Effect of Obesity on Electrocardiographic Left Ventricular Hypertrophy in Hypertensive Patients

The Losartan Intervention For Endpoint (LIFE) Reduction in Hypertension Study

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Abstract—Obesity may limit sensitivity of ECG voltage criteria for left ventricular hypertrophy (LVH) because of the attenuating effects of increased body mass on precordial voltages. However, obesity is associated with an increased prevalence of anatomic LVH, making more accurate ECG criteria in obese patients a clinical priority. ECG LVH by Cornell voltage-duration product and/or Sokolow-Lyon voltage criteria was used to select patients for the Losartan Intervention For Endpoint (LIFE) Reduction in Hypertension Study. Clinical and ECG data were available in 8417 patients (54% women; mean age, 67 ± 7 years); 2519 were overweight and 1573 were obese by gender-specific body mass index criteria. Increased body mass index had significant but directionally opposite effects on ECG LVH by these 2 criteria. Compared with normal-weight patients, obese and overweight patients had lower Sokolow-Lyon voltage and a lower prevalence of ECG LVH by Sokolow-Lyon criteria (10.9% versus 16.2% versus 31.4%; \( P < 0.001 \)). In contrast, obese and overweight patients had higher mean values of the Cornell product and higher prevalences of ECG LVH by this criterion (75.1% versus 69.9% versus 60.7%; \( P < 0.001 \)). After adjustment for age, gender, race, myocardial infarction, and diastolic and pulse pressure with the use of logistic regression analysis, increased body mass remained highly predictive of the presence of ECG LVH. Compared with normal-weight patients, obese patients had a \( 2 \)-fold higher risk of ECG LVH by the Cornell product but a \( 4 \)-fold lower risk of ECG LVH by Sokolow-Lyon voltage; overweight status was associated with intermediate risks, with a \( 151\% \) greater likelihood of ECG LVH by the Cornell product but only \( 44\% \) of the risk of LVH by Sokolow-Lyon voltage criteria compared with normal-weight individuals. Thus, Sokolow-Lyon voltage criteria underestimate the prevalence of anatomic LVH in the presence of obesity, whereas Cornell product criteria for ECG LVH appear to provide a more accurate measure of LVH in obese and overweight patients. (Hypertension. 2000;35:13-18.)

Key Words: blood pressure • electrocardiography • hypertrophy • obesity

Increased left ventricular (LV) mass detected by standard 12-lead ECG1,2 and by echocardiography3,4 has been associated with increased morbidity and mortality. However, low sensitivity of standard voltage criteria for detection of LV hypertrophy (LVH) has limited utility of the ECG for identification of patients with LVH.5–20 Although Cornell voltage criteria modestly improve ECG detection of LVH in hypertensive patients,6,7 the product of Cornell voltage and QRS duration (Cornell voltage-duration product),8,9 an approximation of the area under the QRS,10 appears to further enhance sensitivity of the ECG for LVH while maintaining high specificity. As a consequence, Cornell voltage-duration product criteria were used in combination with Sokolow-Lyon voltage5 to identify hypertensive patients at increased risk of subsequent cardiovascular morbidity and mortality for inclusion in the Losartan Intervention For Endpoint (LIFE) Reduction in Hypertension Study, a prospective trial designed to compare the efficacy of losartan and atenolol in reducing the risk of cardiovascular events.21,22

Obesity has been associated with increases in LV wall thickness, LV mass, and the prevalence of echocardiographic LVH, independent of the impact of blood pressure.23–26 Conversely, obesity has been shown to decrease sensitivity of precordial lead ECG criteria for LVH, presumably because of the attenuating effects of increased distance of exploring electrodes from the LV and attenuation of QRS amplitudes by interposed tissue.11,14–20 However, obesity is common in hypertensive patients,23–26 raising questions regarding the utility of precordial voltage criteria in detecting hypertensive LVH. Moreover, previous studies of the impact of increased...
Electrocardiography

Patients enrolled into LIFE had an additional baseline ECG performed before beginning treatment. All ECGs were interpreted at a central core laboratory by experienced investigators blinded to clinical information. QRS duration was measured to the nearest 4 ms, and R waves in leads aVL, V₅, and V₆ and S waves in leads V₁ and V₃ were measured to the nearest 0.5 mm (0.05 mV). Cornell and Sokolow-Lyon voltages were calculated as noted above, and voltage-duration products were calculated as the product of Cornell or Sokolow-Lyon voltage times QRS duration.

