AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 2, Issue 10, 2024 ISSN (E): 2993-2149

Prognostic Significance of the Ratio of Left Ventricular Myocardial Parameters According to Echocardiography and Electrocardiography Data

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Abstract: A comparison was made of the myocardial mass of the left ventricle of the heart (LVMM), calculated from echocardiography , unaveraged and averaged ECG data, and the effectiveness of these methods in identifying the dynamics of LVMM during antihypertensive therapy in patients was assessed.

Keywords: Angiology, Antihypertensive therapy, Variability of left ventricular myocardial mass, Cardiology, Averaged ECG, Antihypertensive therapy, Left ventricle mass variability, Cardiology, Averaged ECG.

The comparison of the variability of left ventricular mass (LVM) calculated from echocardiography, conventional and signal-averaged ECG and evaluation of the effectiveness of these methods in the detection of the LVM changes during antihypertensive therapy were performed. It was found that the reproducibility of the signal-averaged ECG method of LVM calculation is significantly higher than the conventional one and echocardiography. The use of this method in clinical practice can provide reliability of individualized assessment of LVM changes on single examination and during follow-up. The use of signal-averaged ECG may reduce groups size or the study duration to achieve statistically significant difference in studies with ECG control. Left ventricular hypertrophy (LVH) of the heart in patients with arterial hypertension is a characteristic sign of the formation of a hypertensive heart. The proven unfavorable effect of LVH on cardiovascular prognosis in patients with arterial hypertension and the reduction in cardiovascular risk during the reverse development of this pathological condition [1–3] determine the importance of an individualized assessment of its dynamics against the background of antihypertensive therapy. The current level of development of medical technology makes it possible to accurately determine the mass of the left ventricular myocardium (LVMM) of the heart. For this purpose, diagnostic methods such as 3D echocardiography (3D EchoCG), multislice computed tomography (MSCT), as well as magnetic resonance imaging (MRI), which is considered the standard method today, can be used. However, the use of these methods in real clinical practice, including when examining people with arterial hypertension, is limited by labor intensity, high cost (especially for repeated studies), low availability and lack of reference values for LVMM due to the relatively small amount of accumulated data. In this regard, electrocardiography (ECG) and echocardiography (EchoCG) remain the most

commonly used instrumental methods for detecting and monitoring LVH in the heart both in clinical practice and in research.

The undoubted advantages of echocardiography are the ability to quantitatively assess LVMM and higher sensitivity in recognizing LVH compared to the electrocardiographic method [4, 5]. At the same time, detection of LVH using ECG does not lose its relevance due to its simplicity and accessibility, as well as the high specificity of electrocardiographic indices. In addition, to date, methods have been proposed for calculating LVMM from ECG data, which significantly expands the capabilities of the method when studying LVH [6–8].

The use of these diagnostic methods is associated with a number of factors that can negatively affect the reproducibility of indicators, which can reduce their diagnostic value both in a single-stage study and in dynamic monitoring of LVH. Thus, the assessment of changes in LVMM during an echocardiographic study can be complicated by the dependence of the results on the technical characteristics of ultrasound equipment and the qualifications of the specialist performing the measurements, which leads to random errors. Interpretation of ECG changes during dynamic monitoring of LVH is complicated by the influence on the electrical signal of a large number of external noises, which significantly distort the recorded myocardial potentials.

Some of the shortcomings of the traditional ECG can potentially be eliminated by averaging the cardiac signal , which will help increase the reproducibility and , consequently, the reliability of the results of repeated studies.

Taking into account the above provisions, the purpose of this study was to comparatively assess the variability of LVMM calculated from echocardiography , traditional and averaged ECG, and the effectiveness of these methods in identifying the dynamics of LVMM during antihypertensive therapy in patients with arterial hypertension.

Materials and research methods

At the first stage of the study, LVMM variability was assessed in three separate groups of apparently healthy volunteers.

In group 1 (n = 30), the variability of LVMM according to echocardiography was assessed . Echocardiographic examination according to a standard protocol was performed twice with an interval of 1 week [9].

