Left ventricular mass by 12-lead ECG in healthy subjects: Comparison to cardiac magnetic resonance imaging

[*]Minna Carlsson, [*]Elin Trägårdh, MD, [*]Henrik Engblom, MD, Erik Hedström, [†]Galen Wagner, MD, [*]Olle Pahlm, MD, PhD, [*]Håkan Arheden, MD, PhD

[*]Department of Clinical Physiology, Lund University Hospital, Lund, Sweden,

[†]Duke University Medical Center, Durham, NC, USA

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Address Correspondences to:
Henrik Engblom, MD
Lund University Hospital
S-221 85 Lund, Sweden
Tel: +46 46 173340
Fax: +46 46 151769
E-mail: henrik.engblom@med.lu.se

ABSTRACT

The ability to estimate left ventricular mass (LVM) from the standard 12-lead electrocardiogram (ECG) has been shown to be limited, since there is a considerable variability of the normal 12-lead ECG due to demographic and anthropometric variables. We sought to study LVM, in healthy subjects, and its relationship with QRS duration and established electrocardiographic criteria for left ventricular hypertrophy (LVH). Cardiac magnetic resonance imaging (CMR) was used to measure LVM. Seventy-one healthy volunteers (36 males, age range 21-82 years) were studied. All ECG criteria tested showed a statistically significant relationship with LVM. The highest R-value was found between LVM and QRS duration as well as the 12-lead voltage-duration product ($R = 0.59$, $p < 0.001$ for both). The lowest R-value was found for the Sokolow-Lyon voltage criterion ($R = 0.25$, $p = 0.033$). LVM differed significantly between sexes, as did all ECG criteria except the Sokolow-Lyon criterion. Thus, in healthy subjects, QRS duration alone is equally or more strongly correlated to LVM than are established electrocardiographic LVH criteria.

Keywords: left ventricular mass, magnetic resonance imaging, 12-lead ECG, healthy subjects, left ventricular hypertrophy

INTRODUCTION

The ability to estimate left ventricular mass (LVM) from the standard 12-lead electrocardiogram (ECG) is limited. Demographic and anthropometric variables such as age, sex, height, weight and body fat all contribute to variability of the 12-lead ECG (1-12). Thus, heterogeneity with respect to these determinants may explain the limited accuracy of the 12-lead ECG in estimating LVM. Previous studies (13, 14) have shown that electrocardiographic criteria for left ventricular hypertrophy (LVH) which consider both QRS voltages and QRS duration are more strongly correlated to LVM than are QRS voltage criteria alone.

In recent years, the clinical use of cardiac magnetic resonance (CMR) has increased substantially because of its high image quality in almost all patients and its great ability to depict soft tissue. These features permit CMR to measure cardiac structures and function with high accuracy and reproducibility, often superior to those achieved by other imaging modalities, such as echocardiography (15-17).

Normal variability of QRS duration and voltages due to differences in LVM measured by CMR, in a population of healthy subjects over a wide age range, has not yet been explored. We therefore sought to investigate the relationship between LVM and QRS duration as well as various established electrocardiographic LVH criteria in healthy subjects, and to test the hypothesis that there is a strong relationship between LVM and QRS duration in comparison to the relationship between LVM and established electrocardiographic LVH criteria in this population. We also sought to explore the influence of demographic and anthropometric variables on the various ECG criteria.

MATERIALS AND METHODS

Study population and study design

Seventy-one healthy volunteers (36 males, 35 females; age range, 21-82) were prospectively recruited from the local community in Lund, Sweden. Inclusion criteria were a) no history or clinical signs of cardiovascular disease, systemic or metabolic disease or treatment with medication b) normal 12-lead ECG (no signs of bundle branch block, fascicular block, pre-excitation or ischemic heart disease) c) normal blood pressure (systolic ≤ 140 mmHg and diastolic ≤ 90 mmHg). No subject was excluded on the basis of global or local LV dysfunction or cardiac pathology on CMR. The study was approved by the local ethics committee at Lund University and all subjects gave their written, informed consent to participate in the study.

