Improved sex-specific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: validation with autopsy findings

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ABSTRACT In a previous study of 543 patients we developed, using echocardiographic left ventricular mass as the reference standard, two new sets of criteria that improve the electrocardiographic diagnosis of left ventricular hypertrophy (LVH). One set of criteria, which is suitable for routine clinical use, detects LVH when the sum of voltage in RaVL + SV1 (Cornell voltage) exceeds 2.8 mV in men and 2.0 mV in women. The second set of criteria, suitable for use in interpretation of the computerized electrocardiogram, uses logistic regression models based on electrocardiographic and demographic variables with independent predictive value for LVH, with separate equations for patients in sinus rhythm and atrial fibrillation. To test these criteria prospectively with use of a different reference standard, antemortem electrocardiograms were compared with left ventricular muscle mass measured at autopsy in 135 patients. Sensitivity of standard Sokolow-Lyon voltage (SLV) criteria (SV1 + RV5 or RV6 > 3.5 mV) for LVH was only 22%, but specificity was 100%. The Cornell voltage criteria improved sensitivity to 42%, while maintaining high specificity at 96%. Higher sensitivity (62%) was achieved by use of the new regression criteria, with a specificity of 92%. Overall test accuracy was 60% for SLV criteria, 68% for the Cornell voltage criteria, and 77% for the new regression criteria (p < .005 vs SLV). We conclude that the Cornell voltage criteria improve the sensitivity of the electrocardiogram for detection of LVH and are easily applicable in clinical practice. In addition, the new regression criteria, incorporating the T wave in V1, QRS duration, the magnitude of the negative P terminal force in V1, and patient sex, further improve electrocardiographic accuracy for the detection of LVH and are suitable for computer-based analysis of the electrocardiogram.


RECENT EVALUATIONS of electrocardiographic (ECG) criteria for the detection of left ventricular hypertrophy (LVH) have shown that they recognize LVH poorly, with test sensitivities generally ranging from 20% to below 50%. Since the electrocardiogram is widely used in clinical medicine, often as a screening test, development of more sensitive ECG criteria for early recognition of LVH is highly desirable, providing that high test specificity can be preserved.

In a previous study of two independent, sequential clinical populations, we developed, using echocardiographically determined left ventricular mass as the reference standard, new ECG criteria for LVH with improved sensitivity coupled with high specificity. We previously demonstrated that the magnitude of the S wave in precordial lead V3, the R wave in aVL, the T wave in V1, QRS width, and the magnitude of negative P terminal forces in V1 have independent predictive value for the identification of LVH, and that consideration of patient sex can further improve test accuracy.

Since ECG analyses are currently performed either by clinicians or by computerized systems with physician verification of diagnoses, we formulated new sets of ECG criteria for LVH that either possessed the simplicity requisite for clinical use or optimized the mathematical prediction of LVH from ECG variables by use of a multiple logistic regression model suitable for microprocessor-based interpretation systems. For clinical detection of LVH we chose the simplest of the
sets of criteria we previously developed, in which LVH is diagnosed when the sum of SV$_3$ and RaVL amplitudes (Cornell voltage) exceeds sex-specific cutoffs. The second set of criteria is based on multiple logistic regression equations developed with data from a combined population of 543 patients in our two previous series. The equations use ECG and demographic variables with independent relations to left ventricular muscle mass to predict the presence or absence of LVH. The present study was performed to prospectively test these new voltage and regression criteria with the use of measurements of left ventricular mass obtained at autopsy as the reference standard.

Methods

Autopsy population. Consecutive eligible patients were identified by regular review of the autopsy log of the New York Hospital–Cornell Medical Center from September 1978 to July 1982. Complete clinical data and a 12-lead electrocardiogram in non-paced rhythm obtained within a mean of 10 days from the date of death were available for a total of 135 patients. Women who had undergone a left-sided mastectomy were excluded since a decreased distance from the heart to the chest surface has been shown to increase ECG voltage out of proportion to left ventricular mass.2,5,9 Although pericardial effusions tend to decrease ECG voltage in relation to left ventricular mass, patients with pericardial effusion were not excluded, since this effect is quantitatively small in most instances.10 There were 69 men, with a mean age of 61 years, and 66 women, with a mean age of 63 years. Only seven of 135 patients were under 30 years of age. Cardiac diagnoses were established by review of clinical and laboratory data without knowledge of autopsy findings or ECG measurements. These diagnoses are outlined in table 1.

