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Features of cardiac rhythm disorders and conduction disturbances in patients with arterial hypertension

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Objective – to study features of cardiac rhythm disorders and conduction disturbances in patients with arterial hypertension.

Methods of the study. Under our observation there were 110 patients with first-third degree hypertension stage II, aged 38 to 72 years (mean age – 50.63±1.34 years). The gender distribution of patients was as follows: 61 female (55 %) and 49 male patients (45 %). The control group comprised 30 healthy individuals, of whom 13 were male and 17 female (43 % and 57 % respectively) and whose mean age was 49.75±1.83 years. Cardiac arrhythmias and conduction disorders were detected by means of Holter ECG. Statistical analysis was carried out on a personal computer, using such programs as Excel-7.0 (Microsoft Corp., USA) and Statistica® for Windows 6.0 (StatSoft Inc., License number AXXR712D833214FAN5) through parametric and nonparametric methods.

Results. Cardiac arrhythmias were found in 71 (65 %) patients with arterial hypertension and were characterized by the presence of supraventricular extrasystole in 43 (39 %) patients and paroxysmal atrial fibrillation in 10 (9 %) patients. Ventricular extrasystole and episodes of unstable ventricular tachycardia were diagnosed in 13 (12 %) and 5 (5 %) patients, respectively. In hypertensive patients supraventricular arrhythmias were detected in 2.8 times more likely ($p < 0.01$), and single ventricular premature beats – 6.2 times more likely ($p < 0.01$) than the control group. It was found that in patients with moderate and severe hypertension observed a statistically significant increase in the number of single supraventricular and ventricular premature beats – 21.5 % ($p < 0.05$) and 29.6 % ($p < 0.05$) respectively, compared with the subgroup of mild hypertension.

Conclusions. Patients with arterial hypertension are characterized by a wide range of supraventricular and ventricular arrhythmias, namely extrasystole, atrial fibrillation, ventricular tachycardia.

Ключові слова: гіпертензія, аритмія, екстрасистола, фібриляція передсердь.

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Особливості порушень серцевого ритму та провідності в пацієнтів з артеріальною гіпертензією

А. М. Василенко

Мета роботи – вивчити особливості порушень серцевого ритму та провідності у хворих з артеріальною гіпертензією.

Матеріали та методи. Під нашим наглядом перебували 110 хворих на гіпертонічну хворобу II стадії з 1–3 ступенем артеріальної гіпертензії віком від 38 до 72 років (середній вік – 50,63±1,34 року). За гендерною ознакою пацієнти розподілились так: 61 жінка (55 %) і 49 хворих чоловіки (45 %). Контрольну групу становили 30 здорових осіб, з них 13 були чоловічої та 17 жіночої статі (43 та 57 % відповідно); середній вік – 49,75±1,83 року. Для виключення ішемічної хвороби серця всім пацієнтам виконували тести з фізичним навантаженням (велоергометрія, тредміл). Порушення серцевого ритму та провідності виявлялись шляхом холтерівського моніторування ЕКГ. Статистичний аналіз здійснили на персональному комп'ютері за допомогою таких програм, як Excel-7.0 (Microsoft Corp., США) та Statistica® для Windows 6.0 (StatSoft Inc., ліцензія № AXXR712D833214FAN5) параметричними та непараметричними методами.

Результати. Порушення серцевого ритму виявлені в 71 (65 %) хворого з артеріальною гіпертензією та характеризувались наявністю суправентрикулярної екстрасистолії у 43 (39 %) хворих і пароксизмальної фібриляції передсердь у 10 (9 %) пацієнтів. Шлуночкова екстрасистолія та епізоди нестабільної шлуночкової тахікардії діагностувалися у 13 (12 %) і 5 (5 %) хворих відповідно. У пацієнтів з артеріальною гіпертензією надшлуночкові аритмії та поодинокі вентрикулярні екстрасистоли спостерігалися у 2,8 раза ($p < 0,01$) та в 6,2 раза ($p < 0,01$) відповідно частіше порівняно з контрольною групою. Встановлено, що в пацієнтів із помірною та тяжкою артеріальною гіпертензією спостерігалося статистично значуще збільшення кількості одиничних як надшлуночкових, так і шлуночкових передчасних скорочень – на 21,5 % ($p < 0,05$) та 29,6 % ($p < 0,05$) відповідно порівняно з підгрупою з артеріальною гіпертензією I ступеня.