Magnetic resonance imaging and analysis

MR imaging was performed in supine position with head first on a commercially available 1.5T scanner (Vision, Siemens Medical Solutions, Erlangen, Germany) using a phased-array body coil. As previously described (18) a turbo fast low-angle shot scout imaging protocol permitted identification of the cardiac axis for performance of diagnostic short-axis imaging. Sequential gradient echo short-axis cine images (base to apex; slice thickness 10 mm, field of view 380 mm, matrix 126x256, repetition time 100 ms (echo-shared resulting in phases every 50 ms), time to echo 4.8 ms) covering the entire LV were acquired during breath hold after normal expiration. Three long-axis images (two-, three- and four-chamber views) were also acquired. The acquisition was triggered by ECG.

The gradient echo short-axis images were used to measure LVM by planimetry of the manually defined endocardial and epicardial borders on each short-axis image covering the

entire LV (Fig 1). The measurement was performed in both end-diastole (Fig 1a) and end-systole (Fig 1b) to enable calculation of left ventricular ejection fraction. Papillary muscles were included in the LVM.

To examine the interobserver variability a subset of 20 subjects was analyzed by 2 observers blinded to each other's results.

Electrocardiographic recording and analysis

The 12-lead ECGs were recorded on a MEGACART-R (Siemens-Elema AB, Solna, Sweden) with a sampling rate of 500 Hz and the frequency response set at the range of 0.05-150Hz.

The ECG measurements were performed by computer. Before analysis, the ECGs were screened for abnormalities by an experienced ECG reader (GW).

The following ECG criteria were examined: 12-lead sum of voltages (the sum of Q, R and S wave amplitudes in all 12 leads) (13), Sokolow-Lyon voltage (sum of S-wave amplitude in lead V1 and R-wave amplitude in lead V5 or V6) (19), Cornell voltage (sum of R-wave amplitude in lead aVL and of S-wave amplitude in lead V3) (13), Gubner-Ungerleider voltage (sum of R-wave amplitude in lead I and S-wave amplitude in lead III) (20), RV5 voltage (R-wave amplitude in lead V5) and QRS duration. A voltage-duration product for each criterion was also calculated by multiplying the voltage criterion by QRS duration.

Statistical analysis

All measurements are expressed as mean ± SD. Continuous data were subjected to the Kolmogorov-Smirnov test to determine their distribution. A Gaussian distribution was found for all variables, except for the Gubner-Ungerleider product. However, since a large number of subjects was included in the study, parametric tests were performed throughout. Mean values for males and females were compared using independent Student's t-test. The Pearson correlation coefficient was used to assess the strength of the relationship between LVM and

various ECG criteria. Differences in correlation coefficients between QRS duration and the ECG voltage criteria as well as the difference for each of the corresponding voltages and voltage-duration products were compared by two-tailed tests after application of Fisher's Z transformation. Multiple regression analysis with forward selection was used to assess the influence of LVM, age, height, weight, and BSA on the various ECG criteria. The contributions of individual variables were reported as the partial R-value. Inter-observer variability was assessed by Pearson's correlation coefficient. P-value < 0.05 was considered to indicate statistical significance. SPSS for Windows, version 12.0 (SPSS Inc., Chicago, Il) was used for all statistical analyses.

RESULTS

Study population characteristics

The study population was well distributed into different age groups (Table 1). There was a good balance between sexes. The LVM ranged from 96g – 223g.

Relation between LVM and ECG criteria

The correlations between LVM and the ECG criteria are shown in Table 2. The ECG criteria with the highest R-values were the QRS duration (Figure 2A) and 12-lead voltage-duration product ($R = 0.59$, $p < 0.001$ for both). The Sokolow-Lyon voltage criterion (Figure 2B) showed the lowest R-value ($R = 0.25$, $p = 0.033$). QRS duration was more strongly correlated to LVM than were the Sokolow-Lyon voltage, Gubner-Ungerleider voltage and RV5 criteria ($p = 0.005$, $p = 0.029$ and $p = 0.030$, respectively). However, the differences between QRS duration and Cornell voltage as well as 12-lead sum of voltages were not significant ($p = 0.29$ and $p = 0.32$). For all ECG criteria, the R-value increased when voltage-duration product was considered instead of the voltage criterion alone. This was most prominent for the Sokolow-Lyon criterion. Although the trend was clear, the increase in R-value was not statistically significant for any of the voltage-duration products. The variability of LVM measurement was 0.5 ± 4g between readers ($R = 0.99$).