Clinically normal living subjects. To determine the specificity of newly developed and standard ECG criteria of LVH in apparently healthy adults a separate group of 92 subjects in whom no evidence of any diagnosable form of heart disease was found after complete clinical evaluation. This group comprised 28 men and 64 women ranging in age from 18 to 72 years (mean 33 ± 14 [SD]). Body surface area ranged from 1.50 to 2.21 m$^2$ (mean 1.80). Average blood pressure was 119 ± 12/73 ± 8 mm Hg. Echocardiographic left ventricular mass index obtained by an anatomically validated method11,12 with sex-specific partition values for recognition of LVH13 was used to exclude hypertrophy in these subjects.

Electrocardiography. Standard 12-lead electrocardiograms were recorded at 25 mm/sec and 1 mV/cm standardization by electrocardiographs with frequency response characteristics meeting or exceeding the recommendations of the American

| TABLE 1 | Clinical diagnoses of patients whose data were used for ECG-autopsy correlation |
|---------|-----------------------------|-----------------------------|
| Diagnosis                      | Men | Women |
| Hypertension                   | 8   | 8    |
| Valvular heart disease         | 13  | 6    |
| Coronary artery disease        | 18  | 23   |
| Cardiomyopathy                 | 11  | 2    |
| Pericardial disease            | 3   | 2    |
| Other                          | 16  | 25   |

Heart Association.14 Tracings were coded and interpreted blindly by an investigator without knowledge of clinical or autopsy findings. Two widely used standard ECG criteria for LVH were evaluated for comparison with our newly developed criteria: the Sokolow and Lyon15 precordial voltage criterion (SV$_1$ + RaVL or V$_5$ > 35 mm), and the point score system of Romhilt and Estes.16 Left or right bundle branch block or nonspecific intraventricular conduction defects were classified in the presence of QRS prolongation to at least 0.12 or 0.11 sec, respectively, according to the criteria of the Ad Hoc Working Group of the World Health Organization and the International Society and Federation of Cardiology.17

New criteria developed in previous series (tables 2 and 3). The Cornell voltage criteria for LVH are based on the sum of the R wave voltage in aVL and the S wave voltage in V$_3$. Since normal men and women differ significantly in the magnitude of this combined voltage, sex-specific threshold values were identified, with 28 mm used for recognition of LVH in men and 20 mm used in women. In our previous report these voltage criteria were found, with echocardiographic left ventricular mass as the reference standard, to have a sensitivity of 41% and specificity of 98% for LVH.7

The other set of criteria tested in the present study was developed from multiple logistic regression analyses performed on data from the combined population of 543 patients in our two previous series.7 In multiple logistic regression analysis, the measured value of each variable is multiplied by an empirically derived coefficient, with the sum of these products comprising the exponent in the fundamental equation for this method:

$$ \text{Risk} = \frac{1}{1 + e^{-exponent}} $$

The derived exponents are shown in table 3. Included in the regression analysis were sex and continuous electrocardiographic variables previously found7 to have the strongest independent linear correlation with left ventricular mass. Variables shown to be independently related to LVH in separate “learning” and “test” series were the sum of voltages in RaVL and SV$_3$, and the height of the T wave in V$_1$. In addition, when data from our two previous patient populations were combined, the area of the terminal negative deflection of the P wave in lead

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Cornell voltage criteria for ECG diagnosis of LVH</th>
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<tbody>
<tr>
<td>Men</td>
<td>LVH = SV$_3$ + RaVL &gt; 2.8 mV (28 mm)</td>
</tr>
<tr>
<td>Women</td>
<td>LVH = SV$_3$ + RaVL &gt; 2.0 mV (20 mm)</td>
</tr>
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</table>

For patients in normal sinus rhythm
Exponent = $4.558 - 0.092 \times (RaVL + SV$_3$) - 0.306 \times TV$_1$ - 0.212 \times QRS - 0.278 \times PTFV$_1$ - 0.559 \times sex