TABLE 1. Clinical Characteristics in Normal, Overweight, and Obese Patients With Hypertension

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Weight (n=4325)</th>
<th>Overweight (n=2519)</th>
<th>Obese (n=1573)</th>
<th>Overall P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68.1 ± 7.1</td>
<td>67.1 ± 6.8</td>
<td>65.8 ± 6.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender, % female</td>
<td>49.1</td>
<td>60.9</td>
<td>57.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race, % white/black/other</td>
<td>93.8/4.9/1.3</td>
<td>93.6/4.6/1.8</td>
<td>88.7/9.4/1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Self-reported MI, %</td>
<td>6.5</td>
<td>4.6</td>
<td>5.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>97.2 ± 8.8</td>
<td>98.1 ± 8.7</td>
<td>98.9 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>174.2 ± 14.3</td>
<td>174.7 ± 14.6</td>
<td>174.3 ± 14.0</td>
<td>0.391</td>
</tr>
<tr>
<td>Pulse blood pressure, mm Hg</td>
<td>77.0 ± 15.7</td>
<td>76.5 ± 15.5</td>
<td>75.4 ± 14.9</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Values are mean ± SD. MI indicates myocardial infarction.

Methods

Protocol

LIFE is a prospective, double-blind, randomized study of 9194 patients with hypertension and ECG LVH testing the hypothesis that incidence of cardiovascular death or nonfatal myocardial infarction or stroke will be decreased by at least an additional 15% by use of losartan versus atenolol. Study entry and exclusion criteria and clinical protocols have been published; body mass index (BMI) was calculated from measured height and weight. On the basis of the second National Health and Nutrition Examination Survey (NHANES II), overweight was defined as BMI of 27.8 to 31.0 kg/m² for men and 27.3 to 32.2 kg/m² for women; obesity was defined as higher BMI.

Patients were recruited into LIFE on the basis of LVH on a screening ECG read at a central core laboratory. Based on prior evidence that the product of QRS voltage and duration had the greatest sensitivity at high levels of specificity compared with anatomic and echocardiographic LV mass, the Cornell voltage-duration product (RaVL + SV₃, with 8 mm added in women) was used with a threshold value of 2440 mm·ms to identify LVH. After publication in late 1995 of 2 studies suggesting that a smaller gender adjustment was more appropriate and feedback from field investigators that some otherwise eligible patients had ECG LVH by the insensitive but specific Sokolow-Lyon voltage criteria but not by the Cornell product, the gender adjustment of Cornell voltage was reduced from 8 to 6 mm, and Sokolow-Lyon voltage (SV₁ + RV₅Sa) > 38 mm was accepted as an alternative ECG eligibility criterion for patients enrolled after April 30, 1996.

Statistical Analysis

Data are presented for normal-weight, overweight, and obese groups as mean ± SD for continuous variables and proportions for categorical variables. Differences in prevalences between groups were compared with χ² analyses. Mean values of demographic variables were compared with ANOVA; mean values of ECG measures were compared with 2-way ANOVA to take into account the known impact of gender on these variables. Mean blood pressure values were further examined with 2-way ANOVA to compare differences between patients with and without ECG LVH by weight group. Mean values of ECG criteria were further compared with ANCOVA to adjust for baseline differences in age, gender, race, self-reported myocardial infarction, and diastolic and pulse blood pressure between groups. The independent contribution of overweight and obese status to the risk of ECG LVH was determined with logistic.

