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AUTONOMIC AND ENDOCRINE ACCOMPANIMENTS OF QUANTITATIVE-QUALITATIVE BLOOD PRESSURE CLUSTERS IN PATIENTS OF TRUSKAVETS' SPA

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Abstract

Background. Earlier we showed that profile patients of Truskavets' spa are characterized by a wide range of blood pressure (BP) - from low norm to arterial hypertension III that correspond to the hemodynamics parameters. The **purpose** of this study is to clarify the autonomic and endocrine accompaniments of quantitative-qualitative BP clusters in the same contingent. **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). The parameters of HRV ("CardioLab+HRV", Ukraine), plasma levels of Cortisol, Aldosterone, Testosterone, Triiodothyronine and Calcitonin (ELISA) as well as Ca-P marker of parathyroid hormone were determined. **Results**. In order to identify among the registered parameters, those for which the BP clusters differ from each other, a discriminant analysis was performed. The program forward stepwise included in the discriminant model 29 parameters. The most informative among them are HRV-markers of sympathetic tone and sympathetic-vagal balance as well as testosterone and cortisol, whose levels are maximal in patients with hypertension II, while minimal in patients with low norm BP, on the one hand, and markers of vagal tone and Kerdoe vegetative index, the levels of which are polar, on the other hand. The accuracy of patient classification is 98,9%. **Conclusion**. Autonomic and endocrine accompaniments of quantitative-qualitative

blood pressure clusters corresponding to the existing ideas about the regulation of blood pressure.

Key words: blood pressure, HRV, adaptation hormones, discriminant analysis, Truskavets' spa.

INTRODUCTION

Earlier we showed that profile patients of Truskavets' spa are characterized by a wide range of blood pressure - from low norm to arterial hypertension III [4,15] that correspond to the hemodynamics parameters [14]. Research has shown that the heart communicates to the brain in four major ways: neurologically (through the transmission of nerve impulses), biochemically (via hormones and neurotransmitters), biophysically (through pressure waves) and energetically (through electromagnetic field interactions) [5,28].

The **purpose** of this study is to clarify the autonomic and endocrine accompaniments of quantitative-qualitative blood pressure clusters in the same contingent. Such research remains relevant, as previous research in this area is fragmentary and unsystematic [12,13,16,18,20-24].

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 was measured (by tonometer "Omron M4-I", Netherlands) in a sitting position three times in a row. Then we recorded electrocardiogram in II lead to assess the parameters of HRV [1,2,10] (software and hardware complex "CardioLab+HRV" produced by "KhAI-MEDICA", Kharkiv, Ukraine). For further analysis the following parameters heart rate variability (HRV) were selected. Temporal parameters (Time Domain Methods): heart rate (HR), mode (Mo), the standart deviation of all NN intervals (SDNN), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), the percent of interval differences of successive NN intervals greater than 50 msec (pNN_{50}); triangular index (TNN). Spectral parameters (Frequency Domain Methods): power spectral density (PSD) bands of HRV - high-frequency (HF, range 0,4÷0,15 Hz), low-frequency (LF, range 0,15÷0,04 Hz), very low-frequency (VLF, range 0,04÷0,015 Hz) and ultralow-frequency (ULF, range 0,015÷0,003 Hz). We calculated the Entropy of HRV band [17] and classical indexes LF/HF and LFnu=100%•LF/(LF+HF) as well as (VLF+LF)/HF as Centralization Index. Baevskiy's parameters: the amplitude of mode (AMo) and variational sweep (MxDMn) as well as author's indexes: Baevskiy's Stress Index (BSI=AMo/2•Mo•MxDMn) and Baevskiy's Activity Regulatory Systems Index (BARSI) [1].

In addition, the autonomic reactivity (AR) was assessed by the ratio of Stress Indices in supine and orthostatic positions [1]: $AR=BSI_{orth}/BSI_{sup}$.

