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QUANTITATIVE AND QUALITATIVE BLOOD PRESSURE CLUSTERS IN PATIENTS OF TRUSKAVETS' SPA AND THEIR HEMODYNAMIC ACCOMPANIMENT

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Abstract

Background. The influence of balneotherapy at the Truskavets' spa on the blood pressure (BP) of his patients is still not in the focus of researchers. Therefore, we initiated the project "Neuroendocrine-immune and metabolic mechanisms of the effect of balneotherapy on BP". The first swallow of the project is the analysis of a condition of BP and its hemodynamic support of profile patients of a resort. **Materials and methods.** Under an observations were 44 patients with chronic pyelonephritis and cholecystitis in the phase of remission. Testing was performed twice - on admission and after 7-10 days of standard balneotherapy. The main object of the study was BP (tonometer "Omron M4-I", Netherlands). Simultaneously the parameters of hemodynamics were determined (echocamera "Toshiba-140", Japan). **Results.** The optimal level of systolic BP (range 120÷129 mmHg) stated in 18,2% of cases only, high norm (130÷139 mmHg) in 14,8%, arterial hypertension (AH) I (140÷160 mmHg) – in 39,8%, AH II (over 160 mmHg) in 12,5%, however, in 14,8% of cases the BP was lower than 120 mmHg. In order to identify among the registered parameters of hemodynamics, those for which the BP clusters differ from each other, a discriminant analysis was performed. The program forward stepwise included in the discriminant model 13 parameters out of 17. The most informative among them: contractility index of left ventricle, heart work per minute, ejection fraction and time as well as end-systolic volume. **Conclusion.** Profile patients of

Truskavets' spa are characterized by a wide range of blood pressure - from low norm to arterial hypertension II that correspond to the hemodynamics parameters.

Key words: blood pressure, hemodynamics, discriminant analysis, Truskavets' spa.

INTRODUCTION

The influence of balneotherapy at the Truskavets' spa on the blood pressure of his patients is still not in the focus of researchers, giving way as the object of study first urinary and digestive systems, and then - the neuroendocrine-immune complex. Known publications are few and fragmentary [4,5,7-9,11,12,15-17]. Therefore, we initiated the project "Neuroendocrine-immune and metabolic mechanisms of the effect of balneotherapy on blood pressure". The first swallow of the project is the analysis of a condition of blood pressure and its hemodynamic support of profile patients of a resort.

MATERIALS AND METHODS

Under an observations were 34 males and 10 females by age 24-76 years with chronic pyelonephritis and cholecystitis in the phase of remission. Testing was performed twice - on admission and after 7-10 days of standard balneotherapy (drinking of bioactive water Naftussya, applications of ozokerite, mineral pools).

The main object of the study was blood pressure (BP). Systolic (Ps) and diastolic (Pd) BP as well as heart rate (HR) was measured (by tonometer "Omron M4-I", Netherlands) in a sitting position three times in a row. After that, the parameters of hemodynamics were determined (by echocamera "Toshiba-140", Japan): ejection time (ET), end-diastolic (EDV) and end-systolic (ESV) volumes of left ventricle with the following ejection fraction (EF), general peripheral resistance of vessels (GPRV), cardiac output (CO), heart work per minute (HWM) calculation by classic formulas [1,8,9,14]:

$$EF = 100 \cdot (EDV - ESV) / EDV;$$

$$GPRV = 80 \cdot (0,67 \cdot Pd + 0,33 \cdot Ps) / HR \cdot (EDV - ESV);$$

$$CO = (EDV - ESV) \cdot HR;$$

$$HWM = 0,1332 \cdot 1,055 \cdot (0,67 \cdot Pd + 0,33 \cdot Ps) \cdot (EDV - ESV) \cdot HR.$$

In addition, we calculated the contractility index of left ventricle by Sagawa K [10]:

$$SCI = Ps / ESV$$

as well as by Ruzhylo&Popovych [8,9]:

$$RPCI = 0,1332 \cdot (0,67 \cdot Pd + 0,33 \cdot Ps) \cdot (EDV - ESV) / EDV \cdot ET.$$

Appropriate cardiac output, which is determined by gender, age (A, years), height (H, cm) and body weight (W, kg), was calculated by the formulas [13]:

$$CO \text{ for females} = (9,56 \cdot W + 1,85 \cdot H + 4,67 \cdot A + 65,09) / 281$$

$$CO \text{ for males} = (13,75 \cdot W + 5 \cdot H - 6,75 \cdot A + 66,47) / 281$$

Appropriate ejection time, which is determined by cardiac cycle time (C) calculated by the classic formula: $ET = 0,109 \cdot C + 0,159$.