In groups 2 (n = 27) and 3 (n = 30), the variability of LVMM was studied according to unaveraged and averaged ECG data. In group 2, ECG recordings were performed at intervals of 1 week. In group 3, the time interval between two consecutive electrocardiograms was 1 minute.

At the second stage of the study, a comparative assessment of the effectiveness of EchoCG , non-averaged and averaged ECG was carried out in determining the dynamics of hypertensive changes in the heart against the background of antihypertensive therapy. At this stage, 87 patients with uncomplicated arterial hypertension aged from 37 to 67 years were examined, receiving therapy with antihypertensive drugs with a proven ability to influence LVMM (perindopril , losartan , amlodipine , fixed combination of perindopril and amlodipine) for 3 months. The undoubted advantages of echocardiography are the ability to quantitatively assess LVMM and higher sensitivity in recognizing LVH compared to the electrocardiographic method [4, 5]. At the same time, detection of LVH using ECG does not lose its relevance due to its simplicity and accessibility, as well as the high specificity of electrocardiographic indices. In addition, to date, methods have been proposed for calculating LVMM from ECG data, which significantly expands the capabilities of the method when studying LVH [6–8].

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Repeated studies were carried out under standard conditions (environment, room temperature, position).

Echocardiographic examination was performed using an expert-class ultrasound machine VIVID 9 (General Electric , USA). LVMM according to echocardiography was calculated using the formula recommended by the American Society of Echocardiography (American Society of Echocardiography , ASE): LVMM = 0.8 × [1.04 × (EDR + TZSD + TMVPd)3 – (EDR)3] + 0.6, where LVMM is the mass of the left ventricular myocardium (grams), EDR is end-diastolic left ventricular size (cm), TZSD —thickness of the posterior wall of the left ventricle in diastole (cm), TMVPd —thickness of the interventricular septum in diastole (cm) [9].

To record the ECG, a 12-channel computerized electrocardiograph EK9 Ts-01-KARD from MKS was used . The application of electrodes to the limbs and chest was performed strictly in accordance with anatomical landmarks. Repeated studies in group 3 were carried out without removing the electrodes to exclude random errors associated with their possible displacement relative to the original position. The recording duration for the first and repeat studies was 5 minutes. Registration, archiving, processing and averaging of ECG were carried out using the original HR ECG computer program [10].

To calculate LVMM from ECG data, a previously developed formula was used: LVMM = – 10.523 + 0.706 × age - 32.698 × sex + 2.197 × BMI + 596.973 × Pd + 23.213 × (RAVL + SV3) + 21.860 × (TV1 - TV6), where LVMM — mass of the myocardium of the left ventricle of the heart (grams); age—patient’s age (years); gender — gender of the patient (0 — men, 1 — women); BMI—body mass index (kg/m2) ; Pd —maximum duration of the P wave (seconds); RAVL—amplitude of the R wave in lead AVL (mV); SV3 — amplitude of the S wave in lead V3 (mV); TV1 — amplitude of the T wave in lead V1 (mV); TV6 is the amplitude of the T wave in lead V6 (mV) [8, 11]. The method for determining LVMM using averaged ECG data was developed based on data obtained from a study of 185 volunteers (108 patients with uncomplicated arterial hypertension and 77 people with normal blood pressure aged 35 to 65 years). The proposed model explained 67% of the variability in left ventricular myocardial mass determined from echocardiography data ($R2 = 0.67$; $R = 0.82$; $p < 0.001$).

The research results were processed using the SPSS 13.00 computer program. The reproducibility of the results of repeated studies was calculated using the Bland - Altman method with the determination of the systematic discrepancy, its standard deviation and the coefficient of variability [12]. Between-group differences in LVMM variability were assessed using an unpaired Student's t test with Bonferroni correction for multiple comparisons. A paired Student's

t-test was used to determine the significance of intragroup differences in LVMM across repeated studies . When determining the required sample size to obtain significant intergroup differences in the dynamics of LVMM, the Neyman–Pearson method was used with a specified power of 80% and an error α equal to 5% [13]. At all stages of the study, the null hypothesis was rejected when the p value was less than 0.05.

Results

There were no significant changes in BMI and blood pressure during repeated examination in any of the groups ($p > 0.05$ for all).

