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Research Article

Predictors of Repeated Atrial Fibrillation Paroxism with Patients Having Arterial Hypertension: Analysis of Current Heart Rate Variability and Myocardium Remodeling

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Abstract

Introduction: The prevalence of arterial hypertension and atrial fibrillation had been increasing in most countries of the world. It is known that modern medicine had the problems of arterial hypertension and atrial fibrillation in the center of its attention. It was associated with the increased risk of cardiovascular complications, loss of productivity and mortality among the patients having these diseases. Autonomic influence on the heart played a large part not only in the trigger mechanism, but also in AF progression. At the same time, the severity of atrial fibrillation course depended on the changes in the structure, mass, geometry, and remodeling of the left ventricle. However, the issues of pathogenetic mechanisms and predictors of recurrent atrial fibrillation with arterial hypertension patients having different variants of left ventricular myocardium remodeling are not fully studied and required more detailed coverage.

Objective of the Study: Study the predictors of recurrent paroxysm of atrial fibrillation according to the data of time and spectral analysis of daily heart rate variability with patients having arterial hypertension and different variants of left ventricular myocardium remodeling.

Materials and Methods: In total, 62 patients were examined (average age 58.9 ± 9.2). They complained of "rapid heartbeat and heart failure" attacks 2 - 3 times a month. 18 patients had no arterial hypertension and paroxysmal atrial fibrillation PAF detected. They were included in the 1st group (average age 57.2 ± 7.5). 44 of the examined men and women had AH and PAF found. They were included in the 2nd group (average age 58.4 ± 8.6). As a result, all the patients from the 2nd group were divided into 3 subgroups: 2A - 24 patients with arterial hypertension, paroxysmal atrial fibrillation and concentric left ventricular hypertrophy; 2B - 12 examined patients with arterial hypertension, paroxysmal atrial fibrillation and eccentric left ventricular hypertrophy; 2C - 8 patients with arterial hypertension, paroxysmal atrial fibrillation and left ventricular dilatation. Paroxysmal atrial fibrillation was recorded on the electrocardiogram (ECG). All the patients underwent Holter monitoring (HM) of ECG. Every patient had his daily heart rate variability (HRV) assessed. All the patients underwent echocardiography (EchoCG) and Doppler EchoCG. The analysis of the obtained indicators was carried out using the application software package "Statistica". The following descriptive statistics were made. Methods of parametric and non-parametric statistics were used. Qualitative values were estimated using contingency tables and Pearson's chi-squared test (χ^2) with Yates' correction. To assess the relationship between continuous variables, the Spearman's rank correlation coefficient r_s was used. The significance level of all the statistical tests was accepted as $p < 0.05$.

Results: It turned out that the examined people from 2A subgroup compared to the patients from the 1st group had their VAR, SDNN and SDANN parameters decreased, while AVNN, PNN50, RMSSD and SDNNIDX parameters, on the contrary, increased. We found that AVNN and RMSSD values with the patients from 2A, 2B and 2C subgroups were higher in contrast to similar HRV parameters with the patients from the 1st group (all $p < 0.05$). The high risk of recurrent AF paroxysms was associated with the increase in SDNN, SDANN, RMSSD and PNN50 values. Thus, a positive relationship was found between the parameters of the time and spectral analysis of HRV: VAR SDNN, PNN50, RMSSD, SDANN and TF, VLF, LF ($r_s = 0.47 - 0.97$; $p = 0.012 - 0.048$). We found that HF values with the patients from 2A, 2B and 2C subgroups were higher than in the 1st group (by 2.9; 3.8 and 4.4 times, respectively; all $p < 0.01$).

