

Electrocardiographic Criteria for Left Ventricular Hypertrophy in Children

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Abstract Previous studies to determine the sensitivity of the electrocardiogram (ECG) for left ventricular hypertrophy (LVH) in children had their imperfections: they were not done on an unselected hospital population, several criteria used in adults were not applied to children, and obsolete limits of normal for the ECG parameters were used. Furthermore, left ventricular mass (LVM) was taken as the reference standard for LVH, with no regard for other clinical evidence. The study population consisted of 832 children from whom a 12-lead ECG and an M-mode echocardiogram were taken on the same day. The validity of the ECG criteria was judged on the basis of an abnormal LVM index, either alone or in combination with other clinical evidence. The ECG criteria were based on recently established age-dependent normal limits. At 95% specificity, the ECG criteria have low sensitivities (<25%) when an elevated LVM index is taken as the reference for LVH. When clinical evidence is also taken into account, the sensitivity improved considerably (<43%). Sensitivities could be further improved when ECG parameters were combined. The sensitivity of the pediatric ECG in detecting LVH is low but depends strongly on the definition of the reference used for validation.

Keywords Electrocardiography · Pediatrics · Left ventricular hypertrophy · Echocardiography

Introduction

Left ventricular hypertrophy (LVH) results from adaptation of the heart to increased haemodynamic burden. Therefore, early detection of LVH is important, especially in children. Although the 12-lead electrocardiogram (ECG) is still valued as an initial diagnostic test for LVH, its sensitivity in this respect leaves to be desired. In a recent large study on HIV-infected children, Rivenes et al. [19] found sensitivities of <20% at specificity levels of 88% to 92%. On the other hand, in a number of smaller studies on patients with a specific cardiac disease, the performance of the pediatric ECG was found to be higher [7, 10, 12, 16, 21]. For example, in a group of 19 aortic stenosis patients and 21 normals, Fogel et al. [7] found a sensitivity of 67% at 95% specificity. None of these studies was done on an unselected pediatric hospital population with mixed cardiac abnormalities. For the present investigation we have collected such a population and have sought to improve the sensitivity of the pediatric ECG in detecting LVH by means that issue from the following considerations:

First, in pediatric electrocardiology, only a limited number of criteria have been used for assessing LVH. Several criteria that were shown to improve the detection of LVH in adults have not been tested in children. Pediatric electrocardiographers have focused on the QRS amplitude, although the time-voltage area of the QRS complex or its approximation by the product of maximum QRS voltage and QRS duration was proposed in adults as a useful criterion to improve LVH diagnosis [14]. Likewise, in adults combinations of criteria have been shown to improve

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performance [20, 22, 23], which approach has not yet been attempted for children.

Second, older validity studies have used obsolete limits of normal for the pediatric ECG parameters. In a previous study [17], we established new age-dependent normal limits that differ considerably from the older figures [4, 6]. Hitherto, normal limits have not been revised for LVH detection.

Finally, the reference standard for LVH on the ECG has usually been the left ventricular mass (LVM) as estimated from echocardiographic measurements. This reference has been criticized for being vulnerable to measurement error and for its oversimplification of the geometry of the left ventricle [1, 3]. Alternatively, a combination of increased LVM and clinical evidence of volume or pressure overload of the left ventricle may be a better reference standard for the validity of ECG criteria.

Materials and Methods

Study Population

We collected data on all 904 children from whom a 12-lead electrocardiogram and an echocardiogram were taken on the same day at the Sophia Children's Hospital in Rotterdam in the period 2003 to 2005. We excluded 5 children who had received heart transplantation and 67 children with complete transposition of the great arteries, leaving a study population of 832 children. The age and sex distribution of the population are reported in Table 1.

Clinical data were studied by two pediatric cardiologists (M. W. and A. D. J. H.) who were independently presented with the medical record of each patient. Each cardiologist had to score the likelihood of volume or pressure overload of the right and/or left ventricle on a 3-point scale (0 = absent, 1 = possible, 2 = probable). LVH was considered present in patients with, e.g., aortic stenosis or regurgitation, and RVH in patients with tetralogy of Fallot

Table 1 Age and sex distribution of the study population

Age	Males	Females	Total
0–2 mo	14	18	32
3–5 mo	15	8	23
6–11 mo	18	13	31
1–2 yr	50	45	95
3–4 yr	66	47	113
5–7 yr	77	65	142
8–11 yr	106	82	188
12–15 yr	109	99	208
Total	455	377	832

or pulmonary hypertension. Disagreements, defined as a >1-point scoring difference, were settled by consensus.