The differences in the mean values of LVMM during the first and repeated examinations were statistically insignificant and were: in group 1 - 2.5 ± 18.6 g ($p = 0.56$); in group 2 - 2.7 ± 9.2 g ($p = 0.24$) and 0.5 ± 5.2 g ($p = 0.67$) for the unaveraged and averaged ECG, respectively; in group 3 - –2.6 ± 6.9 ($p = 0.10$) and 0.1 ± 2.8 g ($p = 0.84$) for the unaveraged and averaged ECG, respectively.

The variability of LVMM during repeated studies according to echocardiography was significantly higher in comparison with both traditional and averaged ECG ($p < 0.05$ and $p < 0.01$ for non-averaged and averaged ECG when recorded with an interval of 1 week; $p < 0.01$ and $p < 0.001$ for non-averaged and averaged ECG when recording without electrode displacement between repeated studies, respectively).

Comparison of the variability of the studied sign according to unaveraged and averaged ECG data showed that the averaged ECG is significantly superior to the unaveraged ECG in terms of reproducibility (Table 2).

When comparing the reproducibility of LVMM when recording an electrocardiac signal with an interval of 1 week versus an ECG recorded at a short interval without displacement of the electrodes between repeated studies, for the non-averaged ECG there were no significant differences in the variability of LVMM ($p = 0.23$), while the variability of the averaged The ECG was significantly lower ($p = 0.042$) in the absence of changes in the location of the electrodes between two successive recordings of the cardiac signal .

Sample sizes required to identify statistically significant differences in determining the dynamics of LVMM, taking into account the obtained standard deviation values for the diagnostic methods evaluated in the study and the expected degree of reduction in LVMM.

And the use of echocardiography as a method for monitoring the dynamics of LVMM requires an increase in the sample volume several times in comparison with an ECG, both averaged and non-averaged . In turn, in this regard, the averaged ECG turned out to be more effective than the non-averaged one . The required sample size for an unaveraged ECG was 3 times higher when recording on different days and 6 times higher when excluding the error associated with the error in electrode placement.

For each of the assessed diagnostic methods, the values of change in LVMM in an individual patient were calculated, necessary to register reliable dynamics with repeated measurements, which were 66 g, 33 g versus 19 g, 25 g versus 10 g in accordance with the obtained standard deviations of systematic discrepancy for EchoCG , unaveraged against the averaged ECG with an interval of 1 week and unaveraged against the averaged ECG recorded without electrode displacement, respectively.

Baseline characteristics of patients with arterial hypertension on antihypertensive therapy are presented in Table. 4. The average values of myocardial mass calculated from echocardiography, averaged and traditional ECG data were not statistically different ($p = 0.99$).

The decrease in blood pressure after 3 months of therapy was –24.6 mm Hg. Art. ($p < 0.0001$) and –12.0 mm Hg. Art. ($p < 0.0001$) for systolic and diastolic blood pressure, respectively.

Dynamics of LVMM according to echocardiography , unaveraged and averaged ECG at the end of the observation period.

The decrease in LVMM during antihypertensive therapy was significant according to both unaveraged and averaged ECG data, while the change in LVMM according to EchoCG was not significant.

The relationship between the degree of reduction in LVMM during therapy and the initial values of LVMM according to averaged ECG data is presented. When assessing the distribution of baseline LVMM values by tertiles , the average reduction in LVMM was –3.3 g (95% CI –1.1—5.6 g, $p < 0.01$), –7.1 g (95% CI – 5.1—9.1 g, $p < 0.001$) and –9.6 g (95% CI –6.5—12.8 g, $p < 0.001$) for 1st, 2nd and 3rd th tertiles , respectively, while the differences between the 1st and 3rd tertiles were significant ($p = 0.002$). The data obtained indicate the presence of a direct linear relationship between the values of initial LVMM and the degree of its decrease during therapy.

