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N.V. Kuzminova, A.V. Ivankova, S.E. Lozinsky, I.I. Knyazkova<sup>1</sup>, O.M. Kulchytska, A.O. Gavriluk National Pirogov Memorial Medical University, Vinnytsya <sup>1</sup>Kharkiv National Medical University, Kharkiv

## STATE OF KIDNEY FUNCTION AND FEATURES OF METABOLIC STATUS CHANGES IN PATIENTS WITH HYPERTENSIVE DISEASE WITH DIFFERENT FORMS OF EXTRASYSTOLS

e-mail: Kuzminova5517@gmail.com

156 patients (65 men and 91 women) of middle age with stage II essential hypertension (EH II) were examined. The main group consisted of 124 of them with the evidence of frequent supraventricular (SVPB) (74 persons) or ventricular premature beats (VPB) (50 persons) established by daily ECG monitoring. The comparison group included 32 patients with EH II stage without arrhythmia. Patients in the main group were significantly more likely to have a hypertensive history, they had significantly more burdened cardiovascular heredity, a significant increase in body mass index and incidence of abdominal obesity, fasting glucose and uric acid (p <0.05). The patients with frequent VPB compared with patients with SVPB had more marked differences in most of the analyzed parameters on the background of significant (p <0.05) reduction of the glomerular filtration rate. Therefore, these changes in metabolic status may contribute to the occurrence of VPB in patients with hypertension.

**Keywords:** essential hypertension, arterial hypertension, supraventricular premature beats, ventricular premature beats, uric acid, glomerular filtration rate, body mass index, metabolic status.

The work is a fragment of the research projects "Impairment of endothelial and adipose tissue, their relationship with the functional state of the liver and cardiovascular remodeling and the possibility of their correction in patients with cardiovascular pathology" (state registration No. 0113U007670) and "Metabolic risk factors, cardiovascular remodeling and functional status of the kidney in patients with cardiovascular pathology. Possibilities of pharmacological correction" (state registration No. 0119U101849).

Patients with arterial hypertension (AH) may have a variety of cardiac arrhythmias that contribute to the occurrence of cardiovascular (CV) complications. There is enough attention, paid to the atrial fibrillation (AF) in patients with hypertension but the contributors and mechanisms of occurrence of premature beats, both supraventricular (SVPB) and ventricular (VPB), in patients with hypertension remains studied insufficiently [3, 8, 11, 14].

The linkage between the excess of adipose tissue, obesity, and cardiovascular (CV) diseases has been receiving much attention lately. Obesity is often associated with such diseases and conditions as hypertension, coronary heart disease, dyslipidemia, myocardial infarction, stroke, type 2 diabetes, non-alcoholic fatty liver disease, gout, infertility, "sleep apnea" and others. [6, 7, 9]. Adipose tissue is not passive fat storage, not only an" energy accumulator ". It is an active endocrine organ that is able to synthesize and secrete into the bloodstream variety of biologically active substances of peptide and non-peptide nature (adiponectin) that play an important role in maintaining homeostasis of multiple systems, including cardiovascular system [7, 9, 10].

The linkage between cardiac and renal disorders has been attracting the attention of researchers for a long time. The high risk of cardiac death in terminal renal failure was noted almost immediately after the implementation of hemodialysis into clinical practice, however, only in the last decade, it has become clear that any renal impairment (both acute and chronic) is also associated with a high overall and CV mortality. These data were obtained in large randomized trials and formed the basis for the concept of chronic kidney disease, developed by the National Kidney Foundation, USA. In the future, this concept was the beginning of studies of cardiothoracic interaction [2, 4].

To assess the functional state of the kidneys in clinical practice, the determination of glomerular filtration rate (GFR) is used more often, but its decrease occurs only when the number of functioning nephrons decreases, so it cannot serve as an early marker of kidney damage, which is a prerequisite for finding more sensitive diagnostic methods [4, 5, 13].

Recently a link was discovered between levels of uric acids and (UA) and CV disorders, carbohydrate, and lipid metabolism. According to a number of studies, increase of UA in blood is associated with dysfunction of the endothelium - inhibition of the production of nitric oxide, proliferation of smooth muscle cells of blood vessels, activation of inflammatory sympathoadrenal and reninangiotensin system, diabetes mellitus, hyperinsulinemia, insulin resistance, lipid metabolism, the development and progression of hypertension, target organs' damages and worsening of the general prognosis for such patients [1, 12].

