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Predictors of paroxysmal atrial fibrillation: Analysis of 24-hour ECG Holter monitoring

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Abstract

Aim – to study the features of the ECG records received by 24-hour ECG monitoring in patients with paroxysmal atrial fibrillation (AF) and, based on the data obtained, to determine the main predictors of the development of this arrhythmia.

Material and methods. A single-center, cross-control study was conducted. Of all 6630 protocols analyzed, according to 24-hour ECG monitoring, AF paroxysm was detected in 97 people as an accidental finding. These patients were included in the main study group. The control group consisted of 99 patients from the same cohort without paroxysmal AF, having the anthropometric and comorbidity parameters similar to the patients of the main group.

Results. In the absolute majority (97.9%) of patients in the main group in whom paroxysmal AF was detected, a special variant of extrasystole was revealed – early atrial "P on T" type (versus 4.0% in patients in the control group) [OR 8461.648 (382.1983;187336)]. The number of supraventricular single, paired and group extrasystoles was significantly higher in the main group, but the number of ventricular extrasystoles did not differ significantly.

Conclusion. One of the main ECG predictors for the development of paroxysmal AF in asymptomatic patients is the appearance of supraventricular extrasystole of the "P on T" type. In the mechanism of formation of AF paroxysm during supraventricular extrasystole of the "P on T" type, not only electrophysiological mechanisms play a role, but also the heart biomechanics.

Keywords: extrasystole, predictor of atrial fibrillation, atrial extrasystole, supraventricular extrasystole.

Conflict of interest: nothing to disclose.

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Предикторы развития пароксизмальной фибрилляции предсердий: анализ данных суточного мониторирования ЭКГ по Холтеру

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Аннотация

Цель – изучить особенности ЭКГ-картины по данным суточного мониторирования ЭКГ по Холтеру у пациентов с пароксизмальной фибрилляцией предсердий (ФП) и на основании полученных данных определить основные предикторы развития данного нарушения ритма.

Материал и методы. Проведено одноцентровое исследование по типу кросс-контроля. Из всех проанализированных 6630 протоколов, по данным суточного мониторирования по Холтеру, у 97 человек был выявлен пароксизм ФП как случайная находка. Эти пациенты вошли в основную группу исследования. Группу сравнения составили 99 пациентов без пароксизма ФП из той же когорты, которые по основным антропометрическим показателям и параметрам коморбидности соответствовали основной группе.

Результаты. У абсолютного большинства (97,9%) пациентов основной группы, у которых был выявлен пароксизм ФП, регистрировался особый вариант экстрасистолии – ранней предсердной по типу «P на T» (против 4,0% у пациентов контрольной группы) [OR 8461.648 (382.1983;187336)]. Также достоверно выше в основной группе было количество наджелудочковых экстрасистол, как одиночных, так и парных, и групповых, количество же желудочковых экстрасистол достоверно не отличалось.

Выводы. Одним из основных ЭКГ-предикторов развития пароксизмальной ФП у бессимптомных пациентов является появление наджелудочковой экстрасистолии по типу «P на T». В механизме формирования пароксизма ФП при наджелудочковой экстрасистолии типа «P на T» играют роль не только электрофизиологические механизмы, но и биомеханическая составляющая.

Ключевые слова: экстрасистолия, предиктор фибрилляции предсердий, предсердная экстрасистолия, наджелудочковая экстрасистолия.

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Список сокращений
ФП – фибрилляция предсердий; ЭКГ – электрокардиография; ЧСС – частота сердечных сокращений; ЭС – экстрасистолия; НЖЭ – наджелудочковая экстрасистолия; ЖЭ – желудочковая экстрасистолия; ЭКС – электрокардиостимулятор; ПТ – пароксизмальная тахикардия.

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INTRODUCTION

Atrial fibrillation (AF) is a rhythm disorder prevalent worldwide. Its incidence in the population is ca. 1-2%, the number of patients increasing in the older age groups reaching 5–15% by 80 years [1]. In the coming decades, a further growth of incidence is expected. It is related to an increase of average life expectancy and to a broader diagnostic search [2–4]. Traditional risk factors of AF development include modifiable and non-modifiable risk factors (e.g., smoking, alcohol consumption, abdominal obesity, age, female sex, etc.). Such conditions as arterial hypertension, diabetes, coronary heart disease, chronic heart failure, and chronic kidney disease increase the chance of development of AF [5–11]. In assessing the risk of development of the rhythm disorder, its dependence on the age, genetic, clinical and subclinical factors is also considered [12–14].