For statistical analysis used the software package "Statistica 20".

RESULTS AND DISCUSSION

Standards and gradations are still the object of debate [2,6]. If we take the optimal norm of systolic pressure range 120÷129 mmHg, high norm 130÷139, arterial hypertension (AH) I 140÷160, AH II over 160 mmHg and low norm lower 120 mmHg, the quantitative and qualitative characteristics of the observed contingent will be as follows (Fig. 1).

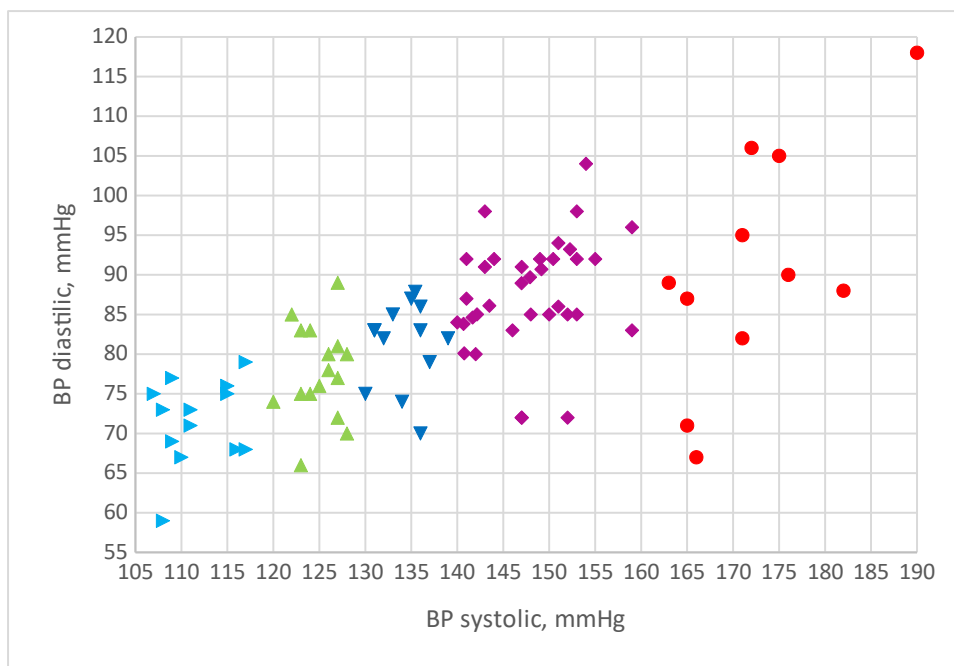


Fig. 1. Diagram of scattering of systolic and diastolic blood pressure of patients of Truskavets' spa

As you can see, the optimal systolic pressure is found only in 18,2% of cases, and in the range of the extended norm fall 47,8% of cases. At the same time in 39,8% of cases AH I was stated, and in 12,5% even AH II. Diastolic pressure is strongly associated with systolic, but not very much ($r=0,67$), so it deserves special attention. For now, we will limit ourselves to stating the different correlation coefficients of both BP parameters with age (0,37 vs 0,18) and sex (-0,19 vs -0,44) (more precisely, with sex-index, when M=1 and F=2) for Ps and Pd, respectively.

By recording BP three times in a row, we noticed that Ps2/Ps1, Ps3/Ps1, Pd2/Pd1, Pd3/Pd1 ratio form at least five patterns that correspond to the parameters of neuroendocrine-immune complex and metabolism (this will be the subject of a separate publication). Therefore, these parameters became the subject of further analysis.