Among hormones determined Cortisol, Aldosterone, Testosterone, Triiodothyronine and Calcitonin (by the ELISA with the use of analyzers "Tecan" and "RT-2100C" and corresponding sets of reagents from "Алкор Био", XEMA Co, Ltd and DRG International Inc).

The level of parathyroid hormone was judged by a coefficient $(Cap•Pu/Pp•Cau)^{0,25}$, based on the direction of its effect on the level of calcium and phosphates in plasma and urine [9].

Finally, the battery of tests included the good old breath-holding Stange's and Gench's tests, which are traditionally considered markers of the state of the cardio-respiratory system [3,19] as well as Kerdö's Vegetative Index [6] and $(Cap/Kp)^{0,5}$ ratio [7] as markers of Sympathetic/Vagal balance.

For statistical analysis used the software package "Statistica 64".

RESULTS AND DISCUSSION

In order to identify among the registered parameters, those for which the blood pressure clusters differ from each other, a discriminant analysis was performed [11]. The program forward stepwise included in the discriminant model 29 parameters (Tables 1 and 2).

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

Step 29, N of vars in model: 29; Grouping: 5 grs; Wilks' Λ: 0,0043; approx. $F_{(116)}=5,6$; $p<10^{-6}$

	Clusters of Blood Pressure (n)					Parameters of Wilk's Statistics						
VARIABLES CURRENTLY IN THE MODEL	AH II (11)	AH I (35)	High N (13)	Norm (16)	Low N (13)	Wilks' Λ	Par-tial Λ	F-re-move (4,55)	p-level	Tole-rancy	Refe-rence (88)	Cv
Blood Pressure Systolic, mmHg	172 2,5	148 0,9	134 0,8	125 0,6	112 1,0	0,004	0,950	0,72	0,580	0,036	125 1	,076
Sex Index (M=1; F=2)	1,36 0,15	1,11 0,05	1,00 0,00	1,25 0,11	1,62 0,14	0,005	0,817	3,08	0,023	0,612	1,23	
LF band HRV, %	30,3 4,3	33,8 2,4	26,2 2,5	40,8 3,6	29,9 4,5	0,005	0,856	2,30	0,070	0,115	26,1 0,9	,312
Blood Pressure Systolic 2, mmHg	168 3,2	136 2,1	132 3,5	125 3,3	108 2,0	0,005	0,849	2,44	0,057	0,003		
Pd3/Pd1 ratio•1000	997 21	1023 8	1014 16	996 14	971 10	0,005	0,778	3,92	0,007	0,225		
$(Cap/Kp)^{0,5}$ as Symp/Vag balance	0,70 0,01	0,73 0,01	0,72 0,01	0,72 0,02	0,68 0,01	0,005	0,814	3,14	0,021	0,518	0,71 0,01	,104
ULF band HRV, %	4,1 1,4	3,1 0,5	5,7 1,3	4,5 1,7	3,3 0,9	0,005	0,856	2,32	0,068	0,282	5,4 0,4	,816
Ps3/Ps1 ratio•1000	944 20	934 11	984 17	964 27	953 18	0,005	0,797	3,50	0,013	0,005		
AMo/MxDMn as Symp/Vag balance	370 92	270 36	240 20	337 87	156 22	0,005	0,854	2,34	0,066	0,009	251 8	,303
Kerdö's Vegetati-ve Index, units	-33 7	-26 3	-17 5	-15 4	-3 3	0,005	0,895	1,61	0,184	0,237	-17 2	**14,6**
Pd2/Pd1 ratio•1000	1000 31	1013 11	1001 18	970 16	976 17	0,005	0,858	2,27	0,073	0,291		
Ps2/Ps1 ratio•1000	975 13	922 13	988 29	1000 26	971 16	0,005	0,866	2,13	0,090	0,004		
Testosterone stand by Sex&Age, Z	0,95 0,57	0,46 0,31	0,46 0,51	-0,11 0,25	0,02 0,33	0,005	0,913	1,32	0,275	0,677	0	
Cortisol Plasma,	469	374	446	386	391	0,005	0,929	1,05	0,391	0,728	370	,303