For patients in atrial fibrillation
Exponent = $5.045 - 0.093 \times (RaVL + SV$_3$) - 0.312 \times TV$_1$ - 0.325 \times QRS - 0.602 \times sex

Partition values of exponent for detection of LVH
In sinus rhythm: LVH < -1.55
In atrial fibrillation: LVH < -1.20

Units of measurement: Voltages of RaVL, SV$_3$, and TV$_1$ in mm (1 mm = 0.1 mV); QRS duration in sec × 100 (hundredths of a second); P terminal force in lead V$_1$ (PTFV$_1$) in mm × sec based on area; sex entered as 1.0 for men and 2.0 for women.
V₁ and QRS duration were also found to be independently related to left ventricular muscle mass, whereas the depth of the T wave in V₆ and patient age were found not to have independent value for prediction of LVH. Based on these findings, our previously reported multiple logistic regression equation was modified to achieve mathematical optimization of ECG prediction of LVH.

Separate regression equations were developed for patients in sinus rhythm and for those in atrial fibrillation since the P terminal force in V₁ is not present in patients in atrial fibrillation. These equations were developed and the values used in this report were obtained with the use of manual measurements of voltages and QRS duration; however, the regression equations predicted LVH at autopsy equally well when computer measurements derived from multiple simultaneous leads were substituted in the 96 of 135 patients for whom these measurements were available.

The coefficients and separate optimal partitions of the composite exponent shown in table 3 for detecting LVH in men and women were determined in the combined population of our previous study and applied prospectively in the present independent series of patients. Partition values were chosen to optimize overall test accuracy in the echocardiographically based series of 543 patients while preserving high test specificity (approximately 95%). These partition values were tested prospectively in the present study.

**Autopsy methods.** Left ventricular mass was measured by the chamber partition method and was corrected for body surface area. Criteria for detection of abnormal left ventricular mass index were derived from 39 autopsied patients with neither intrinsic disease nor hemodynamic load affecting the left ventricle. Upper normal limits of left ventricular mass index as measured at autopsy for men and women were defined as the mean left ventricular mass index in normal subjects of each sex plus 2 SDs, approximately the 97th percentile. From the data, LVH in men was defined as left ventricular mass index greater than 118 g/m² and that in women as left ventricular mass index greater than 104 g/m². LVH was present in 51% (69/135) of patients at autopsy.

Right ventricular mass was also determined by the chamber partition method, with values below 65 g considered to be normal and values above that to represent right ventricular hypertrophy, in accord with the results of previous autopsy studies. Right ventricular hypertrophy was present in 74 of 135 patients or 55% of the present population. The presence and approximate extent of myocardial infarction was determined by visual inspection of both surfaces of 1 cm cross-sectional slices of the ventricular myocardium. Recent or remote myocardial infarction was anatomically documented in 43 patients, 10 of whom had not been diagnosed during life: at least a portion of the infarct was transmural in 22 of these 43 patients. Anatomic LVH was present in 14 of 22 or 64% of the patients with myocardial infarction alone, in 35 or 67% of the 53 patients with right ventricular hypertrophy alone, in 11 of 21 or 52% of the patients with both of these abnormalities, and in nine of 40 or 23% of patients with neither.

**Statistical methods.** Computer analysis was conducted at the Rockefeller University Computer Center with use of BMDP biomedical computer programs to perform multiple logistic regression (described previously) and other statistical analyses. The strength of the relationships between ECG criteria and left ventricular mass index was assessed by least squares linear correlation. The sensitivity, specificity, and positive and negative predictive accuracies of ECG criteria in detecting anatomic LVH were calculated by standard formulas. Applicability of our findings to various clinical populations with lower prevalences of LVH than in our autopsy population was assessed by combining the observed sensitivity and specificity of standard and new ECG criteria with assumed disease (LVH) prevalences of 10%, 20%, and 40% to calculate overall test accuracy in each situation. These prevalences of LVH correspond approximately to those documented by echocardiography in adults 20 to 70 years old in the Framingham general population sample, among elderly adults in the general population, and in patients with essential hypertension, and in patients with essential hypertension evaluated at a referral center.

