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LEADING ARTICLE

Ventricular late potentials in patients with rheumatic heart disease

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Abstract

Objective. *The evaluation of ventricular late potentials (VLPs), its significance and relationship with survival of patients with rheumatic heart disease (RHD).*

Materials and Methods. *The study included 260 patients with mitral stenosis, 103 with aortic stenosis and 81 with mitral valve regurgitation. Patients were followed up for 10 years. Echocardiography was performed on a Philips Affinity 50 apparatus, 24-hour ECG monitoring was performed on a Cardiotechnika-04–3P (M) monitor with an assessment of VLPs: TotQRSF, LAS40, RMS40.*

Results. *The parameters of VLPs significantly changed in patients with RHD during 10-year observation: RMS40 decreased by 9.85 (5.72;13.98) ms and LAS40 increased by 2.83 (5.01;0.65) ms. However, RMS40 and LAS40 did not differ between groups with different types and severity of valvular heart diseases. Patients with prosthetic heart valves had higher LAS40 values of 34.39±15.97 ms and TotQRSF of 94.43±19.64 ms compared with patients who did not underwent surgery: LAS40 of 34.39±15.97 ms and TotQRSF of 87.62±14.76 ms, respectively. The characteristics of LVPs significantly differed between survivors (TotQRSF 88.98±16.59 ms, RMS40 40.67±22.83 ms, LAS40 31.40±12.62 ms) and those who died (TotQRSF 97.00±12.67 ms, RMS40 27.43±15.19 ms, LAS40 36.57±15.25 ms). Increased TotQRS in patients with RHD increased mortality — odds ratio (OR) — 1.026 (1.007;1.046).*

Conclusion. *Patients with RHD showed deterioration of VLP parameters during ten years of observation. Deceased subjects with RHD had more pronounced VLP and increased TotQRSF. VLPs did not differ between groups with various types of valvular heart disease.*

Keywords: *rheumatic heart disease, ventricular late potentials, mitral stenosis.*

Conflicts of interest: none declared.

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Introduction

High-resolution electrocardiography (ECG) with the help of computer processing of the ECG signal detects very low amplitude signals in the ventricles. A standard electrocardiogram that is routinely used to diagnose cardiac arrhythmias cannot detect these signals [1, 2]. Ventricular late potentials (VLPs) are thought to result from fragmentation of electromotive forces in abnormal areas of ventricular myocardium, where activation is delayed by slow conduction, and are considered as independent predictor for the development of life-threatening arrhythmias that lead to sudden cardiac death [3]. VLPs are discussed in the literature from the perspective of patients with chronic heart failure (CHF) with preserved left ventricular ejection fraction (LVEF), since they are associated with diastolic dysfunction. The dysfunction is associated with decreased elasticity of the myocardium due to hypertrophy, fibrosis or sclerosis [4]. VLPs occur in areas with slow conduction of excitation through the myocardium that causes the development of arrhythmogenic zones and contributes to the occurrence of malignant ventricular arrhythmias [5]. The method of VLPs registration is based on the identification of high-frequency (over 20–50 Hz) and low-amplitude (less than 20 μV) signals that occur at the end of the QRS complex [6].

The development of VLPs is associated with slow conduction in abnormal areas of ventricular myocardium. Healthy cardiomyocytes alternate with areas of necrosis and fibrosis or with ischemic areas. This alternation of zones with normal and slow conduction in the myocardium causes the formation of the re-entry phenomenon [7]. The fragmentation of electromotive forces appears is areas with reduced blood supply or small focal necrosis. After the stabilization of patient's condition, for example, in case of unstable angina pectoris, the VLPs parameters improve and they disappear in one third of patients [8]. However, in patients with stable angina pectoris, antianginal pharmacotherapy and angioplasty do not improve the rate of VLPs [8].

In recently published literature, the data on VLPs are contradictory. The value of high-resolution ECG for the assessment of the risk of sudden cardiac death ranges from 7 to 40 %, and the negative predictive value exceeds 95 % [9]. In patients with myocardial infarction (MI), the TotQRSF values are considered to be the most significant for the assessment of the prognosis. The MUSTT study included 1268 patients with LVEF<40 % and unstable ventricular tachycardia and showed that the QRS duration> 114 m/s was associated with higher risk of arrhythmic events during 5-year follow-up in 28 % of cases (compared with 17 % risk in the rest of patients) [10]. However, the results of recent studies bring into question on the value of VLPs [11]. In 968 of patients with MI and percutaneous revascularization [12], VLPs did not have a predictive value for the development of life-threatening arrhythmias or sudden cardiac death [12]. However, even though VLPs cannot be considered as traditional risk factor [13,14], it can have high negative predictive value. This can be useful for the identification of patients with low risk, including patients with chronic rheumatic heart disease (RHD) that can be considered a model of slowly progressive CHF. There are only a few works that studied LVPs in patients with heart valve stenosis, the main focus in the literature is on mitral valve prolapse or the assessment of VLPs after surgery, but the studied samples are small. Therefore, it is interesting to study VLPs in patients with RHD and to assess the changes of its parameters during a long period of time.