nM/L	49	26	56	47	44						12	
Blood Pressure Systolic 3, mmHg	163 4,5	138 1,9	132 2,2	121 3,4	106 2,3	0,005	0,820	3,02	0,025	0,004		
Calcitonin stand by Sex&Age, Z	-0,76 0,27	-0,80 0,08	-0,94 0,19	-0,52 0,31	-0,23 0,32	0,005	0,897	1,59	0,191	0,488	0	
Mode HRV, msec	864 57	859 22	842 33	845 47	850 30	0,005	0,886	1,77	0,148	0,131	875 11	,116
(VLF+LF)/HF as Centralization Ind	19,9 7,2	10,6 1,6	14,9 4,7	14,1 2,6	6,5 1,6	0,005	0,924	1,13	0,351	0,266	6,8 0,4	,554
LFnu HRV, %	74,9 3,9	71,1 2,5	68,6 5,1	79,4 3,6	58,7 5,7	0,004	0,960	0,58	0,680	0,129	64,2 1,4	,201
HF band HRV, msec^2	210 68	485 85	472 235	373 28	712 190	0,005	0,883	1,82	0,138	0,014	350 27	,713
Baevskiy's ARS Index HRV, units	2,64 0,75	3,27 0,43	2,25 0,51	3,43 0,67	2,62 0,60	0,005	0,860	2,24	0,076	0,254	0÷3	
Triangular Index HRV, units	8,4 0,9	11,1 0,7	10,8 0,7	10,2 1,1	13,7 1,1	0,005	0,845	2,52	0,052	0,087	11,2 0,3	,217
VLF band HRV, msec^2	814 145	1216 147	1098 110	1050 271	1535 221	0,005	0,874	1,98	0,111	0,007	1250 76	,572
SDNN HRV, msec	38,5 3,8	48,7 3,4	45,4 4,9	45,0 5,3	58,1 4,5	0,005	0,827	2,88	0,031	0,013	56,2 3,1	,516
Total Power HRV, msec^2	1642 283	2748 354	2402 562	2422 612	3502 558	0,005	0,812	3,18	0,020	0,002	2379 102	,402
AMo HRV, %	53,7 4,9	44,5 2,7	41,8 2,3	47,3 4,7	37,1 2,7	0,005	0,887	1,75	0,153	0,051	39,2 1,2	,298
Gench's Expiration Test, sec	34,5 3,1	31,4 2,0	32,7 3,3	31,5 3,4	33,4 3,7	0,005	0,934	0,97	0,433	0,528	31,0 1,4	,419
Baevskiy's Stress Index HRV, units	243 71	177 26	125 11	214 59	95 14	0,005	0,872	2,03	0,104	0,008	136 6	,417
LF band HRV, msec^2	527 138	1024 156	683 198	916 191	1157 312	0,005	0,886	1,77	0,147	0,013	625 32	,482
VARIABLES CURRENTLY NOT IN THE MODEL	**Clusters of Blood Pressure (n)**					**Parameters of Wilk's Statistics**						
	AH II (11)	**AH I (35)**	**High N (13)**	**Norm (16)**	**Low N (13)**	Wilks' Λ	Partial Λ	F to-enter	p-level	Tolerancy	Reference (88)	Cv
Parathyroid Activity, units	1,80 0,09	1,80 0,05	1,80 0,11	1,77 0,07	1,90 0,07	0,004	0,945	0,78	0,544	0,612	1,82 0,04	,230
Aldosterone Plasma, pM/L	226 5	229 4	232 11	227 6	221 5	0,004	0,972	0,38	0,820	0,417	238 5	,187
Triiodothyronine Plasma, nM/L	1,90 0,16	1,95 0,11	1,72 0,24	2,17 0,31	2,24 0,20	0,004	0,941	0,85	0,502	0,336	2,20 0,05	,227
Blood Pressure Diastolic, mmHg	90,7 4,5	87,6 1,2	81,3 1,5	77,8 1,5	71,5 1,5	0,004	0,957	0,61	0,655	0,284	79 0,5	,054
Blood Pressure Diastolic 2, mmHg	89,9 3,8	88,7 1,4	81,4 2,0	75,5 2,0	70,0 0,8	0,004	0,971	0,40	0,806	0,275		
Blood Pressure Diastolic 3, mmHg	90,2 4,2	89,6 1,4	82,5 2,2	77,5 1,9	69,4 1,5	0,004	0,955	0,63	0,643	0,258		
MxDMn HRV, msec	182 16	212 13	215 15	205 21	264 16	0,004	0,960	0,56	0,691	0,083	244 8	,293
RMSSD HRV, msec	19,5 3,2	30,2 3,0	26,2 4,1	26,4 5,4	37,5 3,9	0,004	0,987	0,18	0,949	0,047	28,8 1,5	,486
pNN$_{50}$ HRV, %	2,8 1,1	10,9 2,1	6,5 2,6	8,4 3,9	14,9 3,8	0,004	0,968	0,44	0,776	0,070	9,0 0,8	,820
ULF band HRV,	81	78	150	83	98	0,004	0,940	0,87	0,489	0,100	122	,892

