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among patients with arterial
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Ereignisse bei Patienten mit
arterieller Hypertonie und
Extrasystolen**

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Cardiovascular event risk factors among patients with arterial hypertension and extrasystole

N. Didyk¹, O. Lysunets², K. Postovitenko³, I. Kurylenko⁴, V. Valentiev⁵

Abstract: The prevalence of hypertension and associated cardiac arrhythmias, including extrasystoles, leads to a more detailed study and analysis of the impact of known risk factors for cardiovascular events on this pathology to develop further preventive measures for complications and mortality. A total of 120 patients with stage 2 hypertension and extrasystole and 30 patients with stage 2 hypertension without signs of extrasystole were examined. 54 patients diagnosed with stage 2 hypertension and supraventricular extrasystole formed the first, 40 the second, and 26 the third clinical study group. The results of the study showed the predominance of stage 2 hypertension of the II–III grade and extrasystole among female patients. It was revealed that the influence of the risk factor for the development of cardiovascular events, the age factor, in patients of the third clinical group is 92.3% and the total risk indicator is significantly higher. High pulse pressure as a risk factor was registered in 13 patients (43.3%) of the control group and in 22 patients (40.7%) of the first clinical study group, which suggests different mechanisms of arrhythmogenesis of supraventricular and ventricular extrasystoles in patients with stage 2 hypertension, as the results of 21 patients (52.5%) of the second and 19 patients (73.1%) of the third clinical study group had no statistical significance. The age factor and the factor of registering a high level of pulse blood pressure should be considered as a component of the pathogenesis of topical variants of extrasystole in combination with stage

2 hypertension, considering their influence when developing prophylactic recommendations for the prevention of stage 2 hypertension and extrasystole in people of different ages.

Key words: arrhythmia, pulse blood pressure, gender factor, mortality of the population, prevention.

Kurzfassung: Risikofaktoren für kardiovaskuläre Ereignisse bei Patienten mit arterieller Hypertonie und Extrasystolen. Die Prävalenz von Bluthochdruck und damit verbundenen Herzrhythmusstörungen, einschließlich Extrasystolen, führt zu einer detaillierteren Untersuchung und Analyse der Auswirkungen bekannter Risikofaktoren für kardiovaskuläre Ereignisse auf diese Pathologie, um weitere Präventionsmaßnahmen für Komplikationen und Mortalität zu entwickeln.

Insgesamt wurden 120 Patienten mit Hypertonie im Stadium 2 und Extrasystolen und 30 Patienten mit Hypertonie im Stadium 2 ohne Zeichen einer Extrasystole untersucht. 54 Patienten mit diagnostizierter Hypertonie im Stadium 2 und supraventrikulärer Extrasystole bildeten die erste, 40 (mit ventrikulärer Extrasystole) die zweite und 26 (mit supraventrikulären und ventrikulären Extrasystolen) die dritte klinische Studiengruppe. Alle Patienten wurden einer allgemeinen klinischen, elektrokardiographischen und echokardiographischen Untersuchung, einem 24h-EKG und einer täglichen Überwachung des Blutdrucks unterzogen.

Die Ergebnisse der Studie zeigten das Vorherrschen von Bluthochdruck Grad II–III und Extrasystolen im Stadium 2 bei weiblichen Patienten. Es zeigte sich, dass der Einfluss des Risikofaktors für die Entstehung kardiovaskulärer Ereignisse, des Altersfaktors, bei Patienten der dritten klinischen Gruppe 92,3 % beträgt und der Gesamtrisikoinikator signifikant höher ist (durchschnittlicher Score 4,1 vs. 5,0). Hoher Pulsdruck als Risikofaktor wurde bei 13 Patienten (43,3 %) der Kontrollgruppe und bei 22 Patienten (40,7 %) der ersten klinischen Studiengruppe registriert, was auf unterschiedliche Mechanismen der Arrhythmogenese von supraventrikulären und ventrikulären Extrasystolen bei Patienten mit Hypertonie-Stadium 2 hindeutet, da die Ergebnisse von 21 Patienten (52,5 %) der zweiten und 19 Patienten (73,1 %) der dritten klinischen Studiengruppe keine statistische Signifikanz hatten.

Der Altersfaktor und der Faktor der Registrierung eines hohen Puls-Blutdrucks sollten als eine Komponente der Pathogenese von topischen Varianten der Extrasystole in Kombination mit Hypertonie im Stadium 2 berücksichtigt werden, um ihren Einfluss bei der Entwicklung von prophylaktischen Empfehlungen zur Prävention von Hypertonie im Stadium 2 und Extrasystole bei Menschen unterschiedlichen Alters zu berücksichtigen. **Z Gefäßmed 2022; 19 (4): 11–20.**

Schlüsselwörter: Arrhythmie, Puls-Blutdruck, Geschlecht, Sterblichkeit der Bevölkerung, Prävention

Introduction

Today, the prevention of complications of hypertension and cardiac arrhythmias, particularly extrasystoles, continues to be a topical and understudied issue both academically and clinically. After all, arterial hypertension and cardiac rhythm disturbances continue to occupy leading positions in the structure of overall mortality and disability of the population of Europe and America. Hypertension is a clinical and social problem. The association between the level of systolic blood pressure and its complications, in particular, ischemic stroke in hypertensive patients, has been demonstrated in the elderly [1]. Thus, regarding the detection of arterial hypertension as a predictor of disability in the population, the age-standardised indicator of disability-adjusted life years (DALYs) as of 2017 was high

blood pressure in four global geographical regions: Central Europe, Eastern Europe, and Central Asia; North Africa and the Middle East; South Asia; South-East Asia, East Asia, and Oceania [2].

As of 2019, hypertension and cardiac rhythm disorders are leading causes of death in both Ukraine and the world. According to the results of „Global Burden of Disease (GBD)“, which determines the severity of health problems among the population in 195 countries, including Ukraine, which is comparative and covers 286 causes of death, 369 diseases and injuries and 87 risk factors in 204 countries and territories, since 1990 (the study is a systematic scientific effort to quantify health loss from diseases, injuries and risks by age, gender in time dynamics and is coordinated by the Institute for Health Metrics and Evaluation (IHME), the global rise in cardiovascular disease cases from 271 million in 1990 to 523 million in 2019 with a corresponding increase in deaths from 12.1 million in 1990 to 18.6 million in 2019 is determined (Roth et al., 2020). In the global community, particularly in India, arterial hypertension is more commonly diagnosed in males over 30 years of age who are overweight and have a high material standard of living [3].