Висновки. Пацієнти з артеріальною гіпертензією характеризуються широким спектром надшлуночкових і шлуночкових аритмій, а саме: екстрасистолією, фібриляцією передсердь, шлуночковою тахікардією.

Ключевые слова: гипертензия, аритмия, экстрасистола, фибрилляция предсердий.

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Особенности нарушений сердечного ритма и проводимости у пациентов с артериальной гипертензией

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Цель работы – изучить особенности нарушений сердечного ритма и проводимости у больных с артериальной гипертензией.

Материалы и методы. Под нашим наблюдением находились 110 больных с гипертонической болезнью II стадии, 1–3 степенью артериальной гипертензии, в возрасте от 38 до 72 лет (средний возраст – 50,63±1,34 года). По гендерному признаку пациенты распределились следующим образом: 61 женщина (55 %) и 49 больных мужского пола (45 %). Контрольную группу составили 30 здоровых человек, из которых 13 были мужского и 17 женского пола (43 % и 57 %

соответственно); средний возраст – 49,75 ± 1,83 года. Для исключения ишемической болезни сердца всем пациентам проводились тесты с физической нагрузкой (велоэргометрия, тредмил). Нарушения сердечного ритма и проводимости выявлялись путём проведения холтеровского мониторирования ЭКГ. Статистический анализ проводился на персональном компьютере с помощью таких программ, как Excel-7.0 (Microsoft Corp., США) и Statistica® для Windows 6.0 (StatSoft Inc., лицензия № AXXR712D833214FAN5) параметрическими и непараметрическими методами.

Результаты. Нарушения сердечного ритма были обнаружены у 71 (65 %) больного с артериальной гипертензией и характеризовались наличием суправентрикулярной экстрасистолии у 43 (39 %) больных и пароксизмальной фибрилляции предсердий у 10 (9 %) пациентов. Желудочковая экстрасистолия и эпизоды нестабильной желудочковой тахикардии диагностировались у 13 (12 %) и 5 (5 %) больных соответственно. У пациентов с артериальной гипертензией наджелудочковые аритмии и единичные вентрикулярные преждевременные сокращения наблюдались в 2,8 ($p < 0,01$) и в 6,2 раза ($p < 0,01$) соответственно чаще по сравнению с контрольной группой. Было установлено, что у пациентов с умеренной и тяжёлой артериальной гипертензией наблюдалось статистически значимое увеличение числа как единичных наджелудочковых, так и изолированных желудочковых экстрасистол – на 21,5 % ($p < 0,05$) и 29,6 % ($p < 0,05$) соответственно по сравнению с подгруппой больных с артериальной гипертензией I степени.

Выводы. Пациенты с артериальной гипертензией характеризуются широким спектром наджелудочковых и желудочковых аритмий, а именно: экстрасистолией, фибрилляцией предсердий, желудочковой тахикардией.

Among cardiovascular diseases the rate of prevalence of all forms of arterial hypertension (AH) in adults in Ukraine is almost 56 % [1]. According to official statistics of the Ministry of Health of Ukraine the number of registered cases is more than 12.5 million, representing 32.2 % of the adult population. Hypertension is regarded as a leading risk factor for cardiac and cerebrovascular disease that significantly affects the after-effects and results in the death rate of 88 % from cardiovascular diseases [2].