In order to identify among the registered parameters of hemodynamics, those for which the blood pressure clusters differ from each other, a discriminant analysis was performed [3]. The program forward stepwise included in the discriminant model 13 parameters out of 17 (Tables 1 and 2).

Table 1. Discriminant Function Analysis Summary for Hemodynamics Variables, their actual levels for Clusters of Blood Pressure as well as Reference levels and Coefficients of Variability

Step 13, N of vars in model: 13; Grouping: 5 grps; Wilks' Λ : 0,021; approx. $F_{(52)}=9,2$; $p<10^{-6}$

VARIABLES CURRENTLY IN THE MODEL	Clusters of Blood Pressure (n)					Parameters of Wilk's Statistics					Reference (88)	Cv
	AH II (11)	AH I (35)	High N (13)	Norm (16)	Low N (13)	Wilks' Λ	Partial Λ	F-remove (4,7)	p-level	Tolerance		
Blood Pressure Systolic, mmHg	172 2,5	148 0,9	134 0,8	125 0,6	112 1,0	0,093	0,223	61,8	10 ⁻⁶	0,588	125 1	,076
Ejection Time, msec	261 11	275 6	292 6	264 9	303 8	0,025	0,829	3,66	0,009	0,063	252 2	,076
1000•Pd3/Pd1 Ratio	997 21	1023 8	1014 16	996 14	971 10	0,023	0,885	2,30	0,067	0,575		
1000•Ps2/Ps1 Ratio	975 13	922 13	988 29	1000 26	971 16	0,023	0,912	1,72	0,155	0,437		
Blood Pressure Diastolic, mmHg	90,7 4,5	87,6 1,2	81,3 1,5	77,8 1,5	71,5 1,5	0,024	0,878	2,47	0,052	0,201	79 0,5	,054
End-diastolic Vol of Left Ventric, mL	122 9	113 2	132 4	111 4	125 5	0,023	0,888	2,25	0,073	0,041	116 1	,115
Ruzhylo-Popovych Contract Ind, kPa/s	34,7 2,4	32,3 1,0	30,2 0,8	32,5 2,1	26,7 0,7	0,025	0,833	3,56	0,010	0,033	35,8 0,9	,223
Ejection Fraction, %c	66,6 2,2	65,8 1,1	66,2 1,3	62,7 2,3	61,1 2,0	0,024	0,880	2,42	0,056	0,016	67,4 1,4	,189
Heart Rate, bpm	70,6 5,2	70,9 2,1	70,6 2,2	68,7 2,4	70,6 2,8	0,023	0,898	2,01	0,102	0,349	68,4 0,9	,120
Heart Work, kJ/min	99 16	83 5	86 5	70 7	65 5	0,022	0,928	1,37	0,253	0,008	76 2	,269
1000•Ps3/Ps1 Ratio	940 20	934 11	984 17	964 27	953 18	0,023	0,916	1,62	0,179	0,429		
End-systolic Vol of Left Ventricle, mL	39 2	39 1	44 2	42 2	48 1	0,023	0,907	1,83	0,133	0,026	36 1	,247
Cardiac Output, L/min	5,87 0,93	5,46 0,29	6,14 0,37	5,17 0,44	5,40 0,42	0,022	0,941	1,10	0,361	0,009	5,43 0,16	,269

VARIABLES CURRENTLY NOT IN THE MODEL	Clusters of Blood Pressure (n)					Parameters of Wilk's Statistics					Reference (88)	Cv
	AH II (11)	AH I (35)	High N (13)	Norm (16)	Low N (13)	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerance		
Stroke Volume of Left Ventricle, mL	82 9	75 2	87 4	73 4	77 5			0,00	1,000		79 2	,271
Gener Periph Resist Vessels, kPa•s/m ³	18,8 2,0	17,0 0,7	13,3 0,7	16,6 1,9	13,9 1,5	0,020	0,961	0,71	0,586	0,066	16,4 0,7	,415
Sagawa Contractility Ind, mmHg/mL	4,48 0,22	4,04 0,21	3,10 0,14	3,11 0,17	2,37 0,06	0,020	0,957	0,79	0,533	0,115	3,78 0,09	,221
1000•Pd2/Pd1 Ratio	1000 31	1013 11	1001 18	970 16	976 17	0,020	0,947	0,97	0,427	0,377		