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In Ukraine, the most common causes of mortality are diseases of the digestive system with 64.3% of cases, neoplasms with 14.1%, digestive diseases with 4.3%, neurological disorders with 3.1% and self-harm and interpersonal violence with 2.7%. And the mortality rate of the population of Ukraine, which was caused by cardiovascular diseases, increased by 8%: from 350,605 deaths in 1990, which was 56.5%, to 449,376 people in 2019, which was 64.3%. From a gender perspective, the specifics of the mortality due to diseases of the cardiovascular system in men and women is that for both the first leading three positions are occupied by mortality associated with coronary heart disease, cerebrovascular pathology, and cardiomyopathy with myocarditis, while the fourth leading cause of mortality in men is a peripheral vascular disease and in women – cardiac rhythm disorders, in particular atrial fibrillation, which ranks sixth among male mortality.

In turn, the pattern of mortality due to hypertension ranks eighth among men and seventh among women, ranking ahead of peripheral vascular disease and other cardiovascular diseases [4]. Statistical indicators of detection of arterial hypertension as a factor of cardiovascular mortality in Ukraine correlate with world indicators [5]. Given the challenges of today, published data on the prevalence of hypertension among patients with COVID-19 show the presence of hypertension in 22%. And chronic diseases of the cardiovascular system were recognised as the dominant risk factors influencing the choice of therapeutic treatment tactics [6]. The increased mortality risk with existing cardiovascular co-morbidities, such as hypertension, obesity, and age, is actively discussed in the world community. Gender occupies a key position in the impact of risk factors on the body, explaining the differentiated approach in the diagnosis of risk of mortality due to cardiovascular events in patients with SARS-CoV-2 [7].

The proportion of cardiovascular disease has continued to rise for a decade in countries with a low gross domestic product, but in some regions, where it has been declining in high-income countries, we have seen the age-standardised rate of cardiovascular disease begin to rise as well. Today, there is an urgent need to develop and implement existing effective strategies for detecting and preventing cardiovascular diseases, followed by a reduction of at least 30% in premature mortality from non-communicable diseases in the world [8]. The issues of lifestyle modification, the management of patients with arterial hypertension, has been presented by a number of scientists in the world community [9–11]. Based on the above, timely diagnosis and preventive measures aimed at reducing risk factors among the population that lead to premature mortality of the latter are key in prolonging the life expectancy indicator and predictors of improving the quality of life of the population.

The impact on reducing cardiovascular disease in Ukraine can be achieved by addressing the major risk factors in the population that lead to premature death. The main risk factors for developing complications of cardiovascular pathology include arterial hypertension, unbalanced diet, hypercholesterolemia, overweight, hyperglycaemia, smoking, low physical activity, factors of air pollution, renal dysfunction, and alcohol consumption [12–14]. Hyperglycaemia with subsequent development of diabetes mellitus is a significant risk factor for cardio-

vascular complications and a factor in determining the quality of life of the population [15]. And today, the results of world studies demonstrate common pathogenetic factors and trends in the development of hyperglycaemia, metabolic syndrome, obesity, diabetes mellitus, arterial hypertension, and complications of these pathological processes [16]. To date, a number of studies, including on animals, have been aimed at developing preventive measures related to overweight [17]. Studies with intermittent animal fasting have shown improvements in cardiometabolic factors, including improved glucose metabolism, reduced inflammation, and lower blood pressure. However, there is still a lack of prospective human trials to confirm the results of animal studies and observational data.

Our study remains relevant to the questions it raises about the influence and role of age factor in the development of cardiovascular risk in patients with hypertension and extrasystoles. There are studies assessing age differences in risk factors for heart failure in the general population that show a clear connection in the occurrence and progression of heart failure with preserved ejection fraction in young people compared to the elderly. Concomitant arterial hypertension, a history of hyperglycaemia with smoking and a history of myocardial infarction – increased the risk of heart failure in young people, compared with participants in the older age category. Arterial hypertension was associated with a threefold increased risk of future heart failure [18].

Considering the epidemiological factor, the role of risk factors for the development of cardiovascular events, our study, which is aimed at determining the diagnostic role, identification and presence of risk factors for the development of cardiovascular complications among people with hypertension and extrasystole, is relevant and appropriate not only from an academic, but also from a practical point of view, and will make it possible to determine a set of measures aimed at improving the quality of life of the population of Ukraine.

The purpose of the study was to investigate the risk factors for cardiovascular events among patients with stage 2 hypertension and symptomatic extrasystole.

■ Materials and Methods

To achieve the goal of an investigation an open-label trial was carried out on the basis of the Department of Internal Medicine No. 3 of the Vinnytsia National Pirogov Memorial Medical University within the research work of the department of “Structural-functional, autonomic, membrane processes in coronary heart disease, hypertension, arrhythmias and other diseases heart and methods of improving the effectiveness and safety of pharmacological correctors” No. of state registration 0198U005613, code 01/11. The study was conducted in accordance with the principles of the Helsinki Declaration. The study protocol was adopted by the Local Ethics Committee of the institution. The patient’s informed consent was obtained for the study. The authors declare no conflict of interest.

Thus, 150 people with arterial hypertension were examined. The specifics of the study were that patients were selected as they were admitted for inpatient treatment and examination in

the Polyclinic Department of the Cardiology Day Hospital No. 3 of Vinnytsia City Clinical Hospital No. 1. All patients, in addition to collecting anamnestic data, underwent the following laboratory and instrumental examinations with a determination of: general blood analysis, general urine analysis, blood glucose, lipid profile, in particular the determination of total cholesterol, high-density lipoprotein cholesterol, triglycerides, atherogenicity index electrocardiography in 12 standard leads, Holter electrocardiography and daily BP monitoring, sonography with a determination of structural features of carotid arteries, echocardiography in M-, B- and D-modes, evaluation of the vasomotor function of the brachial artery. For a more detailed characterisation of the patients' clinical condition, a Visual Analogue Well-being Rating Scale and Physical Activity Rating Scale were used, which reflected the patients' self-assessment of their subjective status.