In view of these problems and the high frequency of hypertension in the national population, the study of various aspects, including impaired renal function, combined course of hypertension and various disorders of the heart rhythm is of great academic and practical interest today.

**The purpose** of the study was to assess the state of renal function and features of the metabolic status in patients with stage II essential hypertension and concomitant frequent premature beats.

**Materials and methods.** Screening, careful collection of complaints and medical history, obtaining of informed consent of the patient to participate in the study in accordance with the ethics of the Declaration of Helsinki were carried out before the study.

The study included 124 patients with stage II hypertension (EH) and frequent symptomatic premature beats between the ages of 27 and 75 (the mean age was  $58.2 \pm 0.9$  years). These patients were the main group. In addition, 32 patients with stage II EH without any cardiac arrhythmias between the ages of 32 and 72 (the mean age was  $55.9 \pm 1.7$  years) were examined. Among the patients of the main group 50 patients (40,3%) were males and 74 (59, 6%) were females. The comparison group consisted of 15 men (46.9%) and 17 women (53.1%). Statistical analysis between the main group and the comparison group showed that there were no significant differences (p > 0.05) in age and gender, indicating the age and gender homogeneity of the examined patients.

The criteria for inclusion of patients in the study were: 1) age from 25 to 75 years; 2) stage II EH according to the unified clinical protocol and the current order of the Ministry of Health of Ukraine, No. 384, May 24, 2012; 3) frequent symptomatic premature beats (> 30 PB per hour) verified by the data of the daily Holter monitoring of the electrocardiogram (DHM); 4) absence of effective antiarrhythmic treatment at the time of inclusion; 5) consent of the patient to participate in the study.

Criteria of non-inclusion were the following: 1) age under 25 and over 75; 2) EH of the I or III stages and symptomatic hypertension; 3) concomitant coronary heart disease, which was excluded in accordance with the recommendations of the Ukrainian Association of Cardiologists (2013) due to the absence of a history of myocardial infarction and typical angina attacks in combination with negative results of the instrumental examination (exercise test); 4) Heart failure (HF) of the III-IV FC by NYHA and the presence of systolic myocardial dysfunction (left ventricular ejection fraction <40%); 5) the presence of prolonged episodes (> 20 s) of AF, persistent AF, or paroxysmal tachycardia; 6) diabetes, impaired carbohydrate tolerance; 7) clinically significant concomitant diseases of internal organs with impaired function; 8) alcohol or drug abuse; 9) severe neurological and mental disorders; 10) refusal of the patient to participate in the study.

Among the 124 patients with EH and concomitant frequent PB, supraventricular (SVPB) and ventricular PB (VPB) were found in 74 cases (59.7%) and in 50 cases (40.3%), respectively. Arrhythmic history ranged from 1 to 27 years and the mean duration was  $8.06 \pm 0.42$  years. 30 patients (24.2%) of the main group experienced arrhythmia during the last year. It was expressed in a form of different subjective symptoms. The most often were feeling of failures and pauses in the heartbeat. Instead, the vast majority (94 patients (75.8%)) experienced episodic arrhythmias as intermittent episodes. The arrhythmia occurred in the active time of a day (from 6 a.m. until 9 p.m.) in 32 patients (25, 8 %). It was associated with physical, psycho-emotional overload, stress. And in 14 persons (11.3%) it occurred in the inactive period of the day (from 9 p.m. until 6 a.m.) at rest in the complete absence of physical and psycho-emotional stress, in a horizontal position and during sleep (according to the data of the DHM). It is worth to note that 48 patients (38.7%) could not notice a clear relationship between arrhythmia and the period of day. The appearance of arrhythmia in these patients was observed regardless of the kind of activity and time of day.

All the patients included in the study were examined and treated during 2016-2019 in the cardiology department of Vinnytsya Regional Pirogov Memorial Clinical Hospital, the clinical-diagnostic department and the department of cardiac rhythm disorders of the Community Institution «Vinnytsya Regional Centre of Cardiovascular Pathology».

All patients underwent clinical, laboratory and instrumental examinations during their inclusion in the study in order to verify the basic diagnosis and concomitant conditions, as well as to assess the metabolic status. After verification of the diagnosis all patients who agreed to participate in the study were provided with 1) general clinical and anthropometric examination, measurement of blood pressure; 2) ECG in 12 leads, DHM, ultrasound of the heart and carotid arteries; 3) assessment of kidney function (blood creatinine with calculation of glomerular filtration rate); 4) laboratory tests: fasting glucose level, serum lipid spectrum level, uric acid level.