msec²	30	22	49	30	26						12	
LF/HF ratio HRV, units	5,07 1,93	3,74 0,51	4,69 1,57	6,83 1,48	2,36 0,63	0,004	0,985	0,21	0,930	0,105	2,86 0,22	,709
Entropy HRV, units•10³	674 53	719 19	736 38	714 27	742 24	0,004	0,979	0,29	0,886	0,151	806 10	,113
VLF band HRV, %	54,5 6,5	48,7 2,9	54,8 4,2	44,7 3,6	45,1 5,0	0,004	0,981	0,26	0,900	0,014	53,9 1,6	,277
HF band HRV, %	11,2 3,0	14,4 1,7	13,4 2,9	10,0 1,8	21,7 4,1	0,004	0,980	0,27	0,894	0,036	14,6 1,3	,859
BSIo/BSIs as Autonomic Reactivity	2,45 0,45	2,60 0,27	2,67 0,42	1,95 0,29	3,42 0,49	0,004	0,992	0,11	0,979	0,518	0,7÷ 1,5	

Table 2. Summary of Stepwise Analysis for Blood Pressure and Neuro-Endocrine Variables, ranked by criterion Lambda

Variables currently in the model	F to enter	p-level	Λ	F-value	p-value
Blood Pressure Systolic, mmHg	298	10^{-6}	0,065	298	10^{-6}
Sex Index (M=1; F=2)	4,95	0,001	0,052	69,0	10^{-6}
LF band HRV, %	2,99	0,024	0,046	39,5	10^{-6}
Blood Pressure Systolic 2, mmHg	2,89	0,027	0,040	28,6	10^{-6}
Pd3/Pd1 ratio	2,76	0,033	0,035	23,0	10^{-6}
$(Cap/Kp)^{0,5}$ as Sympathetic/Vagal balance	2,33	0,063	0,031	19,4	10^{-6}
ULF band HRV, %	1,56	0,194	0,029	16,6	10^{-6}
Ps3/Ps1 ratio	1,40	0,243	0,027	14,7	10^{-6}
AMo/MxDMn as Sympathetic/Vagal balance	1,67	0,165	0,025	13,2	10^{-6}
100(1-Pd/HR) as Kerdö Vegetative Index	2,22	0,075	0,022	12,2	10^{-6}
Pd2/Pd1 ratio	1,41	0,239	0,021	11,3	10^{-6}
Ps2/Ps1 ratio	1,72	0,156	0,019	10,5	10^{-6}
Testosterone standardized by Sex&Age, Z	1,34	0,265	0,017	9,83	10^{-6}
Cortisol Plasma, nM/L	1,87	0,126	0,016	9,35	10^{-6}
Blood Pressure Systolic 3, mmHg	1,22	0,312	0,015	8,81	10^{-6}
Calcitonin standardized by Sex&Age, Z	1,41	0,239	0,014	8,38	10^{-6}
Mode HRV, msec	1,49	0,216	0,012	8,02	10^{-6}
(VLF+LF)/HF as Centralization Index	2,25	0,073	0,011	7,82	10^{-6}
LFnu HRV, %	1,11	0,357	0,010	7,47	10^{-6}
HF band HRV, msec²	1,32	0,272	0,009	7,19	10^{-6}
Baevskiy's Activity Regulatory Systems Index	1,72	0,157	0,009	7,00	10^{-6}
Triangular Index HRV, units	1,01	0,408	0,008	6,72	10^{-6}
VLF band HRV, msec²	1,29	0,285	0,007	6,51	10^{-6}
SDNN HRV, msec	1,62	0,181	0,007	6,36	10^{-6}
Total Power HRV, msec²	1,57	0,194	0,006	6,21	10^{-6}
AMo HRV, %	1,32	0,274	0,006	6,05	10^{-6}
Gench's Expiration Test, sec	1,03	0,400	0,005	5,87	10^{-6}
Baevskiy's Stress Index HRV, units	1,07	0,378	0,005	5,70	10^{-6}
LF band HRV, msec²	1,77	0,147	0,004	5,63	10^{-6}

Next, the 29-dimensional space of discriminant variables transforms into 4-dimensional space of a canonical roots. For Root 1 r*=0,986 (Wilks' Λ=0,0043; $\chi^2_{(116)}$=382; p<10^{-6}), for Root 2 r*=0,727 (Wilks' Λ=0,149; $\chi^2_{(84)}$=133; p=0,0005), for Root 3 r*=0,708 (Wilks' Λ=0,315; $\chi^2_{(54)}$=81; p=0,010) and for Root 4 r*=0,607 (Wilks' Λ=0,632; $\chi^2_{(26)}$=32; p=0,188). The first root contains 92,6% of discriminative opportunities, the second 3,1%, the third 2,7%, the last 1,6%.

Table 3 presents raw and standardized coefficients for discriminant variables. 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 (Figs. 1 and 2).

Table 3. Standardized and Raw Coefficients and Constants for Blood Pressure and Neuro-Endocrine Variables

