Utility of Electrocardiogram for Predicting Increased Left Ventricular Mass in Asymptomatic Men at Risk for Cardiovascular Disease
Nicolas Denarie, Ales Linhart, Jaime Levenson, and Alain Simon

The objective of this study was to test the value of electrocardiogram for predicting left ventricular mass (LVM), assessed echographically in 136 asymptomatic men with at least one major cardiovascular risk factor. We measured the Sokolow-Lyon and Cornell voltages, as well as the ratio of Cornell voltage to QRS voltage in lead II. The prevalence of left ventricular hypertrophy (LVH), defined as LVM of ≥ 125 g/m², was 6%, whereas that of increased LVM, defined as LVM of ≥ 99 g/m², the 90th upper percentile of a control group, was 29%. Receiver operating characteristics curves showed that for predicting LVH at 80% specificity, the Cornell/QRSII voltage ratio had a sensitivity of 75%, whereas those of the Cornell and Sokolow-Lyon voltages were 50% and 12.5%, respectively. For predicting increased LVM at 80% specificity, the Cornell/QRSII voltage ratio had a sensitivity of 56%, whereas the sensitivities of the Cornell and Sokolow-Lyon voltages were 36% and 22%, respectively. We conclude that, in contrast with the Sokolow-Lyon voltage, the new dimensionless Cornell/QRSII voltage shows a sensitivity at a high specificity value at least as acceptable as that of the Cornell voltage for predicting borderline-high LVM in a population with a low prevalence of LVH. Am J Hypertens 1998;11:861–865 © 1998 American Journal of Hypertension, Ltd.

KEY WORDS: Left ventricular hypertrophy, cardiovascular risk factors, prevention.

Left ventricular mass (LVM) detected by echocardiography is an independent predictor of cardiovascular morbidity and mortality, even within normal ranges. However, technical difficulties and economic considerations limit the use of the echocardiogram for evaluating LVM status. There have been serious efforts recently to improve electrocardiographic criteria for left ventricular hypertrophy (LVH), and the superior diagnostic value of new indices, such as the Cornell voltage, in detecting LVH compared with the classical Sokolow-Lyon voltage has been suggested. Nevertheless, these results were obtained mainly in North American populations and their extrapolation to populations at lower cardiovascular risk and with a lower prevalence of LVH may be irrelevant.

The objective of this investigation was to test the value of different electrocardiographic criteria for predicting increased LVM, assessed echocardiographically in a French population of asymptomatic men with at least one major risk factor, such as hypertension, hypercholesterolemia, or current smoking.
MATERIALS AND METHODS

Subjects  Subjects were recruited from an ongoing risk-factor screening program conducted at worksites for employees of several companies within the Paris area by a group of occupational health physicians (Prévention Cardiovasculaire en Médecine du Travail, PCV METRA). Subjects were referred to the hospital because of the presence of cardiovascular risk factors. At the hospital they underwent a multifactorial evaluation of their cardiovascular risk profile during 1 day of hospitalization. Requirements for inclusion in the present study were male gender, complete electrocardiographic and echocardiographic data, presence of at least one risk factor such as essential hypertension, primary hypercholesterolemia, or current smoking, freedom from cardiovascular disease including stroke, transient ischemia, coronary heart disease, congestive heart failure, and intermittent claudication, freedom from significant conduction abnormalities, including left and right bundle branch blocks, and freedom from atrial flutter and fibrillation. Finally, 136 men between the ages of 24 and 73 years (50 ± 8 [SD] years), with a body surface area (BSA) of 1.95 ± 0.12, were included in the study population. Among them, 90 subjects (66%) had mild to moderate hypertension defined by systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg (average of at least three consecutive measurements by standard sphygmomanometric procedure in the supine position), or the presence of antihypertensive drug (33 subjects). Sixty-six subjects (49%) had hypercholesterolemia, defined as a total cholesterol level of ≥ 6.2 mmol/L or the presence of lipid-lowering drug (12 subjects), and 51 subjects (38%) were current smokers, defined as regular smoking each day of the previous 3 months, regardless of the amount smoked.

An additional separate test population of 74 men was used to reassess the analysis performed in the original study population. Subjects were chosen randomly from among patients at cardiovascular risk referred to our clinic. Their anthropometric characteristics were similar to those of the original study population (eg, age of 51 ± 6 years, BSA of 1.91 ± 0.15 m²).