Activation of neurohumoral pressure systems and left ventricle remodeling can lead to the development of a wide range of cardiac arrhythmias, and even to sudden arrhythmogenic death [3]. Improved technology in the study of bioelectric activity of the myocardium allows to record manifestations of electrical in homogeneity of the myocardium as predictors of clinically manifested arrhythmias, even in the absence of clinical symptoms. Hypertension induced cardiac remodeling plays a primary role in the development of electric in homogeneity of the myocardium and is clinically manifested in a wide range of supraventricular and ventricular arrhythmias, namely extrasystole, atrial fibrillation (AF), ventricular tachycardia and sudden arrhythmogenic death etc. [4].

In the mechanism of development of supraventricular arrhythmias in AH an important role is particularly played by the presence of myocardial feedback that leads to a change in electrical processes to mechanical stimuli. Mechanical factors that modulate cardiac electrical activity are myocardial stretch and/or change of contractile capacity of the myocardium caused by increased pressure in the left atrium and left ventricle. Cell sensitivity to stretch increases proportionally to the degree of hypertrophy, reaching its maximum values in ventricular hypertrophy. It is considered as proved that any mechanical cardiac changes, such as, by instance, increased intracardiac pressure, result in cardiac electrical activity modulation. This effect is realized at the cellular level and implies that cardiac muscle stretch leads to initial rapid repolarization of the action potential, emergence of postdepolarization that grows into the extra action potential and induces occurrence of arrhythmias [5].

Extrasystole or atrial tachycardia, or atrial trepidation, are manifestations of atrial electrical in homogeneity, as myocardial pathological condition characterized by a change in its electrophysiological properties and the formation of arrhythmogenic substrate [6]. Numerous studies involving both animals and humans have shown comparable results concerning structural and electrical remodeling of the atrium in hypertension. There were unchanged, increased or reduced to normal dispersion effective refractory periods [7] found in the atria of patients with AH. Other electrical changes in the atria associated with hypertension include conduction with high heterogeneity [8], increased electrogram fractionation [9] and increased dominant frequency. Thus, in a mice model of salt-induced AH, conduction velocity remained unchanged due to hypertensive remodeling [10].

There have been distinguished several main stages in the formation of myocardial electrical instability of left atrium: 1) rapid electrophysiological remodeling that occurs within seconds or minutes against the background of cardiac arrhythmias (extrasystole, paroxysmal supraventricular tachycardia); 2) slow electrical remodeling, which develops during the days or weeks and is characterized by a shift in bioelectric constants of cardiomyocytes. Electrical remodeling contributes to the development and maintenance of cardiac arrhythmias [11].

At the structural level AH led to increased atrial fibrosis and myocytes hypertrophy, which can explain the electrical changes as delayed or high conduction in homogeneities, electrogram fractionation. Refractory atrial variability can be explained by differences in the study models and methods of measurement (*in-vivo* versus *in-vitro),* but the results of observations consisting in increased atrial fibrosis and further changes of its conduction were universal [12].

At present AH is regarded as decisive, independent, potentially reversible risk factor for AF, as confirmed in several large clinical trials: STOP-2, CAPPP, LIFE [13]. Framingham study demonstrated that increased systolic and pulse blood pressure are associated with the development of AF [14].

At present it is admitted that concomitant risk factors determine the development and nature of progression of AF in hypertension. In particular, it is proved that the aging and AH lead to increased thromboembolic events in patients with AF, although pathophysiologic impact or interaction of each factor need further study.

Thus, AH induced cardiac remodeling, consisting of left ventricular hypertrophy and left ventricular diastolic dysfunction, left ventricular enlargement and hyperfunction, plays a pivotal role in the development of electric in homogeneity of the myocardium, clinically manifested through supraventricular and ventricular arrhythmias. High frequency and gradation of ventricular extrasystole, combined with the presence of hypertrophy, are major predictors of death in hypertension. Regression of left ventricular hypertrophy under the influence

of a controlled prolonged antihypertensive treatment is accompanied by a decrease in atrial and ventricular ectopy.