Coefficients	Standardized			Raw		
Variables currently in the model	Root 1	Root 2	Root 3	Root 1	Root 2	Root 3
Blood Pressure Systolic, mmHg	-0,555	1,365	-0,034	-0,114	0,281	-0,007
Sex Index (M=1; F=2)	-0,108	-0,727	-0,114	-0,281	-1,900	-0,297
LF band HRV, %	0,512	-0,082	1,238	0,036	-0,0058	0,0881
Blood Pressure Systolic 2, mmHg	-5,961	1,410	-3,733	-0,504	0,119	-0,316
Pd3/Pd1 ratio	-0,363	0,925	-0,685	-6,832	17,40	-12,87
$(Cap/Kp)^{0.5}$ as Sympathetic/Vagal balance	-0,311	-0,120	0,662	-5,690	-2,205	12,12
ULF band HRV, %	0,622	0,224	0,142	0,140	0,051	0,032
Ps3/Ps1 ratio	-3,393	5,410	-4,221	-45,56	72,65	-56,68
AMo/MxDMn as Sympathetic/Vagal balance	3,321	2,496	2,107	0,014	0,0108	0,0091
100(1-Pd/HR) as Kerdö Vegetative Index	0,008	-0,801	-0,416	0,0004	-0,0441	-0,0229
Pd2/Pd1 ratio	-0,627	-0,162	-0,001	-9,096	-2,35	-0,016
Ps2/Ps1 ratio	5,328	-1,646	3,268	65,71	-20,30	40,30
Testosterone standardized by Sex&Age, Z	-0,208	0,017	-0,296	-0,127	0,010	-0,180
Cortisol Plasma, nM/L	-0,180	-0,260	-0,238	-0,0011	-0,0015	-0,0014
Blood Pressure Systolic 3, mmHg	3,791	-5,203	3,665	0,329	-0,451	0,318
Calcitonin standardized by Sex&Age, Z	0,267	-0,336	0,407	0,313	-0,393	0,478
Mode HRV, msec	-0,224	-1,132	-0,017	-0,0015	-0,0078	-0,0001
(VLF+LF)/HF as Centralization Index	0,171	-0,410	-0,154	0,013	-0,031	-0,012
LFnu HRV, %	-0,176	0,567	0,435	-0,011	0,036	0,027
HF band HRV, $msec^2$	1,811	1,406	2,875	0,0030	0,0023	0,0048
Baevskiy's Activity Regulatory Systems Index	0,675	-0,215	0,180	0,279	-0,089	0,074
Triangular Index HRV, units	1,320	-0,173	-0,384	0,354	-0,046	-0,103
VLF band HRV, $msec^2$	2,588	1,097	4,454	0,0031	0,0014	0,0055
SDNN HRV, msec	1,840	-2,904	2,854	0,099	-0,156	0,153
Total Power HRV, $msec^2$	-8,527	0,285	-10,22	-0,0042	0,0001	-0,0050
AMo HRV, %	0,684	-1,610	0,879	0,046	-0,107	0,059
Gench's Expiration Test, sec	-0,274	-0,244	0,115	-0,022	-0,020	0,009
Baevskiy's Stress Index HRV, units	-3,522	-1,841	-1,699	-0,021	-0,011	-0,010
LF band HRV, $msec^2$	2,342	0,166	2,487	0,0027	0,0002	0,0029
	Constants			33,64	-42,86	8,58
	Eigenvalues			34,03	1,12	1,00
	Cumulative proportions			0,926	0,957	0,984

Table 4 shows the correlation coefficients of blood pressure and neuro-endocrine parameters (discriminant variables) with canonical discriminant roots; the cluster centroids of both roots; and Z-scores of the discriminant variables, as well as not included in the discriminant model. The reason for the last step is our experience that not getting a variable into the model does not always indicate a lack of recognition ability, but may be a consequence of redundancy/duplication of information [17].

Table 4. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Blood Pressure and Neuro-Endocrine Variables