Table 2. Summary of Stepwise Analysis for Hemodynamics Variables, ranked by criterion Lambda

Variables currently in the model	F to enter	p-level	Λ	F-value	p-level
Blood Pressure Systolic, mmHg	298	10 ⁻⁶	0,065	298	10 ⁻⁶
Ejection Time, msec	3,39	0,013	0,056	66,2	10 ⁻⁶
Pd3/Pd1 Ratio	2,89	0,027	0,049	38,1	10 ⁻⁶
Ps2/Ps1 Ratio	2,87	0,028	0,043	27,7	10 ⁻⁶
Blood Pressure Diastolic, mmHg	2,07	0,093	0,039	21,9	10 ⁻⁶
End-diastolic Volume of Left Ventricle, mL	2,77	0,033	0,034	18,7	10 ⁻⁶
Ruzhylo-Popovych Contractility Index, kPa/s	1,68	0,162	0,031	16,1	10 ⁻⁶
Ejection Fraction, %c	1,58	0,188	0,029	14,2	10 ⁻⁶
Heart Rate, bpm	1,15	0,340	0,027	12,7	10 ⁻⁶
Heart Work, kJ/min	1,64	0,174	0,025	11,6	10 ⁻⁶
Ps3/Ps1 Ratio	1,25	0,297	0,023	10,7	10 ⁻⁶
End-systolic Volume of Left Ventricle, mL	1,09	0,368	0,022	9,86	10 ⁻⁶
Cardiac Output, L/min	1,11	0,361	0,021	9,17	10 ⁻⁶

Next, the 13-dimensional space of discriminant variables transforms into 4-dimensional space of a canonical roots, which are a linear combination of discriminant variables. The differentiating ability of the root characterizes the canonical correlation coefficient (r^*) as a measure of connection, the degree of dependence between groups (clusters) and a discriminant function. It is for Root 1 0,976 (Wilks' $\Lambda=0,021$; $\chi^2_{(52)}=302$; $p<10^{-6}$), for Root 2 0,586 (Wilks' $\Lambda=0,435$; $\chi^2_{(36)}=65$; $p=0,002$), for Root 3 0,462 (Wilks' $\Lambda=0,662$; $\chi^2_{(22)}=32$; $p=0,075$) and for Root 4 0,397 (Wilks' $\Lambda=0,843$; $\chi^2_{(10)}=13$; $p=0,205$). The first root contains 95,3% of discriminative opportunities, the second 2,5%, the third 1,3%, the last 0,9%.

Table 3 presents raw (actual) and standardized (normalized) coefficients for discriminant variables. The raw coefficient gives information on the absolute contribution of this variable to the value of the discriminative function, whereas standardized coefficients represent the relative contribution of a variable independent of the unit of measurement. They make it possible to identify those variables that make the largest contribution to the discriminatory function value.

Table 3. Standardized and Raw Coefficients and Constants for Hemodynamics Variables

Variables currently in the model	Coefficients			Standardized			Raw		
	Root 1	Root 2	Root 3	Root 1	Root 2	Root 3	Root 1	Root 2	Root 3
Blood Pressure Systolic, mmHg	1,170	-0,163	-0,158	0,241	-0,034	-0,033			
Ejection Time, msec	0,702	-1,788	2,318	0,022	-0,055	0,072			
Pd3/Pd1 Ratio	0,322	0,342	-0,471	6,050	6,434	-8,866			
Ps2/Ps1 Ratio	0,299	-0,202	-0,620	3,687	-2,497	-7,652			
Blood Pressure Diastolic, mmHg	-0,049	1,232	-0,491	-0,006	0,156	-0,062			
End-diastolic Volume of Left Ventricle, mL	1,263	-1,886	-0,076	0,071	-0,106	-0,004			
Ruzhylo-Popovych Contractility Index, kPa/s	1,322	-2,177	2,775	0,193	-0,318	0,405			
Ejection Fraction, %c	-2,204	2,043	-2,320	-0,308	0,285	-0,324			
Heart Rate, bpm	-0,222	-0,844	0,024	-0,019	-0,071	0,002			
Heart Work, kJ/min	-2,806	1,146	-1,264	-0,094	0,038	-0,042			
Ps3/Ps1 Ratio	-0,382	-0,039	-0,305	-5,135	-0,518	-4,097			
End-systolic Volume of Left Ventricle, mL	-1,768	1,000	-0,980	-0,237	0,134	-0,131			
Cardiac Output, L/min	2,447	0,234	1,394	1,306	0,125	0,744			
				Constants			-27,24	3,719	22,89
				Eigenvalues			20,02	0,52	0,27

