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Electrocardiographic Detection of Left Ventricular Hypertrophy by the Simple QRS Voltage-Duration Product

THOMAS J. MOLLOY, MD, PETER M. OKIN, MD, FACC,
RICHARD B. DEVEREUX, MD, FACC, PAUL KLIGFIELD, MD, FACC
New York, New York

Objectives. The object of this study was to assess the hypothesis that the product of QRS voltage and duration, as an approximation of the time-voltage integral of the QRS complex, can improve the electrocardiographic (ECG) identification of left ventricular hypertrophy.

Background. Electrocardiographic identification of left ventricular hypertrophy has been limited by the poor sensitivity of standard voltage criteria. However, increases in left ventricular mass can be more closely related to increases in the time-voltage integral of the summed left ventricular dipole than to changes in voltage or QRS duration alone.

Methods. Antemortem ECGs were compared with left ventricular mass at autopsy in 220 patients. There were 95 patients with left ventricular hypertrophy, defined by left ventricular mass index >118 g/m^2 in men and >104 g/m^2 in women. The voltage-duration product was calculated as the product of QRS duration and Cornell voltage (Cornell product) and the 12-lead sum of QRS voltage (12-lead product).

Results. At partitions with a matched specificity of 95%, each voltage-duration product significantly improved sensitivity for the detection of left ventricular hypertrophy when compared with simple voltage criteria alone (Cornell product 51% [48 of 95] vs. Cornell voltage 36% [34 of 95], $p < 0.005$ and 12-lead product 45% [43 of 95] vs. 12-lead voltage 31% [30 of 95], $p < 0.001$). Sensitivity of both the Cornell product and 12-lead product was significantly greater than that found for QRS duration alone (28%, 27 of 95, $p < 0.005$) and the Romhilt-Estes point score (27%, 26 of 95, $p < 0.005$), and compared favorably with the sensitivity of the complex Cornell multivariate score (44%, 42 of 95, p = NS). Comparison of receiver operating characteristic curves demonstrated that improved performance of the voltage-duration products for the detection of left ventricular hypertrophy was independent of test partition selection. In addition, test performance of the voltage-duration products was not significantly affected by the presence or absence of a bundle branch block.

Conclusions. These data suggest that the simple product of either Cornell or 12-lead voltage and QRS duration can identify left ventricular hypertrophy more accurately than can voltage or QRS duration criteria alone and may approach or exceed the performance of more complex multiple regression analyses.

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Because left ventricular hypertrophy is associated with an increased risk of future cardiac morbidity and mortality (1–4), its detection by cost-effective screening methods is a clinical priority (5). However, standard voltage criteria based on measured QRS amplitude in single leads or lead combinations of the widely available electrocardiogram (ECG) (6,7) have exhibited poor sensitivity for left ventricular hypertrophy at high levels of specificity (8–12). Additional measurement criteria that incorporate P wave findings, QRS duration, repolarization abnormalities and demographic data into summated scores or frequently complex multivariate regression equations have only modestly improved the overall accuracy of the ECG for left ventricular hypertrophy (8–15).

Increases in left ventricular mass have been associated with both increased magnitude and duration of the vectorcardiographic QRS complex (16–24) and also with an increase in the time-voltage integral of the 126-lead multiple dipole QRS complex (22–24). These findings suggest that the product of QRS duration and ECG voltage, as a simple approximation of the time-voltage area of the QRS complex, might more accurately reflect the presence of hypertrophy than would simple summation of individual variables. Therefore, the purpose of this study was to assess the hypothesis that the product of QRS duration and voltage can improve the ECG identification of left ventricular hypertrophy by comparison with the performance of previously derived ECG criteria with use of left ventricular mass at necropsy as the reference standard.

From the Division of Cardiology, Department of Medicine, The New York Hospital–Cornell Medical Center, New York, New York.

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Address for correspondence: Peter M. Okin, MD, The New York Hospital–Cornell Medical Center, 525 East 68 Street, New York, New York 10021.