Variables currently in the model	Correlations Variables-Roots			AH II (11)	AH I (35)	High N (13)	Norm (16)	Low N (13)
Root 1 (92,6%)	**R 1**	**R 2**	**R 3**	**-10,4**	**-2,5**	**+0,8**	**+4,8**	**+8,9**
Blood Pressure Systolic, Z	**-0,648**	-0,106	0,200	**+5,12**	**+2,48**	**+1,00**	**0,00**	**-1,43**
Blood Pressure Systolic 3, Z	**-0,242**	0,018	-0,054	**+4,08**	**+1,42**	**+0,76**	**-0,48**	**-2,00**
Blood Pressure Systolic 2, Z	**-0,233**	-0,100	-0,075	**+4,66**	**+1,23**	**+0,81**	**0,00**	**-1,79**
AMo HRV, Z	**-0,041**	-0,032	0,089	**+1,26**	**+0,47**	**+0,21**	+0,67	**-0,18**
(VLF+LF)/HF as Centralization	**-0,033**	0,015	-0,068	**+2,74**	+0,93	**+2,02**	+2,05	**+0,04**
Baevskiy's Stress Index HRV, Z	**-0,032**	-0,013	0,151	**+1,51**	**+0,75**	**-0,25**	+1,26	**-0,62**
Testosterone standardized, Z	**-0,032**	-0,017	-0,065	**+0,95**	**+0,46**	**+0,46**	**-0,11**	**+0,02**
AMo/MxDMn as Symp/Vag bal	**-0,031**	-0,006	0,146	**+4,36**	**+2,28**	**+0,99**	+3,61	**-0,11**
Cortisol Plasma, nM/L	**-0,015**	-0,042	-0,159	**+0,89**	+0,04	**+0,68**	+0,15	+0,19
Pd3/Pd1 ratio	**-0,035**	0,249	0,069	0,997	**1,023**	**1,014**	**0,996**	**0,971**
$(Cap/Kp)^{0,5}$ as Sym/Vag balance	**-0,022**	0,279	0,132	-0,15	**+0,24**	**+0,14**	**+0,14**	**-0,48**
Blood Pressure Diastolic, Z	currently not in the model			**+2,75**	**+2,01**	**+0,54**	**-0,30**	**-1,75**
Blood Pressure Diastolic 2, Z	currently not in the model			**+2,56**	**+2,26**	**+0,55**	**-0,83**	**-2,21**
Blood Pressure Diastolic 3, Z	currently not in the model			**+2,58**	**+2,48**	**+0,81**	**-0,36**	**-2,25**
