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The Blood Plasma Aldosterone Concentration in Stage II Hypertension Patients with Comorbid Chronic Coronary Artery Disease, Frequent Ventricular Extrasystoles and Different Clinical Indicators

Introduction. Hypertensive disease (HD) is a major cause of morbidity and mortality. According to the World Health Organization (WHO), 1.28 billion adults aged 30 to 79 years suffer from HD [8, 11].

Aldosterone plays an important role in the regulation of blood pressure (BP) as a component of the renin-angiotensin-aldosterone system (RAAS) [7]. Aldosterone is known to exert arrhythmogenic effect through the stimulation of inhibitor of plasminogen activator-1, which leads to thrombosis and extracellular collagen deposition. It also known as a cause of myocardial fibrosis [12]. There is a high correlation between elevated plasma aldosterone concentrations and inflammation, oxidative stress, endothelial dysfunction, and subclinical atherosclerosis [14].

Many people do not have symptoms HD until severe heart damage, highlighting the need for early diagnosis and effective treatment to prevent its progression and reduce the incidence of complications.

Diagnosis of hyperaldosteronism makes it possible to prescribe specific treatment, which may include mineralocorticoid receptor antagonists, such as spironolactone and eplerenone contributing to improvement of the therapeutic complex.

Aim of the study. To assess the blood plasma aldosterone concentration in stage II hypertension patients with comorbid chronic coronary artery disease, frequent ventricular extrasystoles and different clinical indicators.

Materials and methods. We examined 120 stage II HD patients (34 (28.3 %) women and 86 (71.7 %) men aged 34 to 74 (mean age of the examined patients - 57.3 ± 0.9 years)) with/and without concomitant chronic coronary insufficiency (CCI), frequent ventricular extrasystoles treated at the municipal institution "Vinnytsia Regional Medical and Diagnostic Center of Cardiovascular Pathology". The study was a randomized one with preliminary stratification by stage II HD diagnosis.

Stage II HD was diagnosed in accordance with the recommendations of the European Society of Hypertension 2023 [9] and the clinical protocol for primary and specialized medical care for HD patients 2024 [2]. Concomitant CCI, which was an optional condition for inclusion in the study, was diagnosed instrumentally using stress tests and/or coronary ventriculography, which included only angina of II-III functional classes according to the recommendations of the European Society of Cardiology [13] and the unified clinical protocol "Stable ischemic heart disease" (Order of the Ministry of Health of Ukraine No. 265 dated February 16, 2021) [3]. Cardiac arrhythmia was identified using Holter electrocardiogram monitoring (H-ECG) (Guideline 00051. Outpatient ECG monitoring) [4].

The cohort of examined patients included primarily patients of middle age (45 to 59 years old) - 42.5 % (n = 54) and elderly patient (60 to 74 years old) - 42.5 % (n = 51). The number of young patients (below 44 years old) was only 12.5 % (n = 15). It should be noted that the senile age of patients (over 75 years old) was a criterion for exclusion from the study.

The disease history was: HD - 8.6 ± 6.0 years, CCI - 4.8 ± 2.6 years, and arrhythmia - 3.5±3.0 years. The majority (60.8 %; n = 73) of the examined patients had short hypertensive anamnesis that does not exceed 10 years. 24.2 % (n = 29) of the patients had the history of 10-15 years and only 15.0 % (n = 18) > 15 years.

The analysis of body mass index (BMI) showed that only (9.2 %, n = 11) HD patients had normal body weight

(BMI – 20-25 kg/m^2). 41.7 % (n = 50) of them had excess body weight (BMI – 25-30 kg/m^2) and almost half of them (49.2 %, n = 59) had signs of constitutional-alimentary obesity (BMI > 30 kg/m^2).

The smallest proportion (20.8 %) of the examined patients has stage 1 - mild HD (BP - 140-159/90-99 mm Hg). The proportion of patients with stage 2 (moderate) and stage 3 (severe) HD (BP - 160-179/100-109 and ≥180/≥110 mm Hg, respectively) was practically the same (40.0 and 39.2 %, respectively). Patients with systolic-diastolic HD dominated (90.0 %, n = 108). Patients with isolated systolic and isolated diastolic HD were much less common (7.5 %, n = 9 and 2.5 %, n = 3, respectively) in the general population of HD patients.

The study patients with functional class II and III angina were equally common (41.7 %, n = 925 and 58.3 %, n = 35). Patients with severe angina (functional class IV) were not included in the study.

According to the inclusion criteria, the study involved HD patients with (n=30) and without (n = 30) frequent (>30 episodes of extrasystoles in any hour of the study) symptomatic ventricular extrasystoles, as proven by Holter monitoring. Only 20.0 % (n = 12) of the patients had persistent sensations of arrhythmia, while the vast majority (80.0 %, n = 48) experienced episodical arrhythmia in the form of extrasystolic attacks of varying duration.

According to the developed design, the study involved patients with stages B and C heart failure (HF) according to the Heart Failure Society of America (HFSA), with the preserved ejection fraction (EF) (EF > 50.0 % according to echocardiography results), I-II functional class according to the New York Heart Association (NYHA) and M. D. Strazhesko - V. H. Vasylenko stage 1 HF patients (European Society of Cardiology (ESC) Recommendations, 2023 [10] and All-Ukrainian Association of Cardiologists of Ukraine for Diagnosis, Treatment and Prevention of Chronic HF, 2024 [6]).