Today there is a lack of evidence from international randomized multicentre research study of cardiac rhythm disorders and conduction disturbances in patients with AH.

Objective: to study features of cardiac rhythm disorders and conduction disturbances in patients with arterial hypertension.

Methods of the study

Under our observation there were 110 patients with first-third degree hypertension stage II (established according to classification by International Society of Hypertension, European Society of Cardiology and European Society of Hypertension), aged 38 to 72 years (mean age – 50.63 ± 1.34 years) were included. The gender distribution of patients was as follows: 61 female (55 %) and 49 male patients (45 %). The control group comprised 30 healthy individuals, of whom 13 were male and 17 female (43 % and 57 % respectively) and whose mean age was 49.75 ± 1.83 years.

Inclusion criteria were the presence of stage 2 hypertension, age over 18 years, voluntary written consent for participation in this study. Criteria of exclusion were as follows: secondary arterial hypertension, acute cerebrovascular accidents and syncope during 12 months prior to randomization, coronary heart disease, artificial pacemaker, atrial fibrillation, sinuauricular or atrioventricular block II–III degree, congestive heart failure (III, IV FC by NYHA), cardiomyopathy, congenital and acquired heart disease, peptic ulcer of stomach and duodenum, diabetes mellitus, hypothyroidism and other endocrine diseases, acute stage of chronic inflammatory diseases, cancer.

Analyzing the history of hypertension duration, it should be noted that the number of patients with disease duration of more than 10 years was 67 examinees (61 %) and less than 10 years – 43 patients (39 %). Analysis of the data demonstrated that among the patients with AH grade 1 was observed in 44 patients (40 %), grade 2 was registered in 48 examinees (44 %) and grade 3 – only in 18 patients (16 %).

In all patients tests with physical exercise (bicycle ergometry, tredmill) were performed in order to exclude coronary artery disease.

Cardiac arrhythmias and conduction disorders were detected by means of Holter ECG. Patients followed the usual daily regimen. The duration of monitoring was 24 hours. Throughout the study patient kept so-called patient diary to compare the registered ECG records and patient's actions at this point, and changes to the way the patient feels.

Statistical analysis was carried out on a personal computer, using such programs as Excel-7.0 (Microsoft Corp., USA) and Statistica® for Windows 6.0 (StatSoft Inc., License number AXXR712D833214FAN5) through parametric and nonparametric methods. Data are presented as mean and standard deviation (SD) on condition of the normal distribution. Statistically significant differences between the studied indicators were accepted by significance value p that was not exceeding 0.05.

Results and discussion

According to V. I. Bobrov et al. 2009 about 200 supraventricular and 200 ventricular extrasystoles per day are considered a statistical norm of premature cardiac contractions during the daily ECG monitoring [15].

Cardiac arrhythmias was found in 71 (65 %) patients with AH and characterized by the presence of supraventricular extrasystole in 43 (39 %) patients and paroxysmal atrial fibrillation in 10 (9 %) patients. Ventricular extrasystole and episodes of unstable ventricular tachycardia were diagnosed in 13 (12 %) and 5 (5 %) patients, respectively. As for the rest of cases the mean number of supraventricular and ventricular extrasystoles was below the statistical norm.

The number of supraventricular and ventricular extrasystole in controls was characterized by clinically insignificant values of 11 (37 %) and 8 (27 %) cases respectively. There were no found episodes of unstable ventricular tachycardia, atrial fibrillation and conduction disturbances in control group.

Thus, 10 (9 %) patients with AH showed 1 paroxysm of AF each. The disease duration distribution of patients with this arrhythmia was as follows: 6 patients were with duration of AH more than 10 years, 4 patients – less than 10 years. In addition mild hypertension was observed in 2 patients, moderate hypertension was diagnosed in 3 patients, III degree hypertension – in the rest of cases.