Patients independently assessed their level of well-being and the level of their normal physical activity in the form of a mark per 100 mm segment (visual analogue scale). The length of the marked segment was measured in mm (the maximum value that the patient could mark was 100 mm, the minimum – 0 mm). Contraindications for the inclusion of patients in the study were the lack of informed consent of the patient to participate in the clinical trial, the presence of hypertension in stages 1 and 3, heart failure in stages 2A-3 according to the classification of N.D. Strazhesko and V.H. Vasilenko and stages III-IV according to the classification of the New York Heart Association (NYHA) of 1995, the diagnosis of left ventricular systolic dysfunction (ejection fraction less than 45%), tachycardia, asymptomatic extrasystole and an extrasystole that, according to the current recommendations of the European Society of Cardiology (ESC), does not require continuous antiarrhythmic drug therapy [19], the presence of persistent and permanent forms of atrial fibrillation, premature excitation syndrome and ventricular preexcitations, the presence of significant somatic pathology, in particular, neoplasms, tuberculosis, metabolic disorders, infectious and psychiatric diseases. The main clinical and control groups of the study of patients were formed in accordance with the study design (Tab. 1).

Statistical processing of the obtained data was performed using Statistica 10.0 software packages (StatSoft, Inc., USA, 2011). Quantitative values are represented by the mean and its standard deviation ($x \pm SD$) and in the form of the median and interquartile range (25 and 75 percentiles) are given in the text and tables. Relative values are represented as percentages (%). To determine the probability of the difference between the samples were used criteria χ^2 Pearson, Wilcoxon, Mann-Whitney U-test with statistical significance $p < 0.05$.

Thus, the control group was represented by 30 patients with stage 2 hypertension without diagnosed signs of frequent extrasystole, which would require constant antiarrhythmic medication correction. The age of patients in the control group was between 40 and 74 years, with an average of 55.0 ± 1.7 years (median – 56, interquartile range 48 and 1.7 years). Gender characteristics of patients in the control group were characterized by the presence of 13 men, which was 43.3%, and 17 women, who made up 56.7% of patients in the control group of the study. The ratio of women to men was 1.3:1.

Table 1. Gender and age characteristics of patients with stage 2 hypertension and stage 2 hypertension and extrasystole.

Parameters	Control group (n = 30)	Study group (n = 120)
Gender		
Men, n	13	42
Women, n	17	78
Age, years	55 ± 1.7	59.8 ± 1.0

120 patients with stage 2 hypertension and frequent extrasystoles (more than 30 extrasystoles per study hour), which require continuous antiarrhythmic drug treatment, formed three clinical trial groups. The main criterion for dividing patients into study groups was the presence of a topical variant of extrasystole: supraventricular, ventricular, or combined (supraventricular and ventricular). The age of patients was in the range of 27–81 years, the average was 59 ± 1.0 years (median – 61, interquartile range – 56 and 67). The gender characteristics of patients in the three clinical study groups were characterized by the presence of 78 females (65.0%) and 42 males (35.0%). The ratio of women to men was 1.9:1.

According to topical extrasystole variants, all 120 patients were divided into three clinical groups. Thus, the first clinical group consisted of 54 patients (45.0%) with diagnosed stage 2 hypertension and supraventricular extrasystole. Gender composition of the group: 32 women (59.3%), 22 men (40.7%). The ratio of women to men was 1.5:1. The second clinical group of the study consisted of 40 people with diagnosed stage 2 hypertension and ventricular extrasystole. Among the patients in the second clinical group of the study, there were 27 female patients (76.5%) and 13 male patients (32.5%). The third clinical group of the study was formed by patients with stage 2 hypertension and combined (supraventricular and gastric) extrasystole consisting of 26 people. Among them were 19 women (73%) and 7 men (27.0%). The ratio of women to men reached 2.7:1.

Considering the specifics of patient selection (study groups were formed according to patients' admission to inpatient examination and treatment in the cardiology department), the age distribution data (Fig. 1) show certain statistical differences in the formed study groups.

The above study design demonstrated the absence of gender and age randomization between different patient groups. Namely, female patients predominated in all groups, with a more significant female predominance in the group of patients with stage 2 hypertension combined and ventricular extrasystole (second clinical trial group) and stage 2 hypertension with combined (supraventricular and ventricular) extrasystole (third clinical group). In turn, young and middle-aged patients formed the control group and the first clinical group of the study.

■ Results

The obtained data of visual analogue scales showed that the self-assessment of well-being on the visual analogue scale was in the range of 55.7–49.8, and the level of physical activity was 51.0–54.6 mm, respectively (Fig. 2). A small range of average