Timely diagnostics and periodic screening are vital for the finding of AF in patients from high-risk groups. They include post-stroke patients [15]. Despite the state of knowledge of major risk factors of AF, to date there is no unified prognosis score of this rhythm disorder, and the existing models of prognosis (C_2HEST score, MHS, CHARGE-AF score, FHS score and others) found no wide application [16–19]. Among the electrophysiological causes, the importance of the mechanism of re-entry in the start and continuation of AF, and the structure of pulmonary veins characterized with a shorter refractory time, are mentioned as highly important [20]. Some studies describe more frequent development of AF in patients with extrasystole and regard it as a predictor of AF in the future [21–23]. However, they do not indicate which specific variant of extrasystole is the most frequent predictor of AF, and do not account for specific characteristics of intracardiac and intra-arterial circulatory dynamics. In our preceding papers we showed and provided experimental proof of existence of the so called 'surging shock', a phenomenon that occurs in rhythm disorders and serves as the basis of circulatory dynamic changes in arrhythmias [24–27].

AIM

To study the features of the ECG records received by 24-hour ECG monitoring in patients with paroxysmal atrial fibrillation and, based on the data obtained, to determine the main predictors of the development of this arrhythmia.

MATERIAL AND METHODS

A single-center, cross-control study was conducted involving 6630 patients. The object was the 24-hour ECG Holter monitoring database. The study was performed on an elective basis to identify disorders of heart rhythm and control the ST segment dynamics. The patients had never complained of any malfunction in the heart rate, had never been diagnosed with AF in their history, had never had any pathology of the thyroid gland. Of all 6630 protocols analyzed, according to 24-hour ECG monitoring, AF paroxysm was detected in 97 people as accidental finding. These patients were included in the main study group. The control group consisted of 99 patients from the same cohort without paroxysmal AF, having the anthropometric and comorbidity parameters similar to the patients of the main group. All patients

underwent the standard laboratory (including lipid profile and thyroid hormone levels) and instrumental tests: apart from the 24-hour ECH Holter monitoring, they had transthoracic echocardiography (EchoCG), Doppler ultrasonic examination of brachiocephalic artery (BA USDG), and, when indicated, stress EchoCG with exercising or adenosine, or coronary arteriography.

24-hour ECG Holter monitoring was performed using the "Myocard-Holter-2" device manufactured by NIMP ESN LLC, Sarov, Nizhny Novgorod Region (sensitivity: 99.99%, specificity: 100%; detection of atrial complexes: sensitivity: 99.57%, specificity 99.84%). In the 24-hour ECG monitoring the following major parameters were analyzed: sinus node; heart rate analysis, including circadian rhythm that was matched against the patient's physical activity journal; supraventricular and ventricular ectopic activity; pauses and blocks; ST segment and PQ and QT interval dynamics; heart rate variability.

Statistical processing of data involved principles of evidence-based medicine. First, the normality of distribution of analyzed parameters was determined. In the event of normal distribution, parametric criteria were applied (quantitative variables were characterized by finding the mean value and standard deviation, intergroup comparisons by single-factor dispersion analysis with indication of the F criterion, 'df' degree of freedom and 'p' statistical significance); in the event of abnormal distribution, non-parametric criteria were applied (for quantitative values, medians and quartiles 1 and 3 were indicated, Q1 and Q3, and intergroup comparisons were performed by Kruskal-Wallis method using the statistics values H and 'p'). We considered differences between groups at $p \leq 0.05$ to be statistically significant.

RESULTS

The main group and the control group had similar anthropometric indicators and comorbidities. When performing the analysis of the 24-hour ECG Holter monitoring, there were registered statistically reliable differences in the supraventricular and ventricular ectopic activity (**Table 1**).

The groups were comparable in sex and age (no statistically significant differences). The indicators of 24-hour ECG Holter monitoring (heart rate, number and type of extrasystoles, availability of 'P on T' and 'R on T') proved to occur more frequently and have higher values in the main study group with paroxysmal AF. Thus, the absolute majority (97.9%) of the patients in the main study group, in which the AF paroxysm was found, showed a special variation of the extrasystole: early atrial 'P on T' type (vs. 4.0% in the control group patients) [OR 8461.648 (382.1983;187336)]. The number of supraventricular extrasystoles in the main study group was also reliably higher, singular, paired, and grouped alike, the number of ventricular extrasystoles not being reliably different.