Methods  A standard 12-lead electrocardiogram (ECG) was recorded using the classic calibration scale (1 mV = 10 mm) and chart speed (25 mm/sec), executed by a trained nurse supervised by a physician (ND) who verified the standard position of the precordial electrodes and calibration. ECG recordings were analyzed by a single reader (ND). R and S wave amplitudes were measured in all leads and total amplitude of QRS was computed. From these parameters, the following indices were calculated: Sokolow-Lyon voltage, defined as SV1 + RV5 or V6; Cornell voltage was defined as RVL + SV3. Finally, a new dimensionless index discovered a priori in our study population and calculated as the ratio of Cornell voltage to QRS voltage in lead II (Cornell/QRSII voltage ratio) was used. The QRS voltage in lead II represents the height of the QRS wave (ie, the sum of the absolute value of R and S wave heights).

A real-time B-mode ultrasound system (Ultramark 9-HDI, Advanced Technology Laboratories, Les Ulis, France) with a 2–3-MHz broadband electronic phased array probe was used for echocardiographic examinations, all of which were performed by a single investigator (AL). Patients were examined in the lateral decubitus position. A complete examination allowed us to rule out in all study subjects the presence of hemodynamically significant valvular heart disease, left ventricular regional wall motion abnormalities, or previously unrecognized congenital heart disease. Two-dimensionally guided M-mode recording was obtained from the parasternal window. All measurements were performed online at least three times from three different cardiac cycles, and the average values of each parameter were calculated. The recommendations of the American Society of Echocardiography (ASE) were applied to all measurements for calculating the LVM with the Devereux-modified cube formula. LVM was expressed in g/m² as the ratio of left ventricular mass to BSA. LVH was defined as LVM value > 125 g/m² (the standard threshold). Increased LVM was defined as LVM value > 99 g/m², which is the 90th percentile of LVM obtained in a control group of 44 healthy male volunteers free from any cardiovascular risk factor and having the same mean age (49 ± 9 years) as the study population.

Statistical Analysis  Receiver operating characteristics (ROC) curves compared sensitivity and specificity of the three electrocardiographic criteria over a wide range of cutoff values for predicting increased left ventricular mass (LVM > 99 g/m²) and left ventricular hypertrophy (LVM > 125 g/m²) for the three ECG criteria (Figure 2). We compared areas under the ROC curves using the method of Hanley and McNeil.

RESULTS

The prevalence of increased LVM was 29%, whereas that of LVH was 6%. In the study population, LVM correlated significantly with the Cornell voltage (r = 0.34, P < .001) and the Cornell/QRSII voltage ratio (r = 0.48, P < .001), but not with the Sokolow-Lyon voltage (Figure 1). When reassessing this univariate analysis in the separate test population, we obtained the same findings as in the original study population (Figure 1).

The ROC curves show the overall performance of the Cornell/QRSII voltage ratio, the Cornell voltage, and the Sokolow-Lyon voltage for predicting both
increased LVM and LVH (Figure 2). For predicting increased LVM, at matched specificities of 80% and 95%, the Cornell/QRS\textsubscript{II} voltage ratio had sensitivities of 56% and 26%, respectively (cutoff values: 2.5 and 3.4), whereas the sensitivities of the Cornell voltage were 36% and 10%, respectively (cutoff values: 1.8 and 2.3 mV) and those of the Sokolow-Lyon voltage were 22% and 10%, respectively (cutoff values: 2.7 and 3.1

FIGURE 1. Correlations of the Sokolow-Lyon voltage, Cornell voltage, and Cornell/QRS\textsubscript{II} voltage ratio with left ventricular mass index (LVMI) in the original study population (top panels) and in a separate reassessed test population (bottom panels). Continuous lines represent linear regression lines. \( n \) = number of patients.

FIGURE 2. ROC curves for Sokolow-Lyon voltage, Cornell voltage, and Cornell/QRS\textsubscript{II} voltage ratio, plotted for various cutoff values, for determining increased LVM (left panel) and LVH (right panel), defined in the text (see Materials and Methods).
TABLE 1. COMPARISON OF THE AREAS UNDER RECEIVER OPERATING CHARACTERISTICS (ROC) CURVES FOR PREDICTING SUBJECTS WITH LEFT VENTRICULAR HYPERTROPHY (LVH) OR INCREASED LEFT VENTRICULAR MASS (LVM) IN THE STUDY POPULATION (N = 136)

<table>
<thead>
<tr>
<th>Predicted Alteration</th>
<th>ROC Curve Area</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sokolow-Lyon Voltage (1)</td>
<td>Cornell Voltage (2)</td>
</tr>
<tr>
<td>LVH</td>
<td>0.506 (0.106)</td>
<td>0.691 (0.107)</td>
</tr>
<tr>
<td>Increased LVM</td>
<td>0.359 (0.054)</td>
<td>0.668 (0.054)</td>
</tr>
</tbody>
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Values are mean (SE).

mV). For predicting LVH at matched specificities of 80% and 95%, the Cornell/QRSII voltage ratio had sensitivities of 75% and 12.5%, respectively (cutoff values: 2.7 and 3.6), whereas the sensitivities of the Cornell voltage were 50% and 0%, respectively (cutoff values: 1.9 and 2.4 mV) and those of the Sokolow-Lyon voltage were 12.5% and 12.5%, respectively (cutoff values: 2.7 and 3.2 mV).