The general clinical examination included the identification of indications and contraindications for the inclusion in the study, the establishment of the basic diagnosis and concomitant pathology, the evaluation of the anamnesis and the formation of study groups. The anthropometric examination was performed to determine the body weight and height of the patients, followed by the calculation of body

mass index (BMI) by the Kettle formula as the ratio of body weight in kilograms to height in meters, raised to the square (kg/m²). The waist circumference (WC) and hip circumference (HC) were measured.

Blood pressure was measured according to the Guidelines of the Ukrainian Cardiologists Association (2013) using sphygmomanometer (Microlife) [6].

Electrocardiography was performed according to the standard procedure in 12 leads on the electrocardiograph "YUKARD" (Hungary).

DHM was performed using the equipment «DiaCard» (JSC «Solvaig», Ukraine) using the standard protocol. According to the DHM, such indicators characterized the structure of the daily heart rate were evaluated: daily average, daytime, and nighttime heart rate (AHR, DHR, and NHR, respectively) and the circadian index (CI), which was calculated by the formula CI = DHR/NHR. The following parameters were determined to assess the attributes of the arrhythmias: the number of SVPB and VPB per 24 hours; the amount of SVPB and VPB per hour (SVPB<sub>1</sub> and VPB<sub>1</sub>, respectively); the number of patients with paired and group VPB (VPBp) and the number of VPBp per 24 hours.

Assessment of the structural-functional state of the heart was performed using echocardiography in one-dimensional and two-dimensional modes with color, pulse and constant-wave Doppler imaging by the equipment «My Lab 25» (Italy).

The structural and functional state of the vessels of the neck was determined by the duplex scanning and color Doppler mapping using linear sensor 6.5-13 MHz of the «Logiq - 500 MO» (GE, USA) equipment.

The spectrophotometric method was applied for the determination of serum lipid spectrum such as total cholesterol (TCL), cholesterol in high-density lipoproteins (HDL-C) and triglycerides (TG). For these purpose standard sets of reagents «Cholesterin-F», «Trygliceridy-F», «HDL- cholesterin» manufactured by "Philicit-Diagnostics" (Ukraine) were used. The level of cholesterol in very-low-density lipoproteins (LDL) was determined by the formula:  $TG \times 0.45$ . The level of cholesterol in LDL was calculated using the formula of W. Friedwald: LDL-C = TCL HDL – HDL-C - (0.45 x TG).

Assessment of kidney function was carried out using the following tests: 1) determining of blood creatinine level in mmol/l with the help of kinetic modified Jaffe method on the analyzer Cobas 6000 (c 501 module) using a test system Roche Diagnostics (Switzerland); 2) calculation of glomerular filtration rate according to the formula CKD-EPI using the online calculator. Uric acid (UA) level was determined in µmol/l with the help of enzymatic colorimetric method on analyzer Cobas 6000 (c 501 module) using test kits Roche Diagnostics (Switzerland).

Statistical processing of the study results was performed using software «Statistica» v. 12 .0 by «StatSoft» company according to the recommendations for the processing of biomedical data. The results were presented as the mean (M) and the error of the mean (m) for quantitative values and as a percentage (%) for relative values. Comparisons of relative values (%) were performed using the criterion  $\chi^2$ . Quantitative values in independent samples were compared by t-test for independent samples.

**Results of the study and their discussion.** It was found that the mean duration of hypertensive history was significantly higher in the main clinical group compared with the comparison group (10.88 vs. 7.75 years, respectively, p = 0.01) (table 1). In addition, a significantly lower incidence of hypertensive history of up to 5 years was determined in the main clinical group compared with patients without cardiac arrhythmias (21.0% versus 40.6%, respectively, p = 0.02).

There is some practical and academic interest in the study of risk factors for various CV complications. For this reason, we conducted an analysis of well-known risk factors in the examined groups of patients (Tab.1). The fundamental differences between the groups were found in the parameters of fasting glucose and the rate of burdened CV heredity. Thus, fasting glucose of 5.6-6.9 mmol/l range and the number of burdened CV heredity cases were significantly more frequently registered in patients of the main clinical group (29.8% vs 12.5%, p = 0.04 and 73.4 % vs 53.1%, p = 0.03, respectively). In addition, there was a clear trend of increasing incidence of cases with exceeding WC (74.2% versus 59.4%, p = 0.09) compared to the comparison group. It indicated the presence of abdominal type of distribution of adipose tissue in patients with stage II EH with frequent premature beats.