The duration of the intervals (ventricular and supraventricular pause, QT, RR) was significantly higher in the main study group with paroxysmal AF. The frequency of ventricular extrasystoles, atrioventricular blockades, and depression of the ST segment was consistent among the groups. In other words, the patients with paroxysmal AF in the main group showed characteristic changes in the rhythm and conductivity that were more marked as compared with the control group. The groups were comparable in the main demographic characteristics.

Parameter		Main group n=97	Control n=99	Statistics
Sex, n (%)	F	53 (27,04%)	53 (27,04%)	χ^2=0,000, p=0,991
	M	44 (22,45%)	46 (23,47%)	
Age, years, median (Q1, Q3)		72,0 (65,0, 78,0)	71,0 (64,0, 79,0)	H=0,007, p=0,933
Monitoring time, h, median (Q1, Q3)		22,7 (21,9, 23,2)	22,3 (21,4, 23,1)	H=1,376, p=0,120
AF time, s,median (Q1, Q3)		81,0 (14,0, 8925,0)	0,0 (0,0, 0,0)	H=167,876, p<0,001
HR during AF, median (Q1, Q3)		107,0 (94,0, 117,0)	0,0 (0,0, 0,0)	H=167,142, p<0,001
Supraventricular PT, s, median (Q1, Q3)		5,0 (0,0, 34,0)	0,0 (0,0, 9,0)	H=9,840, p=0,002
Ventricular PT, s, median (Q1, Q3)		0,0 (0,0, 0,0)	0,0 (0,0, 0,0)	H=0,099, p=0,753
Number of supraventricular extrasystoles, median (Q1, Q3)		633,0 (284,0, 2098,0)	79,0 (27,5, 349,5)	H=40,635, p<0,001
Singular SVEs, median (Q1, Q3)		461,0 (238,0, 1767,0)	69,0 (22,5, 315,0)	H=37,952, p<0,001
Paired and grouped SVEs, median (Q1, Q3)		26,0 (6,0, 93,0)	4,0 (1,0, 12,0)	H=38,272, p<0,001
Allorhythmia in SVE, median (Q1, Q3)		24,0 (1,0, 401,0)	0,0 (0,0, 9,5)	H=31,647, p<0,001
Atrial extrasystole, median (Q1, Q3)		602,0 (262,0, 2028,0)	74,0 (27,5, 314,0)	H=36,843, p<0,001
Number of ventricular extrasystoles, median (Q1, Q3)		24,0 (3,0, 149,0)	16,0 (3,0, 488,5)	H=0,176, p=0,675
Singular ventricular extrasystoles, median (Q1, Q3)		20,0 (2,0, 143,0)	14,0 (2,0, 328,5)	H=0,121, p=0,727
Paired ventricular extrasystoles, median (Q1, Q3)		0,0 (0,0, 6,0)	0,0 (0,0, 2,0)	H=2,100, p=0,147
Allorhythmia in ventricular extrasystoles, median (Q1, Q3)		0,0 (0,0, 0,0)	0,0 (0,0, 3,0)	H=0,193, p=0,661
R on T, median (Q1, Q3)		2,0 (1,0, 5,0)	0,0 (0,0, 0,0)	H=74,763, p<0,001
P on T, n (%)	Y	95 (97,9%)	4 (4,0%)	χ^2= 172,81, p<0,001
	N	2 (2,1%)	95 (96%)	
QT max interval, s, median (Q1, Q3)		0,5 (0,5, 0,6)	0,5 (0,5, 0,6)	H=2,495, p=0,114
RR max, s, median (Q1, Q3)		1,7 (1,6, 1,9)	1,5 (1,4, 1,8)	H=14,172, p<0,001
QRS drop-out, median (Q1, Q3)		0,0 (0,0, 2,0)	0,0 (0,0, 0,0)	H=11,732, p=0,001
ST depression, n (%)	No	84 (42,86%)	91 (46,43%)	χ^2=2,377, p=0,305
	Yes	13 (6,63%)	8 (4,08%)	
Pacemaker, n (%)	No	95 (48,47%)	99 (50,51%)	χ^2=0,526, p=0,468
	Yes	2 (1,02%)	-	

Notes. *Normal distribution of characteristics was not observed.*
Примечания. *Нормальность распределения признаков не соблюдалась.*

