage area of the QRS complex, had the greatest sensitivity at high levels of specificity compared with anatomic and echocardiographic reference standards of LV mass,14,15 the product of QRS duration times the Cornell voltage combination (RV5/6 + SV3, with 8 mm added in women)14,15 was used with a threshold value of 2440 mm · msec to identify LVH. After publication of two studies suggesting that a smaller gender adjustment was more appropriate,17,18 and after feedback from field investigators that a number of otherwise eligible hypertensive patients had ECG LVH by insensitive but highly specific Sokolow-Lyon voltage criteria but not by the Cornell product, two changes were made in ECG entry criteria that affected patients enrolled in LIFE after 30 April 1996: the gender adjustment of Cornell voltage was reduced from 8 to 6 mm, and Sokolow-Lyon voltage (SV1 + RV5/6) > 38 mm was accepted as an alternative ECG eligibility criterion.13

All ECG were interpreted at the Core Laboratory at Sahlgrenska University Hospital/Östra in Göteborg, Sweden. The QRS duration was measured to the nearest 4 msec, and the R-wave amplitudes in leads aVL, V5, and V6 and the S-wave amplitudes in leads V1 and V3 were measured to the nearest 0.5 mm (0.05 mV) using calipers. The presence of ECG LVH by Sokolow-Lyon voltage criteria was defined according to the preselected partition value of 38 mm used to determine LIFE study eligibility, as defined above.12,13 Because patients were recruited into LIFE using two different gender adjustments for Cornell product calculations, ECG LVH according to Cornell product criteria was defined for this study using previously determined gender-specific partitions of 1713 mm · msec in women and 2647 mm · msec in men,15,19 based on unadjusted voltage measurements.

Echocardiography

Studies were performed using standardized recording procedures and measurements as previously reported in detail.20 The LV internal dimension and wall thicknesses were measured at end-diastole following the American Society of Echocardiography (ASE) recommendations.21 When optimal orientation of M-mode recordings could not be obtained, correctly oriented linear dimension measurements were made using two-dimensional imaging by the leading-edge ASE convention.22 The LV mass was calculated using an anatomically validated formula23 and rela-
Table 1. Clinical, demographic, and electrocardiographic characteristics according to the persistence or absence of Cornell voltage-duration product and/or Sokolow-Lyon voltage criteria on the baseline LIFE study electrocardiogram

<table>
<thead>
<tr>
<th>Variable</th>
<th>CP-/SL- (n = 228)</th>
<th>CP-/SL+ (n = 162)</th>
<th>CP+/SL- (n = 410)</th>
<th>CP+/SL+ (n = 106)</th>
<th>Overall P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>65.0 ± 7.0</td>
<td>65.8 ± 7.0</td>
<td>67.0 ± 6.9</td>
<td>67.4 ± 6.9</td>
<td>.002</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>42.1</td>
<td>19.1</td>
<td>52.2</td>
<td>34.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Race (% white/African American/other)</td>
<td>89.0/9.2/1.8</td>
<td>71.6/27.2/1.2</td>
<td>88.3/9.0/2.7</td>
<td>77.4/19.8/2.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Self-reported MI (%)</td>
<td>4.5</td>
<td>4.4</td>
<td>6.5</td>
<td>4.9</td>
<td>.648</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>170.5 ± 15.1</td>
<td>174.8 ± 14.5</td>
<td>173.3 ± 13.7</td>
<td>178.0 ± 13.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>98.4 ± 8.6</td>
<td>98.3 ± 10.2</td>
<td>97.9 ± 8.7</td>
<td>99.3 ± 8.4</td>
<td>.539</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.6 ± 4.2</td>
<td>25.5 ± 3.2</td>
<td>28.2 ± 5.3</td>
<td>26.5 ± 3.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage (mm)</td>
<td>27 ± 7</td>
<td>45 ± 6</td>
<td>26 ± 7</td>
<td>46 ± 8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cornell product (mm · msec)</td>
<td>1805 ± 445</td>
<td>1514 ± 548</td>
<td>2983 ± 1049</td>
<td>3388 ± 1240</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

LIFE = Losartan Intervention for Endpoint Reduction in Hypertension; CP/SL = Cornell product/Sokolow-Lyon; MI = myocardial infarction; BP = blood pressure.