Electrocardiography

Twelve-lead ECGs were recorded by means of a PC-based acquisition system (Welch Allyn Cardio Control, Delft, The Netherlands) at a sampling rate of 1200 Hz. Following common practice at the Department of Pediatric Cardiology in Rotterdam, V3 was moved to the V3R position, and V5 was moved to the V7 position. All ECGs were processed by the pediatric ECG computer program PEDMEANS [18]. To reduce noise, PEDMEANS computes a representative averaged beat for each of the 12 leads, from which ECG measurements are derived. Wave onsets and offsets as found by PEDMEANS were visually checked.

A total of 15 ECG parameters for diagnosing LVH in children were evaluated (Table 2). In addition to the standard pediatric parameters, we included parameters based on V3R and V7 and defined an additional version of the Sokolow-Lyon criterion by using V3R and V7 instead of V1 and V6. Furthermore, the sum of the R- and S-wave amplitudes in all leads (12-lead sum) and the QRS voltage-duration product and voltage-time integral versions of the Sokolow-Lyon and 12-lead sum criteria were added. The sensitivities of the voltage-duration product version and the voltage-time integral version were compared with their amplitude versions by means of the McNemar's modification of the chi-square method for paired proportions.

Table 2 Evaluated ECG parameters for left ventricular hypertrophy

Parameter	Description
SV3R	S-wave amplitude in V3R
SV1	S-wave amplitude in V1
RV6	R-wave amplitude in V6
RV7	R-wave amplitude in V7
TV6	Inverted T wave in V6
TV7	Inverted T wave in V7
SV1 + RV6	Sokolow-Lyon voltage
(SV1 + RV6) × QRS _d	Sokolow-Lyon voltage-duration product
(SV1 + RV6) area	Sokolow-Lyon voltage-time integral
SV3R + RV7	Additional Sokolow-Lyon voltage
(SV3R + RV7) × QRS _d	Additional Sokolow-Lyon voltage-duration product
(SV3R + RV7) area	Additional Sokolow-Lyon voltage-time integral
12-lead sum	Sum of top-top deflections of all leads
12-lead sum × QRS _d	12-lead sum voltage-duration product
12-lead sum area	12-lead sum voltage-time integral

The polarity of the T wave in V6 or V7 was taken as a binary value. For all other parameters, reference values were derived from a normal population of 1912 children aged 11 days to 16 years [17]. The 98th percentile of the parameter distribution was taken as the upper limit of normal (ULN). We estimated age-dependent percentile curves using a two-stage parametric approach described before [17]. As an illustration, the age-dependent normal curve for the 12-lead sum is presented in Fig. 1. For each LVH parameter, the difference between the parameter value and its corresponding normal limit was taken for further processing.

Echocardiography

The echocardiograms were recorded with a Philips Sonos 5500 (Philips, Best, The Netherlands). The following M-mode measurements were obtained according to the American Society of Echocardiographers’ convention [9]: interventricular septum thickness at end diastole (IVSd), posterior wall thickness at end diastole (PWLvd), and left ventricular internal dimension at end diastole (LVIDd).

Left ventricular mass (LVM) was calculated with the anatomically validated formula of Devereux [5]:

$$LVM = 0.8 \times [1.04 \times (IVSd + PWLVd + LVIDd)^3 - LVIDd^3] + 0.6 \text{ [g]}$$

The LVM index (LVMI) adjusts for body size and is taken as LVM (g) divided by body weight (kg). As shown in Fig. 2, we estimated a partition value of 3 for LVMI, based on a set of 587 normal echocardiograms of 361 boys and 226 girls aged birth to 18 years previously described by Overbeek et al. [15]. We calculated the LVM using the