HFSA stage C HF patients significantly prevailed over stage B chronic HF, M. D. Strazhesko - V. H. Vasylenko stage 1 HF patients (64.2 %, n = 77 versus 35.8 %, n = 43); all patients had an intact EF phenotype.

We considered inappropriate to diagnose the functional class of HF patients since half (50.0 %) of the examined subjects were diagnosed with stable angina pectoris of II-III functional class. Therefore, the NYHA functional class was assessed only in the cohort of non-CCI patients (n = 60). The majority of patients (70.0 %, n = 42) reported no limitations of daily physical activity (functional class 0). 16.7 % (n = 10) of patients reported limitations of physical activity associated with extreme or high loads (functional class I), and even smaller number of patients (13.3 %, n = 8) reported them in usual physical loads (functional class II). NYHA FC 0 patients significantly prevailed among HD patients without concomitant CCI.

All examined patients received RAAS blockers as antihypertensive medicines: Angiotensin-converting enzyme inhibitors (ACEI) and Angiotensin II receptor blockers (sartans) for 68.3 % (n = 82) and 31.7 % (n = 38), accordingly. 83.3 % (n = 100) of patients used thiazide/thiazide-like diuretics, more often in fixed combinations with RAAS blockers, while 60.8 % (n = 73) and 56.7 % (n = 68) of patients administered calcium channel blockers and beta-blockers, respectively. A fairly high percentage of examined patients at the outpatient stage used prognosis-modifying medicines, such as antiplatelet agents and antilipidemics in 84.2 % (n = 101) and 81.7 % (98) of cases, accordingly.

Most patients (68.3 %, n = 82) used three medicines for antihypertensive purposes, much less patients (16.7 %, n = 20) used two medicines to control BP, even less often - four (10.8 %, n = 13) and more than four (4.2 %, n = 5) antihypertensive medicines, respectively.

All patients examined at the outpatient stage received prescribed combined antihypertensive therapy before their inclusion in the study. The results of efficacy assessment over the last three months showed that only 26.7 % (n = 32) of the patients achieved the target BP (<140/<90 mm Hg) for most of a day (controlled HD), while the majority of patients (73.3 %, n = 68) presented with uncontrolled BP exceeding the target figure (uncontrolled HD).

Taking into account the diagnosis of concomitant CCI and frequent ventricular extrasystoles, the study was divided into four separate groups: 1-st one (n = 30, mean age 52.1 ± 11.1) consisting of HD patients without concomitant CCI and ventricular extrasystoles, 2-nd one (n = 30, mean age 53.9 ± 7.7) included HD patients with frequent ventricular extrasystoles, 3-rd group (n = 30, mean age 61.7 ± 7.5) involved HD patients with concomitant CCI, and the 4-th group (n = 30, mean age 61.6 ± 8.1) consisted of HD patients with concomitant CCI and frequent ventricular extrasystoles.

The ethylenediaminetetraacetic acid (EDTA) plasma aldosterone concentration (blood collected in EDTA tubes) was measured by enzyme-linked immunosorbent assay (ELISA) using a commercial kit "Aldosterone ELISA" (Dia Metra, Italy) according to the manufacturer's instructions, as 50.0 µl of standard solution (with known aldosterone concentrations – 0.0; 20.0; 80.0; 300.0; 800.0; 2000.0 pg/ml), control samples and blood plasma samples were placed to the wells of plates, where antibodies to aldosterone were adsorbed, after which 100.0 µl of conjugate (aldosterone conjugated with horseradish peroxidase) was added and incubated for 1 hour at 37.0 °C. The wells were washed three times to remove excessive unbound reagents, after which 100.0 µl of chromogen - tetramethylbenzidine (TMB substrate) - was added and incubated for 20.0 min at 22.0-28.0 °C. The reaction stopped with 100.0 µl of stop solution and photometered at 450.0 nm (differential filter 630.0 nm) using automatic STAT FAX 303/PLUS analyzer.

The obtained results were statistically processed by variational statistics methods using Microsoft Excel (2019) and Statistica 12.0 (Statsoft, USA). The values were presented as n (%) - absolute number (percentage) and M±σ - mean value ± standard deviation of the mean.

Given the vast variety of comparisons, the obtained results are descriptive in nature, therefore the C. E. Bonferroni correction was not used in the study.

Quantitative values were presented as median and interquartile range (25-th and 75-th percentiles) because of abnormal distribution of W-test sample indicators (S. S. Shapiro - M. B. Wilk test). Relative values reflecting the frequency of a parameter in the sample were presented in percentage form (%). Intergroup reliability of the quantitative results was determined by W. H. Kruskal - W. A. Wallis ANOVA & Median Test (four groups of 30 patients each) and by H. B. Mann - D. R. Whitney U-test (two groups of 60 patients each), and of the relative values (%) – by the χ^2 criterion for independent samples.

The study protocol was developed taking into account the ethical standards of the 1975 Declaration of Helsinki (1983 Revision) and was approved by the Ethics Committee of the National Pirogov Memorial Medical University (Minutes No. 8 dated October 5, 2017).