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Table 1. Cardiac Diagnoses in 220 Autopsy Subjects

	Autopsy Subjects		Proportion With LVH	
	No.	% of Total Group (n = 220)	No.	% of Diagnostic Group
Hypertension	53	24	38 of 53	72
Coronary artery disease	78	35	45 of 78	58
Aortic stenosis	17	8	16 of 17	94
Aortic regurgitation	3	1	2 of 3	67
Mitral stenosis	6	3	4 of 6	67
Mitral regurgitation	9	4	8 of 9	89
Dilated cardiomyopathy	23	10	16 of 23	70
Restrictive cardiomyopathy	1	0.5	1 of 1	100
Pericardial disease	13	6	4 of 13	31
Cor pulmonale	5	2	0 of 5	0
No significant heart disease	73	33	10 of 73	14

LVH = left ventricular hypertrophy.

Methods

Study group. Cases were selected from review of the autopsy log of the Hospital of the University of Pennsylvania between January 1975 and April 1976 and by regular review of the autopsy log of The New York Hospital–Cornell Medical Center during several periods between October 1978 and March 1990. Complete clinical data and a 12-lead ECG of adequate technical quality in a nonpaced rhythm obtained within a mean of 16 days of death were available for a total of 220 patients, 119 men and 101 women, with a mean age of 60 years. Women with a left-sided mastectomy were excluded because a decreased distance from the heart to the chest surface has been shown to increase ECG voltage out of proportion to left ventricular mass (25,26). Clinical diagnoses are listed in Table 1.

Electrocardiography. Standard 12-lead ECGs were recorded at 25 mm/s and 1 mV/cm standardization with equipment whose frequency response characteristics met recommendations of the American Heart Association (27). Tracings were coded and interpreted by a single investigator who had no knowledge of clinical or autopsy findings. QRS duration was measured by computer to the nearest ms on digitized ECGs (n = 117) and to the nearest 10 ms with use of a magnifying graticule on analog ECGs (n = 103). Complete right bundle branch block was defined when, in the presence of the standard pattern, QRS prolongation was ≥0.12 s; complete left bundle branch block was defined when QRS prolongation was ≥0.14 s (28). In the absence of these criteria, intraventricular conduction defect was defined by a QRS duration ≥0.10 s (29).

Several widely used simple and complex ECG criteria for the detection of left ventricular hypertrophy were examined. Simple ECG criteria were based on QRS duration, single-lead QRS voltages or linear sums of QRS voltages alone. These include QRS duration; the amplitude of the R wave in lead aVL; Gubner-Ungerleider voltage (sum of the amplitude of the R wave in lead I and the amplitude of the S wave in lead III) (7); Sokolow-Lyon voltage (sum of the amplitude of the S wave in lead V_1 and the amplitude of the R wave in lead V_5 or V_6) (6); gender-specific Cornell voltage (sum of the amplitude of the R wave in lead aVL and the amplitude of the S wave in lead V_3 adjusted by the addition of 8 mm [0.8 mV] for female gender) (9) and the sum of QRS voltage in all 12 leads (30). More complex ECG criteria for hypertrophy based on weighted scores that incorporate QRS duration, QRS voltages, repolarization changes and P wave abnormalities, the Romhilt-Estes point score (31) and the Cornell multivariate regression-based score (9) were also determined. To test the hypothesis that an approximation of the time-voltage area under the QRS may be a useful marker for left ventricular hypertrophy, a voltage-duration product was calculated for each simple voltage criterion as the product of QRS duration and voltage.

Autopsy methods. Left ventricular mass was measured by the chamber partition method (32) and was normalized for body surface area. Left ventricular hypertrophy was defined as left ventricular mass index >118 g/m^2 in men and >104 g/m^2 in women, which approximate the upper 97th percentile of normal left ventricular mass index in a subset of 39 autopsy patients with neither intrinsic disease nor hemodynamic load affecting the left ventricle (9). According to these partitions, hypertrophy was present in 43% (95 of 220) of patients at autopsy.