TABLE 2. ECG LVH Criteria in Normal, Overweight, and Obese Patients With Hypertension

<table>
<thead>
<tr>
<th>ECG Criteria for LVH</th>
<th>Normal Weight (n=4325)</th>
<th>Overweight (n=2519)</th>
<th>Obese (n=1573)</th>
<th>Overall P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornell voltage, mm</td>
<td>24.2 ± 8.1</td>
<td>24.8 ± 6.7</td>
<td>25.0 ± 7.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cornell product, mm·ms</td>
<td>2470 ± 1110</td>
<td>2518 ± 931</td>
<td>2613 ± 923</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage, mm</td>
<td>32.6 ± 10.8</td>
<td>28.2 ± 9.7</td>
<td>25.5 ± 9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sokolow-Lyon product, mm·ms</td>
<td>3251 ± 1178</td>
<td>2824 ± 1077</td>
<td>2625 ± 1015</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
regression analyses. For all tests, a 2-tailed $P$ value <0.05 was required for statistical significance.

**Results**

**Relation of Clinical Characteristics to Body Habitus**

Clinical, demographic, and ECG data were available for analysis in 8417 patients (54% women; mean age, 67±7 years). Obesity was present in 1573 patients (19%), 2519 patients (30%) were overweight, and 4325 patients (51%) had normal BMI values. Clinical characteristics according to BMI group are shown in Table 1. Compared with normal-weight patients, obese and overweight patients were younger, were more likely to be black than either overweight or normal-weight patients. Mean systolic blood pressure was identical across groups, but increased BMI was associated with higher diastolic blood pressures and consequently lower pulse pressures.

**Effect of Body Habitus on ECG LVH Criteria**

Increased BMI had significant but directionally opposite associations with mean values and prevalences of ECG LVH according to Cornell and Sokolow-Lyon voltage and voltage-duration product criteria (Table 2, Figures 1 and 2). Compared with normal-weight patients, overweight and obese patients had higher mean values of Sokolow-Lyon voltage and Cornell product measurements (Table 2, Figures 1 and 2). In contrast, compared with normal-weight patients, overweight and obese patients had higher mean values of Cornell voltage and Cornell product measurements (Table 2, Figures 1 and 2).

**TABLE 3. Systolic Blood Pressure in Normal, Overweight, and Obese Patients With Hypertension According to the Presence or Absence of ECG LVH**

<table>
<thead>
<tr>
<th>ECG Criteria for LVH</th>
<th>Normal Weight (n=4325)</th>
<th>Overweight (n=2519)</th>
<th>Obese (n=1573)</th>
<th>Weight Group P</th>
<th>ECG LVH P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ECG LVH−</td>
<td>ECG LVH+</td>
<td>ECG LVH−</td>
<td>ECG LVH+</td>
<td>ECG LVH−</td>
</tr>
<tr>
<td>Cornell voltage</td>
<td>172.5±14.3</td>
<td>175.6±14.2</td>
<td>172.5±14.3</td>
<td>175.9±14.6</td>
<td>171.9±14.1</td>
</tr>
<tr>
<td>Cornell product</td>
<td>173.2±14.5</td>
<td>174.7±14.1</td>
<td>173.3±14.4</td>
<td>175.2±14.7</td>
<td>172.9±14.0</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage</td>
<td>173.3±14.3</td>
<td>175.9±14.2</td>
<td>174.1±14.5</td>
<td>177.5±15.0</td>
<td>173.6±13.9</td>
</tr>
<tr>
<td>Sokolow-Lyon product</td>
<td>173.3±14.3</td>
<td>175.5±14.3</td>
<td>174.0±14.5</td>
<td>176.5±14.9</td>
<td>173.5±13.9</td>
</tr>
</tbody>
</table>

Values are mean±SD.

with parallel higher prevalences of ECG LVH by both voltage (52.0% versus 62.4% versus 62.3%; $P<0.001$) and voltage-duration product criteria (60.7% versus 69.9% versus 75.1%; $P<0.001$) (Figures 1 and 2). These differences in mean values remained significant after adjustment for baseline demographic and blood pressure differences with the use of ANCOVA.