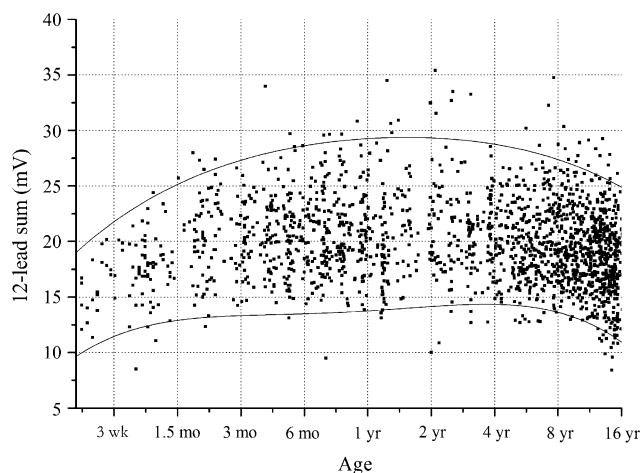


Fig. 1 Scatter diagram for the 12-lead sum versus age. The solid lines indicate the 2nd and 98th percentile curves

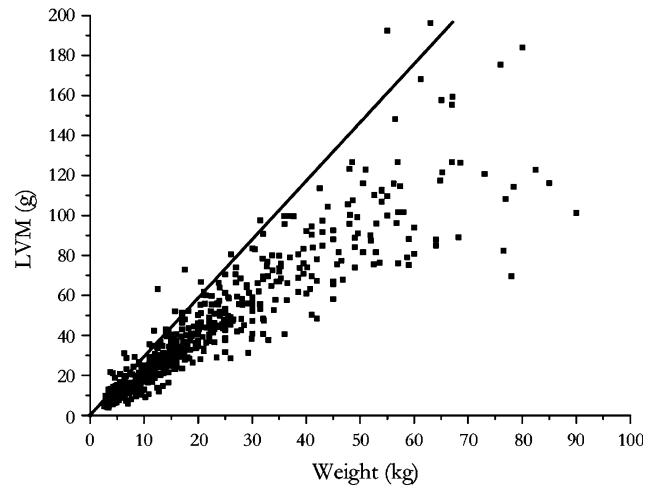


Fig. 2 Left ventricular mass (LVM) calculated on 587 normal echocardiograms plotted against body weight. The solid line represents the partition value of the LVM index, $LVM_I = LVM / \text{weight} = 3$

formula of Devereux from the measurements provided to us by Overbeek.

Reference Standards for LVH

The ECG criteria for LVH were validated using two different reference standards. As in other validation studies, one standard is based only on the LVMI. LVH was considered present at $LVM_I > 3$, which is indicated by LVM+. In the second standard the clinical evidence of LVH is also taken into consideration and LVH was defined at two different likelihood levels. LVH was assumed to be present at the first level if $LVM_I > 3$ and at least one cardiologist scored “possible” (indicated by LVM+, L1), and at the second level if $LVM_I > 3$ and at least one cardiologist scored “probable” (LVM+, L2). Note that the difference between the two cardiologists can never be higher than 1 scoring point due to the consensus rule. The cases with a $LVM_I \leq 3$ were classified as non-LVH.

Combination of ECG Parameters

Combinations of LVH-ECG parameters were evaluated using our EXPLORE induction algorithm [8]. EXPLORE can search for the decision rule that has the highest sensitivity at a user-specified level of specificity. In this study, we wanted EXPLORE to find the best decision rule consisting of two ECG parameters at a specificity of 95%. EXPLORE takes as its input a set of ECGs, each presented by a set of parameters, and a label indicating whether or not LVH is present. We searched for the best parameter combination for each of the three LVH definitions: LVM+; LVM+, L1; and LVM+, L2.

Results

Performance of Individual LVH-ECG Parameters

Table 3 reports the diagnostic performance of all ECG parameters for different age groups and for the total study population, taking LVM+ as LVH definition. In the complete set (0–15 years), the additional version of the Sokolow-Lyon parameter (SV3R + RV7) performs best, with 25.3% sensitivity. Multiplying by QRS duration or taking the voltage-time integral does not improve this criterion. However, there is an increase in sensitivity of 31% by the area version compared to the amplitude-only version of the 12-lead sum in the complete set ($p = 0.045$).