Statistical methods. The strength of the relation between ECG criteria and left ventricular mass index was assessed by least square linear correlation. Coefficients of correlation (r) were compared statistically with use of a two-tailed Fisher Z transformation. Definitions of sensitivity and specificity conform to standard use. Comparison of test sensitivity of the voltage-duration product with simple and complex ECG criteria was performed at matched specificity of 95% with McNemar's modification of the chi-square method for paired proportions.

Because sensitivity and specificity of a test are dependent on the partition value chosen for test positivity, test accuracy of the voltage-duration products and simple and complex ECG criteria were also compared with use of receiver operating characteristic curve analysis. Receiver operating characteristic curves were compared statistically by means of a univariate Z score test of the difference between the areas under two curves (33). Because the clinically relevant area of interest of the performance of ECG criteria for the detection of left ventricular hypertrophy is in the range of test specificities from 90% to 100%, overall performance of each criterion was also compared with performance of the voltage-duration product by means of a univariate Z score test of the difference between the partial areas under respective receiver operating characteristic curves at specificities between 90% and 100% (34). Comparison of proportions between groups was performed using a two-tailed Fisher exact test. For all tests, a p value of < 0.05 was required for rejection of the null hypothesis.

Table 2. Correlation Between ECG Criteria and Left Ventricular Mass Index at Autopsy

	Correlation Coefficients With Mass Index		
	Voltage	p Value	Voltage-QRS Duration Product
Voltage criteria			
Cornell voltage	0.47*	< 0.05	0.57
12-lead QRS sum	0.50*	< 0.01	0.64
Sokolow-Lyon voltage	0.43†	< 0.001	0.60
Gubner-Ungerleider voltage	0.32‡	NS	0.43†
Amplitude of R wave in aVL	0.30‡	NS	0.41†
Other criteria			
QRS duration	0.53		
Romhilt-Estes point score	0.46*		
Cornell multivariate score	0.60		

*p < 0.05, †p < 0.01, ‡p < 0.001 versus Cornell multivariate score and product of QRS duration with the 12-lead QRS sum, Cornell voltage and Sokolow-Lyon voltage.

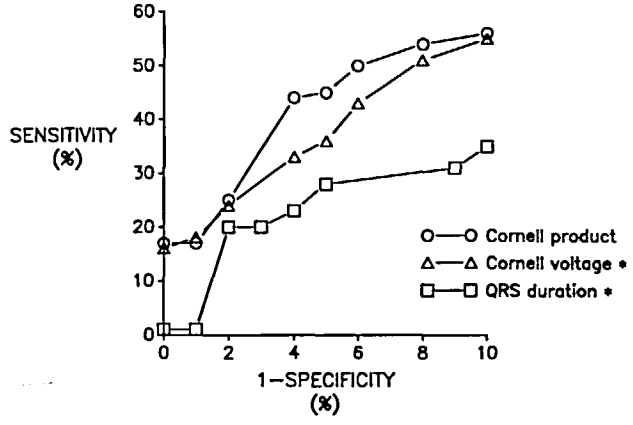


Figure 1. Receiver operating characteristic curves comparing performance of QRS duration, Cornell voltage and the Cornell product for the identification of left ventricular hypertrophy. *p < 0.05 versus Cornell product.

Results

Relation of ECG criteria to left ventricular mass index. The linear correlates of ECG findings with left ventricular mass index are shown in Table 2. There were only modest relations between left ventricular mass index and QRS voltage criteria alone. Correlation of QRS duration alone with left ventricular mass index was significantly greater than that for Gubner-Ungerleider voltage or Sokolow-Lyon voltage and was similar to the correlations of Cornell voltage and Romhilt-Estes point score with indexed mass. Correlation with left ventricular mass index was significantly improved by the product of QRS duration with Cornell, 12-lead and Sokolow-Lyon voltage, with coefficients of correlation similar to the regression-based Cornell multivariate score and greater than any of the pure voltage criteria or the Romhilt-Estes point score.