Results

Patient Characteristics

At study baseline, only 678 patients (75%) who met LIFE screening ECG criteria had persistent ECG LVH, and 228 no longer met either Cornell voltage-duration product or Sokolow-Lyon voltage criteria for LVH. Of the 678 patients with persistent ECG LVH by these criteria, 162 patients had LVH by Sokolow-Lyon voltage-only, 410 patients had LVH by Cornell voltage-duration product criteria only, and 106 patients had persistence of ECG LVH by both criteria. Clinical, demographic, and electrocardiographic characteristics of patients according to the persistence or absence of ECG LVH by these criteria are shown in Table 1. Compared with patients who no longer met either Sokolow-Lyon voltage or Cornell product LVH criteria, patients with ECG LVH by either or both criteria were older, were more likely to be African American, and had higher SBP with the highest values in patients with ECG LVH by both criteria. Patients with ECG LVH by Cornell product criteria only were more likely to be female and significantly more obese than patients with Sokolow-Lyon voltage criteria. Patients who met Sokolow-Lyon voltage criteria were significantly more likely to be African American than patients who did not have ECG LVH by this criterion. There were no significant differences in the rate of self-reported myocardial infarction or in diastolic BP between groups, and the mean values of Sokolow-Lyon voltage and Cornell voltage-duration product were directly related to group definitions. Of note, the mean values of Cornell product and Sokolow-Lyon voltage in patients without ECG LVH by either criteria at baseline exceeded the 85th and 80th percentile values, respectively, in a separate population of 175 normal subjects.

Statistical Analysis

Data management and analysis were performed with SPSS version 9 software (SPSS, Chicago, IL); data are presented as means ± SD for continuous variables and proportions for categoric variables. Differences in prevalences between groups were compared using χ² analyses. Mean values of demographic variables were compared using analysis of variance (ANOVA); mean values of echocardiographic measures were compared using two-way ANOVA to take into account the known impact of gender, and were further compared using analysis of covariance (ANCOVA) to adjust for baseline differences in age, gender, race, systolic blood pressure (SBP), and body mass index (BMI) between groups. The independent relation of echocardiographic LVH to the persistence of ECG LVH by Cornell product or Sokolow-Lyon voltage criteria was determined using logistic regression analyses. For all tests, a two-tailed P value < .05 was required for statistical significance.

dative wall thickness as end-diastolic posterior wall thickness/LV radius. The LV mass was indexed for body surface area and alternatively for height²alysis. Using predefined criteria chosen on the basis of their ability to predict an adverse prognosis, LVH was considered to be present if LVMI was >104 g/m² in women and >116 g/m² in men. Hypertrophy was considered concentric if LV relative wall thickness was >0.43 and eccentric if relative wall thickness was in the normal range; patients with normal LV mass were considered to have normal LV geometry if relative wall thickness was ≤0.43 or to have concentric remodeling if relative wall thickness was increased. Alternative analyses used LV mass/height² partition values of 46.7 and 49.2 g/m²² in women and men, respectively.

Results

Patient Characteristics

At study baseline, only 678 patients (75%) who met LIFE screening ECG criteria had persistent ECG LVH, and 228 no longer met either Cornell voltage-duration product or Sokolow-Lyon voltage criteria for LVH. Of the 678 patients with persistent ECG LVH by these criteria, 162 patients had LVH by Sokolow-Lyon voltage-only, 410 patients had LVH by Cornell voltage-duration product criteria only, and 106 patients had persistence of ECG LVH by both criteria. Clinical, demographic, and electrocardiographic characteristics of patients according to the persistence or absence of ECG LVH by these criteria are shown in Table 1. Compared with patients who no longer met either Sokolow-Lyon voltage or Cornell product LVH criteria, patients with ECG LVH by either or both criteria were older, were more likely to be African American, and had higher SBP with the highest values in patients with ECG LVH by both criteria. Patients with ECG LVH by Cornell product criteria only were more likely to be female and significantly more obese than patients with Sokolow-Lyon voltage criteria. Patients who met Sokolow-Lyon voltage criteria were significantly more likely to be African American than patients who did not have ECG LVH by this criterion. There were no significant differences in the rate of self-reported myocardial infarction or in diastolic BP between groups, and the mean values of Sokolow-Lyon voltage and Cornell voltage-duration product were directly related to group definitions. Of note, the mean values of Cornell product and Sokolow-Lyon voltage in patients without ECG LVH by either criteria at baseline exceeded the 85th and 80th percentile values, respectively, in a separate population of 175 normal subjects.