Increased atrial fibrosis as a universal morphological manifestation is probably the final phase of restructure, which affects the stability of AF. Several pathophysiological signaling pathways are involved in a variety of structural heart disease and cause the manifestation of hypertrophy and fibrosis. Recent preclinical studies focused on the role of inflammation in hypertensive atrial remodeling, which had not previously been subject to detailed review. A large animal "one-kidney, one-clip" hypertensive model demonstrated an increased infiltration of inflammatory cells on condition of short-term hypertension and its statistically significant correlation with the atrial conductivity disorders, possible development of AF. Kume et al. 2011 confirmed the involvement of pro-fibrotic inflammatory mechanisms on the example of pressure overload models in small animals [16]. These data are confirmed by clinical studies that detected an association between the high level of C-reactive protein and increased risk of arrhythmias aggravated by AF in hypertension. Besides, they confirm the involvement of CD-68-positive macrophages found in atrial endocardium to active inflammation and immune response. These macrophages probably trigger atrial fibrosis by generating reactive oxygen species, release of cytokines, growth factors, pro-fibrotic enzymes [17].

In group patients with AH among conduction disorders 6 examinees had atrioventricular block stage I. However, 4 patients with this type of heart block were with disease duration of more than 10 years and hypertension II–III degree; 2 of examined patients were with disease duration of less than 10 years and with mild hypertension.

The literature lacks data on the prevalence of conduction disorders in patients with AH. So, Uhm J.S. in his work showed that among 3816 patients with hypertension the number of patients with atrioventricular block stage 1 was 14.3 %. It was demonstrated that atrioventricular block stage 1 is an independent factor in the future development of AF and left ventricle dysfunction in these patients [18]. Iskenderov B.G. et al. studied the frequency and nature of heart block in patients with essential hypertension with different clinical and pathogenetic variants of the disease.

The authors draw the conclusion that in the general group of patients conduction disorders were observed in 55.3 % of cases. Intraventricular conduction disorders were more typical for the hyperhydration variant of essential hypertension, atrioventricular block on various stages – for hyperreninemic. Calcium-dependent variant of the disease was characterized by the cardiac conduction disorders mentioned above [19].

Quantitative analysis of the structure of cardiac arrhythmias (*Table 1*) was conducted only in patients with AH and clinically significant arrhythmias (61 of 110). As a comparison, the control group data, where a clinically significant arrhythmia was not observed.

Thus, the data analysis demonstrated that in patients with essential hypertension, unlike the controls, both supraventricular and ventricular cardiac arrhythmias with clinical significance are observed and amounted to 6 % and 10 % respectively. In hypertensive patients supraventricular arrhythmias were detected in 2.8 times more likely ($p < 0.01$), and single ventricular premature beats – 6.2 times more likely ($p < 0.01$) than the control group.

Regarding the correlation between the presence of supraventricular and ventricular arrhythmias and hypertension there is no consensus found. Thus, the study by Conen D. et al. demonstrated no statistically significant connection between the frequency of supraventricular extrasystole and hypertension [20]. Ofoma U. et al. found that ventricular and supraventricular arrhythmias occurred in 4.9 % and 5.5 % of patients respectively. In addition, significant association between the mean number of ventricular extrasystole and hypertension was established ($p < 0.05$) [21]. Published data indicate the occurrence of ventricular arrhythmias in 15 % of patients with hypertension [22] that does not contradict the results.

It is known that the disease contributes to myocardial electric heterogeneity, which, in turn, is one of the main risk factors of ventricular extrasystole. Among the potentially fatal complications of hypertension paroxysmal ventricular tachycardia and sudden arrhythmic death have been confirmed in recent years and verified in 16.2 % and 4.2 % of cases respectively [23].