Electrocardiographic identification of left ventricular hypertrophy. Relative performance of ECG criteria for the identification of left ventricular hypertrophy and the effect of the simple product of QRS duration with voltage on test performance is examined in Table 3 and Figures 1 to 4. At matched specificity of 95%, individual QRS voltage and duration criteria had poor sensitivity for hypertrophy, ranging from 13% for the R wave in lead aVL to 36% for Cornell voltage (Table 3). Test performance of Cornell voltage was enhanced by multiplication by the QRS duration; at a matched specificity of 95%, the Cornell voltage-duration product identified left ventricular hypertrophy with a sensitivity of 51% (48 of 95), which was significantly higher than the sensitivity of either QRS duration or Cornell voltage criteria alone. Relative to simple voltage criteria, test sensitivity of the 12-lead sum and Sokolow-Lyon voltage were also improved by creation of a voltage-duration product, but there was no significant change in test performance for the

Table 3. Sensitivity of Electrocardiographic Criteria for the Identification of Left Ventricular Hypertrophy at Partitions With Matched Specificity of 95%

	Voltage			Voltage-QRS Duration Product	
	Partition (mm)	Sensitivity (%)	p Value	Partition (mm·ms)	Sensitivity (%)
Voltage criteria					
Cornell voltage	28*	36†	<0.005	2,436*	51
12-lead QRS sum	179	31†	<0.001	17,472	45
Sokolow-Lyon voltage	31	24‡	<0.05	2,880	34†
Gubner-Ungerleider voltage	19	19‡	NS	1,980	15‡
Amplitude of R wave in aVL	9	13‡	NS	968	15‡
Other criteria	Partition				
QRS duration	120 ms	28†			
Romhilt-Estes point score	5	27†			
Cornell multivariate score	0.746	44			

*Adjusted for gender (see text). †p < 0.005, ‡p < 0.001 versus product of QRS duration and Cornell voltage.

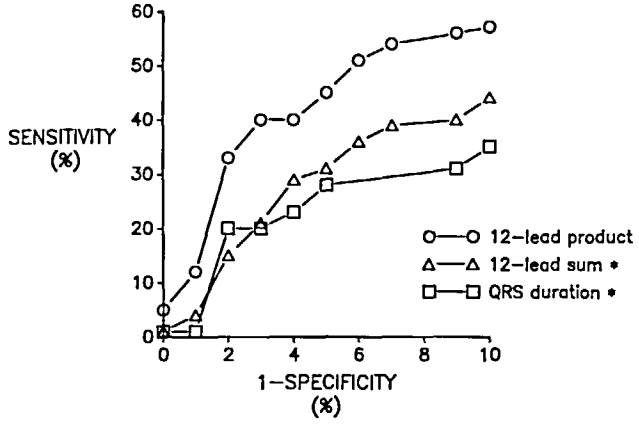


Figure 2. Receiver operating characteristic curves comparing performance of QRS duration, 12-lead voltage and the 12-lead product for the identification of left ventricular hypertrophy. *p < 0.05 versus 12-lead product.

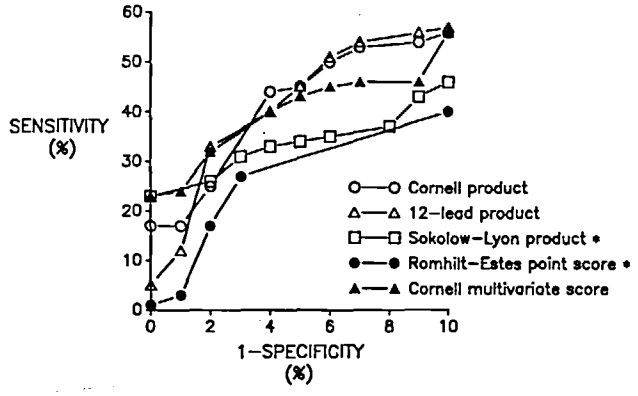
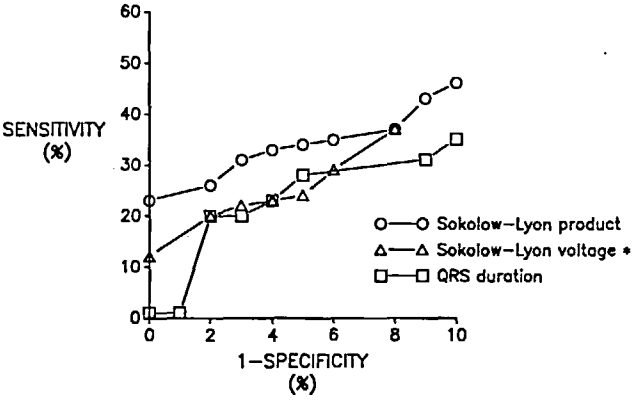