**Results**

**Relation of standard and new ECG criteria to left ventricular mass measured at autopsy.** The relationships of standard and new ECG criteria to left ventricular mass index are shown in table 4. Moderate correlations (r = .41 to .54) were found between left ventricular mass index and Sokolow-Lyon precordial voltage and the Romhilt-Estes point score. Correlations of left ventricular mass index with Cornell voltage were stronger for both men (r = .57) and women (r = .60). The strongest correlations with left ventricular mass index were observed with the regression equations for men in sinus rhythm (r = .62) and in atrial fibrillation (r = .61), and for women in sinus rhythm (r = .70) and in atrial fibrillation (r = .70) (both p < .05 vs Sokolow-Lyon voltage and Romhilt-Estes point score).

When patients were divided into subgroups according to the presence or absence of right ventricular hypertrophy and myocardial infarction, the closest correlation between left ventricular mass index at autopsy and the regression equations was in patients with neither of these abnormalities (r = .65, p < .001, SEE = 22 g/m²), followed closely by that in patients with right ventricular hypertrophy without infarction (r = .63, p < .001, SEE = 38 g/m²), those with myocardial infarction without right ventricular hypertrophy (r = .57, p < .005, SEE = 20 g/m²), and those with both right ventricular hypertrophy and myocardial infarction (r = .49, p < .01, SEE = 30 g/m²). A similar and

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*Savage DD: Personal communications*
generally superimposable pattern of relationships between Cornell voltage and left ventricular mass index was also observed in the respective subgroups, albeit with slightly lower correlation coefficients. The distribution of points relating each ECG variable to left ventricular mass index was similar in all subgroups, however, and neither right ventricular hypertrophy nor myocardial infarction systematically altered the sensitivity or specificity of either ECG criterion.

**Diagnostic utility of ECG criteria.** Diagnostic performance of the tested ECG criteria for detection of LVH was assessed in terms of sensitivity and specificity, as illustrated in figure 1. The precordial voltage of Sokolow and Lyon was 100% specific but not at all sensitive (22%) for LVH in the present study. A Romhilt-Estes score of 4 or more points had a sensitivity of 54%, but a specificity of only 85%. When 5 or more points were used, Romhilt-Estes specificity improved to 94%, but sensitivity fell to 33%. The Cornell voltage criteria had a sensitivity of 42% with a specificity of 96%. The regression equations improved sensitivity to 62%, while maintaining specificity at 92% for the entire study population.

The sensitivity of the Cornell voltage criteria in the 31 patients with conduction defects was 50%, with a specificity of 82%, while sensitivity was 85% and specificity was 73% for the new regression equations in these patients. Of the 104 patients without conduction defects, sensitivity of the Cornell voltage criteria was 39% with specificity of 98%, and the new regression criteria had sensitivity of 59% with specificity of 98%. Examination of results in patients with specific conduction defects (table 5) revealed a trend toward reduced sensitivity of Cornell voltage criteria for detection of LVH in patients with right bundle branch block, both in the presence and absence of coexistent left anterior fascicular block.

Positive and negative predictive value of standard criteria with specificity over 90% and new ECG criteria are shown in figure 2. Sokolow-Lyon voltage criteria had the best positive predictive value (100%), but the worst negative predictive value (55%) and overall accuracy of 60%. A Romhilt-Estes point score of 5 or more had a positive predictive value of 85%, negative predictive value of 57%, and accuracy of 63%. The Cornell voltage criteria had high positive predictive value (91%), with improved negative predictive value (61%) and improved accuracy of 68%. The new regression criteria achieved the best overall accuracy (77%) and the best negative predictive value (70%), while maintaining high positive predictive value (90%). The lowest calculated likelihood of LVH identified as positive by our regression equation partition values was 83% for patients in sinus rhythm and 77% for patients in atrial fibrillation.

**Specificity of ECG criteria in living normal subjects.** Since numerous metabolic and other abnormalities exist in autopsied subjects whose left ventricles appear anatomically normal, the test specificity of ECG criteria may appear to be lower in such patients than it would be in a population of living normal subjects. Therefore, we also examined test specificity of the new criteria in a separate clinically normal population of 92 subjects in whom echocardiographic left ventricular mass index measured by an anatomically validated method was used as the reference standard for exclusion of LVH. As shown in figure 3, in comparison with the 96% specificity of the Cornell voltage criteria in the autopsy population, specificity was 97% in clinically normal subjects. Similarly, in comparison with the 92% test specificity for the new regression criteria in the autopsy population, specificity was 98% in the clinically normal population.