Conclusion: Patients with arterial hypertension and concentric left ventricular hypertrophy during the study of daily heart rate variability had repeated PAF associated with the simultaneous disturbance in the balance of the effects of sympathetic and parasympathetic parts of the autonomic nervous system on the heart rate with increased sympathetic stimulation. With the progression of myocardium remodeling in the form of the development of eccentric hypertrophy and left ventricular dilatation, an increase in the activity of parasympathetic nervous system was noted. According to the time and spectral analysis of heart rate variability with patients having arterial hypertension and concentric left ventricular hypertrophy, the decrease in VAR and SDNN values below 805.1 and 116.2 ms, respectively, could be the predictors of recurrent atrial fibrillation paroxysm; patients with arterial hypertension, eccentric hypertrophy or left ventricular dilatation showed the increase in PNN50 and RMMSD values of more than 7.5% and 24.7 ms, respectively. Recurrent atrial fibrillation paroxysm with patients having arterial hypertension, regardless of the variant of left ventricular myocardium remodeling, was associated with the increase in the power of VLF, LF and HF spectral analysis waves above 1132.7 ms^2, 446.8 ms^2 and 171.8 ms^2, respectively.

Keywords: *Atrial Fibrillation; Arterial Hypertension; Myocardium Remodeling*

Introduction

The prevalence of arterial hypertension (AH) and paroxysmal atrial fibrillation (PAF) had been increasing in most countries of the world [9,10,14]. It is known that modern medicine had the problems of AH and PAF in the center of its attention [2,7,8,18]. It was associated with the increased risk of cardiovascular complications, loss of productivity and mortality among the patients having these diseases. The main pathogenetic mechanisms of AH and PAF development were well studied. Most patients had some imbalance in the influence of autonomic nervous system (ANS) on the function of cardiovascular system [5,6,15,20]. The dominance of sympathetic nervous system (SNS) was associated with increased blood pressure and appearance of AF attacks. Autonomic influence on the heart played a large part not only in the trigger mechanism, but also in AF progression [1,3,12,13]. At the same time, the severity of AF course depended on the changes in the structure, mass, geometry, and remodeling of the left ventricle. However, the issues of pathogenetic mechanisms and predictors of recurrent AF with AH patients having different variants of left ventricular (LV) myocardium remodeling are not fully studied and required more detailed coverage [4,11,16,17,19].

Objective of the Study

Study the predictors of recurrent paroxysm of atrial fibrillation according to the data of time and spectral analysis of daily heart rate variability with patients having arterial hypertension and different variants of left ventricular myocardium remodeling.

Materials and Methods

In total, 62 patients were examined (average age 58.9 ± 9.2). They complained of "rapid heartbeat and heart failure" attacks 2 - 3 times a month. The attacks lasted from 2 - 3 to 30 minutes and stopped on their own without taking medicines. 18 patients had no AH and PAF detected. They were included in the 1st group (average age 57.2 ± 7.5). 44 of the examined men and women had AH and PAF found [4]. They were included in the 2nd group (average age 58.4 ± 8.6). AH and PAF diagnoses were made during anamnestic, clinical and instrumental examination. Exclusion criteria from the study were: permanent AF, heart defects, ischemic heart disease, thyroid diseases, obesity, diabetes mellitus, WPW syndrome, cerebral vascular disorders, atrial or ventricular tachycardia, disorder of atrioventricular conduction, sick sinus syndrome or sinus node dysfunction and digestive system pathology. AF paroxysm was recorded on the electrocardiogram (ECG). All the patients underwent Holter monitoring (HM) of ECG. HM ECG lasted 24 hours. The examined people adhered to their usual daily routine, marking the main points in their observation diaries. Every patient had his daily heart rate variability (HRV) assessed. The following time characteristics of HRV were calculated:

- VAR in milliseconds (ms) - Variation range as the difference between the maximum and minimum values of RR interval;
- AVNN (ms) - Average duration of normalized RR interval, SDNN (ms) - root mean square deviation of RR intervals;
- PNN50 - Proportion of adjacent RR intervals with the differences of more than 50 ms between them;
- RMSSD (ms) - Root mean square deviation of interval differences;
- SDNNIDX (ms) - Average from 5-minute standard deviations over the entire record;
- SDANN (ms) - Root mean square deviation of RR intervals, which are averaged over each 5 minutes of recording.

Spectral analysis was carried out with the calculation of spectral power density (ms^2) according to the following frequency ranges:

- TP (Total Power - Total spectrum power, in ms^2);
- VLF (Very Low Frequency - Very low spectrum frequencies, in ms^2);
- LF (Low Frequency - Low spectrum frequencies, in ms^2);
- HF (High Frequency - High spectrum frequencies, in ms^2).