	Cumulative proportions	0,953	0,978	0,991
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The calculation of the discriminant root values for each person as the sum of the products of raw coefficients to the individual values of discriminant variables together with the constant enables the visualization of each patient in the information space of the roots (Fig. 2).

Table 4 presents the full structural coefficients, that is, the coefficients of correlation between the discriminant root and variables. The structural coefficient shows how closely variable and discriminant functions are related, that is, what is the portion of information about the discriminant function (root) contained in this variable. There are also average values (centroids) of Roots and Z-scores of Variables.

Table 4. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Hemodynamics Variables

Variables currently in the model	Correlations Variables-Roots			Low N (13)	Norm (16)	High N (13)	AH I (35)	AH II (11)
	R 1	R 2	R 3					
Root 1 (95,3%)				-6,76	-3,40	-1,38	2,05	8,04
Blood Pressure Systolic, Z	0,847	-0,033	-0,005	-1,43	0	+1,00	+2,48	+5,12
Blood Pressure Diastolic, Z	0,177	0,279	0,047	-1,75	-0,30	+0,54	+2,01	+2,75
Ruzhylo-Popovych Contr Ind, Z	0,172	0,185	-0,127	-0,48	-0,20	-0,99	-0,42	+0,62
Heart Work, Z	0,073	-0,091	-0,142	+0,81	+0,04	-0,04	+0,27	+2,16
Ejection Fraction, Z	0,054	0,050	-0,130	+0,42	-0,15	-0,53	-0,20	+0,87
Heart Rate, Z	0,006	-0,022	0,072	+0,23	+0,08	+0,30	+0,23	+0,31
Sagawa Contractility Index, Z	currently not in the model			-1,08	-0,64	-1,06	+0,32	+1,54
End-systolic Volume Left Vent, Z	-0,079	-0,346	-0,057	+0,76	+0,96	+1,70	+0,65	+0,21
Ejection Time, Z	-0,064	-0,259	0,227	+2,77	+0,68	+2,21	+1,34	+0,43
Root 2 (2,5%)				-0,91	+0,56	-0,40	+0,58	-1,11
End-diastolic Vol Left Ventr, Z	-0,023	-0,416	-0,292	+1,76	+0,03	+0,67	-0,28	+1,04
Cardiac Output, Z	0,015	-0,130	-0,140	+1,55	+0,22	-0,04	-0,03	+1,28
Ps2/Ps1 Ratio	-0,037	-0,246	-0,539	0,971	1,000	0,988	0,922	0,975
Stroke Volume Left Ventricle, Z	currently not in the model			+1,30	+0,06	-0,10	-0,20	+1,25
Pd3/Pd1 Ratio	0,044	0,324	-0,073	0,971	0,996	1,014	1,023	0,997
Pd2/Pd1 Ratio	currently not in the model			0,976	0,970	1,001	1,013	1,000
General Periph Resist Vessels, Z	currently not in the model			-0,54	+0,26	+0,08	+0,50	+0,16
Root 3 (1,3%)				+0,65	-0,51	-0,82	+0,33	-0,10
Ps3/Ps1 Ratio	-0,027	-0,102	-0,377	0,953	0,964	0,984	0,934	0,944

The localization of the patients with AH II along the first root axis (Fig. 2) in the extreme right (positive) zone reflects combination of significantly elevated BP with maximum for sampling levels of myocardial contractility indices, ejection fraction and heart work, on the one hand, and minimum ESV and ejection time levels on the other hand. Consecutive decrease in BP is accompanied by a decrease/increase in these hemodynamic parameters. Additional differentiation of patients with AH I occurs along the axis of the second root, the upper position of which reflects the minimum for sampling EDV, cardiac output and Ps2/Ps1 ratio, while the maximum levels of Pd3/Pd1 ratio and general peripheral resistance of vessels.