Results and discussion. We used the method of variational statistics to find out that plasma aldosterone concentration in the total cohort of patients (n = 120) varied from 42.8 to 285.0 pg/ml, with an average of 158.1 ± 55.5 pg/ml. Due to abnormal distribution of the indicator in the sample calculated by the S. S. Shapiro - M. B. Wilk test (W = 0.92, p = 0.04), the results were presented as median and interquartile range (25-th - 75-th percentiles), 152.5 pg/ml and 116.5 - 204.5 pg/ml, respectively. For analytical comparison, the aldosterone result was dichotomized around the median. The rounded median value (153.0 pg/ml) was taken to distinguish groups with relatively small (≤153.0 pg/ml) and relatively large marker content (> 153.0 pg/ml) in the examined cohort of patients (hereinafter RSC and RLC).

The results of the study show that the plasma aldosterone concentration in 50.0 %, 25.0 %, and remaining 25.0 % of patients was within the range of 116.5-204.5 pg/ml, less than 116.5 pg/ml and over 204.5 pg/ml, respectively.

Analysis of plasma aldosterone concentration in patients of different clinical groups (Fig. 1) showed a significant increase in the index in groups 3 and 4 compared to group 1 (162.0 and 195.0 vs. 125.5 pg/ml, p = 0.03 and < 0.0001, respectively), and in group 4 compared to group 2 (195.0 vs. 140.5 pg/ml, p = 0.02).

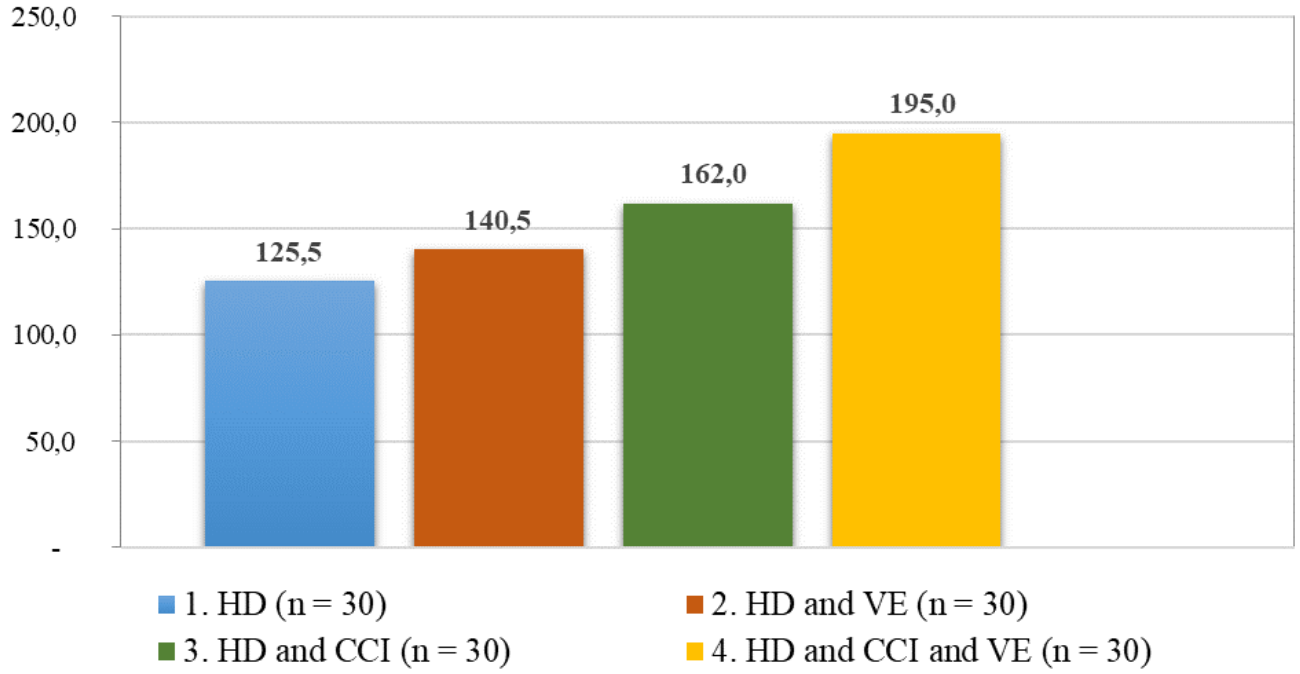

Fig. 1. Variations in aldosterone concentration in patients of different clinical groups (median, 25-th and 75-th percentiles).

Note: Intergroup reliability of results was determined by W. H. Kruskal - W. A. Wallis ANOVA & Median Test: p_{1-2} = 0.43; p_{1-3} = 0.03; p_{1-4} < 0.0001; p_{2-3} = 1.0; p_{2-4} = 0 .02; p_{3-4} = 0.41.

The presented results of the study demonstrate, on the one hand, that significantly higher aldosterone plasma levels were recorded in groups with concomitant CCI and, on the other hand, absence of changes in the marker level in groups with frequent ventricular extrasystoles (absence of significant changes between groups 1 and 2 and 3 and 4).

The distribution of the selected gradations of plasma aldosterone concentration (RSC and RLC) in different groups (Fig. 2) confirms the pattern described above.