**Overall accuracy of ECG criteria in populations with lower prevalences of left ventricular hypertrophy.** When the prevalence of LVH in a population was assumed to be 10%, similar to that recently documented by echocardiographic methods in a general population sample, application of the Cornell voltage criteria dou-

![FIGURE 1. Diagnostic performance of standard and new ECG criteria for recognition of LVH, with sensitivity displayed above the centerline and specificity below it. The new Cornell voltage and regression equation criteria exhibit the highest sensitivity of any criteria, with over 90% specificity.](image-url)
bled the sensitivity of Sokolow-Lyon voltage for LVH from 22% to 42%, while (with specificity derived from clinically normal subjects) maintaining an equal overall test accuracy of 92% (table 6). As assumed LVH prevalence was increased to 20% and 40%, overall test accuracy of the Cornell voltage criteria exceeded that of Sokolow-Lyon voltage criteria by 2% and 5%, respectively. At each level of prevalence of LVH, the overall accuracy of Cornell voltage was 4% higher than that obtained with a Romhilt-Estes score of 5 points or more, and ranged from 1% (at 40% LVH prevalence) to 10% (at 10% LVH prevalence) higher than that obtained with a Romhilt-Estes score of 4 points or more.

Overall test accuracy with the new regression equations in similar calculations ranged from 94% with a population prevalence of LVH of 10% to 80% when LVH prevalence was 40%. In this prevalence range, this represents a 6% to 12% improvement in percent correct diagnosis over standard criteria for LVH.

**Discussion**

In the present study, recently developed Cornell voltage criteria and separate multiple logistic regression equation criteria for patients in sinus rhythm or atrial fibrillation performed better than standard ECG criteria for detection of LVH when prospectively tested against the reference standard of left ventricular mass index at autopsy. These results are similar to those obtained in two previous patient populations in which echocardiography was used to measure left ventricular mass. The improved performance of the new criteria compared with previously available standard criteria was reflected in closer correlations with left ventricular mass at autopsy (table 4), better sensitivity and specificity (figure 1), improved overall accuracy, and higher predictive values of positive and negative

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**TABLE 5**  
Performance of Cornell voltage and regression equation criteria in patients with ventricular conduction defects

<table>
<thead>
<tr>
<th>Conduction defect</th>
<th>n</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBBB 12</td>
<td>1/6 (17%)</td>
<td>6/6 (100%)</td>
<td>3/6 (50%)</td>
<td>5/6 (83%)</td>
<td></td>
</tr>
<tr>
<td>LBBB 6</td>
<td>4/5 (80%)</td>
<td>0/1 (0%)</td>
<td>5/5 (100%)</td>
<td>0/1 (0%)</td>
<td></td>
</tr>
<tr>
<td>IVCD 13</td>
<td>5/9 (56%)</td>
<td>3/4 (75%)</td>
<td>9/9 (100%)</td>
<td>3/4 (75%)</td>
<td></td>
</tr>
<tr>
<td>Total 31</td>
<td>10/20 (50%)</td>
<td>9/11 (82%)</td>
<td>17/20 (85%)</td>
<td>8/11 (73%)</td>
<td></td>
</tr>
</tbody>
</table>

IVCD = nonspecific intraventricular conduction defect; LBBB = left bundle branch block; RBBB = right bundle branch block.
tests for detection or exclusion of anatomic LVH (figure 2). Neither pathologically documented myocardial infarction nor right ventricular hypertrophy systematically altered relationships between left ventricular mass and Cornell voltage or regression equations, suggesting that our criteria may be successfully applied to patients with these anatomic abnormalities.