The comparison of the areas under the ROC curves for predicting LVH showed a significant difference between the Cornell/QRSII voltage ratio and the Sokolow-Lyon voltage (P = .02), but no difference between the Cornell and Sokolow-Lyon voltages and between the Cornell/QRSII voltage ratio and the Cornell voltage (Table 1). The comparison of the areas under the ROC curves for predicting subjects who had increased LVM also showed a significant difference between the Cornell/QRSII voltage ratio and the Sokolow-Lyon voltage (P < .01), but no significant difference between the Cornell and Sokolow-Lyon voltages and between the Cornell/QRSII voltage ratio and the Cornell voltage (Table 1).

When reassessing the overall ECG test performance using ROC curves for predicting increased LVM in the test population, we obtained the same findings as in the original study population: the ROC curve area for the Sokolow-Lyon voltage (0.550 ± 0.093) was lower (P < .05) than for the Cornell/QRSII voltage ratio (0.765 ± 0.084), but not different than for the Cornell voltage (0.720 ± 0.089). No significant difference existed between ROC curve areas for the Cornell voltage and the Cornell/QRSII voltage ratio. In contrast, the ROC curves for predicting LVH could not be used in this additional test population because of the low prevalence of LVH (1%) in this population.

DISCUSSION

Because of the requirement of ECG detection of LVH for identifying patients at high risk for cardiovascular disease, the application of improved ECG criteria appears of major importance. In the present study, we have used two classic ECG criteria, the Sokolow-Lyon voltage and the Cornell voltage. We have also introduced a new criterion representing the ratio of Cornell voltage to QRS in lead II, which was not based on a specific physiopathologic rationale. We observed in our population study that among the correlations of LVM with a number of ECG criteria, the strongest were the positive correlation between Cornell voltage and LVM and the negative correlation between QRS voltage in lead II and LVM. It ensued that the construction of a ratio of Cornell voltage to QRS voltage in lead II potentiated the strength of the relation with LVM. This finding was not specific to our original study population. It was confirmed by the analysis of a separate reassessed test population showing that the Cornell/QRSII voltage ratio remained strongly correlated with LVM.

In agreement with previous studies, our results demonstrate that the classic Sokolow-Lyon voltage had the lowest performance for estimating both increased LVM and LVH when tested against the reference standard of left ventricular mass assessed echographically. The comparison of areas under ROC curves for predicting increased LVM and LVH confirms that the Cornell/QRSII voltage ratio was clearly superior to the Sokolow-Lyon voltage. In contrast, the comparison of the area under the ROC curve of the Cornell voltage with the area of the Sokolow-Lyon voltage and area of the Cornell/QRSII voltage ratio showed no clearcut difference. Such findings were confirmed by the analysis of ROC curves in the separate test population, at least for predicting increased LVM, as the low prevalence of LVH in this test population did not allow us to use ROC curves for predicting LVH adequately. Because the great majority of our subjects do not have LVH, we have tested the value of ECG criteria for increased LVM by using a high test specificity to reduce false-positive diagnoses and obtain an acceptable predictive value of a positive test. Thus, at 95% specificity, the sensitivity of the Cornell voltage was 2.6 times lower than that of the Cornell/QRSII voltage ratio and similar to that of the Sokolow-Lyon voltage for predicting increased LVM. Therefore, the Cornell voltage appears of lesser value than the Cornell/QRSII voltage ratio for predicting increased LVM in a population with a low prevalence of LVH.
As the Cornell/QRS$_{III}$ voltage ratio is simple to calculate and dimensionless, i.e., unaffected by calibration errors, it may be particularly useful for screening for borderline-high LVM in asymptomatic adults at risk for cardiovascular disease and for better stratifying the global cardiovascular risk in individuals, as the increase in LVM is associated with a continuous increase in cardiovascular morbidity and mortality.\textsuperscript{1}

There were, however, some study limitations, including potential selection bias and the use of increased LVM, in addition to LVH, for testing the utility of the electrocardiographic criteria. The results of this study may not be applied to screening of the general population because our population was selected on the basis of the presence of established risk factors and women were not included. Furthermore, the upper normal limit of LVM, defined as the 90th upper percentile of a control group of healthy male volunteers, may be also difficult to extrapolate to other populations for defining increased LVM.

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REFERENCES