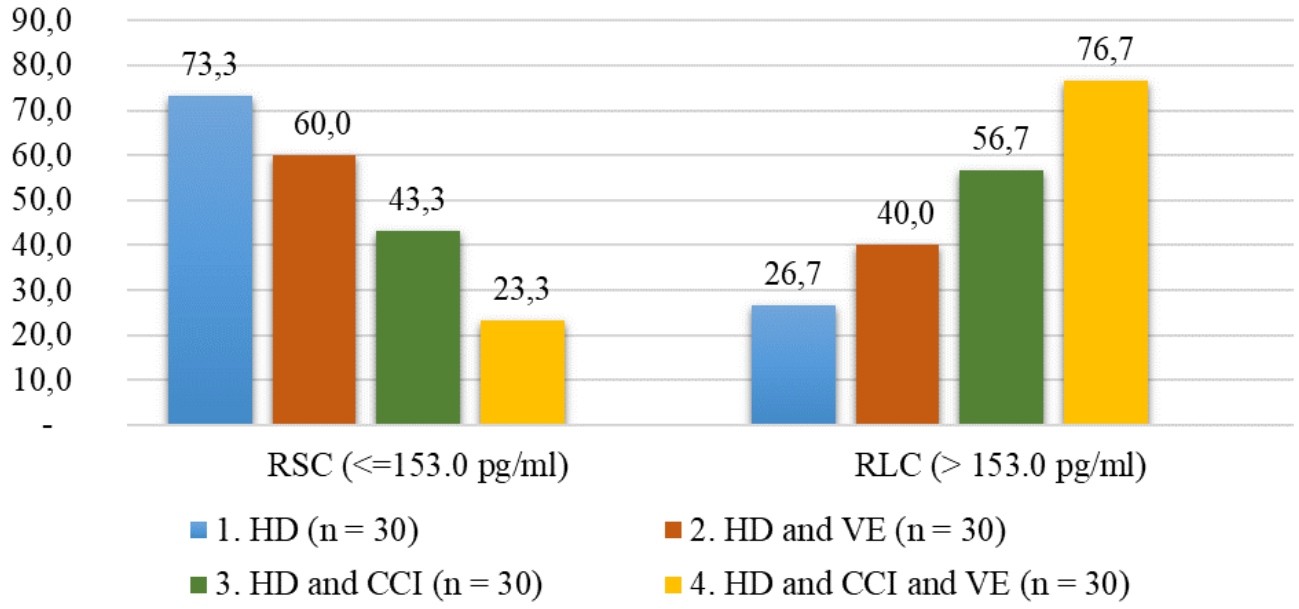

Fig. 2. Gradation of aldosterone concentration in patients of different clinical groups.

Note: The intergroup statistical reliability of the results was determined by e χ^2 criterion for independent samples: $p_{1-2}=0.27$; $p_{1-3}=0.02$; $p_{1-4}=0.0001$; $p_{2-3}=0.20$; $p_{2-4}=0.004$; $p_{3-4}=0.10$.

Thus, aldosterone RSC was significantly more frequently determined in patients of group 1 compared to groups 3 and 4 (73.3 % vs. 43.3 and 23.3 %, $p = 0.02$ and 0.0001, respectively), and in patients of group 2 compared to group 4 (60.0 % vs. 23.3 %, $p = 0.004$).

Aldosterone RLC was significantly more frequently determined in patients of groups 3 and 4 compared to group 1 (76.7 and 56.7 % vs. 26.7 %, $p = 0.02$ and 0.0001, respectively), and in patients of group 4 compared to group 2 (76.7 vs. 40.0 %, $p = 0.004$). Thus, a higher aldosterone concentration in HD patients was determined in association with concomitant CCI, while such pattern was not common with groups with concomitant frequent ventricular extrasystoles. See the analysis of dependence of aldosterone level on various clinical characteristics in the Table 1 below.

Table 1

Aldosterone concentration (pg/ml) in the total cohort of patients depending on various clinical indicators (n; median (pg/ml); 25-th - 75-th percentiles)

Description	Number of patients	Median, pg/ml	25th-75th percentiles
1	2	3	4
Sex			
1. Women	34	179.5	132.0-203.0
2. Men	86	147.0	108.0-211.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2}=0.11$		
WHO age classification			
1. Young age (below 44)	15	77.7	59.7-90.1
2. Average age (45-59)	54	149.0	112.0-208.0
3. Elderly age (60-74)	51	182.0	136.0-217.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2}<0.0001$; $p_{1-3}<0.0001$; $p_{2-3}=0.24$		
Hypertension history			
1. Below 10 years	73	132.0	100.0-176.0
2. From 10 to 15 years	29	194.0	155.0-217.0
3. Over 15 years	18	184.0	140.0-227.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2}=0.0002$; $p_{1-3}=0.007$; $p_{2-3}=1.00$		
Arrhythmia history			
1-5 years	46	163.0	125.0-217.0
2. > 5 years	14	203.0	149.0-224.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2}=0.37$		
Patients' BMI			
1. Normal body weight (BMI 20.0-25.0 kg/m^2)	11	125.0	112.0-131.0
2. Excessive body weight (BMI 25.0-30.0 kg/m^2)	50	147.5	112.0-201.0
3. Constitutional-alimentary obesity (BMI > 30.0 kg/m^2)	59	177.0	127.0-215.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2}=0.65$; $p_{1-3}=0.06$; $p_{2-3}=0.22$		
HD stage			
1. 1-st (mild HD)	25	180.0	130.0-215.0