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Table 2. Echocardiographic left ventricular dimensions and mass in relation to the persistence or absence of Cornell voltage–duration product and/or Sokolow-Lyon voltage criteria for left ventricular hypertrophy on the baseline LIFE study electrocardiogram

<table>
<thead>
<tr>
<th>Echocardiographic Variable</th>
<th>CP–/SL– (n = 228)</th>
<th>CP–/SL+ (n = 162)</th>
<th>CP+/SL– (n = 410)</th>
<th>CP+/SP+ (n = 106)</th>
<th>Overall P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV internal dimension in diastole (cm)</td>
<td>5.16 ± 0.53</td>
<td>5.27 ± 0.55</td>
<td>5.31 ± 0.57</td>
<td>5.49 ± 0.63</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV septal wall thickness in diastole (cm)</td>
<td>1.12 ± 0.14</td>
<td>1.14 ± 0.13</td>
<td>1.16 ± 0.15</td>
<td>1.23 ± 0.18</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV posterior wall thickness in diastole (cm)</td>
<td>1.04 ± 0.11</td>
<td>1.07 ± 0.11</td>
<td>1.07 ± 0.12</td>
<td>1.12 ± 0.15</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>215 ± 11</td>
<td>229 ± 11</td>
<td>236 ± 11</td>
<td>268 ± 11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV mass/body surface area (g/m²)</td>
<td>114 ± 21</td>
<td>121 ± 21</td>
<td>129 ± 25</td>
<td>140 ± 31</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV mass/height².⁷ (g/m².⁷)</td>
<td>52 ± 11</td>
<td>53 ± 11</td>
<td>59 ± 16</td>
<td>62 ± 15</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.41 ± 0.06</td>
<td>0.41 ± 0.06</td>
<td>0.41 ± 0.07</td>
<td>0.41 ± 0.08</td>
<td>.924</td>
</tr>
</tbody>
</table>

LV = left ventricular; other abbreviations as in Table 1.

Echocardiographic Findings in Relation to Electrocardiographic Left Ventricular Hypertrophy

The relationship of LV dimensions and LV mass to the persistence or absence of ECG LVH is shown in Table 2. Compared to that in patients without ECG LVH at study baseline, persistence of ECG LVH was associated with greater LV internal dimension and wall thicknesses during diastole, with consequent greater LV mass, and LV mass indexed for either body surface area or for height².⁷. Patients who met both Cornell voltage–duration product and Sokolow-Lyon voltage criteria at baseline had the greatest LV dimensions, wall thicknesses, and both unadjusted and adjusted LV mass values. The statistical significance of these differences was unchanged after adjusting for baseline differences between groups in age, gender, race, SBP, and BMI using ANCOVA.

The prevalence of echocardiographic LVH was strongly related to the persistence or absence of ECG LVH on the baseline ECG (Fig. 1), ranging from 54.6% in patients without ECG LVH by either Sokolow-Lyon voltage or Cornell product criteria on the second tracing to 85.8% in patients with persistence of ECG LVH by both of these criteria. Of note, when patients meeting only one of the ECG LVH criteria were examined, the 77.5% prevalence of echocardiographic LVH in those with only Cor-
nell product criteria for ECG LVH was significantly greater than the 62.3% prevalence in those with only Sokolow-Lyon voltage criteria ($\chi^2 = 12.85$, $P < .001$). Alternative analyses using gender-specific partitions of LV mass indexed for height did not substantially alter the relationship of echocardiographic LVH to the persistence or absence of ECG LVH: anatomic LVH by these criteria was present in 64.3% of patients without ECG LVH, in 63.4% of patients with Sokolow-Lyon voltage only, in 81.6% of patients with Cornell product criteria only, and in 86.4% of patients with both ECG LVH criteria (overall $\chi^2 = 41.32$, $P < .001$), and was significantly higher in patients meeting Cornell product criteria only, as compared with patients meeting only Sokolow-Lyon voltage criteria for LVH ($\chi^2 = 17.71$, $P < .001$).

The relationship of echocardiographic LV geometry to persistence or absence of ECG LVH is shown in Table 3. Normal LV geometry was more common in patients without ECG LVH at baseline and in those with only Sokolow-Lyon LVH than in patients meeting Cornell product criteria for LVH. Both eccentric and concentric geometric patterns of LVH increased in prevalence with the presence of one or both ECG LVH criteria for LVH, being most common in patients with both Cornell product and Sokolow-Lyon voltage for LVH. In contrast, concentric remodeling was significantly less prevalent in patients with ECG LVH than in patients without either ECG criterion for LVH. The relationship of abnormal LV geometry (echocardiographic LVH or concentric remodeling) to the persistence or absence of ECG LVH is illustrated in Fig. 2. Abnormal LV geometry was most prevalent in patients with persistent ECG LVH by both criteria (93%), and was significantly more common in patients with ECG LVH by Cornell product criteria only (86%) than in patients with Sokolow-Lyon voltage only (71%) or without ECG LVH by either criterion (73%).