Objective

The evaluation of VLPs, its significance and relationship with survival rate of patients with RHD.

Materials and methods

The study included 444 patients (17.12 % — men, 82.88 % — women) with average age of 58.06±9.65 years who were diagnosed with RDH and signed written informed consent. After the analysis of medical records, we identified 260 patients (from RDH group) with mitral stenosis (191 patients) and combined mitral and aortic stenosis (69 patients), 103 with aortic stenosis and 81 with mitral regurgitation. According to current guidelines on the management of valvular heart disease, acute rheumatic fever is the main cause of mitral or combined mitral and aortic stenosis; aortic — calcific aortic stenosis; mitral valve regurgitation — degenerative disease. The exclusion criteria were: decompensation of CHF at the time of inclusion and severe concomitant pathology that potentially negatively affects life expectancy; life-threatening arrhythmias. Patients were followed up for ten years. The incidence of concomitant diseases at the time of inclusion: arterial hypertension — 44.6 %, atrial fibrillation — 49.1 %, angina pectoris — 17.3 %. The frequency of prescribed drug therapy: ACE inhibitors / sartans — 86.7 %, β-blockers — 57.7 %, spironolactone — 80.3 %. The groups were comparable

by the frequency of prescribed pharmacotherapy for CHF and concomitant cardiovascular diseases.

All the patients underwent echocardiography on the Philips Affinity 50 apparatus. Holter ECG monitoring with the assessment of VLPs was performed on the cardiorespiratory monitor «Cardiotekhnika-04–3R (M)» by "Inkart" company. The ECG signal was processed and filtered between 40–250 Hz in order to obtain the resulting filtered QRS complex [15]. The program calculated the duration of the filtered QRS complex on the vectorcardiography (TotQRSF), the mean square amplitude of the last 40 m / s of the QRS complex on the vectorcardiography (RMS40); the duration of the section from the end of the QRS complex on the vectorcardiography (points S) to the beginning of the QRS complex over 40 μV (LAS40). The following values were considered as pathology: TotQRSF> 114–120 m/s, LAS40> 38 m / s, RMS40<20 μV [9].

The statistical analysis of the obtained data was performed in the IBM SPSS Statistics 23.0 software. The assessment of the normality of the distribution of quantitative variables was carried out using the Shapiro-Wilk test. We also performed logistic regression analysis with the assessment of the odds ratio (OR) and linear regression analysis with the estimation of the regression coefficient — B, and the coefficient of determination — R2. The t-test was for paired samples was performed. We calculated mean (M); confidence interval (CI) was set up as 95% for the mean; standard deviation (SD); the level of significance (p). The differences were considered statistically significant with p<0.05.

Results

When we compared the results of high-resolution ECG parameters (Table 1) during 10-year follow-up, we have found that TotQRSF increased by 1.33 m/s; LAS40 by 2.83 m/s, and RMS40 decreased by 9.85 μV, however, only the change of the last two indicators were statistically significant.

Due to the fact that many participants with RHD had aortic stenosis, we assessed the effect of VLPs parameters of combined mitral and aortic stenosis. The difference was significant for the TotQRSF parameter (p=0.001): in patients with mitral stenosis — 88.84 (87.73; 90.25) m/s; in patients with combined mitral and aortic stenosis — 97.64 (94.27; 101.02) m/s. The groups did not differ by the RMS40 and LAS40 parameters. The comparison of patients with RHD and patients only with aortic stenosis also revealed significant difference (p= 0.001) in TotQRSF by 91.13±17.55 m/s (aortic stenosis — 100.33± 25.19 m/s). As well as the comparison with patients with only mitral regurgitation (p= 0.001): TotQRSF 86.35± 10.72. The values of RMS40 and LAS40 parameters in patients with RHD, mitral regurgitation and isolated aortic stenosis did not differ significantly. We also assessed the effect of VLPs on the severity of mitral stenosis. Patients were divided into two groups depending on the area of the mitral valve orifice: less than 1.5 cm^2 and over 1.5 cm^2, that is the criterion for surgical treatment of the defect. However, these groups of patients with RHD did not differ by the VLPs parameters: TotQRSF 88.82 (87.20; 90.44) m/s (SMo<1.5 cm^2 – 89.96 (87.95; 91.97) m/s); RMS40 44.65 (41.17; 48.12) μV (SMo<1.5 cm^2–41.63 (38.58; 44.68) μV); LAS40 32.23 (31.06; 33.39) m s (SMo<1.5cm^2 – 30.49 (29.20; 31.78) m/s).

Initially, participants with RHD were divided into two groups depending on the presence of pulmonary hypertension (Table 2). The group with pulmonary hypertension showed the decrease of the following indicators: RMS40 (B= –5.288 (–9.731; –0.845), p=0.020, R2–0.009); TotQRSF (B= –2.266 (–4.411; –0.122), p= 0.038, R2–0.007) and almost significant change of LAS40 (B= –2.767 (–5.535; 0.002), p= 0.050, R2–0.006).