It is interesting that dyslipidemia was diagnosed in the vast majority of patients with stage II essential hypertension both with and without concomitant arrhythmias (84.4% and 88.7%, respectively, p> 0.05). In this case, the cut-off levels for TCL > 5 mmol/l or LDL-C > 3 mmol/l or TG > 1.7 mmol/l were applied. Structural remodeling of the carotid arteries (TIM > 0.9 mm) was revealed in half of patients (53.1% and 51.6%, respectively, p> 0.05). Hemodynamically insignificant atherosclerotic plaques (from 15 to 30% of vessels diameter) in the pull of the carotid arteries were found in 25.0% and 23.4% of patients, respectively (p> 0.05). The obtained results indicate that there are more factors of increase of cardiovascular risk in patients with hypertension and rhythm disorders, compared with patients with EH without arrhythmias and coincide with some literature data [3, 8].

Table 1 Clinical characteristics of patients with stage II hypertension in the main and comparison groups

Features	Comparison group (n = 32)	Main group ( n = 124)	p
Mean duration of EH (years)	$7.75 \pm 1.16$	$10.88 \pm 0.55$	0.01
Duration of EH up to 5 years	13 (40.6 %)	26 (21.0 %)	0.02
Duration of EH is 5-10 years	10 (31.3 %)	42 (33.9 %)	0.78
Duration of EH > 10 years	9 ( 28.1 %)	56 (45.2 %)	0.08
AH 1 degree	7 (21.9 %)	19 (15.3 %)	0.38
AH 2 degrees	16 (50.0 %)	65 (52.4 %)	0.81
AH 3 degrees	9 (28.1 %)	40 (32.3 %)	0.65
Percentage of uncontrolled AH	21 (65.6%)	62 (50.0%)	0.11
Age (m. > 55 and in w. > 65 years)	14 (43.8 %)	71 (57.3%)	0.17
PBP > 60 mm Hg	10 (31.3%)	58 ( 46.8 %)	0.11
Smoking	11 (34.4%)	47 (37.9%)	0.71
Dyslipidemia (TCL > 5 mmol / 1 or LDL-C > 3 mmol / 1 or TG > 1.7 mmol / 1)	27 (84.4%)	110 (88.7%)	0.50
Fasting glucose of 5.6-6.9 mmol / l	4 (12.5%)	37 (29.8%)	0.04
WC (in m. > 102 and in w. > 88 cm)	19 (59.4%)	92 (74.2%)	0.09
Burdened CV heredity	17 (53.1%)	91 (73.4%)	0.03
The presence of AP in the CA pool	8 (25.0%)	29 (23.4% )	0.84
TIM > 0.9 mm	17 (53.1%)	64 (51.6%)	0.87
High CVR	13 (40.6%)	41 (33.1%)	0.42
Very high CVR	19 (59.4%)	83 (66.9%)	0.42
BMI, kg / m <sup>2</sup>	$30.21 \pm 0.93$	$31.93 \pm 0.42$	0.046
NW (BMI $18.5 - 25.0 \text{ kg} / \text{m}^2$ )	8 (25.0%)	8 (6.5%)	0.002
BMI (BMI - 25-30 kg / m <sup>2</sup> )	12 (37.5%)	41 (33.1%)	0.64
Ob $(BMI > 30 \text{ kg} / \text{m}^2)$	12 (37.5%)	75 (60.5%)	0.02
Ob of I degree (BMI - 30-35 kg / m <sup>2</sup> )	8 (25.0%)	38 (30.6%)	0.53
Ob of II degree (BMI - 35-40 kg/m <sup>2</sup> )	3 (9.4%)	28 (22.6%)	0.10
Ob of III degree (BMI $> 40 \text{ kg} / \text{m}^2$ )	1 (3.1%)	9 (7.3%)	0.39

Notes (hereinafter): 1. EH – essential hypertension; AH - arterial hypertension; m. – men; w. – women; PBP - pulse blood pressure; TCL - total cholesterol; LDL-C - low density lipoprotein cholesterol; TG - triglycerides; WC - waist circumference; AP - atherosclerotic plaques; CA - carotid arteries; TIM - thickness of intima/media ratio; CVR - cardiovascular risk; BMI - body mass index; NW – normal weight; OW - overweight; Ob - obesity; 2. Intergroup significance of the difference between mean values calculated by T-test for independent samples, % - by criterion  $\chi^2$ 