Because persistence of ECG LVH was associated with older age, higher SBP, a higher prevalence of African

**Table 3.** Echocardiographically determined left ventricular geometry in relation to the persistence or absence of Cornell voltage–duration product and/or Sokolow-Lyon voltage criteria for left ventricular hypertrophy on baseline LIFE study electrocardiogram*

<table>
<thead>
<tr>
<th>Left Ventricular Geometry</th>
<th>CP−/SL− ($n = 228$)</th>
<th>CP−/SL+ ($n = 162$)</th>
<th>CP+/SL− ($n = 410$)</th>
<th>CP+/SL+ ($n = 106$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (%)</td>
<td>26.9</td>
<td>29.0</td>
<td>13.9</td>
<td>7.5</td>
</tr>
<tr>
<td>Concentric remodeling (%)</td>
<td>18.5</td>
<td>8.6</td>
<td>8.6</td>
<td>6.6</td>
</tr>
<tr>
<td>Eccentric hypertrophy (%)</td>
<td>38.8</td>
<td>40.2</td>
<td>50.6</td>
<td>55.7</td>
</tr>
<tr>
<td>Concentric hypertrophy (%)</td>
<td>15.8</td>
<td>22.2</td>
<td>26.9</td>
<td>30.2</td>
</tr>
</tbody>
</table>

Abbreviations as in Tables 1 and 2.

* Overall $\chi^2 = 62.76$, 9 degrees of freedom, $P < .001$.

![Figure 2](https://example.com/fig2.png)

**FIG. 2.** Prevalence of abnormal left ventricular (LV) geometry (concentric remodeling, eccentric hypertrophy, or concentric hypertrophy) according to the persistence or resolution of ECG LV hypertrophy (LVH) by Cornell product (CP) or Sokolow-Lyon (SL) voltage criteria.
American ethnicity, and differences in BMI and gender (Table 1), the independence relationship of echocardiographic LVH to persistence or absence of ECG LVH was further examined using logistic regression analysis (Table 4). After controlling for these factors, persistence of ECG LVH on the baseline ECG remained associated with an increased risk of echocardiographic LVH. Compared with patients with neither ECG criteria for LVH, patients with only Sokolow-Lyon voltage criteria had a nonsignificant 1.2-fold increased risk of echocardiographic LVH, those with only Cornell product criteria had a 2.7-fold increased risk, and patients with both ECG criteria present had a 4.1-fold increased risk of echocardiographic LVH.

Discussion

Persistent ECG LVH by Cornell voltage–duration product or Sokolow-Lyon voltage criteria between screening and LIFE study baseline identifies patients with greater LV mass and a higher prevalence of echocardiographic LVH compared to patients in whom ECG LVH was no longer manifest. Indeed, the presence of ECG LVH by both criteria was associated with a > than 4-fold higher risk of echocardiographic LVH compared to the absence of these criteria, even after factoring in the older age, higher SBP, and greater BMI in these patients. These findings suggest that persistence of LVH on serial ECG may identify patients at especially high risk of subsequent morbid and mortal events.

Persistence of ECG LVH by these criteria was associated with higher SBP and with older age, consistent with the role of long-standing hypertension in development of hypertrophy, and also with increased body mass index, consistent with the known relation of LVH to obesity. Compared with Sokolow-Lyon voltage criteria, persistence of Cornell product criteria had a higher positive predictive value for echocardiographic LVH and was associated with higher LV mass, further supporting the use of the Cornell product for detection of hypertrophy.

Short-term reproducibility of ECG voltage measurements plays a significant role in the current findings. Previous studies of short-term variability of the QRS voltage combinations used in ECG criteria for LVH demonstrated that the coefficient of variability ranged from 10% to 24.8% and reclassification rates ranged from 0% to 17% when electrode positions were not marked. The lower coefficient of day-to-day variability of QRS duration (3.1%) suggests that voltage–duration product criteria may vary less than ECG criteria based solely on QRS voltages. The 25% reclassification rate of ECGs in the current study is higher than would be expected from previous studies of hypertensive patients in which 10% of Sokolow-Lyon voltage and 5% of Cornell voltage were reclassified to LVH or no LVH on serial tracings. However, the vast majority of patients in the previous study had ECG with QRS amplitudes well within the normal range, such that even significant changes in QRS voltages would not result in the recoding of their tracings. In contrast, the current study included only hypertensive patients who met screening ECG criteria for LVH and, by study design, therefore included a high proportion of patients in whom Sokolow-Lyon or Cornell product measurements on their screening ECG were only minimally elevated above the threshold levels required to define LVH. As a consequence, even modest decreases in these values on the subsequent baseline ECG would be more likely to result in these patients no longer meeting criteria for LVH, as seen in the present study. This concept is supported by the higher than normal range of Cornell product and Sokolow-Lyon voltage findings in patients without either criterion for LVH at study baseline (Table 1).