Figure 4. Receiver operating characteristic curves comparing performance of the voltage-duration products, the Romhilt-Estes point score and the Cornell multivariate score for the identification of left ventricular hypertrophy. *p < 0.05 versus Cornell product, 12-lead product and Cornell multivariate score.

voltage-duration product of either Gubner-Ungerleider voltage or the R wave in lead aVL (Table 3). Comparison of receiver operating characteristic curves confirmed that the superior performance of the Cornell product (Fig. 1) and 12-lead product (Fig. 2) relative to simple voltage and QRS duration was independent of partition value selection. Overall performance of the Sokolow-Lyon product was significantly greater than that of simple Sokolow-Lyon voltage criteria alone but was not statistically better than QRS duration alone (Fig. 3).

The performance of the voltage-duration products relative to complex ECG criteria that incorporate QRS voltages, QRS duration, repolarization changes and P wave abnormalities is examined in Table 3 and Figure 4. At a matched specificity of 95%, the 51% sensitivity of the Cornell product for the detection of left ventricular hypertrophy was significantly greater than the 34% sensitivity of the Sokolow-Lyon product and the 27% sensitivity of a Romhilt-Estes point score of >5 but was not significantly greater than the 45% sensitivity of the 12-lead product or the 44% sensitivity of the Cornell multivariate regression-based score. Comparison of receiver operating characteristic curves revealed no significant difference in overall performance of the Cornell product, the 12-lead product and the Cornell multivariate score and demonstrated superior overall performance of these three methods relative to the Sokolow-Lyon product and the Romhilt-Estes point score (Fig. 4).

Figure 3. Receiver operating characteristic curves comparing performance of QRS duration, Sokolow-Lyon voltage and the Sokolow-Lyon product for the identification of left ventricular hypertrophy. *p < 0.05 versus Sokolow-Lyon product.



Effect of bundle branch block on electrocardiographic identification of left ventricular hypertrophy. The effects of underlying right or left bundle branch block on the correlation of ECG findings with indexed left ventricular mass are examined in Table 4. Compared with patients without bundle branch block, the small subset of patients with bundle branch block exhibited trends toward poorer correlation of

Table 4. Effect of Bundle Branch Block on the Correlation Between Electrocardiographic Criteria and Left Ventricular Mass Index

Electrocardiographic Criteria	Correlation Coefficients With Mass Index*	
	Patients Without BBB (n = 195)	Patients With BBB (n = 25)
Cornell product	0.60	0.40
12-lead product	0.58	0.74
Sokolow-Lyon product	0.60	0.64
12-lead sum	0.48†	0.66
Cornell voltage	0.55	0.37
Sokolow-Lyon voltage	0.47†	0.60
QRS duration	0.49†	0.50
Cornell multivariate score	0.60	0.55

*There were no significant differences in correlation coefficients between patients with and without bundle branch block. †p < 0.05 versus Cornell product, Sokolow-Lyon product and Cornell multivariate score in patients without bundle branch block. BBB = bundle branch block.