Contin of the Table 1

Contin of the Table 1

1	2	3	4
2. 2-st (moderate HD)	48	142.0	117.0-203.5
3. 3-rd (severe HD)	47	149.0	112.0-194.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2} = 0.54$; $p_{1-3} = 0.43$; $p_{2-3} = 1.00$		
Hemodynamic HD variants			
1. Systolic-diastolic HD	108	149.5	112.0-203.5
2. Isolated systolic HD	9	182.0	137.0-223.0
3. Isolated diastolic HD	3	148.0	113.0-164.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2} = 0.68$; $p_{1-3} = 1.00$; $p_{2-3} = 0.97$		
Concomitant CCI			
1. CCI diagnosed	60	183.0	134.5-224.5
2. CCI not diagnosed	60	132.0	100.5-174.0
p H. B. Mann – D. R. Whitney U test	$p_{1-2} = 0.003$		
Angina functional class			
1. II functional class	25	167.0	133.0-217.0
2. III functional class	35	186.0	137.0-235.0
p H. B. Mann – D. R. Whitney U test	$p_{1-2} = 0.34$		
Frequent ventricular extrasystoles			
1. Frequent ventricular extrasystoles diagnosed	60	183.0	134.5-224.5
2. Frequent ventricular extrasystoles not diagnosed	60	132.0	100.5-174.0
p H. B. Mann – D. R. Whitney U test	$p_{1-2} < 0.0001$		
Ventricular extrasystoles variant			
1. Allorhythmia	12	167.5	125.0-239.0
2. Episodic ventricular extrasystoles	48	177.0	136.0-223.0
p H. B. Mann – D. R. Whitney U test	$p_{1-2} = 0.42$		
HFSA HF stage			
1. Stage B	43	132.0	96.6-180.0
2. Stage C	77	169.0	128.0-215.0
p H. B. Mann – D. R. Whitney U test	$p_{1-2} = 0.002$		
NYHA HF functional class			
1. 0 functional class	42	132.0	112.0-171.0
2. I functional class HF	10	135.5	61.4-189.0
3. II functional class HF	8	118.0	84.8-163.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2} = 1.00$; $p_{1-3} = 0.92$; $p_{2-3} = 1.00$		
Use of certain classes of antihypertensive medicines			
1. ACEI	82	140.5	112.0-189.0
2. Not used	38	178.5	130.0-227.0
p H. B. Mann – D. R. Whitney U test	$p_{1-2} = 0.02$		
1. Sartans	38	177.0	130.0-225.0

End of the Table 1

1	2	3	4
2. Not used	82	141.0	112.0-194.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2} = 0.05$		
1. Beta-blockers	68	155.0	111.0-208.0
2. Not used	52	150.0	125.0-199.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2} = 0.95$		
1. Thiazide diuretics	100	156.0	125.0-211.0
2. Not used	20	130.0	90.1-171.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2} = 0.06$		
1. CC blockers	73	149.5	122.5-202.0
2. Not used	47	159.0	112.5-210.0
p H. B. Mann – D. B. Whitney U tes	$p_{1-2} = 0.72$		
1. Antiplatelet medicines	101	166.0	131.0-211.0
2. Not used	19	90.1	70.0-125.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2} < 0.0001$		
1. Statins	98	167.0	132.0-211.0
2. Not used	22	92.1	72.0-125.0
p H. B. Mann – D. B. Whitney U test	$p_{1-2} < 0.0001$		
Number of antihypertensive medicines administered by out-patients			
1. Two medicines	20	132.5	93.3-180.0
2. Three medicines	82	152.5	125.0-203.0
3. Four medicines	13	157.0	121.0-177.0
4. Morethan four medicines	5	227.0	204.0-238.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2} = 0.87$; $p_{1-3} = 1.00$; $p_{1-4} = 0.03$; $p_{2-3} = 1.00$; $p_{2-4} = 0.04$; $p_{3-4} = 0.08$		
Efficacy of antihypertensive out-patient treatment			
1. Controlled HD	32	134.0	99.3-207.5
2. Uncontrolled HD	68	162.0	128.5-207.0
3. Untreated	20	147.5	109.0-183.0
p W. H. Kruskal – W. A. Wallis ANOVA test	$p_{1-2} = 0.57$; $p_{1-3} = 1.00$; $p_{2-3} = 0.88$		

The main portion of the examined patients were men, which demonstrated gender heterogeneity ($\chi^2 = 46.1$; $p < 0.0001$) of the examined patients and a significant predominance of males. The ratio of men to women was 2.5 to 1.0. However, no statistically significant ($p = 0.11$) difference in plasma aldosterone concentration of patients of different genders was determined (only a disposition).

We found a dependence of aldosterone level on age, as middle-aged and elderly patients had significantly higher concentration than young patients (149.0 and 182.0 versus 77.7 pg/ml, $p < 0.0001$ and < 0.0001, respectively). However, we did not determine any statistically significant ($p = 0.24$) difference in the aldosterone concentration in middle-aged and elderly patients (only a disposition). The dependence of plasma aldosterone concentration on the HD history was also found. Patients

with HD history from 10 to 15 years and more than 15 years had aldosterone concentration significantly higher compared to those with a shorter hypertension history (below 10 years) (194.0 and 184.0 vs. 132.0 pg/ml, $p = 0.0002$ and 0.007, respectively).

One study demonstrated an association of high plasma aldosterone levels with high BP and more severe disturbances in daily BP and heart rate regulation in young and middle-aged stage II HD patients [5].

Patients with constitutional alimentary obesity (BMI > 30.0 kg/m^2) demonstrated only a trend towards a significant increase in plasma aldosterone concentration compared to patients with normal body weight (BMI 20.0-25.0 kg/m^2) (177.0 vs. 125.0 pg/ml, $p = 0.06$), which can be explained by the small number of patients in the normal body weight group reducing the statistical significance of the difference in results.