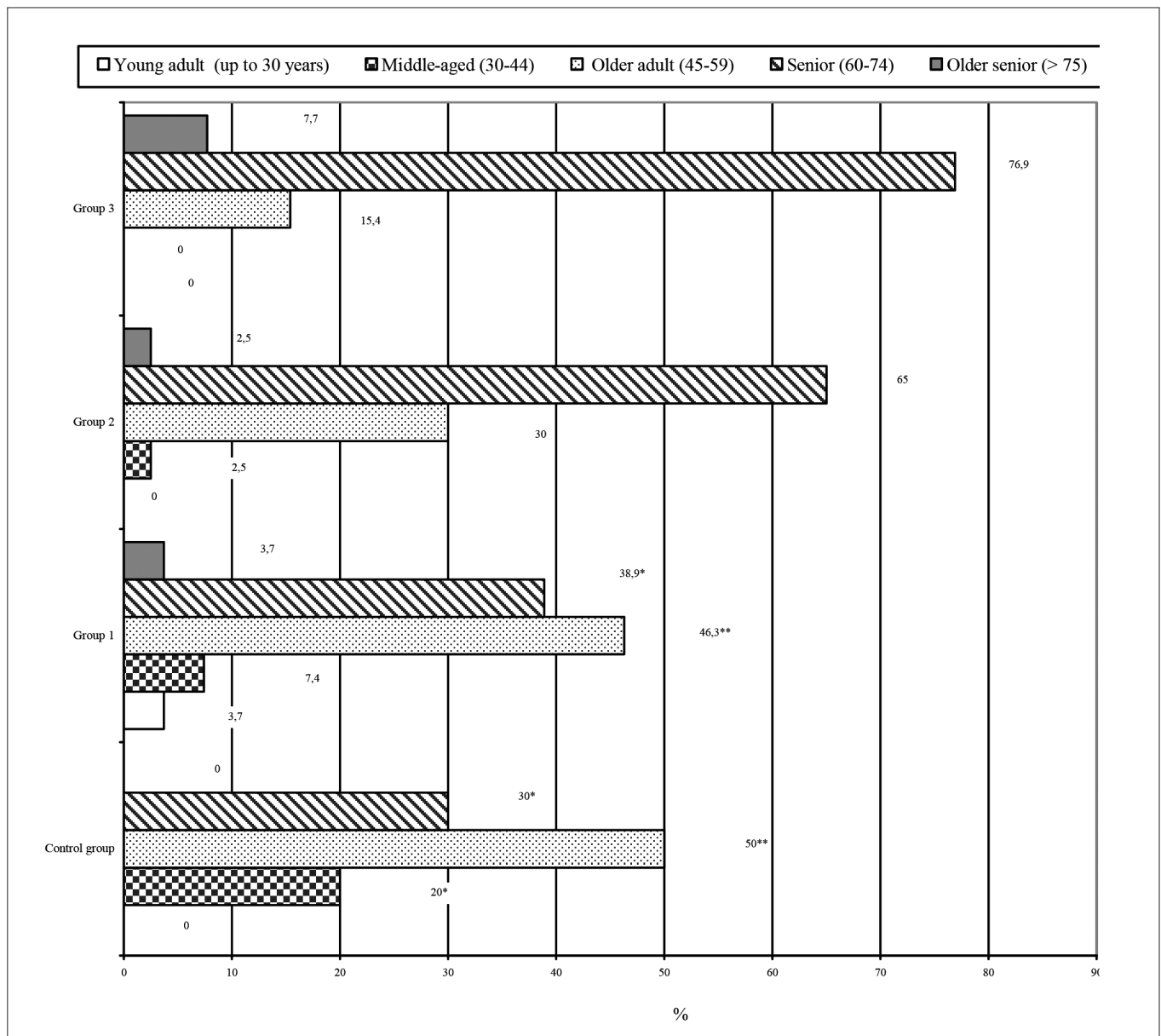


Figure 1. Age distribution in the control and clinical groups.

Note: The reliability of the percentage difference between groups is calculated using the χ^2 criterion; * indicates reliability with the second and third clinical groups, ** with the third clinical group ($p < 0.05$).

values in the clinical groups of the study showed a comparable subjective state and physical activity in different groups of patients. Significant differences were diagnosed only in the mean well-being score in the control group compared to the third clinical group (55.7 ± 1.5 vs 49.8 ± 2.3 , $p < 0.05$).

Dividing patients into clinical groups (patients with stage 2 hypertension and extrasystole) – the first clinical group of the main clinical array study and the control group – patients with hypertension without signs of extrasystole, the following results were obtained (Tab. 2). The control group had a history of hypertension duration of 9.9 ± 1.0 years, with an average of 10.5 (interquartile range of 4.0–15.0). The duration of hypertension under 5 years was documented in 11 patients, accounting for 36.7% of patients in the control group. Four people had a history of hypertension of 5–10 years, representing 13.3% of control group patients, and 15 people had a history of hypertension of more than 10 years, representing 50.0% of control group patients.

In the control group, 3 patients were diagnosed with stage 1 hypertension. It was observed in 10.0% of patients in the clinical group. Stage 2 hypertension was registered in 12 people – about 40.0% of patients in the control group. And stage 3 hypertension was recorded in 15 patients (50.0%) in the control group. The following results in the control group patients were obtained by examining the distribution of major cardiovascular event risk factors. So, the 1st, age factor: age of male patients > 55 years and female patients > 65 years (according to ESC data). There were no old senior patients (> 75 years old) in the control group. 6 people (20.0%) were middle-aged (aged 30 to 44 years). Older adults (aged 45 to 59 years) numbered 15 patients (50.0%) in the control group and 9 patients (30.0%) were seniors (aged 60 to 74 years). Thus, the diagnosis and impact of the age factor were recorded in 22 patients of the control group, which was 73.3% of the cases.

The 2nd factor is the level of pulse blood pressure (more than 60 mmHg), diagnosed in 13 patients with stage 2 hypertension,

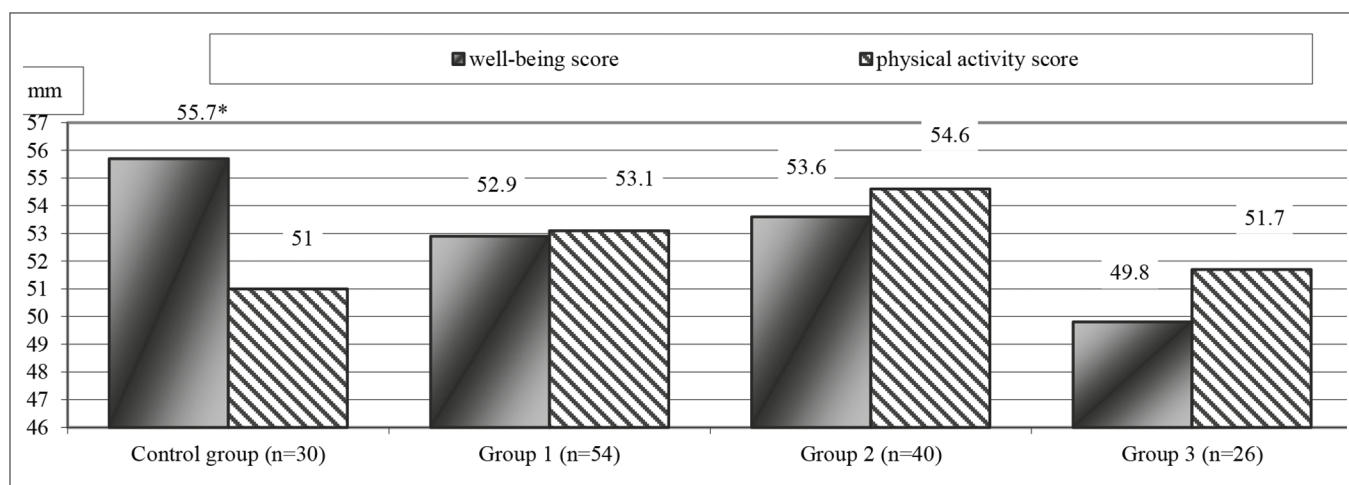


Figure 2. Assessment of well-being and physical activity on a visual analogue scale in the control and clinical groups.

Note: The reliability of the difference in average values between groups is calculated according to the Wilcoxon signed-rank test; * indicates reliability with the third clinical group ($p < 0.05$).