Discussion

Monitoring the dynamics of LVMM seems to be an urgent and at the same time quite difficult task. Of the limited number of diagnostic techniques currently available in everyday practice for the purpose of assessing changes in LVMM, echocardiography is considered to be a reliable method. However, there are a number of factors that can affect the reproducibility of indicators used to determine LVMM according to echocardiographic studies. Among such factors, one can highlight the dependence of the study results on the technical characteristics of the ultrasound scanner, the experience of the specialist conducting the study, as well as the characteristics of ultrasound imaging in a particular patient. When using recommended models for determining LVMM, linear parameters are cubed [9], so even small errors in measurements will lead to a significant deviation of the calculation result from the true value of LVMM.

EchoCG parameters , according to published data, is quite high and, depending on the scanning mode used, can reach 15% [14–16], which is comparable to the results we obtained. In real clinical practice, where repeated examinations are often performed on ultrasound machines with different technical characteristics by specialists with different levels of training, higher rates of variability should be expected.

The use of an ECG to assess the dynamics of LVH is also associated with a high probability of random error, since, even with strict adherence to the rules for ECG registration, the cardiac signal can be distorted due to the influence of external interference, the activity of skeletal muscles and respiratory movements of the chest, the appearance of artifacts when the electrodes come into contact with skin, as well as displacement of the electrodes from the original location during repeated examination.

Averaging the electrocardiographic signal makes it possible to eliminate some of the shortcomings of the traditional ECG by summing up many cardiac cycles , when random deviations of the electrocardiographic curve will tend to zero, while the stable component of the ECG is fully preserved.

The reproducibility of LVMM according to both traditional and averaged ECG data in comparison with EchoCG in our study was significantly higher. At the same time, when comparing the unaveraged and averaged ECG, the variability of LVMM for the average ECG was 2–2.5 times lower under the same recording conditions. It was also noteworthy that there were no significant differences in the variability of the unaveraged ECG depending on the time interval between repeated studies, while the variability of the averaged ECG in the absence of electrode displacement between repeated studies was significantly lower compared to registration after 1 week. The results obtained, on the one hand, indicate a significant impact on the reproducibility of ECG indicators from changes in the location of the electrodes relative to the initial position during repeated testing. At the same time, even if the study is carried out, when the random error caused by the displacement of the electrodes is completely excluded, the

variability of the cardiac signal during traditional recording of myocardial electrical potentials remains quite high due to the influence of other factors. Averaging the electrocardiosignal , in turn, makes it possible to minimize the influence of random interference, increasing the reliability of the method for dynamic ECG monitoring.

The high variability of LVMM according to echocardiography did not allow us to assess the effectiveness of antihypertensive therapy during a relatively short treatment period. According to the results obtained, the change in LVMM according to echocardiography was –0.3 g. These changes were statistically insignificant. At the same time, the ECG method was able to detect significant dynamics of LVMM in a relatively short period of time, which confirms its greater accuracy in dynamic control.

We analyzed a number of studies with a total number of participants of 1564 people, in which, using EchoCG control, the effect of various antihypertensive drugs and their combinations on LVH in patients with arterial hypertension was assessed [3, 17–24]. The analysis included studies that presented the initial values of LVMM and those achieved during therapy or the average values of the linear dimensions of the left ventricle, on the basis of which it was possible to calculate this indicator. Depending on the duration of therapy (3, 6, 12, 24 months), separate analyzed groups were formed, for each of which the average values of changes in LVMM during treatment for arterial hypertension were calculated .

As can be seen from the presented graph, the most rapid decrease in LVMM is observed in the initial stages of therapy (3–6 months) and after 3 months, according to echocardiography, the average is 14.0 g. Taking into account the data we obtained when determining the sample size necessary to identify significant dynamics of LVMM (Table 3), such a change in the indicator could be recorded according to EchoCG data already during the examination of 22 individuals, however, with a larger number of participants in the present study, significant changes in LVMM according to EchoCG data were not detected. This contradiction may be due to the fact that among the individuals we examined at the second stage, LVH according to echocardiography was detected only in 20% of cases, and the initial LVMM was lower than in the analyzed studies, in which individuals with LVH predominated (185.0 g versus 259.2 g, respectively). Taking into account the presence of a direct linear relationship between the initial LVMM and the degree of its decrease during therapy identified in our study (Fig. 1), the result in our sample should have been lower, and indeed, according to the averaged ECG, the decrease in LVMM was on average 6 .7 g. Subject to the inclusion in this study of persons with the same LVMM as in those analyzed by us works , according to the regression equation (Fig. 1), the change in LVMM after 3 months would be 14.5 g, which is comparable to the meta-analysis data . In turn, taking into account the standard deviation of the systematic discrepancy for EchoCG , which was obtained in this study, to register a significant decrease in LVMM by 6.7 g according to ultrasound, the sample size should have been 96 people, which is significantly larger than our sample size, then how to register the same change in LVMM according to non-averaged and averaged ECG data, 24 and 8 repeated observations, respectively, would be sufficient .