Quantitative analysis of the structure of cardiac arrhythmias depending on the degree of hypertension (*Table 2*) also was conducted only in patients with AH and clinically significant arrhythmias (61 of 110). As a comparison, the control group data, where a clinically significant arrhythmia was not observed. Thus, it was found that in patients with moderate and severe hypertension observed a statistically significant increase in the number of single supraventricular and ventricular premature beats – 21.5 % ($p < 0.05$) and 29.6 % ($p < 0.05$) respectively, compared with the subgroup of mild hypertension. However, in the analyzed subgroups did not reveal significant differences in the number of registered paired and polymorphic ventricular premature beats.

Table 1. Quantitative characteristics of cardiac arrhythmias

The type of arrhythmias	Controls	Patients with arterial hypertension (n=61)
Supraventricular arrhythmias	114.92±14.3	325.26±18.9*
Single ventricular extrasystole	40.84±9.7	249.89±17.7*
Polymorphic ventricular extrasystole	-	37.50±11.3
Pair ventricular extrasystole	-	19.53±6.6
The episodes of ventricular tachycardia	-	3.14±1.2

*: Significant differences from the controls ($p < 0.01$).

Quantitative analysis of the structure of cardiac arrhythmias depending on the duration of hypertension (*Table 3*) also was conducted only in patients with AH and clinically significant arrhythmias (61 of 110). As a comparison, the control group data, where a clinically significant arrhythmia was not observed.

Thus, in subgroup of patients with AH duration more than 10 years was detected a statistically significant increase in the number of single supraventricular and ventricular premature beats –23.7 % ($p < 0.05$) and 26.1 % ($p < 0.05$) respectively, also a statistically significant increased frequency of pair ventricular extrasystole (in 2.9 times) compared with the subgroup of patients with AH duration less than 10 years. However, did not reveal significant differences in the number of polymorphic ventricular premature beats between subgroups of hypertensive patients.

Conclusions

1. Patients with arterial hypertension are characterized by a wide range of supraventricular and ventricular arrhythmias, namely extrasystole, atrial fibrillation, ventricular tachycardia.

2. In hypertensive patients supraventricular arrhythmias were detected in 2.8 times more likely ($p < 0.01$), and single ventricular premature beats – 6.2 times more likely ($p < 0.01$) than in the control group.

Table 2. Quantification of cardiac arrhythmias in patients with essential hypertension depending on severity of the disease

The type of arrhythmias	Controls	Patients with I degree AH (n=26)	Patients with II-III degree AH (n=35)
Supraventricular arrhythmias	114.92±14.3	268.35±16.4*	325.96±21.0*#
Single ventricular extrasystole	40.84 ± 9.7	223.25±14.2*	289.47±19.3*#
Polymorphic ventricular extrasystole	–	32.71±15.9	50.85±14.8
Pair ventricular extrasystole	–	14.87±6.1	21.08±7.1

*: Significant differences from the controls ($p < 0.01$); #: Significant differences from the subgroup of patients with mild hypertension ($p < 0.05$).

Table 3. Quantification of cardiac arrhythmias in patients with essential hypertension depending on duration of the disease

The type of arrhythmias	Controls	Patients with AH duration less than 10 years (n=23)	Patients with AH duration more than 10 years (n=38)
Supraventricular arrhythmias	114.92±14.3	254.88±17.2*	314.43±19.9*#
Single ventricular extrasystole	40.84±9.7	218.93±12.7*	275.06±16.1*#
Polymorphic ventricular extrasystole	–	26.34±11.4	38.59±13.7
Pair ventricular extrasystole	–	9.19±4.8	27.12±6.6#

*: Significant differences from the controls ($p < 0.01$); #: Significant differences from the subgroup of patients with less than 10 years hypertension ($p < 0.05$).

3. The duration and severity of hypertension significantly increase the detection rate of supraventricular, single and paired ventricular premature beats.

The prospect of further scientific research in this direction is to study the best ways of pharmacological therapy of cardiac arrhythmias in patients with hypertension.

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