The total number of patients with mitral stenosis was 260 and 83 patients underwent valve surgery, the time after the intervention before VLPs was 4.95± 2.24 years. The analysis of the VLPs in the group of

Table 1. **The dynamics of VLPs parameters**

ECG paramters	Initial M±SD	After 10-year follow-up M±SD	The difference between parameters M (95% CI)	p
TotQRSF, m/s	88.13±11.35	89.46±16.14	1.33 (–3.54; 0.89)	0.237
RMS40, μV	47.81±27.37	37.96±21.49	9.85 (5.72; 13.98)	0.001
LAS40, m/s	29.89±9.26	32.72±14.76	2.83 (5.01; 0.65)	0.012

Table 2. **VLPs parameters in patients with pulmonary hypertension**

ECG parameters	RHD without pulmonary hypertension; M (95% CI)	RHD with pulmonary hypertension; M (95% CI)	p
TotQRSF, m/s	92.66 (89.99;95.32)	89.89 (88.54; 91.24)	0.050
RMS40, μV	45.62 (42.06;49.18)	40.33 (37.55; 43.11)	0.020
LAS40, m/s	33.75 (31.82;35.68)	31.48 (30.32; 32.65)	0.038

patients with RHD who underwent surgical treatment of the defect showed that the frequency of VLPs significantly increased in the operated group (Table 3): TotQRSF up to 94.43± 1.79 m/s (OR 1.088 (1.038; 1.139), p= 0.001) and LAS40 up to 34.39± 1.43 m/s (OR 1.127 (1.038; 1.224), p= 0.004). There were no differences in RMS40 between the groups, however, OR was 1.041 (1.012; 1.070), p= 0.005.

During the follow-up period 30 patients died out of 260 patients with RHD, the main cause of death was RHD. The comparison VLP parameters in deceased and survived patients is presented in table 4. Deceased patients had significantly higher TotQRSF 97.00± 12.67 m/s (p= 0.008, OR 1.026 (1.007; 1.046)) and LAS40 indices 36.57±15.25 m/s (p= 0.029, OR 0.964 (0.933; 0.996)), and showed significant decrease of RMS40 to 27.43±15.19 μV (p=0.439, OR 0.995 (0.982; 1.008)).

Discussion

VLPs that are known to reflect electrical and anatomical heterogeneity of the myocardium with the development of zones with normal and delayed conduction [7], changed in patients with RHD during ten-year follow-up — the RMS40 decreased and LAS40 increased. These changes reflect the processes in ventricular myocardium in patients with RHD. However, the influence of valvular heart disease: mitral and aortic stenosis, mitral regurgitation, combined mitral and aortic stenosis, on VLPs parameters (RMS40 and LAS40) has not been shown previously. This may be partly explained by the absence differences in the number of foci with delayed fragmented activity [3] in patients with various valvular heart diseases. The exception was significant change of TotQRSF parameter in these groups of patients. This may indicate higher number of zones with slow conduction of excitation and increased risk of life-threatening arrhythmias according to the TotQRSF parameter in patients with valve stenosis and lower number — with mitral valve regurgitation. The results were similar in patients with different severity of mitral stenosis.

However, in patients with pulmonary hypertension, the changes were less severe (according to TotQRSF and LAS40 parameters). Although patients with pulmonary hypertension are expected to have higher number of zones with electrical heterogeneity in the myocardium. The obtained results may be explained by the fact that most changes on echocardiography in patients with mitral stenosis appear in the right ventricle and atrium, while there were no significant differences of the parameters in the left cavities and ventricular hypertrophy between groups. In the group of patients who underwent surgery, we expected the decrease of VLPs parameters due to the improvement of hemodynamics; however, in patients with prosthetic valves, these parameters were significantly higher. The reason for such results may be postoperative changes in the myocardium [4] or initially high VLPs parameters in these patients.

One of the most significant results was obtained in this study when comparing VLPs parameters in deceased and survived patients. It has been shown not only significant change of all VLPs parameters in deceased patients, but also the influence of these indicators on the outcome [8] in patients with RHD. Therefore, the dynamics of VLP parameters determines the need for its further investigation and control in patients with RHD.

Conclusion

Therefore, patients with RHD showed the deterioration of VLP parameters with the severity of valvular heart disease, and deceased subjects with RHD had more pronounced VLP and increased TotQRSF. VLPs did not differ between groups with various types of valvular heart disease.

Conflict of interest: none declared

Table 3. **VLPs in participants with and without surgery**

ECG parameters	Patients with RHD after surgery M±SD	Patients with RHD without surgery M±SD	p
TotQRSF, m/s	87.62±14.76	94.43±19.64	0.001
RMS40, μV	40.05±20.89	39.55±26.74	0.856
LAS40, m/s	30.70±11.28	34.39±15.97	0.023

Table 4. **VLPs in deceased and survived patients with RHD**

ECG parameters	Survived patients with RHD M±SD	Deceased patients with RHD M±SD	p
TotQRSF, m/s	88.98±16.59	97.00±12.67	0.013
RMS40, μV	40.67±22.83	27.43±15.19	0.001
LAS40, m/s	31.40±12.62	36.57±15.25	0.041

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