Taking into account rather high incidence of abdominal obesity, determined by waist to hip ratio, and the increase in BMI, we performed a more detailed analysis of BMI level and type of fat distribution. Thus, it was found that in the main group of patients (n = 124) the mean value of BMI was  $31.40 \pm 0.43$  kg/m $^2$  with a range from 20.0 to 46.0 kg/m $^2$  compared with BMI in the comparison group  $30.21 \pm 0.93$  kg/m $^2$  (p = 0.046). Only 16 persons (10.3%) had normal weight when 53 - excess weight (34.0%), and 87 patients (55.8%) had an abdominal type of obesity. The obesity of I degree (BMI - 30-35 kg/m $^2$ ) was established in 46 (52.9%) patients with abdominal obesity, II degree (BMI - 35-40 kg/m $^2$ ) - in 31 (35.6%), and III degree (BMI> 40 kg/m $^2$ ) - in 10 (11.5%), respectively.

In the group of patients with frequent PB normal weight (BMI 18.5 -  $25 \text{ kg/m}^2$ ) occurs significantly less than in the comparison group (6.5% vs. 25.0%, p = 0.002). Also the significantly higher rate of the abdominal obesity (60.5% vs. 37.5%, p = 0.02) was observed in this group. It may indicate the association between the presence of metabolic disorders and the development of extrasystolic arrhythmias in patients with hypertension and coincides with some research findings by other scientists [9, 12].

The features of clinical characteristics of subgroups of patients with EH were analyzed depending on the presence of frequent supraventricular or ventricular PB. These data suggest that there are fundamental differences between subgroups in risk factors such as the degree of hypertension, smoking rate, fasting glycemia rate, the rate of structural remodeling of carotid arteries (IMT> 0.9 mm), the value of BMI, the rate of abdominal obesity, the level of CVR (table 2).

Grade 1 hypertension and fasting glucose level within 5.6-6.9 mmol / 1 were significantly more frequently reported in patients with SVE (37.8% vs 18.0%, p = 0.02 and 21.6% vs 6.0%, p = 0.02, respectively). In contrast, the patients with stage II EH and concomitant VPB had slightly older age (p = 0.04). They had more marked rates of III degree AH (46.0% vs. 23.0%, p = 0.007), smoking (50.0% vs. 29.7%, p = 0.02), signs of structural remodeling of the carotid artery (64.0% vs. 43.2%, p = 0.03) and very high CV risk (80.5 % vs. 58.1%, p = 0.01). Also they had higher BMI and their rates of abdominal obesity and obesity of III degree (BMI> 40 kg / m $^2$ ) were higher (72.0% vs. 52,7%, p = 0.03 and 14% vs 2.7%, respectively, p = 0.02) ( Table 2 ). The obtained data indicate that patients with II stage EH and concomitant PB has more severe disorders, which to some extent can contribute to the progression of both, PB and CV complications [6].

Clinical characteristics of subgroups of patients with essential hypertension and different types of premature beats