Despite widespread ideas about the reliability of the echocardiography method , it turned out to be unacceptable for a personalized assessment of cardiac changes during antihypertensive therapy. The calculated reduction in LVMM by 66 g, necessary for a reliable assessment of the dynamics of this indicator in an individual according to echocardiography , is not observed even after 2 years of therapy (Fig. 2) and can hardly be achieved in the future, given the parabolic shape of the curve. In turn, an averaged ECG will make it possible to record significant changes in LVMM in an individual patient after 3–6 months (calculated difference -19 g), and if the possibility of electrode displacement between repeated studies is eliminated, such changes can be recorded in less than 3 months from start of therapy (calculated difference –10 g). The use of the traditional method of ECG recording is associated with delayed assessment of the effectiveness of therapeutic interventions. Reliable individual dynamics of LVMM using a non-averaged ECG

can only be assessed after 1–2 years of treatment (calculated value of the difference is 33 g), which will not allow a temporary change in the antihypertensive therapy regimen.

The results of this study indicate greater reliability of the averaged ECG method in comparison with traditional ECG and EchoCG in assessing the dynamics of LVMM, including when used for the purpose of individualized monitoring of changes in this indicator. However, it should be noted that the comparison of the effectiveness of diagnostic methods for dynamic monitoring of LVMM in our study was carried out on a small sample of individuals using a previously developed method for determining LVMM using averaged ECG data [8], the information content of which in comparison with reference methods for assessing this indicator requires further study.

Traditionally, LVH is assessed using indexed indicators that take into account body surface area (BSA). The present study assessed the variability of LVMM in terms of the possibility of detecting regression of hypertensive changes in the myocardium during antihypertensive therapy, rather than the LVMM index. Based on the characteristics of the indexed indicator, a decrease or increase in the patient's weight during therapy may distort data on real changes in the heart muscle when indexed by PPT. Our study, like a number of others, showed that the incidence of LVH in the general population of patients with uncomplicated arterial hypertension is low [25, 26]. In addition, the work demonstrated that a significant decrease in LVMM under the influence of antihypertensive therapy occurs even with initial values that do not fit into the criteria for LVH determined on the basis of indexed values. Thus, it seems to us more reasonable to use LVMM as a control indicator of the effectiveness of therapeutic interventions, especially with individualized assessment.

Conclusions

1. The echocardiographic method has low reproducibility , which reduces the reliability of a one-time assessment of LVMM, leads to a significant overestimation of the required sample size in studies with dynamic control and does not allow the use of this method for individualized monitoring of the dynamics of LVMM in patients with arterial hypertension during antihypertensive therapy.
2. The reproducibility of LVMM according to ECG data is higher in comparison with EchoCG .
3. ECG averaging allows you to minimize the error in determining LVMM during repeated measurements, which will reduce the size of groups or time to obtain a statistically significant result when used in prospective studies in comparison with both echocardiography and traditional ECG.
4. If the obtained data are confirmed in larger studies, the use of an averaged ECG in clinical practice will allow for an individualized assessment of changes in LVMM already in the early stages of antihypertensive therapy with the possibility of timely correction, while the use of a traditional ECG provides a delayed assessment that cannot affect treatment tactics.
5. The averaged ECG method provides a reliable assessment of changes in the myocardial mass of the left ventricle of the heart against the background of antihypertensive therapy in patients with arterial hypertension, regardless of its initial values, including in persons without left ventricular hypertrophy, determined by generally accepted criteria.

Books

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