All the patients underwent echocardiography (EchoCG) and Doppler EchoCG. End-Diastolic Size of Left Ventricular (EDS LV) and End-Systolic Size of Left Ventricular (ESS LV) in centimeters, End-Diastolic Volume of Left Ventricular (EDV LV) and End-Systolic Volume of Left Ventricular (ESV LV) in milliliters, Thickness of InterVentricular Septum (TIVS) and Thickness of the Left Ventricle Posterior Wall (TLVPW) in centimeters, Myocardium Mass of Left Ventricular (MM LV) in grams, Left Atrial Diameter (LAD) in centimeters were calculated.

The 2nd group included men and women with left ventricular hypertrophy (LVH). LVH was ascertained after calculating myocardial mass (MM) and LV MM index (LVMM and LVMMi, respectively). The thickness of interventricular septum and the thickness of the left ventricle posterior wall were measured [2]. Among the patients with AH and LVH, we selected the patients with concentric left ventricular hypertrophy and eccentric left ventricular hypertrophy (KLVH and ELVH, respectively). Groups of patients with left ventricular dilatation (LVD) were selected from the group of patients with ELVH [3]. As a result, all the patients from the 2nd group were divided into 3 subgroups: 2A - 24 patients with AH, PAF and KLVH; 2B - 12 examined patients with AH, PAF and ELVH; 2C - 8 patients with AH, PAF and LVD. Comparison of the obtained HRV data was carried out between the patients of the 1st group and the patients of 2A, 2B and 2C subgroups. The analysis of the obtained indicators was carried out using the application software package "Statistica". The following descriptive statistics were made: means (M), boxplots, median, minimum, maximum, standard deviation (SD), ± 95% confidence intervals (CI). Normality of continuous quantities distribution was checked using the Shapiro-Wilk W-test. Methods of parametric and non-parametric statistics were used to compare quantitative indicators. Student's t-test, Mann-Whitney U-test, Kruskal-Wallis H-test were applied. Qualitative values were estimated using contingency tables and Pearson's chi-squared test (χ^2) with Yates' correction. To assess the relationship between continuous variables, the Spearman's rank correlation coefficient r_s was used. The significance level of all the statistical tests was accepted as $p < 0.05$.

Results and Discussion

The results of the analysis of descriptive statistics of EchoCG data in patients of groups 1 and 2 are presented in table 1.

Parameter	Groups of patients	M	SD	± 95% CI
EDS LV	1st	4,37	0,28	4,12 - 4,56
	2nd	4,92*	0,45	4,51 - 5,43
EDV LV	1st	86,92	13,12	73,54 - 99,27
	2nd	115,19*	23,89	102,42 - 129,89
ESS LV	1st	2,91	0,11	2,51 - 3,35
	2nd	3,26*	0,46	2,97 -3,51
ESV LV	1st	32,28	2,97	29,23 - 35,84
	2nd	44,22*	4,26	39,67 - 48,69
TLVPW	1st	0,91	0,08	0,77 - 1,12
	2nd	1,07*	0,14	0,89 - 1,08
TIVS	1st	1,05	0,12	0,91 - 1,11
	2nd	1,16*	0,13	1,02 - 1,24
MM LV	1st	143,92	10,69	127,83 - 155,39
	2nd	205,29*	45,79	181,4 - 227,86
LAD	1st	3,46	0,42	3,24 - 3,57
	2nd	3,95*	0,51	3,65 - 4,21

Table 1: *The results of the analysis of descriptive statistics of EchoCG data in patients of 1st and 2nd groups.*
*Note: *: Statistical significance between the patients from the 1st and 2nd groups of the patients is p < 0.01.*

It was found that in group 2 patients, the values of EDS LV, EDV LV, ESS LV, ESV LV, TLVPW, TIVS, MM LV, LAD were higher than in group 1 patients (by 12,6%; 32,5%; 12,0%; 36,9%; 17,5%; 10,4%; 42,3%; 14,1% respectively; all p = 0.001). The results of a comparative analysis of EchoCG data in patients of groups 1 and 2 are presented in table 2.