The analysis confirmed an increase of aldosterone concentration in HD patients with concomitant CCI (183.0 in the group with CCI versus 132.0 pg/ml in patients without CCI, $p = 0.003$).

We obtained a statistically significant dependence of aldosterone concentration on HFSA HF stage (169.0 for stage C versus 132.0 pg/ml for stage B, $p = 0.002$) with no difference in the marker level for different NYHA functional classes ($p > 0.90$).

A highly statistically significant dependence of aldosterone level on diagnosed frequent ventricular extrasystoles was determined in the general cohort of patients, while no such a dependence was observed in clinical groups (Fig. 1 and 2). Thus, HD patients with frequent ventricular extrasystoles demonstrated significantly higher aldosterone concentration than those without FVE (183.0 versus 132.0 pg/ml, $p < 0.0001$). This statistical dissonance is largely preconditioned by a different number of patients taken for different tests and fundamentally different statistical methods: in the first case, four groups of 30 patients each (W. H. Kruskal - W. A. Wallis ANOVA test), in the second case, two groups of 60 patients each (H. B. Mann - D. B. Whitney U-test). The difference between multivariate and simple groupings may be explained by different statistical power of samples.

V. P. Ivanov and T. D. Danilevych [1] found an association between relatively high aldosterone concentrations (>184.0 pg/ml) and high mean daily heart rate and circadian index; elevated frequency of atrial fibrillation attacks, their number and total duration per day; increased frequency of ventricular extrasystoles, both individual and group, in stage II HD patients with frequently recurring atrial fibrillation.

Analysis of the dependence of aldosterone concentration on antihypertensive therapy received by patients at outpatient stage showed the higher level in the group of patients who used more than four antihypertensive medicines compared to the groups that used two, three and four medicines (227.0 vs. 132.5, 152.5 and 157.0 pg/ml, $p = 0.03$, 0.04 and 0.08, respectively). The results of the study confirm the fact of high plasma aldosterone concentration in patients with resistant HD using a large number of antihypertensive medicines for BP control. The aldosterone concentration was significantly higher in the group of patients not taking ACEI inhibitors (178.5 vs. 140.5 pg/ml, $p = 0.02$), which can be explained by the blocking effect of ACE on the renin-angiotensin-aldosterone system, which is known to play a leading role in the HD pathogenesis. It is quite difficult to explain the higher aldosterone level in the group of patients administered sartans (177.0 vs. 141.0 pg/ml, $p = 0.05$), thiazide and thiazide-like diuretics (156.0 vs. 130.0 pg/ml, trend towards significance - $p = 0.06$), antiplatelet medicines (166.0 vs. 90.1 pg/ml, $p < 0.0001$), and statins (167.0 vs. 92.1 pg/ml, $p < 0.0001$). It is clear that antiplatelet medicines and statins were administered in patients with a high probability of various cardiovascular events, in whom the increase of aldosterone concentration, in our opinion, was preconditioned by special aspects of etiological factors and comorbidity rather than the effect of medicines. The analysis of associations with medicine management is descriptive and does not exclude the influence of a combination of factors.

Conclusions. We established that stage II hypertension patients with/without concomitant chronic coronary artery disease and frequent ventricular extrasystoles (n = 120) had the average plasma aldosterone concentration 158.1 ± 55.5 pg/ml (median - 152.5, interquartile range 116.5 and 204.5 pg/ml, respectively). The rounded value of the median indicator (153.0 pg/ml) was taken to distinguish groups with relatively low (≤ 153.0 pg/ml) and a relatively high concentration of the marker (> 153.0 pg/ml) in the total cohort of patients.

The obtained data suggest that significantly higher plasma aldosterone concentration was found in middle-aged and elderly patients compared to young patients, in case of hypertension history over 10 years, in patients with constitutional-alimentary obesity (body mass index > 30.0 kg/m^2), in groups of patients with concomitant chronic coronary disease, in patients diagnosed concomitant chronic coronary disease and frequent ventricular extrasystoles in the general sample of patients with stage C disease according to the Heart Failure Society of America.

The association between aldosterone concentration and administration of such classes of medicines as Angiotensin-Converting Enzyme inhibitors, sartans, thiazide and thiazide-like diuretics, antiplatelet and antilipid agents, and the number of antihypertensive medicines was found.

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Conflict of interests
The author declare no conflict of interests.

The Blood Plasma Aldosterone Concentration in Stage II Hypertension Patients with Comorbid Chronic Coronary Artery Disease, Frequent Ventricular Extrasystoles and Different Clinical Indicators

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Introduction. Hypertensive disease (HD) remains a leading cause of death worldwide. Aldosterone is involved in the regulation of blood pressure, has proarrhythmic effects, and can induce myocardial fibrosis, contributing to myocardial electrical instability.

The aim of the study. To assess the plasma aldosterone concentration variations in stage II hypertension patients with comorbid chronic coronary artery disease, frequent ventricular extrasystoles and different clinical indicators.

Materials and methods. We examined 120 stage II HD patients (34 (28.3 %) women and 86 (71.7 %) men aged 34 to 74 (mean age of the examined patients - 57.3 ± 0.9 years)) with/and without concomitant chronic coronary insufficiency (CCI), frequent ventricular extrasystoles treated at the municipal institution "Vinnytsia Regional Medical and Diagnostic Center of Cardiovascular Pathology". The study was a randomized one with preliminary stratification by stage II HD diagnosis.