Table 1. *Main parameters of 24-hour ECG Holter monitoring in patients of the main and control groups*
Таблица 1. *Основные данные анализа суточного мониторирования ЭКГ по Холтеру у пациентов основной и контрольной групп*

DISCUSSION

The papers published to date have no unanimous opinion on the efficacy of prognosis of paroxysmal AF in the population. The existing scores of forecasting the risk of development of this rhythm disorder have found no broad application. The most widely studied C2HEST score, validated on the Asian and Caucasian populations involving over 711,000 people, include the following in the risk parameters of AF: chronic obstructive pulmonary disease, arterial hypertension, age, systolic heart failure, diseases of the thyroid [20]. Other prognostication scores (FHS score, CHARGE-AF score, ARIC score, WHS score, MHS, JMC score, Shandong score), studied on smaller cohorts, include anthropometric parameters and secondary illnesses as risk factors, and take into account the dimensions of the cardiac chambers. Not a single model takes into account the specifics of the ECG pattern. When possible mechanisms of paroxysmal AF are explained, researcher focus specifically on the electrophysiological component of arrhythmia. We believe that the biomechanical component is also to be taken into consideration, as well as intracardiac hemodynamics that can explain, among other things, the processes of heart remodeling that occur during AF.

With the premature atrial extrasystole 'P on T', the systole of atria in the axtrasystolic beat usually occurs at the peak or the descent of the T wave of the preceding beat. At that moment, the period of ventricular emptying is over. The increase of pressure to the atrial systole will not be sufficient with this variant of the extrasystole to overcome the intraventricular pressure and create conditions for the atrioventricular valves to open. Therefore, the atrial contraction under extrasystole 'P on T' may be considered isometric or isovolumic since there is no movement of blood to the ventricles. In our opinion, this may end up in creation of conditions for the dilatation of the left and the right atria, especially if the onset of the 'P on T' extrasystole is frequent or regular or there appears atrial paroxysmal tachycardia. The changes in the biomechanics and hemodynamics similar to the ones described above may occur during the extrasystole from the atrioventricular node with simultaneous excitation of the atria and ventricles and during extrasystole from the atrioventricular node with excitation of ventricles preceding excitation of atria.

Considering our clinical experience, we can state that the pharmacological therapy of these specific variants of extrasystole with anti-arrhythmia drugs seems, in our opinion, the optimal prevention of AF paroxysms.

CONCLUSION

One of the main ECG predictors for the development of paroxysmal AF in asymptomatic patients is the appearance of supraventricular extrasystole of the "P on T" type.

In patients newly diagnosed with paroxysmal AF, this rhythm disorder precedes the paroxysm and is seen in 95 (97.9%) patients, whereas in the control group only in 2 (2.1%) individuals [OR 8461.648 (382.1983;187336)]. This means that the possibility of development of paroxysmal AF in patients with this variant of extrasystole is 8461 higher than with its absence.

Considering the data obtained, the patients with supraventricular extrasystole of the 'P on T' type are recommended a long-term ECG Holter monitoring (three or more days) to diagnose paroxysmal AF; in the event the latter is diagnosed, respective treatment compliant with applicable standards is recommended, including prevention of cacrdioembolic stroke for this category of patients.

In the mechanism of formation of AF paroxysm during supraventricular extrasystole of the "P on T" type, not only electrophysiological mechanisms play a role, but also the heart biomechanics.

ADDITIONAL INFORMATION	ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ
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Conflict of Interest. The authors declare that there are no obvious or potential conflicts of interest associated with the content of this article.	***Конфликт интересов.*** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.
Contribution of individual authors. O.A. Germanova – was responsible for data analysis, wrote the first draft of the manuscript. G. Galati – provided final revision of the manuscript. L.D. Kunz – performed the scientific data collection. A.A. Usenova – managed the study. Yu.B. Reshetnikova – was responsible for data systematization. A.V. Germanov – developed the study concept and design. A. Stefanidis – provided final revision of the manuscript.	***Участие авторов.*** О.А. Германова – анализ данных, текст статьи. Дж. Галати – окончательная правка. Л.Д. Кунц – сбор данных. А.А. Усенова – постановка задач исследования. Ю.Б. Решетникова – систематизация материала. А.В. Германов – идея и дизайн исследования. А. Стефанидис – окончательная правка.
All authors gave their final approval of the manuscript for submission, and agreed to be accountable for all aspects of the work, implying proper study and resolution of issues related to the accuracy or integrity of any part of the work.	Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.

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