Variable	Mann-Whitney U Test By variable Patient groups Marked tests are significant at p <,05000							
	Rank Sum 2nd group	Rank Sum 1st group	U	Z	p-value	Z adjusted	p-value	2*1sided exact p
EDS LV	8616,0	1254,0	624,0	5,837	0,001	5,857	0,001	0,001
EDV LV	8616,0	1254,0	624,0	5,837	0,001	5,857	0,001	0,001
ESS LV	8494,0	1376,0	746,0	5,251	0,001	5,294	0,001	0,001
ESV LV	8494,0	1376,0	746,0	5,251	0,001	5,294	0,001	0,001
TLVPW	8787,0	1083,0	453,0	6,661	0,001	6,749	0,001	0,001
TIVS	8145,5	1724,5	1094,5	3,573	0,001	3,621	0,001	0,001
MM LV	9018,5	851,5	221,5	7,77	0,001	7,783	0,001	0,001
LAD	8594,5	1275,5	645,5	5,734	0,001	5,769	0,001	0,001

Table 2: *Results of the comparative analysis of EchoCG data in patients of 1st and 2nd groups.*

Boxplots of EchoCG indicators were analyzed. The results of comparing the most significant indicators in patients of groups 1 and 2 are shown in figure 1.

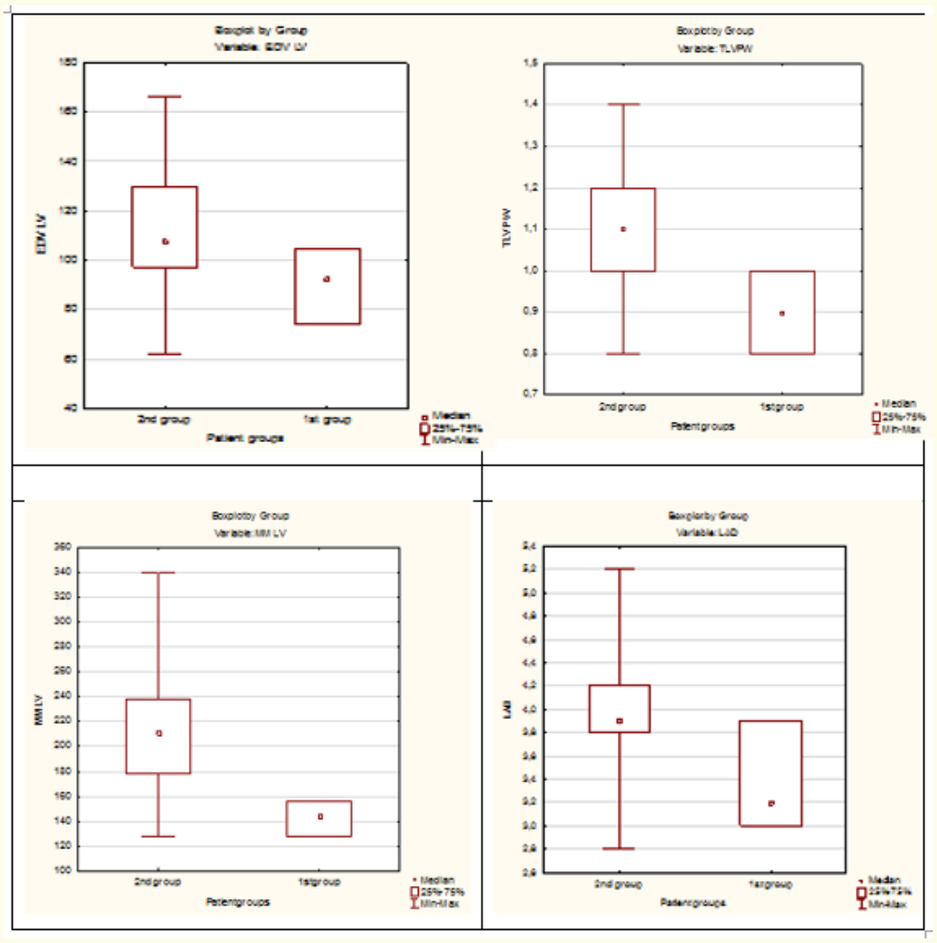

Figure 1: *The results of comparing the most significant indicators in patients of groups 1 and 2.*

It was found that the maximum value and median values of EDV LV, TLVPW, MM LV, and LAD in group 2 patients were higher than in group 1. The results of the comparative analysis of time and spectral HRV characteristics with patients from the 1st group and patients from 2A, 2B and 2C subgroups are presented in table 3.