Table 2. Duration of hypertensive history in patients of different clinical study groups.

Duration of hypertension history	Control group (n = 30)	First clinical group (n = 54)	Second clinical group (n = 40)	Third clinical group (n = 26)
Duration of hypertension (years)	9.9 ± 1.0	9.9 ± 0.8	11.6 ± 0.8	10.2 ± 0.9
Duration of hypertension under 5 years	11 (36.7%)*,**	17 (31.5%)**	6 (15.0%)**	0 (0)
Duration of hypertension 5–10 years	4 (13.3%)**	16 (29.6%)**	12 (30.0%)**	16 (61.5%)
Duration of hypertension > 10 years	15 (50.0%)	21 (38.9%)	22 (55.0%)	10 (38.5%)

Note: Absolute values are presented as mean value x and its standard deviation SD the reliability of the percentage difference between groups is calculated using the χ^2 criterion; * indicates reliability with the second, ** reliability with the third clinical group, $p < 0.05$

Table 3. Distribution of patients according to the determination of the total risk of cardiovascular events and the controllability of the course of hypertension in the control and clinical groups of the study.

The total risk of cardiovascular complications	Control group (n = 30)	First clinical group (n = 54)	Second clinical group (n = 40)	Third clinical group (n = 26)
High cardiovascular risk	15 (50.0%)*,**	22 (40.7%)	10 (25.0%)	6 (23.1%)
Very high cardiovascular risk	15 (50.0%)*,**	32 (59.3%)	30 (75.0%)	20 (76.9%)
Uncontrolled hypertension	19 (63.3%)	31 (57.4%)	24 (60.0%)	19 (73.1%)

Note: The reliability of the percentage difference between groups is calculated using the χ^2 criterion, * indicates reliability with the second, ** with the third clinical group, $p < 0.05$.

which is 43.3% of the control group. Third, the factor of limited bad habits, including smoking – was diagnosed in 12 patients of the control group and accounted for 40.0% of patients in the control group. Fourth, a factor of lipid metabolism disorder, namely dyslipidaemia (total cholesterol > 5 mmol/L or low-density lipoprotein cholesterol > 3 mmol/L, or triglycerides > 1.7 mmol/L) was reported in 27 individuals in the control group, representing 90.0% of the group. The 5th is the factor of fasting hyperglycaemia, in particular, fasting heart glucose of 5.6–6.9 mmol/L, was present in 4 patients, which made up 13.3% of the control group. Sixth, the factor of abdominal obesity, namely: waist circumference > 102 cm in men and > 88 cm in women was registered in 27 patients, which was 90.9%.

The 7th, a factor of family history of cardiovascular disease, was recorded in 17 people in the control group, which was 56.7% of patients. The total indicator of risk factors in patients of the

control group was 4.1 ± 0.2 , median 4 (interquartile range 3; 5). The total risk of cardiovascular complications in patients of the clinical group was recorded as a “high” cardiovascular risk in 15 people, which was 50.0% of the examined patients in the control group and a “very high” cardiovascular risk, which was recorded in 15 patients (50.0%) in the control group (Tab. 3). Such a characteristic of the course of nosology hypertension as controllability of blood pressure levels and uncontrolled course of hypertension was diagnosed in 19 patients, who made up 63.3% of the control group.

Considering the results of the study among patients of the first clinical group (patients with stage 2 hypertension and verified supraventricular extrasystole, which, according to modern recommendations of the *European Society of Cardiology*, requires constant drug antiarrhythmic therapy), the following factors were obtained. The first factor is the duration of hypertension in years. It was 9.9 ± 0.8 years, the median was 9.0 (interquartile

range 4.0 and 16.0). In this clinical group, 17 people, who made up 31.5% of patients with stage 2 hypertension and supraventricular extrasystole, had hypertension for under 5 years. In 16 patients (29.6%) of this clinical group, stage 2 hypertension was registered for 5–10 years. And the duration of stage 2 hypertension for more than 10 years was diagnosed in 21 patients, which accounted for 38.9% of people in this clinical group of the study.

Analyzing the results of determining the grade of arterial hypertension in patients with stage 2 hypertension and supraventricular extrasystole, 2 people were diagnosed with the first grade of arterial hypertension, which accounted for 3.7% of patients in the first clinical group of the study. Stage 2 hypertension of the second grade was registered in 24 people, which accounted for 44.4% of patients in this clinical group. And in 51.9% of cases, namely, in 28 patients with stage 2 hypertension and supraventricular extrasystole, hypertension of third grade was registered. Regarding the controllability of the nosology of stage 2 hypertension in the patients of the first clinical group of the study, the course of hypertension was classified as uncontrolled in 31 patients, which was 57.4% of cases.

Considering the diagnosis of the main risk factors for the development of cardiovascular pathology in this first clinical group of the study, the first, age-related factor was registered in 55.6% of cases of the first clinical group and was detected in 30 patients. The age-related characteristics of patients in the 1st clinical group are as follows. Young adult patients (up to 30 years old) in the number of 2 people accounted for 3.7% of the first clinical group of the study. 4 middle-aged adults (30–44 years old) accounted for 7.4% of cases, older adults (45–59 years old) accounted for 25 patients (46.3%). In this clinical group, there were 21 seniors (60–74 years old), which accounted for 38.9% of cases, and 2 old seniors (over 75 years old), which accounted for 3.7% of cases.

The 2nd factor, pulse blood pressure > 60 mmHg, was diagnosed in 22 people, who accounted for 40.7% of patients in this clinical study group. The 3rd factor, smoking, was detected in 44.4% of patients with stage 2 hypertension and supraventricular extrasystole and was diagnosed in 24 people. The 4th factor, the level of dyslipidaemia: the level of total cholesterol > 5 mmol/L or cholesterol of low-density lipoproteins greater than 3 mmol/L, or triglycerides > 1.7 mmol/L was manifested in 49 patients, which made up 90.7% of people in this 1st clinical study group. The 5th factor was fasting hyperglycaemia: fasting glucose of 5.6–6.9 mmol/L was recorded in 17 patients, representing 31.5% of cases in clinical group 1. Sixth, the factor of abdominal obesity, namely: waist circumference > 102 cm in men and > 88 cm in women, was recorded in 43 patients in the 1st clinical group of the study, which was 79.6%. The 7th, a factor of family history of cardiovascular disease, was registered in 29 people, which accounted for 53.7% of cases in this clinical study group. Calculating the total indicator of risk factors in patients of the 1st clinical study group, their score was 4.3 ± 0.2 (median 4, interquartile range 3; 5). The total risk of developing cardiovascular complications was recorded as “high” in 22 people, which accounted for 40.7% of cases. But the cumulative risk of cardiovascular events as “very high” was diagnosed in 32 people, representing 59.3% of cases in the 1st clinical study group.