It is important to the overall design of the LIFE study to understand that the < 100% prevalence of echocardiographic LVH in the present study, as reflected by the 25% to 30% false-positive rate for our ECG criteria, was expected based on the known imperfect sensitivity and specificity of these ECG criteria and does not reflect a study.

Table 4. Multivariable relation of echocardiographic left ventricular hypertrophy to the persistence or absence of Cornell voltage–duration product or Sokolow-Lyon voltage criteria for left ventricular hypertrophy on the baseline LIFE study electrocardiogram*

<table>
<thead>
<tr>
<th>Persistence or Absence of ECG LVH</th>
<th>β Coefficient</th>
<th>Standard Error</th>
<th>P Value</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornell product –/Sokolow Lyon voltage–</td>
<td>0.197</td>
<td>0.216</td>
<td>.361</td>
<td>1.22</td>
<td>0.80–1.86</td>
</tr>
<tr>
<td>Cornell product –/Sokolow-Lyon voltage+</td>
<td>0.974</td>
<td>0.183</td>
<td>&lt;.0001</td>
<td>2.65</td>
<td>1.85–3.79</td>
</tr>
<tr>
<td>Cornell product +/- Sokolow-Lyon voltage–</td>
<td>1.415</td>
<td>0.315</td>
<td>&lt;.0001</td>
<td>4.12</td>
<td>2.22–7.63</td>
</tr>
</tbody>
</table>

* Adjusted for age, gender, race, systolic blood pressure, and body mass index using logistic regression analysis; overall χ² = 42.16, P < .0001.

CI = confidence interval; ECG = electrocardiographic; LVH = left ventricular hypertrophy.
design flaw. Based on previous observations of sensitivity and specificity of about 45% to 50% and 95%, respectively, for the combination of Cornell product and Sokolow-Lyon voltage criteria for the detection of anatomic LVH,14,15 and based on an approximately 20% to 22% prevalence of ECG LVH estimated from a pilot sample of patients who met LIFE eligibility requirements, a 69% to 74% prevalence of echocardiographic LVH was predicted using the revised LIFE ECG criteria. Thus, the 70% to 75% overall prevalence of echocardiographic LVH in the present study, corresponding to the 25% to 30% false-positive rate depending on the method chosen for indexing LV mass, was consistent with the diagnostic accuracy of the ECG criteria used and with the estimated prevalence of LVH among hypertensive patients being screened for LIFE. These findings highlight the need for ECG LVH partitions with high specificity when using imperfect screening methods in populations with relatively low prevalences of true hypertrophy.

Although fully 25% of the study population did not have echocardiographic LVH by LV mass indexed for body surface area, these patients by no means had normal LV mass or geometry. Mean values of LV mass index in patients without echocardiographic LVH were substantially higher than in previously studied groups of hypertensive patients or normal reference subjects for both men (102 ± 10 vs 96 ± 21 g/m²) and women (93 ± 9 vs 87 ± 17 g/m²).29,30 In addition, the 36% prevalence of concentric LV geometry (LVH or remodeling) was significantly greater than the 14% prevalence among hypertensives (χ² = 35.80, P < .0001) and the 5% prevalence in normal subjects (χ² = 63.67, P < .0001).29,30 These findings suggest that LIFE patients who did not meet threshold criteria for echocardiographic LVH are still at increased risk for subsequent morbidity and mortality.3

Limitations and Implications

Because electrode positions were not marked, it remains unclear to what degree the changes in ECG LVH between tracings reflect differences in precordial electrode placement as opposed to measurement or true biologic variability.28 The lower day-to-day variability previously found for QRS duration measurements26 suggests that use of voltage–duration product criteria should decrease day-to-day variability. The 2.7- to 4-fold greater risk of having echocardiographic LVH when Cornell product criteria were present on both screening and baseline ECG further suggest that requiring Cornell product criteria to be present on serial ECG can increase the prevalence of true anatomic LVH in a study population compared to when only a single ECG meeting screening criteria is required, or compared to the use of other ECG criteria for LVH. Finally, despite these potential limitations, it is worth emphasizing that even patients in whom ECG LVH was not present on the second ECG had a > 50% likelihood of having LVH by echocardiogram, further illustrating the clinical value of ECG methods for identifying hypertensive patients at high risk.

References

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