The effect of age on the results is mixed. For different age groups different parameters perform best, and the improvement of the 12-lead sum is not consistent in all age groups. However, this may be accounted for by the lower number of LVH cases in the higher age groups. For SV1, SV3R, RV6, RV7, TV6, and (SV1 + RV6) × QRS duration, an increasing performance is seen with age. In all age groups, SV3R appears to perform better than SV1, and RV7 better than RV6.

Table 4 reports the diagnostic performance of the individual ECG parameters for the different definitions of LVH. The sensitivity of all ECG criteria improves considerably when, apart from LVM+, the clinical evidence of LVH is also entered in the definition of LVH. The more certain the cardiologists were about the presence of LVH, the better the ECG performs. The additional Sokolow-Lyon

Table 3 Sensitivity (%) at 95% specificity for three age groups and for the total population taking left ventricular mass index >3 as definition of left ventricular hypertrophy

Parameter	0–5 yr	6–11 yr	12–15 yr	0–15 yr
SV3R	16.5	17.1	19.4	16.7
SV1	18.3	20.0	33.3	20.4
RV6	12.2	15.7	16.7	16.3
RV7	19.1	20.0	25.0	22.2
TV6	7.0	10.0	13.9	9.0
TV7	17.4	14.3	25.0	15.8
SV1 + RV6	20.0	22.9	19.4	22.2
(SV1 + RV6) × QRS _d	16.5	21.4	22.2	24.0
(SV1 + RV6) area	19.1	21.4	19.4	24.4
SV3R + RV7	29.6	18.6	27.8	25.3
(SV3R + RV7) × QRS _d	22.6	20.0	22.2	23.1
(SV3R + RV7) area	20.0	20.0	19.4	20.8
12-lead sum	15.7	17.1	22.2	17.2
12-lead sum × QRS _d	19.1	17.1	22.2	18.6
12-lead sum area	22.6	14.3	27.8	22.6
No. cases (LVH+/LVH–)	115/225	70/214	36/172	221/611

Table 4 Sensitivity (%) at 95% specificity for three left ventricular hypertrophy (LVH) definitions

Parameter	LVM+	LVM+, L1	LVM+, L2
SV3R	16.7	21.1	30.0
SV1	20.4	25.9	33.8
RV6	16.3	19.0	26.3
RV7	22.2	25.9	36.3
TV6	9.0	10.9	12.5
TV7	15.8	20.4	26.3
SV1 + RV6	22.2	25.2	35.0
(SV1 + RV6) × QRS _d	24.0	29.9	31.3
(SV1 + RV6) area	24.4	30.6	41.3
SV3R + RV7	25.3	30.6	42.5
(SV3R + RV7) × QRS _d	23.1	28.6	37.5
(SV3R + RV7) area	20.8	26.5	37.5
12-lead sum	17.2	21.1	33.8
12-lead sum × QRS _d	18.6	21.8	33.8
12-lead sum area	22.6	27.9	37.5
No. cases (LVH+/LVH–)	221/611	147/611	80/611

Note. LVM+, left ventricular mass index >3; L1, at least one cardiologist scored possible LVH; L2, at least one cardiologist scored probable LVH

criterion (SV3R + RV7) performs best for all reference standards. Removal of all LVH cases from the LVM+, L2 group which were also marked by at least one cardiologist as probable RVH ($n = 15$) hardly changed the performance of the parameters.

Performance of a Combination of Two LVH-ECG Parameters

Using the EXPLORE algorithm, we found that for all definitions of LVH the best rule consisted of (SV3R + RV7) area in conjunction with 12-lead sum area. The threshold values of these parameters were optimized by EXPLORE to ensure 95% specificity. Table 5 reports that this combination improves the sensitivity by 21%–25% compared to the best single parameter (SV3R + RV7).