The findings of the study of the second clinical group, which consisted of patients with stage 2 hypertension and ventricular extrasystole, which according to the current recommendations of the *European Society of Cardiology* requires continuous antiarrhythmic drug treatment, are summarized below. Thus, the duration of stage 2 hypertension in patients in the second clinical group of the study was in the range of 11.6 ± 0.8 years and the median was 14.0 (interquartile range 8.0 and 16.0). The duration of stage 2 hypertension for under 5 years was recorded in 6 people, which accounted for 15% of cases. The duration of stage 2 hypertension with a period of 5–10 years was recorded in 12 people, which accounted for 30.0% of cases in this clinical group, and in 22 people, which was 55.0% of cases, the duration of hypertension was more than 10 years.

As for the grade of arterial hypertension in patients with stage 2 hypertension and ventricular extrasystole, in 5.0% of cases, that is, in 2 patients, the first grade of hypertension was also registered. In 14 people, which accounted for 35.0% of cases, hypertension of the second grade was diagnosed. And 60.0%, that is, 24 people, were diagnosed with arterial hypertension of the third grade.

Characterizing the risk factors for cardiovascular events, the age factor (age > 55 years in men and > 65 years in women) was present in 75.0% of patients with stage 2 hypertension and ventricular extrasystole and was recorded in 30 patients and had the following characteristics. There were no young adult patients in this clinical group. One person of middle age (30–44 years) and one of old senior age (over 75 years) each accounted for 2.5% of cases, and 12 older adults (45–59 years), accounting for 30, 0% of cases and 26 (65.0%) seniors (60–74 years) were registered.

The factor of recording the level of pulse blood pressure > 60 mm Hg manifested in 21 patients of this clinical study group, that is, 52.5% of cases. Smoking occurred as a factor in cardiovascular events in 45% of cases (reported in 18 patients). As for dyslipidaemia (total cholesterol > 5 mmol/L or low-density lipoprotein cholesterol > 3 mmol/L, or triglycerides > 1.7 mmol/L), it was diagnosed in 33 patients, which is 82.5% of cases in this clinical group. Hyperglycaemia, fasting glucose 5.6–6.9 mmol/L, was diagnosed in 7 people, which is 17.5% of all cases. The factor of abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women), was detected in 87.5%, i.e., it was present in 35 people with stage 2 hypertension and ventricular extrasystole.

21 patients (52.5%) had a family history of cardiovascular disease. The cumulative risk factor score for patients in this clinical group was within 4.5 ± 0.2 ; median 4 (interquartile range 4; 6). The cumulative risk of cardiovascular complications was recorded as “high” in 10 people, which is 25.0%, and as “very high” in 30 people (75.0%). At the same time, the indicator of controllability of hypertension as an “uncontrolled” course of arterial hypertension was diagnosed in 60%, which is 24 patients in this clinical study group.

Indicators of the results of the study in the third clinical group of patients with stage 2 hypertension and mixed (supraventricular and ventricular) extrasystole, which, according to the existing

Table 4. Identification of statistically significant risk factors for cardiovascular events.

Main risk factors (ESC)	Control group (n = 30)	First clinical group (n = 54)	Second clinical group (n = 40)	Third clinical group (n = 26)
Age (> 55 years for men; > 65 years for women)	22 (73.3%)	30 (55.6%)*	30 (75.0%)	24 (92.3%)
Pulse blood pressure > 60 mmHg	13 (43.3%)*	22 (40.7%)*	21 (52.5%)	19 (73.1%)

Note: The reliability of the percentage difference between groups is calculated using the χ^2 criterion, * with the third clinical group, $p < 0.05$.

recommendations of the European Society of Cardiology, requires constant drug antiarrhythmic treatment, are as follows. Thus, in this group of patients, hypertension persisted for 10.2 ± 0.9 years, the median – 9.0 (interquartile range 7.0 and 16.0). In the third clinical group, the duration of hypertension for more than 5 years was absent. At the same time, hypertension had been registered in 16 people for 5–10 years, or 61.5% of cases. 10 patients, who accounted for 38.5% of cases, were diagnosed with hypertension for a period of more than 10 years.

Regarding the severity of arterial hypertension in patients with hypertension in this clinical trial group, grade I hypertension was not diagnosed. Grade 2 hypertension was registered in 10 patients, which accounted for 38.5% of cases, and grade 3 arterial hypertension was registered in 16 patients, which accounted for 61.5% of cases. The obtained factors for the development of cardiovascular events (ESC), the age factor (age > 55 years in men and > 65 years in women) was recorded in 24 patients, which accounted for 92.3% of cases in the third clinical group of the study and had the following characteristics. In the third clinical group of the study, there were no patients of young adult (up to 30 years) and middle (30–44 years) age. The seniors (60–74 years) comprised the main age group of 20 patients, accounting for 76.9% of cases, followed by 4 patients (15.4%) of older adult age (45–59 years) and 2 patients (7.7%) of older senior age (>75 years).

A risk factor such as pulse BP > 60 mmHg was evident in 19 people with stage 2 hypertension with mixed (supraventricular and ventricular) extrasystoles, representing 73.1% of cases. Smoking was registered in 10 people. They accounted for 38.5% of patients in the third clinical group of the study. Cardiovascular events such as lipid profile abnormalities (total cholesterol > 5 mmol/L or low-density lipoprotein cholesterol > 3 mmol/L, or triglycerides > 1.7 mmol/L) were recorded in 21 patients, 80.8% of cases of the third clinical group of the study. A fasting glycaemic index of 5.6–6.9 mmol/L was recorded in 7 people with stage 2 hypertension and mixed (supraventricular and ventricular) extrasystoles, which was 26.9%. A risk factor such as abdominal obesity (waist circumference >102 cm in men and >88 cm in women) was reported in 92.3% of cases in this clinical group of the study, namely: 24 people. Family history of cardiovascular disease, as a risk factor for cardiovascular events, was diagnosed in 16 patients in the third clinical group of the study, which accounted for 61.5% of cases. The controllability of hypertension treatment was qualified as uncontrolled in 73.1% of cases in the third clinical group. The total risk of developing cardiovascular complications (ESC) was recorded as a “high” cardiovascular risk in 6 people, accounting for 23.1% of cases, and as a “very high” cardiovascular risk was diagnosed in 76.9% of cases, which accounted for 20 patients.