Table 5. Effect of Bundle Branch Block on the Sensitivity and Specificity of Electrocardiographic Criteria for the Identification of Left Ventricular Hypertrophy

Criteria	Sensitivity (%)			Specificity (%)		
	Patients Without BBB (n = 76)	p Value	Patients With BBB (n = 19)	Patients Without BBB (n = 119)	p Value	Patients With BBB (n = 6)
Cornell product	51	NS	50	95	NS	100
12-lead product	39	NS	58	96	NS	83
Sokolow-Lyon product	34*	NS	32	95	NS	100
Cornell voltage	38*	NS	26	95	NS	100
12-lead sum	33*	NS	21	95	NS	100
Sokolow-Lyon voltage	27†	NS	11*	95	NS	100
Gubner-Ungerleider voltage	14‡	NS	5*	95	NS	100
Amplitude of R wave in aVL	13‡	NS	11*	93	NS	100
QRS duration (120 ms)	12‡	<0.001	100*	97	<0.01	50
Romhilt-Estes score	26†	NS	32	97	NS	100
Cornell multivariate score	43	NS	47	95	NS	100

*$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$ versus Cornell product in patients with or without bundle branch block. BBB = bundle branch block.

the Cornell product and simple Cornell voltage criteria with indexed left ventricular mass, but there was no difference in the correlation of QRS duration, the Sokolow-Lyon product or the Cornell multivariate score. There were trends toward a higher correlation of the 12-lead sum and product and of Sokolow-Lyon voltage in patients with bundle branch block. Among the large subset of patients without bundle branch block, correlation with left ventricular mass index remained significantly greater for the voltage-duration product and the Cornell multivariate score than for QRS duration alone or for any of the simple voltage criteria except Cornell voltage.

Performance of ECG criteria for the detection of left ventricular hypertrophy in relation to the presence or absence of complete left or right bundle branch block is examined in Table 5. As expected, performance of QRS duration alone for the identification of hypertrophy was significantly affected by the presence or absence of bundle branch block. By group definition, a QRS duration of 120 ms had 100% sensitivity for left ventricular hypertrophy among patients with bundle branch block, whereas nonspecific intraventricular conduction defects of equal duration were present in only a small proportion of patients who had hypertrophy in the absence of a bundle branch block. However, specificity of this QRS duration partition was significantly lower in patients with bundle branch block (50% [3 of 6] vs. 97% [116 of 119], $p < 0.01$). In contrast, there was no significant difference in test sensitivity or specificity of the Cornell product, the 12-lead product, the Sokolow-Lyon product, the Cornell multivariate score, the Romhilt-Estes point score or any of the simple voltage criteria between patients with and without bundle branch block, although there was a trend toward lower sensitivity of simple Cornell, 12-lead and Sokolow-Lyon voltage among patients with bundle branch block.

Among the small subset of patients with left ventricular hypertrophy and bundle branch block, the 50% sensitivity of the Cornell product was significantly greater than the 11% sensitivity of Sokolow-Lyon voltage and the R wave amplitude in lead aVL and significantly greater than the 5% sensitivity of Gubner-Ungerleider voltage, with a trend toward better performance than simple Cornell and 12-lead voltage, the Sokolow-Lyon product and the Romhilt-Estes point score. In contrast, among the larger subset of patients with left ventricular hypertrophy and no bundle branch block, the 51% sensitivity of the voltage-duration product was significantly greater than the 12% sensitivity of QRS duration alone and was also significantly greater than the sensitivity of the simple voltage criteria and the Romhilt-Estes point score. Test specificity of the voltage-duration product and the other ECG criteria was similarly high among patients with and without bundle branch block.

Discussion

These data demonstrate that multiplication of several standard voltage criteria by QRS duration results in simple voltage-duration products that can improve ECG identification of left ventricular hypertrophy. These findings support the concept that a time-voltage integral of the QRS complex more accurately reflects left ventricular mass than do individual QRS amplitude or duration findings alone.

Relation of QRS voltage and duration to left ventricular mass. *QRS voltage and left ventricular hypertrophy.* Increased QRS voltage, attributed to the increased size of the electrical activation boundary according to solid angle theory (35), is a highly specific but poorly sensitive finding in left ventricular hypertrophy (8–12). Attempts to increase sensitivity of the ECG for the identification of left ventricular hypertrophy have focused on summing up additional ECG and demographic variables into complex linear scores that have modestly improved performance of the ECG for the detection of hypertrophy (8–15). However, these multivariate criteria may be closer to models of clinical decision

making than to fundamentally improved interpretation of the ECG.