To determine whether the decreasing frequency of ECG LVH by Sokolow-Lyon voltage and voltage-duration product criteria as BMI increased was associated with identification of a subset of obese patients with more severe hypertension, mean values of systolic blood pressure in normal, overweight, and obese patients were further examined in patients with or without ECG LVH (Table 3). The proportionally fewer patients with ECG LVH by Sokolow-Lyon voltage criteria as body mass increased had proportionally higher mean systolic pressure ($P=0.004$), as did, to a lesser degree, patients with ECG LVH by Sokolow-Lyon product criteria ($P=0.035$). In contrast, the increasing proportion of patients with ECG LVH by Cornell voltage or voltage-duration product criteria as body mass increased had similarly elevated systolic pressures across weight groups. Of note, patients with ECG LVH by any of the 4 criteria examined had higher systolic pressures than patients who did not meet these criteria for LVH on their baseline ECGs, and systolic pressure did not vary with increasing obesity among patients with no evidence of ECG LVH (Table 3).

The independent contribution of overweight and obesity to the likelihood of ECG LVH was assessed with logistic regression analysis (Table 4). After we controlled for the possible effects of demographic variables and blood pressure on ECG LVH prevalence, increased body mass remained highly predictive of the presence of ECG LVH (Table 4). Compared with normal-weight patients, obese patients had a
TABLE 4. Multivariate Logistic Regression Model to Assess Contribution of Overweight and Obese Status to the Risk of Having ECG LVH*

<table>
<thead>
<tr>
<th>ECG Criteria for LVH</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \chi^2 )</td>
<td>( P )</td>
</tr>
<tr>
<td>Cornell voltage</td>
<td>47.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cornell product</td>
<td>140.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage</td>
<td>329.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sokolow-Lyon product</td>
<td>227.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

See text for definition of normal, overweight, and obese.
*Adjusted for age, gender, race, diastolic blood pressure, pulse pressure, and self-reported myocardial infarction.
†Relative risk calculated compared with patients with normal weight.

Discussion

These findings demonstrate that the prevalence and degree of ECG LVH by Cornell and Sokolow-Lyon criteria in hypertensive patients are strongly affected by obesity. The significantly lower prevalence of LVH by Sokolow-Lyon voltage and voltage-duration product criteria in obese and overweight patients suggests that these criteria may underestimate the presence of anatomic LVH in the presence of obesity. In contrast, the higher prevalence and severity of Cornell product and voltage criteria with greater body mass, paralleling the known association of anatomic LVH with obesity, suggest that these criteria provide a more accurate measure of LVH in obese and overweight individuals.

LVH and Obesity

A number of previous studies have examined the relationship of LVH by ECG criteria to obesity, predominantly finding decreased sensitivity of precordial lead voltage criteria in overweight patients. Levy et al11 found a negative association between sensitivity of predominantly precordial lead voltage criteria and quartile of BMI in 4684 subjects from the Framingham Heart Study. Abergel et al16 found sensitivity of Sokolow-Lyon voltage to be significantly lower in obese hypertensive patients than in nonobese patients but found no significant differences in sensitivity of Cornell voltage according to body habitus. Similar effects of obesity on sensitivity of Sokolow-Lyon voltage and Cornell voltage were found in a study of 212 patients from our laboratory. Among 7543 participants in the Hispanic Health and Nutrition Examination Survey, R-wave amplitude in V5 was lower in overweight subjects and both R-wave amplitude in aVL and Cornell voltage were higher in overweight than normal-weight subjects. However, after adjustment for the effects of age, QRS axis, gender, and race, obesity was not independently associated with ECG LVH by Cornell voltage.

The present study extends these observations to a large, heterogeneous population of hypertensive patients, demonstrating strong negative associations of obesity with Sokolow-Lyon voltage and voltage-duration product and equally strong positive associations of obesity with Cornell voltage and voltage-duration product, even after the impact of blood pressure and other clinically relevant variables was taken into account (Table 4). Moreover, among the criteria examined, the Cornell voltage-duration product identified the highest prevalence of ECG LVH in obese patients, consistent with the positive impact of obesity on anatomic LVH. In this context, it is notable that multiplication of Sokolow-Lyon voltage by QRS duration attenuated the negative relation between obesity and LVH by Sokolow-Lyon voltage ECG criteria. Given that voltage-duration product criteria are, in effect, approximations of the area under the QRS, these findings support previous observations in a small population that true time-voltage area criteria for ECG LVH may be less affected by obesity. It is intriguing to note that the Perugia score, which combines Cornell voltage, the Romhilt-Estes point score, and the presence or absence of the “strain” pattern in lateral precordial leads, behaved quite similarly to Cornell criteria in the present population. ECG LVH by the Perugia score was present in 70.1% of normal-weight patients, 74.9% of overweight patients, and 75.3% of obese hypertensive patients (\( \chi^2=26.09, P<0.001 \) for trend), suggesting that accuracy of this ECG criterion may also be relatively independent of obesity.