An intergroup analysis of the manifestation of extrasystole factors in patients with stage 2 hypertension revealed the influence of two statistically significant factors - age and the factor of pulse blood pressure level > 60 mmHg (Tab. 4)

■ Discussion

The gender and age composition of the control group and the 3 clinical study groups show the predominance of females: the ratio of females to males in the control group and the 1st clinical study group and the diagnosis of statistically significant female predominance among patients in the 2nd (hypertension and ventricular extrasystoles) and third clinical study groups (hypertension with combined supraventricular and ventricular extrasystoles).

There are few data in the literature describing the effect of gender specifically on the development of extrasystoles in patients with stage 2 hypertension. Although, there are presented gender and age features of morpho-functional changes of the myocardium in stage 2 hypertension [20]. And morpho-functional changes in the myocardium occupy leading positions in the pathogenesis of extrasystole development. If the occurrence of extrasystoles is considered a predictor of heart rhythm disturbances such as atrial fibrillation – a clear link can be seen between the influence of risk factors according to the article. Thus, the prevalence of atrial fibrillation in women is lower than in men. However, in prognostic terms, it is the females who have atypical symptoms of atrial fibrillation, an increased risk of stroke and mortality. Gender variability in risk factors, pathophysiology, treatment strategies, and complications require further consideration in large-scale population-based studies or randomized clinical trials [21].

A study that assessed the severity of symptoms, quality of life, functional status, and emotional status of atrial fibrillation showed a poorer clinical picture of the disease among women [22]. Heart rhythm disturbances such as extrasystole were diagnosed in our study. Physical activity scores on the visual analogue scale in the range of 55.7–49.8 and the level of physical activity 51.0–54.6 mm. The range of mean values in the clinical and study groups showed comparable subjective state and physical activity. Significant differences were diagnosed only up to the average score of well-being in the control group compared to the third clinical group (55.7 ± 1.5 vs. 49.8 ± 2.3 , $p < 0.05$).

This makes it possible to assert various pathophysiological mechanisms of the development of extrasystole and atrial fibrillation, which require further study. Ventricular arrhythmias, including extrasystoles, are one of the factors in the development of fatal cardiovascular events [23]. The research of the

world community is aimed at studying and searching for new, pharmacologically safe, measures to prevent the development of the latter [24]. Although, the risk factors that lead to the development of rhythm disorders are identical: gender, body weight, hypertension, smoking, hyperglycaemia, concomitant pathology, in particular, the diagnosis of congestive heart failure. These findings correlate with global research confirming a higher prevalence of hypertension specifically in females [25] and the very prevalence of hypertension also in paediatric populations is worrying [26, 27].

The American Academy of Paediatrics Clinical Practice Guidelines (AAP CPG) 2017 for screening and management of high blood pressure in children and adolescents includes new normative blood pressure tables for children and adolescents aged 1 to 17 years and new definitions for stage 1 hypertension [28]. In analyzing the gender-specific prevalence of arterial hypertension, the findings from a study on the reduction of blood pressure in children, based on the addition of seaweed to their diet, are also noteworthy [29]. These studies showed a difference in results from a gender perspective: the consumption of seaweed by girls had no effect on blood pressure levels, while the consumption of seaweed by boys had a decrease in blood pressure, which suggests that seaweed consumption is appropriate for the prevention of high blood pressure.

Describing in detail such a risk factor for the development of cardiovascular events as age, which has demonstrated its significance in patients with stage 2 hypertension and extrasystole of various topical variants (in this case), the correlation of the age factor in studies of the world medical community is apparent. Similarly to the study of gender characteristics of the spread of extrasystole in hypertension, few studies have been published that allow definite conclusions to be drawn regarding the influence of age on the development of extrasystoles in hypertension. From this perspective, the results of the present research are unique. Patients with hypertension and ventricular extrasystole and hypertension and mixed (supraventricular and ventricular) extrasystole had a significantly higher median age (64 and 65 versus 56 and 57, respectively) in hypertensive patients with supraventricular extrasystole ($p < 0.001$). The same pattern was also determined when dividing patients into generally accepted age gradations.

Patients with hypertension and supraventricular extrasystole were more often found to be middle-aged (30–44 years) compared to patients in the second and third clinical groups of the study (statistical significance was found between patients in the control and second and third groups, $p < 0.017$) and older adult (45–59 years old) patients (statistical significance was found between patients in the control group and the 1st and 3rd study groups, $p < 0.007$) and less frequently senior (60–74 years old) (statistical significance was found between patients in the control group and the 1st, 2nd and 3rd groups, $p < 0.017$). The data from this study show that it is precisely in older seniors (75 years) and seniors (60–74 years) that the presence of an extrasystole may be considered more dangerous in prognostic terms. On the other hand, younger patients formed the control group (patients with stage 2 hypertension) and the first clinical group of the study (patients with stage 2 hypertension and supraventricular extrasystole).

The role of age has also been demonstrated in a study examining risk factors for atrial fibrillation [30]. According to researchers, risk factors for cardiovascular events such as age, smoking, type 2 diabetes mellitus, arterial hypertension, body mass index, rhythm disturbances such as atrial fibrillation, myocardial infarction, left ventricular hypertrophy are studied and closely associated with the development of heart failure in both sexes ($p < 0.001$) [31]. From this perspective, the lack of randomisation by sex in our study had no influence on the formation of the conclusions and the prospects for further developments.

According to the findings of our study, in patients with hypertension stage I and hypertension stage 2 and extrasystoles, the duration of hypertension for under 5 years and the period of 5–10 years, which had statistical reliability in our study groups, and the manifestation of such indicators as patient age (in men over 55 years and women over 65 years), the diagnosis of pulse BP over 60 mmHg; determination of the total risk factor score and diagnosis of cardiovascular risk as high and very high in our patients.