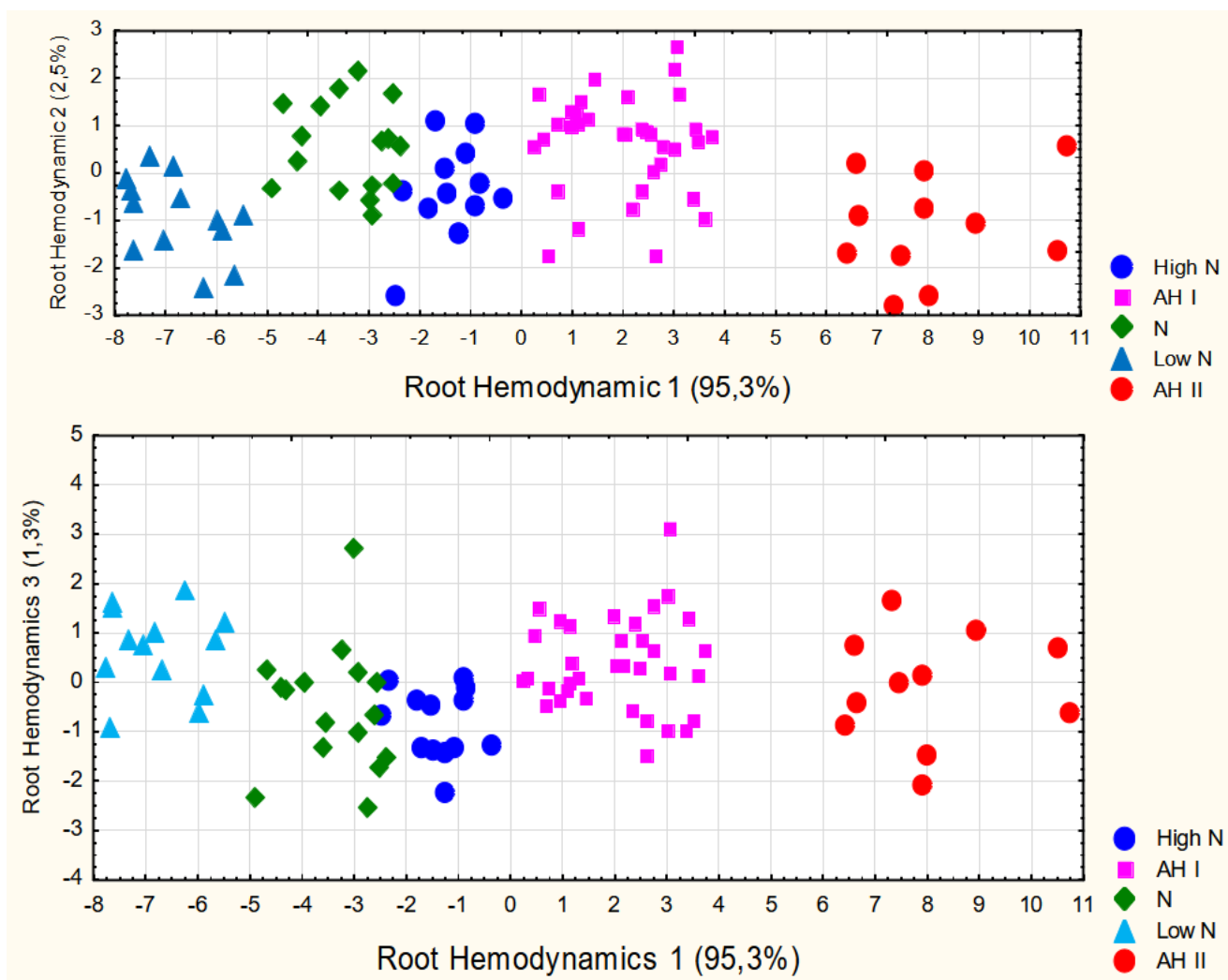


Fig. 2. Scattering of individual values of the first and second (top) and first and third (bottom) discriminant hemodynamic roots of patients of different blood pressure clusters

Along the axis of the third root patients with High N BP are allocated as the maximum for sampling of Ps3 / Ps1.