Features	SVPB ( n = 74 )	VPB ( n = 50 )	p
Mean age, years	56.67 ± 1.26	60.46 ± 1.29	0.04
Mean duration of EH (years)	$10.26 \pm 0.69$	$11.80 \pm 0.91$	0.17
Duration of EH up to 5 years	19 (25.7%)	7 (14.0%)	0.12
Duration of EH is 5-10 years	24 (32.4%)	18 (36.0%)	0.68
Duration of EH > 10 years	31 (41.9%)	25 (50.0%)	0.37
AH 1 degree	16 (21.6%)	3 (6.0%)	0.02
AH 2 degrees	41 (55.4%)	24 (48.0%)	0.42
AH 3 degrees	17 (23.0%)	23 (46.0%)	0.007
Percentage of uncontrolled AH	39 (52.7%)	23 (46.0%)	0.46
Age (in m. > 55 and in w. > 65 years)	42 (56.8%)	29 (58.0%)	0.89
PBP > 60 mmHg. Art.	31 (41.9%)	27 (54.0 %)	0.18
Smoking	22 (29.7%)	25 (50.0 %)	0.02
Dyslipidemia (TCL > 5 mmol / 1 or LDL-C > 3 mmol / 1 or TG > 1.7 mmol / 1)	68 (91.9%)	42 (84.0 %)	0.17
Fasting glucose of 5.6-6.9 mmol / 1	28 (37.8%)	9 (18.0 %)	0.02
WC (in m. > 102 and in w. > 88 cm)	52 (70.3%)	40 (80.0 %)	0.22
Burdened CV heredity	5 8 (78.4 %)	3 3 (6.0 %)	0.13
The presence of AP in the CA pool	13 ( 1 7, 6%)	16 (32, 0 %)	0.06
TIM > 0.9 mm	32 (43.2 %)	32 (64, 0%)	0.03
High CVR	31 (41.9%)	1 0 (20.0%)	0.01
Very high CVR	43 (58.1%)	40 (80.0%)	0.01
BMI, kg / m <sup>2</sup>	$30.66 \pm 0.61$	$32.64 \pm 0.77$	0.02
NW (BMI 18.5 - 25 kg / m <sup>2</sup> )	6 (8.1%)	2 (4.0%)	0.36
OW (BMI - 25-30 kg / m <sup>2</sup> )	26 (35.1%)	15 (30.0%)	0.55
Ob (BMI $> 30 \text{ kg} / \text{m}^2$ )	39 (52.7%)	36 (72.0%)	0.03
Ob I degree (BMI - 30-35 kg / m <sup>2</sup> )	20 (27.0%)	18 (36.0%)	0.29
Ob II degree (BMI - 35-40 kg / m <sup>2</sup> )	17 (23.0%)	11 (22.0%)	0.90
Ob III degree (BMI $> 40 \text{ kg} / \text{m}^2$ )	2 (2.7%)	7 (14.0%)	0.02

Notes: 1. SVE – supraventricular premature beats; 2. VE - ventricular premature beats.

Table 3 Markers of the state of kidneys function and uric acid levels in patients with EH stage II and different forms of extrasystoles

Indexes	EH II without arrhythmias ( n = 32)	EH II and SVE ( n = 74)	EH II and VE ( n = 50)	P
	1	2	3	
Creatinine, μmol / L	78 (66; 97)	81 (62; 100)	86 (70; 100)	P1-2 = 0, 12 P1-3 = 0.04 P2-3 = 0.90
GFR, ml / min / 1.73 m $^2$	81 (74; 100)	77 (68; 95)	71 (59; 88)	P1-2 = 0, 22 P1-3 = 0.009 P2-3 = 0.04
UA, μmol / L	321 (294; 378)	356 (340; 403)	387 (353; 433)	P1-2 = 0.02 P1-3 = 0.001 P2-3 = 0.01
The incidence of UA > 420 (3 6 0) m k mol / L, to% (%)	3 (9.4%)	20 (27.0%)	20 (40.0%)	P1-2 = 0, 10 P1-3 = 0.007 P2-3 = 0.27

Notes: 1. EH - essential hypertension; SVE - supraventricular extrasystoles; VE - ventricular extrasystoles; GFR - glomerular filtration rate; UA - uric acid; P1-2, P1-3, P2-3 - significance of differences between subgroups of patients. 2. The significance of differences was performed according to Kruskal - Wallis ANOVA & Median test for all groups, % - by the  $\chi^2$  criterion.

The analysis of the functional state of the kidneys and the level of uric acid in patients with stage II EH without rhythm disorders and with various variants of premature beats was performed. These data suggests that in patients with essential hypertension and frequent PB there is a significant increase in the mean UA level, compared with patients without arrhythmias. The level of UA was highest in the group of patients with VPB compared with patients who had SVPB or no arrhythmias (p = 0.01 and p = 0.001, respectively) (Table 3). Our findings confirm the possible link between plasma uric acid levels and an increased risk of cardiovascular disease in essential hypertension [12]. It should be noted that the hyperuricemia rate (UA level> 420 (360)  $\mu$ mol / l) was also significantly higher in patients with EH and VPB compared to patients without arrhythmia (p = 0.007).

The fact of significant (p = 0.04) increase in creatinine level in the subgroup of patients with PB compared with patients without rhythm disorders was rather interesting, although it did not exceed the reference values. Calculation of the glomerular filtration rate showed that the average GFR level in all subgroups of patients was below 90 ml/min/ 1.73m $^2$ , indicating a slight decrease in renal function. In the subgroup of stage II EH and VPB GFR was significantly lower compared to the corresponding values in patients without arrhythmias and with the presence of SVPB (p = 0.009 and p = 0.04, respectively).