The ethylenediaminetetraacetic acid (EDTA) plasma aldosterone concentration (blood collected in EDTA tubes) was measured by enzyme-linked immunosorbent assay (ELISA) using a commercial kit "Aldosterone ELISA" (Dia Metra, Italy) according to the manufacturer's instructions.

The disease history was: HD - 8.6 ± 6.0, CCI - 4.8 ± 2.6, and arrhythmia - 3.5 ± 3.0 years. The majority (60.8 %, n = 73) of the examined patients had short hypertensive anamnesis not exceeding 10 years. 24.2 % (n = 29) of the patients had the history ranging from 10 to 15 years and only 15.0 % (n = 18) of the subjects had the history exceeding 15 years.

Taking into account the diagnosis of concomitant CCI and frequent ventricular extrasystoles, the study was divided into four separate groups: 1-st one (n=30, mean age 52.1 ± 11.1) consisting of HD patients without concomitant CCI and ventricular extrasystoles, 2-nd one (n = 30, mean age 53.9 ± 7.7) included HD patients with frequent ventricular extrasystoles, 3-rd group (n = 30, mean age 61.7 ± 7.5) involved HD patients with concomitant CCI, and the 4-th group (n = 30, mean age 61.6 ± 8.1) consisted of HD patients with concomitant CCI and frequent ventricular extrasystoles.

The obtained results were statistically processed by variational statistics methods using Microsoft Excel (2019) and Statistica 12.0 (Statsoft, USA). The values were presented as n (%) - absolute number (percentage) and M ± σ - mean value ± standard deviation of the mean.

Results. We used the method of variational statistics to find out that plasma aldosterone concentration in the total cohort of patients (n = 120) varied from 42.8 to 285.0 pg/ml, with an average of 158.1 ± 55.5 pg/ml. Due to abnormal distribution of the indicator in the sample calculated by the S. S. Shapiro-M. V. Wilk test (W = 0.92, p = 0.04), the results were presented as median and interquartile range (25-th - 75-th percentiles), 152.5 pg/ml and 116.5-204.5 pg/ml, respectively. For analytical comparison, the aldosterone result was dichotomized around the median. The rounded median value (153.0 pg/ml) was taken to distinguish groups with relatively small (≤153.0 pg/ml) and relatively large marker content (>153.0 pg/ml) in the examined cohort of patients (hereinafter RSC and RLC).

The results of the study show that the plasma aldosterone concentration in 50.0 %, 25.0 %, and remaining 25.0 % of patients was within the range of 116.5-204.5 pg/ml, less than 116.5 pg/ml and over 204.5 pg/ml, respectively.

Conclusions. We established that stage II hypertension patients with / without concomitant chronic coronary disease and frequent ventricular extrasystoles (n = 120) had the average plasma aldosterone concentration 158.1 ± 55.5 pg/ml (median - 152.5, interquartile range 116.5 and 204.5 pg/ml, respectively). The rounded value of the median indicator (153.0 pg/ml) was taken to distinguish groups with relatively low (≤153.0 pg/ml) and a relatively high concentration of the marker (>153.0 pg/ml) in the total cohort of patients.

The obtained data suggest that significantly higher plasma aldosterone concentration was found in middle-aged and elderly patients compared to young patients, in case of hypertension history over 10 years, in patients with constitutional-alimentary obesity (body mass index >30.0 kg/m^2), in groups of patients with concomitant chronic coronary artery disease, in patients diagnosed concomitant chronic coronary artery disease and frequent ventricular extrasystoles in the general sample of patients with stage C disease according to the Heart Failure Society of America.

The association between aldosterone concentration and administration of such classes of medicines as Angiotensin-converting enzyme inhibitors, sartans, thiazide and thiazide-like diuretics, antiplatelet and antilipid agents, and the number of antihypertensive medicines was found.

Keywords: aldosterone, hypertension, chronic coronary artery disease, ventricular extrasystoles.

Уміст альдостерону в плазмі крови у пацієнтів із гіпертонічною хворобою II стадії, його зміни за наявности коморбідних хронічної коронарної хвороби і частої шлуночкової екстрасистолії, а також різних клінічних показників

Ю. Ю. Маслюк

Вступ. Гіпертонічна хвороба (ГХ) є основною причиною смертности у всьому світі. Альдостерон бере участь у регуляції артерійного тиску, крім цього, має аритмогенний ефект і може спричинити фіброз міокарда, що призводить до електричної нестабільности міокарда.

Мета. Дослідити вміст альдостерону в плазмі крови у пацієнтів із гіпертонічною хворобою II стадії і його зміни за наявности коморбідних хронічної коронарної хвороби та частої шлуночкової екстрасистолії, а також різних клінічних показників.

Матеріяли й методи. Обстежено 120 пацієнтів (34 (28,3 %) жінки і 86 (71,7 %)) чоловіків віком від 34 до 74 (середній вік обстежених хворих – 57,3 ± 0,9 року)), які лікувалися на базі комунального закладу «Вінницький регіональний клінічний лікувально-діагностичний центр серцево-судинної патології», із ГХ II стадії з/ і без супутньої хронічної коронарної хвороби (ХКХ) з/ і без частої шлуночкової екстрасистолії (ШЕ). Дослідження проводили в рандомізований спосіб, із попередньою стратифікацією за наявности ГХ II стадії.