In general, all clusters on the planes of three roots are quite clearly delineated, which is documented by calculating the Mahalanobis distances (Table 5).

Table 5. Squared Mahalanobis Distances between Blood Pressure Clusters and F-values (df=13,7; for High N/N $p < 10^{-3}$, for others $p < 10^{-6}$)

Blood Pressure Clusters	High N	AH I	N	Low N	AH II
High N	0	14,4	6,83	31,9	91,0
AH I	8,96	0	31,1	80,0	39,2
N	3,22	22,5	0	15,2	134
Low N	13,6	49,9	7,15	0	220
AH II	35,7	21,6	57,4	86,1	0

The same discriminant parameters can be used to identify the belonging of one or another person to one or another cluster. This purpose of discriminant analysis is realized with the help of classifying functions (Table 6). These functions are special linear combinations that maximize differences between groups and minimize dispersion within groups. An object belongs to a group with the maximum value of a function calculated by summing the products of the values of the variables by the coefficients of the classifying functions plus the constant.

Table 6. Coefficients and Constants for Classification Functions for Blood Pressure Clusters

Blood Pressure Clusters	High N	AH I	Norm	Low N	AH II
Variables currently in the model	p=,148	p=,398	p=,182	p=,148	p=,125
Blood Pressure Systolic, mmHg	6,942	7,683	6,371	5,591	9,177
Ejection Time, msec	0,297	0,400	0,224	0,315	0,592
Pd3/Pd1 Ratio	751,9	765,9	736,0	699,0	791,9
Ps2/Ps1 Ratio	390,6	394,2	384,2	363,9	426,5
Blood Pressure Diastolic, mmHg	-1,737	-1,707	-1,672	-1,917	-2,017
End-diastolic Volume of Left Ventricle, mL	-3,884	-3,751	-4,137	-4,222	-3,145
Ruzhylo-Popovych Contractility Index, kPa/s	4,286	5,172	3,889	4,103	6,770
Ejection Fraction, %c	16,51	15,29	17,12	17,44	13,02
Heart Rate, bpm	1,369	1,235	1,334	1,506	1,241
Heart Work, kJ/min	-1,733	-2,035	-1,441	-1,268	-2,605
Ps3/Ps1 Ratio	147,5	121,4	147,8	164,8	89,51
End-systolic Volume of Left Ventricle, mL	16,19	15,34	16,71	17,18	13,73
Cardiac Output, L/min	13,72	18,76	10,35	7,131	25,55
Constants	-1817	-1868	-1725	-1644	-2065

In this case, we can retrospectively recognize patients with AH I and II as well as with low norm BP **unmistakably**, the patients with high norm BP are classified with one mistake, and with norm BP with two errors. Overall classification accuracy is 96,6% (Table 7).

Table 7. Classification Matrix for Blood Pressure Clusters

Group	Rows: Observed classifications Columns: Predicted classifications					
	Percent Correct	High N p=,14773	AH I p=,39773	Norm p=,18182	Low N p=,14773	AH II p=,12500
High N	92,3	12	0	1	0	0
AH I	100,0	0	35	0	0	0
Norm	87,5	2	0	14	0	0
Low N	100,0	0	0	0	13	0
AH II	100,0	0	0	0	0	11
Total	96,6	14	35	15	13	11

Thus, profile patients of Truskavets' spa are characterized by a wide range of blood pressure - from low norm to arterial hypertension II that correspond to the hemodynamics parameters. Subsequent publications will analyze the neurogenic, endocrine, metabolic and immune accompaniments of blood pressure.

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ACCORDANCE TO ETHICS STANDARDS

Tests in patients are conducted in accordance with positions of Helsinki Declaration 1975, revised and complemented in 2002, and directive of National Committee on ethics of scientific researches. During realization of tests from all parent of participants the informed consent is got and used all measures for providing of anonymity of participants.

For all authors any conflict of interests is absent.

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