HRV indicators	Groups of patients			
	1st group (n = 18)	2A subgroup (n = 24)	2B subgroup (n = 12)	2C subgroup (n = 8)
VAR	855,7 ± 179,1	805,1 ± 88,8*	891,6 ± 222,1*	861,4 ± 110,5
AVNN	814,2 ± 118,6	891,5 ± 176,7*	917,4 ± 176,7*	929,8 ± 161,6**
SDNN	121,5 ± 19,5	116,2 ± 23,2	144,3 ± 20,2*	127,6 ± 28,7
PNN50	1,8 ± 0,6	7,6 ± 6,5**	7,5 ± 4,9**	9,2 ± 6,3**
RMSSD	15,5 ± 5,2	28,2 ± 23,5**	24,7 ± 11,7**	21,8 ± 10,4**
SDNNIDX	34,2 ± 13,1	36,1 ± 13,4	52,8 ± 5,6*	45,8 ± 13,8
SDANN	113,7 ± 15,3	98,7 ± 26,8	122,8 ± 15,7**	119,8 ± 26,4
VLF	912,5 ± 501,1	1132,7 ± 538,1*	1885,6 ± 181,6**	1361,8 ± 652,1**
LF	386,2 ± 280,5	446,8 ± 336,4*	633,6 ± 271,3**	466,2 ± 269,6*
HF	58,5 ± 28,4	171,8 ± 91,4**	223,6 ± 271,4**	253,8 ± 183,9**

Table 3: *Results of the comparative analysis of heart rate variability with patients from the 1st group and patients from 2A, 2B and 2C subgroups (M ± SD).*

*Note: *: Statistical significance between the patients from the 1st group and the patients from 2A, 2B and 2C subgroups is p < 0.05;*

***: Statistical significance between the patients from the 1st group and the patients from 2A, 2B and 2C subgroups is p <0.01.*

Undoubtedly, the question of assessing the risk of complications of cardiovascular diseases is essential [2]. At the same time, the problem of finding PAF predictors has aroused certain scientific and practical interest [3]. In this regard, the study of prognostic value of HRV indicators seemed to be very relevant. According to the authors' data, AF paroxysms were divided into vagal, sympathoadrenal and mixed types However, pure vegetative paroxysms were extremely rare. Though, ANS dystonias were found with the significant part of patients having AH and PAF [4,5].