Influence of demographic and anthropometric variables

The influence of demographic and anthropometric variables on the ECG criteria is shown in Table 3. LVM was the only independent predictor of the Cornell voltage and voltage-duration product criteria as well as the RV5 voltage-duration product criterion. In addition to LVM,

height remained significant for prediction of QRS duration. Of interest, LVM was not an independent predictor of the Sokolow-Lyon voltage criterion.

Sex differences

The sex differences in demographic and anthropometric variables as well as the various ECG criteria are shown in Table 4. LVM differed significantly between males and females (186g ± 21g vs. 138g ± 23g). A significant sex difference was also found for all other demographic and anthropometric variables except for age ($p = 0.75$). Furthermore, a significant difference was found between males and females for all ECG criteria, except for the Sokolow-Lyon voltage criterion ($p = 0.13$).

DISCUSSION

The main result of this study was that in healthy subjects QRS duration alone is equally or more strongly correlated to LVM than are established electrocardiographic LVH criteria.

Influence of demographic and anthropometric variables on the QRS complex

The data show a clear trend towards increased correlation coefficients for LVM and established electrocardiographic LVH criteria when multiplying the voltage criterion with QRS duration (voltage-duration product). Sugita et al (10) have previously shown that the correlation between LVM assessed by echocardiography and RV5 is significantly better in adolescents within the low and middle body-fat range than adolescents in the high body-fat range. It may be that in the absence of conduction disturbances due to LVH, the amount of body fat affects QRS voltages more than QRS duration, thus explaining why R-values for voltage-duration products are equal or lower than that of QRS duration alone in subjects with no cardiac disease. Body fat was, however, not considered in the present study.

All ECG criteria that depend on absolute voltages in single leads (all ECG criteria except QRS duration and the12-lead sum of voltages in the present study) are sensitive to the electrical axis in the frontal or horizontal plane. Hence, independence of electrical axis might explain why QRS duration and 12-lead voltage-duration product showed higher correlation coefficients than the other electrocardiographic LVH criteria.

The finding that the correlation coefficients increased for all ECG criteria when the QRS voltage-duration product was considered instead of the simple voltage criteria is supported by the findings in a previous study by Okin et al (14) in which LVM was assessed by echocardiography. In that study, however, QRS duration alone was not as strongly correlated

to LVM as for instance the Sokolow-Lyon voltage criterion, which showed the weakest correlation to LVM in the present study.

Left ventricular hypertrophy versus physiological differences in LVM

Previous animal and human studies have shown that the pathologically changed myocardium found in LVH differs from the healthy myocardium at molecular, cellular and tissue level (21-27). Thus, LVH may lead to changes in the myocardial conduction properties and alter the ECG in different ways than a physiologically large heart. Changes in QRS-duration with increasing LVM within normal physiological limits may be attributed to a longer time required to activate the increased amount of myocardium itself.

Sex differences

There was a significant difference between males and females with regard to all variables examined except age and the Sokolow-Lyon voltage criterion. These findings are in accordance with previous reports on sex differences of LVM and ECG measures (1, 16, 28, 29). The lower voltages found in females might be explained by the lower LVM, height, weight and body surface area found in this group. It has previously been shown, however, that some sex differences in ECG measures persist after correcting for these anthropometric variables (5). Another variable potentially contributing to differences in voltages between males and females might be the increased distance between the precordial leads and the myocardium in females caused by increased amount of breast tissue in this group (30). In fact, increased QRS voltages have been found after mastectomy (31).