The decreased prevalence and sensitivity of precordial lead voltage criteria for detecting anatomic LVH in obese patients, despite the recognized increased prevalence of echocardiographic LVH with higher body mass, have been attributed to attenuating effects of increased distance of exploring electrodes from the LV and attenuation of precordial QRS amplitudes by interposed tissue. Horton et al28 demonstrated that Sokolow-Lyon voltage was inversely related to the square of the distance from the anterior chest wall to the mid-LV and that this distance correlated directly with body surface area, suggesting that Sokolow-Lyon voltage varies inversely with increasing body size. Devereux et al15 demonstrated that patients with false-negative Sokolow-Lyon voltage for LVH had both increased...
body weight and increased distance from the chest wall to the LV compared with patients with true-positive ECG LVH findings. Rautaharju et al.28 also found that increasing chest size was associated with lower Sokolow-Lyon voltage and further demonstrated that Cornell voltage increased with greater chest dimension, but they did not examine the relation of increased chest size to body mass.

Although female gender was strongly associated with increased BMI (Table 1), gender did not play a significant role in the observed lower prevalence and severity of Sokolow-Lyon criteria with increasing body mass (Table 4). This finding contrasts with previous suggestions that breast tissue importantly attenuates precordial ECG voltages.29 The present findings are supported by observations by Rautaharju et al.28 that, although increasing breast size was associated with lower Sokolow-Lyon voltage and greater Cornell voltage, these effects were small in magnitude (≥15 μV for each 1-cm increment in breast size) with R values <0.10, suggesting that breast size alone accounted for <1% of ECG amplitude variations.

The association of anatomic LVH with increasing BMI23–26 and lower sensitivity of many ECG criteria in obese patients11,14–20 led investigators to incorporate BMI into regression equations with ECG voltage in attempts to improve ECG sensitivity for LVH.12,20 However, further examination revealed that sensitivity of BMI-adjusted voltage criteria for anatomic LVH was highly dependent on body habitus, with lower ECG sensitivities in normal-weight than in obese subjects.17,18 Indeed, adjusting the Cornell product for BMI, age, and gender20 in the present population produced substantially lower prevalences of ECG LVH in normal-weight patients (18.9%), overweight patients (19.1%), and obese patients (26.1%) compared with unadjusted Cornell product criteria (P<0.001) and still left a significant residual association with increasing BMI group (χ²=40.35, P<0.001 for trend). Although anatomic LVH has been linked to increasing body mass and obesity,23–26 recent observations suggest that LV mass is more strongly related to fat-free body mass than to either adipose mass or BMI, and that normalizing LV mass for fat-free body mass appears to increase sensitivity for detection of anatomic LVH.26 The strong positive relation of fat-free body mass to both total body weight and BMI suggests that increased fat-free body mass may have similar implications of LVH by Sokolow-Lyon criteria with increasing BMI, suggesting that voltage-duration products may be the most accurate conventional ECG method to detect anatomic LVH, independent of body habitus. These findings, as well as previous studies showing increased accuracy of true time-voltage area criteria for LVH and the independence of area criteria performance from the effects of obesity,10,18 suggest that true time-voltage area ECG criteria for LVH will provide the most stable and accurate test performance, independent of body habitus. Analyses in the echocardiographic substudy that enrolled >10% of LIFE patients will provide greater insight into the impact of obesity on the accuracy of standard ECG criteria; further study in additional populations will be required to more fully assess the value of time-voltage area criteria in relation to body habitus. Because the present study was, by design, limited to patients with hypertension and target organ damage, further study of this issue in normotensive and less highly selected hypertensive patients will be of importance.

Acknowledgment

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