The obtained data give some reasons to believe that the presence of frequent PB in patients with stage II EH is accompanied by significant disorders of the metabolic status of the organism. They are more pronounced and accompanied by a significant decrease in glomerular filtration rate in patients with frequent VPB.

#### Conclusions

- 1. Patients with stage II EH and concomitant frequent PB, compared with patients with EH without cardiac arrhythmias has significantly longer hypertensive history, significantly higher rate of burdened hereditary history of cardiovascular pathology, significant increase in BMI, fasting glucose and uric acid. It can be assumed that the identified changes may serve as predictors of frequent premature beats in patients with stage II EH.
- 2. Patients with stage II and frequent VPB compared with patients with frequent SVPB were significantly older, had significantly higher rates of smoking, AH of III degree (46.0% vs. 23.0%, p = 0.007), signs of structural remodeling of carotid arteries, very high CV risk, exceeding BMI and abdominal obesity (p < 0.05). These changes and smoking can be considered as predictors of the occurrence of VPB in patients with stage II EH.
- 3. In patients with stage II GC, the presence of frequent extrasystolic arrhythmia was accompanied by a significant increase in plasma levels of UA. Significantly higher levels of UA and a decrease in GFR were observed in patients with stage II EH and frequent VPB compared with patients without arrhythmia or with frequent SVPB. It can be suggested that increased plasma levels of UA contribute to the development of arrhythmias in patients with EH. Certain changes in metabolic status can contribute to the occurrence of cardiac arrhythmias, in particular, frequent VPB, in patients with stage II EH. The presence of frequent VPB can serve as a marker of more severe metabolic disorders in patients with uncomplicated AH. However, there is a need to continue scientific research in this area to clarify the mechanisms of arrhythmias and to identify early predictors of metabolic disorders, kidney function, and rhythm disorders in patients with hypertension to improve prognosis, optimize treatment, and reduce cardiovascular risk.

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#### Реферати

#### СТАН ФУНКЦІЇ НИРОК ТА ОСОБЛИВОСТІ ЗМІН МЕТАБОЛІЧНОГО СТАТУСУ У ХВОРИХ НА ГІПЕРТОНІЧНУ ХВОРОБУ ІЗ РІЗНИМИ ФОРМАМИ ЕКСТРАСИСТОЛІЙ

Кузьмінова Н.В., Іванкова А.В., Лозінський С.Е., Князькова І.І., Кульчицька О.М., Гаврилюк А.О.

Обстежено 156 пацієнтів (65 чоловіків та 91 жінка ) середнього віку із гіпертонічною хворобою II стадії (ГХ II). Основну групу склали 124 з них, які за даними добового моніторування електрокардіограми мали часту суправентрикулярну (СВЕ) (74 особи) або шлуночкову екстрасистолію (ШЕ) (50 осіб). В групу порівняння увійшли 32 хворих на ГХ II ст. без аритмії. У пацієнтів основної групи визначено достовірно триваліший гіпертензивний анамнез, значно частіше обтяжений спадковий анамнез по серцево-судинній патології, вірогідне збільшення індексу маси тіла і випадків абдомінального частоти ожиріння. підвищення рівня глюкози натще та рівня сечової кислоти (р<0,05). Найбільші розбіжності проаналізованих показниках на фоні достовірного (р<0,05) зниження величини швидкості клубочкової фільтрації спостерігались в групі хворих з частою ШЕ порівняно з пацієнтами з СВЕ. Отже, зазначені зміни метаболічного статусу можуть сприяти виникненню ШЕ у хворих з артеріальною гіпертензією.

**Ключові слова:** гіпертонічна хвороба, артеріальна гіпертензія, суправентрикулярна екстрасистолія, шлуночкова екстрасистолія, сечова кислота, швидкість клубочкової фільтрації, індекс маси тіла, метаболічний статус.

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# СОСТОЯНИЕ ФУНКЦИИ ПОЧЕК И ОСОБЕННОСТИ МЕТАБОЛИЧЕСКОГО СТАТУСА У БОЛЬНЫХ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ С РАЗНЫМИ ФОРМАМИ ЭКСТРАСИСТОЛИЙ

Кузьминова Н.В., Иванкова А.В., Лозинский С.Э, Князькова И.И., Кульчицкая Е.Н., Гаврилюк А.А.