In our study, we found that the patients from 2A subgroup in contrast to the patients from the 1st group had certain particularities in HRV indices. It turned out that the examined people from 2A subgroup compared to the patients from the 1st group had their VAR, SDNN and SDANN parameters decreased, while AVNN, PNN50, RMSSD and SDNNIDX parameters, on the contrary, increased. Further progression of LV remodeling with patients from 2B and 2C subgroups was associated with the increase in all HRV indices [1,9,14,16,17]. According to the literature, the increase of the VAR value for over 500 ms could reflect the increase in parasympathetic nervous system (PSNS) effect on the heart rate and the increase in the risk of heart rhythm disorders [2,4,8,9]. We found that AVNN and RMSSD values with the patients from 2A, 2B and 2C subgroups were higher in contrast to similar HRV parameters with the patients from the 1st group (all $p < 0.05$). In 2A, 2B and 2C subgroups AVNN and RMSSD values were higher than in the 1st group. The prevalence of PSNS tone was also indicated by higher AVNN and RMSSD values (by 9.4%; 12.6%; 14.2% and 86.7%; 60.0%; 46.7%, respectively; all $p < 0.05$). This indicated the predominance of parasympathetic nervous system tone with patients of these subgroups. According to the literature, the increase in PSNS effects on the heart was associated with the decrease in the duration of transmembrane potential of cardiomyocytes action, with the shortening of atrial myocardium refractory period and with the lengthening in the period of vulnerability for extrasystoles. Ultimately, the "readiness" for AF development increased [20]. The high risk of recurrent AF paroxysms was associated with the increase in SDNN, SDANN, RMSSD and PNN50 values . Although, the patients from 2A subgroup had their SDNN and SDANN values lower than the patients from the 1st group (by 4.1% and 13.2%). At the same time, the differences were not reliable. In contrast, SDNN and SDANN were higher in 2B and 2C subgroups than in the 1st group. Indicators PNN50 and RMSSD in 2A, 2B and 2C subgroups were also higher than in the 1st group. One can conclude that our results do not contradict the data in the literature. In our study, we performed the correlation analysis of the indicators of HRV time and spectral analysis with patients from 2A, 2B and 2C subgroups. As a result, certain particularities were revealed. Thus, a positive relationship was found between the parameters: VAR and TF ($r_s = 0.71$; $p = 0.031$), VAR and VLF ($r_s = 0.77$; $p = 0.012$), VAR and LF ($r_s = 0.63$; $p = 0.012$), SDNN and TF ($r_s = 0.72$; $p = 0.021$), SDNN and VLF ($r_s = 0.74$; $p = 0.043$), SDNN and LF ($r_s = 0.53$; $p = 0.039$), PNN50 and TF ($r_s = 0.79$; $p = 0.007$), PNN50 and VLF ($r_s = 0.71$; $p = 0.048$), PNN50 and LF ($r_s = 0.69$; $p = 0.029$), RMSSD and TF ($r_s = 0.53$; $p = 0.045$), SDNNIDX and TF ($r_s = 0.97$; $p = 0.029$), SDNNIDX and VLF ($r_s = 0.96$; $p = 0.037$), SDNNIDX and LF ($r_s = 0.83$; $p = 0.041$), SDANN and TF ($r_s = 0.62$; $p = 0.045$), SDANN and VLF ($r_s = 0.64$; $p = 0.033$), SDANN and LF ($r_s = 0.47$; $p = 0.048$). We found that HF values with the patients from 2A, 2B and 2C subgroups were higher than in the 1st group (by 2.9; 3.8 and 4.4 times, respectively; all $p < 0.01$). This could indicate the increase in the influence of parasympathetic division of autonomic nervous system on the heart rate and was one of the risk factors for the development of repeated paroxysms with the patients having AH and PAF [9,10]. In addition, in our study we noted the synchronous increase in the power of HF and LF components of HRV spectral analysis with the patients having AH and PAF. It can be assumed that these results reflected the simultaneous increase in both sympathetic and parasympathetic influences on the heart rate [12]. Apparently, the simultaneous increase in parasympathetic and sympathetic influences on the chronotropic function of the heart can be considered the conditions for recurrent AF occurrence [5]. We believe that the patients with AH and PAF in our study had their electrical properties of the atrial myocardium changed; electrophysiological prerequisites for the re-entry circle formation, the refractory period dispersion, and the atrial electrical remodeling were created. Ultimately, this could lead to repeated attacks of atrial fibrillation with AF patients having unfavorable variants of left ventricular myocardium remodeling [1,2,19,20].

Conclusion

1. Patients with arterial hypertension and concentric left ventricular hypertrophy during the study of daily heart rate variability had repeated AF paroxysms associated with the simultaneous disturbance in the balance of the effects of sympathetic and

parasympathetic parts of the autonomic nervous system on the heart rate with increased sympathetic stimulation. With the progression of myocardium remodeling in the form of the development of eccentric hypertrophy and left ventricular dilatation, an increase in the activity of parasympathetic nervous system was noted.

2. According to the time and spectral analysis of heart rate variability with patients having arterial hypertension and concentric left ventricular hypertrophy, the decrease in VAR and SDNN values below 805.1 and 116.2 ms, respectively, could be the predictors of recurrent atrial fibrillation paroxysm; patients with arterial hypertension, eccentric hypertrophy or left ventricular dilatation showed the increase in PNN50 and RMMSD values of more than 7.5% and 24.7 ms, respectively.

3. Recurrent atrial fibrillation paroxysm with patients having arterial hypertension, regardless of the variant of left ventricular myocardium remodeling, was associated with the increase in the power of VLF, LF and HF spectral analysis waves above 1132.7 ms^2, 446.8 ms^2 and 171.8 ms^2, respectively.

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