Arterial hypertension is still a major risk factor for various cardiovascular diseases. Rhythm disturbances are common in patients with hypertension. Left ventricular hypertrophy and diastolic dysfunction, and left atrium enlargement – all of these have been suggested as major risk factors for supraventricular and ventricular arrhythmias in hypertensive patients [32]. The findings on the absence of common pathophysiological mechanisms of vascular dysfunction and pathogenetic arrhythmogenesis in patients with stage 2 hypertension and extrasystoles have prompted further research into the provoking factors for extrasystoles in these patients [33].

Regarding control of the course of hypertension (stated as uncontrolled in our study), our investigation compares the prevalence of hypertension among people of low socioeconomic status [34]. Unfortunately, our study also showed similar indicators: uncontrolled hypertension was diagnosed in 63.3% of patients in the control group, 57.4% of people with hypertension and supraventricular extrasystole, 60.0% of patients with hypertension and ventricular extrasystole, and 73.1% of patients with hypertension and combined (supraventricular and ventricular extrasystole). The latter suggests that it is the control of blood pressure levels that can be a predictor of the severity of extrasystole development and in the prognostic direction is more unfavorable in terms of the development of fatal cardiovascular events.

A separate discussion, according to the results of our study, requires such an indicator (risk factor for cardiovascular events) as the level of blood pressure in patients with hypertension as a separate nosology and, in this case, combined with extrasystole. A number of world studies confirm that the level of blood pressure is an independent factor in the development of cardiovascular events. Thus, it was found that high systolic blood pressure is independently associated with the risk of the first ischemic stroke in hypertensive patients over 60 years of age and is a factor that increases the risk of developing the first ischemic stroke among older senior patients with a history of hypertension [1]. Similar results were demonstrated by this study. The role of high pulse BP in the development of gastric and combined extra-

systoles in senior and older senior patients with a history of stage 2 hypertension has been revealed and confirmed: patients in the third clinical group had a high pulse BP (> 60 mmHg) compared to patients in the control group and clinical group 1 (73.1% vs 43.3% and 40.7%, respectively, $p < 0.04$).

Heart rate variability represents the activity and balance of the autonomic nervous system and its ability to respond to internal and external stimuli, which underlies the development of both hypertension and extrasystole. As an indicator of overall homeostasis in the body, heart rate variability is associated with lifestyle factors and with morbidity and mortality [35]. Weight loss, effects of physical activity and dietary intervention can be monitored by heart rate variability parameters, including its temporal and frequency components. Parameters of heart rate variability can be controlled by performing an electrocardiogram (ECG) and indexes showing a decrease in heart rate and the number of premature ventricular complexes, along with an increase in the mean-square deviation of the normal and premature stroke intervals (SDNN) [36], which correlates with the results of this study.

The link between the occurrence of ectopic supraventricular and ventricular complexes associated with features of anthropometric data, diet has been revealed in a study, which found that heart rate variability has an inverse relationship with body fat mass (MBF) ($p = 0.015$) [37], which correlates with the results of our study, revealing increased body fat mass among 90.0% of control group patients, 79.0% of subjects in the first clinical group, 88% of patients in the second clinical group and 92.0% in the third clinical group.

Based on the above, it can be argued that overweight is an independent risk factor for hypertension, however, there is no reason to consider weight gain as a predictor of the development of a topical variant of extrasystole. Recent data are also confirmed by a study that examines the role of lifestyle modification, obesity, and age factors as the basis for the development of arterial hypertension [38]. Weight loss, as a modified risk factor for developing cardiovascular complications, is achieved through a comprehensive approach that includes balancing a person's diet, physical activity, and lifestyle in general. There is no doubt about the utility of the Dietary Approaches to Prevent Hypertension (DASH) recommendations for hypertension and extrasystole, but there is a suggestion that a diet associated with intermittent fasting may reduce the risk of cardiovascular disease with improved weight control, hypertension, dyslipidaemia, and diabetes. Intermittent fasting can have its effects through a variety of modalities, including reducing oxidative stress, optimizing circadian rhythms and ketogenesis [39, 40]. The results of a study of dyslipidaemia in patients with stage 2 hypertension and extrasystole have been previously presented in detail [41]. They demonstrated significant impairment of blood lipid transport function in patients with stage 2 hypertension and extrasystole [42, 43].

Thus, this study demonstrated the place and role of risk factors for cardiovascular events in patients with stage 2 hypertension and extrasystole in the context of modern arrhythmology. The data obtained were crucial for the influence of the age-related factor and the factor of the pulse arterial pressure level on the

formation of extrasystolic complexes in patients with stage 2 hypertensive disease and extrasystoles.

■ Conclusions

For further development of practical recommendations on preventive measures to reduce the development of fatal complications in stage 2 hypertension and extrasystole, the influence of modified (hyperglycaemia, excess body weight, physical activity level, blood pressure, family history, lifestyle, diet and unmodified (age, gender) risk factors for cardiovascular events will guide our work. And, if in this case, the age factor cannot be influenced, it is possible to at least predict the probability of developing ventricular and mixed (supraventricular and ventricular) extrasystole with stage 2 hypertension in seniors (60–74 years) and older seniors (> 75 years), which will be investigated in further analysis of our study data. Being familiar with the various pathophysiological mechanisms of different topical variants of extrasystoles in individuals of different ages provides a preventive strategy in ways to improve a patient's quality of life, regardless of the country's level of socioeconomic development.

The study of the pathophysiological features of extrasystole development dependent on cardiovascular risk factors, at the present stage, requires academic and clinical investigation in people of different racial backgrounds in general, on a differential approach and, depending on age structure. Finally, the effects of the COVID-19 virus on the various physiological homeostasis links in the body cannot be overlooked.

■ Conclusions and prospects of the study:

- 1) The age factor is key in predicting the development of ventricular and combined (ventricular and supraventricular) extrasystole in patients with stage 2 hypertension.
- 2) The factor of recording high pulse blood pressure should be considered a leading risk factor for cardiovascular events in patients with stage 2 hypertension and extrasystole.
- 3) The pathophysiological mechanisms of extrasystole development of various topical variants in patients with arterial hypertension are based on various developmental mechanisms that require further study.

■ Conflict of interest

There is no conflict of interest.

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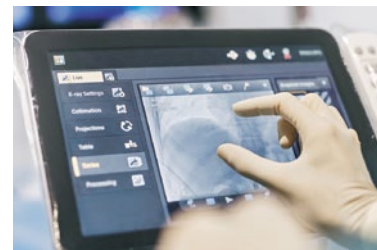
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