Обследовано 156 пациентов (65 мужчин и 91 женщина) среднего возраста с гипертонической болезнью (ГБ) II стадии. Основную группу составили 124 из них, которые по данным суточного мониторирования электрокардиограммы имели частую суправентрикулярную (СВЭ) (74 человека) либо желудочковую экстрасистолию (ЖЭ) (50 человек). В группу сравнения вошли 32 больных ГБ II ст. без аритмии. У пациентов основной группы выявлено достоверно более продолжительный гипертензивный анамнез, значительно чаще отягощенный наследственный анамнез по сердечно-сосудистой патологии, значительное увеличение индекса массы тела, частоты случаев абдоминального ожирения, повышение уровня глюкозы крови натощак и уровня мочевой кислоты (р<0,05). Наибольшие расхождения в проанализированных показателях на фоне достоверного (р<0,05) снижения величины скорости клубочковой фильтрации наблюдались в группе больных с частой ЖЭ по сравнению с пациентами с СВЭ. Исходя из этого, вышеперечисленные изменения метаболического статуса могут способствовать возникновению ЖЭ у больных с артериальной гипертензией.

**Ключевые слова:** гипертоническая болезнь, артериальная гипертензия, суправентрикулярная экстрасистолия, желудочковая экстрасистолия, мочевая кислота, скорость клубочковой фильтрации, индекс массы тела, метаболический статус.

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## Н.В. Кузьмінова, В.О. Романова, В.К. Сєркова, О.М. Біловол <sup>1</sup>, І.І. Князькова <sup>1</sup>, А.О. Гаврилюк

Вінницький національний медичний університет імені М.І. Пирогова, Вінниця <sup>1</sup>Харківський національний медичний університет, Харків

## НОВІ МОЖЛИВОСТІ КОРЕКЦІЇ КЛІНІЧНОГО СТАНУ ТА ЕНДОТЕЛІАЛЬНОЇ ДИСФУНКЦІЇ У ХВОРИХ НА ІШЕМІЧНУ ХВОРОБУ СЕРЦЯ

e-mail: Kuzminova5517@gmail.com

Обстежено 112 хворих на ішемічну хворобу серця (IXC): 76 з них мали діагноз стабільної IXC, 36 пацієнтів, госпіталізовані з гострим коронарним синдромом. Для оцінки ефективності лікування хворі були розподілені на дві групи. Перша група (n=69) отримувала комплексну базисну терапію IXC. Пацієнти 2-ої групи (n=43) додатково до базисної терапії приймали фіксовану комбінацію мельдонію (180 мг) з гамма-бутиробетаїном (60 мг) перорально по 2 капсули двічі на добу протягом 4 тижнів. Комплексна терапія хворих на IXC з додаванням комбінації мельдонію з гамма-бутиробетаїном (оцінювали через 1 місяць від початку) сприяла достовірному (p<0,05) покращенню клінічного стану пацієнтів (якості життя, зменшенню частоти нападів стенокардії, підвищенню задоволеності лікуванням) та функціонального стану ендотелію, а саме його судиннорухливої та адгезивної функцій порівняно з традиційною терапією. Ключові слова: ішемічна хвороба серця, ендотеліальна дисфункція, мельдоній, гамма-бутиробетаїн.

Робота є фрагментом НДР «Порушення функції ендотелію та жирової тканини, їх зв'язок з функціональним станом печінки та серцево-судинним ремоделюванням та можливості їх корекції у хворих з серцево-судинною патологією» (№ державної реєстрації 0113U007670) та «Метаболічні фактори ризику, серцево-судинне ремоделювання та функціональний стан нирок у хворих з серцево-судинною патологією. Можливості фармакологічної корекції» (№ державної реєстрації 0119U101849).

Згідно даних ВООЗ, серцево-судинні захворювання (ССЗ) є одними з найважливіших причин смертності та інвалідизації в країнах Європи, обумовлюючи 4,3 млн смертей на рік. Україна ж посідає одне з перших місць в Європі за показниками серцево-судинної (СС) смертності як серед всього, так і серед працездатного населення [4, 12]. На жаль, рівень смертності від ССЗ в останні роки невпинно зростає – сьогодні в Україні цей показник: перевищив 1000 на 100 тис. населення (1009,5 на 100 тис.