QRS duration and left ventricular hypertrophy. QRS duration has also been found to correlate with left ventricular mass (16–24,36,37). The mechanism for QRS prolongation in left ventricular hypertrophy has yet to be determined. However, it may be related to the longer time required to activate myocardium that is increasingly distant from specialized conduction tissue (16,37), to decreased upstroke velocity of the action potential in hypertrophied myocardium (38) or to changes in activation sequence or changes in the relative conductivity of fibrotic intracellular and extracellular spaces (17,39,40). Although QRS duration alone has also proved to be poorly sensitive at clinically relevant levels of specificity, incorporation of QRS duration into linear scores has resulted in modest improvements in the sensitivity of complex ECG criteria for left ventricular hypertrophy and in their correlation with left ventricular mass (8,9,14).

Voltage-duration product and left ventricular hypertrophy. Observations that the time-voltage integral of the orthogonal lead vectorcardiographic QRS complex and the summed time-strength left ventricular dipole can improve ECG correlation with left ventricular mass (16–24) suggest that an ECG representation of the time-voltage integral of ventricular activation should more accurately reflect increases in left ventricular mass. The present study extends these findings to the 12-lead ECG, showing that the simple voltage-duration product, as an approximation of the time-voltage area of the QRS complex, can improve ECG correlation with left ventricular mass and ECG identification of left ventricular hypertrophy. These findings suggest that increases in left ventricular mass may result in subtle increases in both QRS voltage and duration that together produce a proportionally greater increase in the area under the QRS complex than in either QRS voltage or duration alone. Thus, the voltage-duration product may more accurately reflect the presence and severity of hypertrophy than ECG scores that incorporate both QRS voltage and duration only as linear weighted sums, such as the Romhilt-Estes point score and the Cornell multivariate score.

Effect of bundle branch block on the ECG identification of left ventricular hypertrophy. Although autopsy (41) and echocardiographic (42,43) studies suggest that a high proportion of patients with left bundle branch block have anatomic left ventricular hypertrophy, most previous studies of ECG identification of left ventricular hypertrophy have either excluded patients with conduction blocks because of uncertainty regarding test applicability in the presence of prolonged QRS duration or have derived separate criteria for these patients. The present findings confirm the high prevalence of left ventricular hypertrophy in patients with bundle branch block (78%, 18 of 23) and the poor performance of standard voltage criteria for the detection of hypertrophy in this group. In contrast, performance of the voltage-duration products and other criteria incorporating both QRS duration and voltage was not substantially affected by conduction abnormalities, maintaining similarly high specificity and equivalent sensitivity for left ventricular hypertrophy independent of the presence or absence of a bundle branch block.

Clinical implications. Clinical usefulness of ECG criteria for the detection of left ventricular hypertrophy has been limited by the low sensitivity of simple voltage criteria at acceptable levels of test specificity (8–12). Although complex regression-based equations linking ECG and clinical variables such as the Cornell multivariate score have significantly improved test sensitivity, these methods require computer-assisted calculation (8,9,14).

Conclusions. The present study suggests that the simple product of Cornell voltage and QRS duration can significantly improve the sensitivity of ECG identification of left ventricular hypertrophy at acceptably high levels of test specificity. It is necessary to have further study of these methods and verification of criteria partitions in less highly selected clinical groups with use of echocardiographic left ventricular mass determinations. The voltage-duration product can be readily calculated by most commercially available ECG systems and can be easily calculated even in the absence of computer-measured QRS duration and voltage. Because test performance of the Cornell product does not appear to be significantly affected by conduction system disease, application of this method need not be limited to patients without bundle branch blocks. These findings suggest that more precise measurement of the time-voltage integral of the area under the QRS complex available with signal-averaged ECG techniques may further enhance the accuracy of the ECG for the detection of left ventricular hypertrophy (44,45) and provide future direction for continued investigation.

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