ГХ II стадії визначали за рекомендаціями Європейського товариства гіпертензії, (2023), а також Клінічним протоколом первинної і спеціялізованої медичної допомоги пацієнтам з ГХ, (2024). Супутню ХКХ, яка була необов'язковою умовою включення, діягностували інструментально за допомогою стрес-тестів і/або коронаровентрикулографії і включали лише стенокардію навантаження II-III функційних класів згідно з рекомендаціями Європейського товариства кардіологів, (2024) та уніфікованого клінічного протоколу «Стабільна ішемічна хвороба серця». Визначено порушення серцевого ритму за допомогою холтерівського моніторування електрокардіограми. Вміст альдостерону в плазмі крови, зібраній у пробірки з етилендіямінтетраоцтовою кислотою (ЕДТА) визначали імуноферментним методом з використанням комерційного набору «Альдостерон ІФА» (DiaMetra, Італія) відповідно до інструкції фірми-виробника.

Тривалість анамнезів становила: ГХ – 8,6 ± 6,0, ХКХ – 4,8 ± 2,6, аритмологічного – 3,5 ± 3,0 років.

Із урахуванням наявности або відсутности супутньої ХКХ і частої ШЕ виділено чотири групи пацієнтів: 1-ша (n = 30, середній вік 52,1 ± 11,1 року) – пацієнти з ГХ без супутніх ХКХ і ШЕ, 2-га (n = 30, середній вік 53,9 ± 7,7 року) – пацієнти з ГХ і частою ШЕ, 3-тя (n = 30, середній вік 61,7 ± 7,5 року) – пацієнти з ГХ і супутньою ХКХ, 4-та (n = 30, середній вік 61,6 ± 8,1 року) – пацієнти з ГХ і супутніми ХКХ та частою ШЕ.

Результати. Визначено, що вміст альдостерону в плазмі крови у загальній когорті пацієнтів (n=120) міститься в діяпазоні від 42,8 до 285,0 пг/мл і в середньому становить 158,1 ± 55,5 пг/мл. У зв'язку з ненормальним розподілом показника у вибірці, що визначено за W-test (критерій S. S. Shapiro – M. B. Wilk) – W = 0,92, p = 0,04, результати подані у вигляді медіяни та інтерквартильного розмаху (25-й і 75-й персентилі). Медіяна показника становить 152,5 пг/мл, інтерквартильний розмах – 116,5 і 204,5 пг/мл. Показник альдостерону дихотомізовано за медіяною. Заокруглене значення медіяни (153,0 пг/мл) взято для виокремлення груп із відносно малим (≤153,0 пг/мл) і відносно великим умістом маркера (>153,0 пг/мл) у загальній когорті пацієнтів.

Відносно малий уміст альдостерону значно частіше визначали у пацієнтів 1-ї групи, порівняно з 3-ю і 4-ю (73,3 % проти 43,3 і 23,3 %, p = 0,02 і 0,0001 відповідно), та у пацієнтів 2-ї групи, порівняно з 4-ю (60,0 % проти 23,3 %, p = 0,004).

Відносно великий уміст альдостерону значно частіше реєстрували у пацієнтів 3-ї і 4-ї груп, порівняно з 1-ю (76,7 і 56,7 % проти 26,7 %, p = 0,02 і 0,0001 відповідно), та у пацієнтів 4-ї групи, порівняно з 2-ю (76,7 % проти 40,0 %, p = 0,004). Отже, більший уміст альдостерону у пацієнтів із ГХ визначали за наявности супутньої ХКХ, а в групах із частою супутньою ШЕ такої закономірности не фіксували.

Висновки. Визначено, що у пацієнтів із гіпертонічною хворобою II стадії з/ і без супутньої хронічної коронарної хвороби і частої шлуночкової екстрасистолії (n = 120) середнє значення альдостерону в плазмі крови становить 158,1 ± 55,5 пг/мл (медіяна показника 152,5, інтерквартильний розмах 116,5 і 204,5 пг/мл відповідно). Заокруглене значення медіяни показника (153,0 пг/мл) взято для виокремлення груп із відносно малим (≤153,0 пг/мл) і відносно великим умістом маркера (>153,0 пг/мл) у загальній когорті пацієнтів.

Значно більший уміст альдостерону в плазмі крови визначається у пацієнтів середнього і похилого віку, ніж у пацієнтів молодого віку; у разі тривалости анамнезу гіпертонічної хвороби понад 10 років; за наявности конституційно-аліментарного ожиріння (індекс маси тіла >30,0 кг/м^2); у групах пацієнтів із супутньою хронічною коронарною хворобою; за наявности супутньої хронічної коронарної хвороби і частої шлуночкової екстрасистоли у загальній вибірці хворих і за наявности стадії C за Heart Failure Society of America.

Визначено асоціяції, що вміст альдостерону залежить від застосування таких класів лікарських засобів, як інгібітори ангіотензинперетворювального ферменту, сартани, тіязидні й тіязидоподібні діуретики, антитромбоцитні й антиліпідні засоби, та кількости застосованих антигіпертензивних лікарських засобів.

Ключові слова: альдостерон, гіпертонічна хвороба, хронічна коронарна хвороба, шлуночкова екстрасистолія.

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