Table 5 Sensitivities (%) for the best single parameter (SV3R + RV7) and the best combination of two parameters ([SV3R + RV7] area with 12-lead sum area) for the three LVH definitions at 95% specificity

LVH definition	1 parameter	2 parameters	% increase
LVM+	25.3	31.7	25.3
LVM+, L1	30.6	38.1	24.5
LVM+, L2	42.5	51.3	20.7

Note. LVM+, left ventricular mass index >3; L1, at least one cardiologist scored possible LVH; L2, at least one cardiologist scored probable LVH

Discussion

We performed the first large study on the validity of ECG criteria for detecting LVH in an unselected pediatric hospital population with up-to-date reference standards for both electrocardiographic and echocardiographic parameters. The unreliability of reference standards for both the ECG criteria and the echocardiographic-based criteria may previously have been accountable for the disappointing performance of the ECG. Rivenes et al. [19] demonstrated that the often used standard of normal ECG limits of Davignon et al. [4] needed to be revised. They derived new age-adjusted reference values for their HIV-uninfected group of children <6 years old. With these new normal values the sensitivity decreased slightly (from <20% to <17%) while the specificity improved (from 88%–92% to 94%–100%). Regarding the echocardiogram, a recent study provided echocardiographic dimensions that differed significantly from previous data, probably owing to improved measuring techniques [15].

The sensitivity of the ECG for detecting LVH in children is relatively low when LVM+ is taken as the LVH definition (Table 3). The best single parameter is (SV3R + RV7), with a sensitivity of 25.3% at 95% specificity. Notably, SV3R, RV7, and (SV3R + RV7) perform better than SV1, RV6, and (SV1 + RV6), respectively. The best-performing parameter that uses leads from the standard 12-lead ECG is the voltage-time integral version of the Sokolow-Lyon criterion, with a sensitivity of 24.4%. Further, the use of voltage-duration product and voltage-time integral of the 12-lead sum resulted in higher sensitivities than the amplitude-only version in the total population. However, overall the use of voltage-duration products and voltage-time integrals for the diagnosis of LVH remains less effective than in adults.

In most studies on the usefulness of the ECG in detecting LVH, echocardiographic-determined LVM has been taken as the reference standard. However, we believe that the ECG should not only be judged by taking LVM as the reference. LVM determination suffers from large measurement errors in both directions [1, 3]. When underestimated, this will go unnoticed because of the high specificity levels to which the criteria are set. When LVM is overestimated, however, the ECG is penalized for stating normal. We therefore also used combinations of increased LVM and clinical indexes of volume or pressure overload to ascertain the validity of ECG criteria. We found that the ECG performs considerably better when there is more certainty about the presence of LVH on clinical grounds. Fogel et al. [7] showed that the sensitivity was 67% in a small group of 19 children with aortic stenosis. Unfortunately, we could not collect a large enough group of aortic

stenosis patients without other abnormalities to make a better comparison with Fogel's data.

The combination of different ECG LVH parameters is known to improve performance in adults [20, 22, 23]. The combination of highly specific criteria can be a fruitful approach to increase sensitivity without generating an unacceptable number of false-positives. We restricted the search of our EXPLORE algorithm to combinations of only two parameters because more parameters might introduce overspecialization on a data set of our size. A combination of (SV3R + RV7) area and 12-lead sum area was found to improve the sensitivity by 25% in the LVM+ and LVM+, L1 groups and by 21% in the LVM+, L2 group, at 95% specificity. Combination of parameters can thus be useful in the pediatric population also.

Our study has several limitations. First, we validated the ECG criteria for LVH using LVM as measured by M-mode echocardiography. However, there are studies in adults suggesting that cardiac MRI can more accurately and reproducibly measure LVM [1, 11]. In children this has not yet been confirmed. Second, in our study V3 was moved to the V3R position, and V5 was moved to the V7 position. Therefore, the 12-lead sum included these leads instead of V3 and V5, which makes comparison with other studies using standard lead sets more difficult. Third, we could not determine the effect of concomitant RVH on the performance of the ECG in detecting LVH due to the low number of cases scored as probable RVH by the cardiologists ($n = 15$). Fourth, we could not establish the effect of gender because of the limited size of the study population. In adults gender influences the performance of the ECG criteria for LVH [1, 2, 13]. In our normal pediatric ECG population we did find gender differences in QRS duration for all ages and in R- and S-wave amplitudes for children aged 12 to 16 years [17]. The effect of gender on ECG-LVH criteria in the pediatric population awaits investigation on a larger population.

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