Limitations of the study

In the present study a relatively small number of subjects was studied, compared to previous studies comparing LVM and ECG criteria (10, 14, 32). In these previous studies, however, LVM was assessed by echocardiography, which has considerably lower accuracy than CMR for quantitative measurements of LVM (17). Furthermore, the range of LVM was limited compared to these previous studies since only healthy subjects were studied. The ECG criteria tested were all developed to diagnose LVH. The aim of the present study was, however, to study how these ECG criteria vary with LVM in healthy subjects. Furthermore, the study population was well balanced regarding both sexes and age. The gradient-echo MR technique used in the present study has been shown to slightly overestimate LVM (33) compared to the more recent developed steady state free precession MR technique. It does, however, not affect the relationship between LVM and the ECG criteria examined in the present study, since this was a systematic difference.

CONLUSION

In healthy subjects QRS duration alone is equally or more strongly correlated to LVM than are established electrocardiographic LVH criteria.

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FIGURE LEGENDS

Figure 1

Delineation of endocardium and epicardium on cardiac magnetic resonance short-axis images. The left ventricular mass was delineated in both end-diastole (A) and end-systole (B) to enable determination of left ventricular ejection fraction.

Figure 2

The relationship between LVM and (A) QRS duration and (B) the Sokolow-Lyon voltage criterion. QRS duration showed the highest R-value and Sokolow-Lyon voltage criterion the lowest of the ECG criteria examined.

Table 1. Study population characteristics

	mean ± SD
Age (yrs)	47 ± 17
20 - 29	n = 13
30 - 39	n = 15
40 - 49	n = 13
50 - 59	n = 14
60 - 69	n = 7
> 70	n = 9
Sex (males/females)	36/35
Weight (kg)	74 ± 13
Height (cm)	175 ± 9
Body surface area (m^2)	1.89 ± 0.19
Left ventricular mass (g)	162 ± 32
End-diastolic volume (ml)	140 ± 31
End-systolic volume (ml)	55 ± 18
Ejection fraction (%)	61 ± 8

Table 2. The univariate relationships between electrocardiographic criteria and left ventricular mass

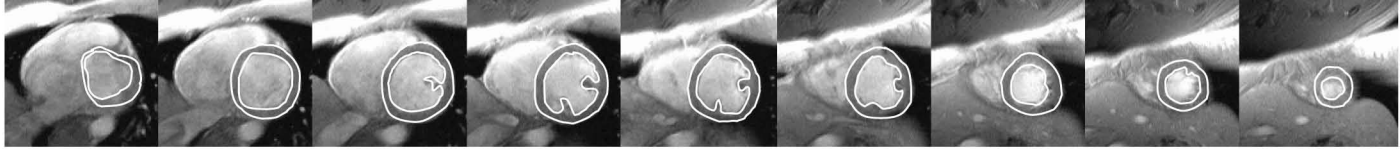
	Voltage alone		Voltage-duration product	
ECG criterion	R (R^2)	P value	R (R^2)	P value
Sokolow-Lyon	0.25 (0.06)	0.033	0.42 (0.18)	<0.001
Gubner-Ungerleider	0.32 (0.10)	0.007	0.42 (0.18)	<0.001
RV5	0.36 (0.13)	0.002	0.47 (0.22)	<0.001
Cornell	0.49 (0.24)	<0.001	0.57 (0.32)	<0.001
12-lead sum	0.49 (0.24)	<0.001	0.59 (0.35)	<0.001
QRS duration	0.59 (0.35)	<0.001	-	-

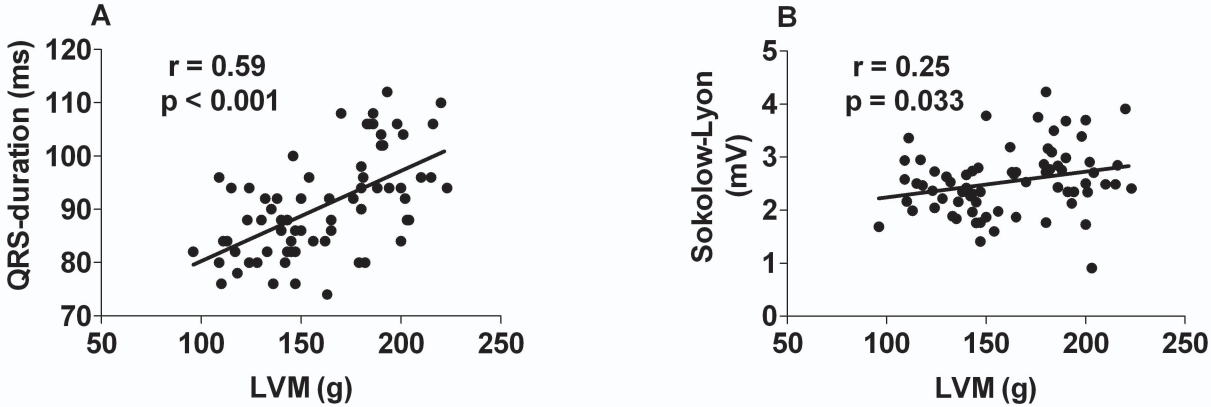
Table 3. Stepwise multiple linear regression analysis of electrocardiographic criteria with demographic and anthropometric variables.