Extrapolation of our data to populations with prevalences of LVH of 10% to 40% demonstrated up to 12% improvement in overall diagnostic accuracy of the new criteria compared with those of Sokolow and Lyon and Romhilt and Estes. Furthermore, the performance of our computerized regression equation is significantly better than that of the widely used IBM-Bonner ECG interpretation program. The similarity between the results of the present study, in which left ventricular mass at autopsy was used as the reference standard, and our previous study, in which echocardiography was used in a diverse clinical population, suggests that our findings are not strongly dependent on the high prevalence of patients with severe LVH or cardiac cachexia found in the autopsy population. It should be emphasized that our criteria have been developed and tested in populations generally exceeding 30 years of age. Therefore, extrapolation of these data to younger populations in which normal voltage and other ECG findings may differ should be approached with caution.

Specificity of ECG criteria. The prevalence of anatomic LVH in an unselected adult population or in patients with uncomplicated mild essential hypertension, the clinical condition under which ECG screening for LVH would be most commonly used, probably ranges between 10% and 20%. Because the majority of subjects in relatively unselected populations do not have LVH, it is essential that test specificity be high to reduce false-positive diagnoses in normal subjects and maintain an acceptable predictive value of a positive test. Although test specificities of our new criteria are high, ranging from 92% to 96% in this autopsy population, even higher specificities are desired for application in unselected populations.

However, in ambulatory normal subjects, test specificities were found to be 97% and 98% for the new voltage and regression equation criteria, respectively. To ascertain why specificity of the new criteria differed between autopsy and ambulatory populations, we examined clinical findings in the patients in the autopsy series who had false-positive ECG diagnoses of LVH. There were three false-positive results when Cornell voltage criteria were used in the autopsy series, each in women dying of adenocarcinoma. Two were severely cachectic, a condition that decreases the distance from the heart to the chest surface, and has been shown in previous studies to increase ECG voltage out of proportion to left ventricular mass.

There were five false-positive responses for the new regression criteria. These included one of the three women in the previous false-positive group and four additional men. Among the men, three had severely dilated hearts despite normal left ventricular mass. These observations suggest that preterminal morbidity can reduce ECG specificity for LVH, but that test accuracy is higher in ambulatory populations.

Effect of conduction defects on ECG criteria. Although autopsy and echocardiographic studies suggest that a high proportion of patients with left bundle branch block have anatomic LVH, most previous criteria for ECG recognition of LVH have excluded patients with prolonged QRS durations because of uncertainty regarding test applicability in the presence of conduction abnormalities. Inclusion of 31 patients with bundle branch block or nonspecific intraventricular conduction defects in the present study might, accordingly, have affected diagnostic performance of the new criteria. However, voltage has been related to LVH in patients with conduction disease and our criteria performed in subsets of patients with left bundle branch block or nonspecific intraventricular conduction abnormalities and in those with normal QRS duration with comparable sensitivity. Although test specificity in these patients requires further analysis in larger groups, these findings provisionally suggest that patients with left ventricular conduction abnormalities can be included in populations to which our new criteria are applied, while our results in the small group of patients with right bundle branch block suggest that Cornell voltage criteria have low sensitivity in the presence of this conduction defect.

Clinical implications. The practical significance of the improvement in ECG detection of LVH by the new voltage and regression criteria is highlighted by the
widespread use of electrocardiography. Based on Fisch’s estimate that over 100,000,000 ECG examinations are performed annually in the United States, the 8% increase in overall diagnostic accuracy we observed with the Cornell voltage criteria compared with standard ECG criteria would result in approximately 3,000,000 to 5,000,000 more overall correct diagnoses of the presence or absence of LVH each year, since a disproportionate number of ECG examinations are performed in clinical populations with a 20% or higher prevalence of LVH. An even greater increase in overall diagnostic accuracy, ranging from 9% to 17%, would result from use of our multiple logistic regression equations. Commercially available computerized ECG interpretation systems, which provide the computational assistance for such calculations, are becoming more widely used in hospitals and in large practice groups, the settings in which most electrocardiograms are obtained. Based on our observed sensitivity and specificity data, it can be estimated that when 50% of ECG examinations are performed by computerized systems, use of our new regression equations could result in 4,000,000 to 8,000,000 more correct diagnoses of the presence or absence of LVH yearly. Because of the important implications of ECG detection of LVH for judging the severity of cardiovascular disease and identifying patients at above-average risk, application of improved ECG criteria appears to be worthy of pursuit.

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