ECG criteria	β-coefficient	Partial R	Overall R	P value
Sokolow-Lyon voltage			0.53	<0.001
Age	-0.32	-0.35		0.003
Height	0.60	0.45		<0.001
Weight	-0.51	-0.39		0.001
Sokolow-Lyon product			0.62	<0.001
LVM	0.40	0.33		0.007
Age	-0.24	-0.28		0.021
Height	0.51	0.39		0.001
Weight	-0.55	-0.42		<0.001
Gubner-Ungerleider voltage			0.45	<0.001
LVM	0.39	0.39		0.001
Age	0.32	0.33		0.005
Gubner-Ungerleider product			0.50	<0.001
LVM	0.48	0.48		<0.001
Age	0.29	0.31		0.008
RV5 voltage			0.51	<0.001
LVM	0.43	0.33		0.006
Height	0.42	0.30		0.012
Weight	-0.52	-0.36		0.002
RV5 product			0.47	<0.001
LVM	0.47			<0.001
Cornell voltage			0.49	<0.001
LVM	0.49			<0.001
Cornell product			0.57	<0.001
LVM	0.57			<0.001
12-lead sum voltage			0.63	<0.001
LVM	0.69	0.54		<0.001
Age	-0.27	-0.32		0.008
Weight	-0.38	-0.34		0.004
12-lead sum product			0.66	<0.001
LVM	0.74	0.58		<0.001
Age	-0.20	-0.25		0.036
Weight	-0.30	-0.28		0.018
QRS duration			0.62	<0.001
LVM	0.40	0.36		0.002
Height	0.28	0.25		0.034

Table 4. Sex differences (mean ± SD).

	Males	Females	P value
Age (yrs)	46 ± 16	47 ± 17	0.75
Weight (kg)	81 ± 9	67 ± 13	< 0.001
Height (cm)	181 ± 6	169 ± 6	< 0.001
BSA (m^2)	2.01 ± 0.13	1.76 ± 0.17	< 0.001
LVM (g)	186 ± 21	138 ± 23	< 0.001
QRS duration (ms)	96 ± 9	85 ± 6	< 0.001
12-lead sum of voltages (mV)	16.8 ± 3.6	14.0 ± 2.8	0.001
12-lead sum product	1630 ± 446	1193 ± 257	< 0.001
RV5 (mV)	1.8 ± 0.5	1.4 ± 0.4	0.002
RV5 product	127 ± 57	122 ± 34	< 0.001
Sokolow-Lyon voltage	2.7 ± 0.7	2.4 ± 0.6	0.13
Sokolow-Lyon product	258 ± 74	207 ± 53	0.001
Cornell voltage	1.5 ± 0.5	0.9 ± 0.3	< 0.001
Cornell product	144 ± 52	80 ± 29	< 0.001
Gubner-Ungerleider voltage	1.0 ± 0.2	0.8 ± 0.5	0.02
Gubner-Ungerleider product	95 ± 47	65 ± 21	0.001


A
B


A
QRS-duration (ms)
120
110
100
90
80
70
r = 0.59
p < 0.001
50
100
150
200
250
LVM (g)
B
Sokolow-Lyon (mV)
5
4
3
2
1
0
r = 0.25
p = 0.033
50
100
150
200
250
LVM (g)