100•(1-Pd/HR) as Kerdö's VI, Z	**0,087**	-0,089	-0,123	**-0,42**	**-0,17**	**+0,34**	**+0,41**	**+1,08**
Triangular Index HRV, Z	**0,051**	-0,046	-0,033	**-1,13**	**-0,04**	-0,15	-0,40	**+1,03**
SDNN HRV, Z	**0,037**	-0,053	0,011	**-0,50**	**-0,26**	-0,35	-0,43	**-0,02**
Total Power HRV, Z	**0,032**	-0,021	0,026	**-0,40**	**+0,35**	+0,18	-0,07	**+0,89**
VLF band HRV PS, Z	**0,030**	-0,033	0,005	**-0,47**	**-0,07**	-0,12	-0,32	**+0,30**
HF band HRV PS, Z	**0,029**	-0,012	-0,030	**-0,16**	**+0,44**	**+0,54**	-0,16	**+0,87**
LF band HRV PS, Z	**0,024**	-0,010	0,120	**+0,27**	**+1,39**	+0,34	+0,75	**+1,19**
Entropy HRV, units	currently not in the model			**-1,28**	**-0,94**	-0,75	-1,07	**-0,81**
pNN_{50} HRV, Z	currently not in the model			**-0,75**	**+0,20**	-0,24	-0,06	**+0,76**
Root 2 (3,1%)	**R 1**	**R 2**	**R 3**	-1,59	+0,43	**+1,37**	+0,32	-1,58
Sex Index (M=1; F=2)	0,036	**-0,450**	0,006	1,36	1,11	**1,00**	1,25	1,62
Calcitonin standardized, Z	0,034	**-0,169**	0,055	-0,76	-0,80	**-0,94**	-0,52	-0,23
Mode HRV, Z	-0,007	**-0,021**	0,019	-0,16	-0,11	**-0,37**	-0,34	-0,21
Triiodothyronine Plasma, Z	currently not in the model			-0,60	-0,50	**-0,95**	-0,06	+0,09
ULF band HRV PS relative, Z	0,004	**0,076**	-0,130	-0,46	-0,53	**+0,12**	-0,15	-0,41
Ps3/Ps1 ratio	0,018	**0,070**	-0,150	0,944	0,934	**0,984**	0,964	0,953
ULF band HRV PS, Z	currently not in the model			-0,38	-0,40	**+0,25**	-0,36	-0,22
Aldosterone Plasma, Z	currently not in the model			-0,28	-0,20	**-0,14**	-0,24	-0,37
Root 3 (2,7%)	**R 1**	**R 2**	**R 3**	-0,51	+0,61	-1,92	**+1,01**	-0,53
LF/TP ratio HRV, Z	0,010	0,031	**0,297**	+0,87	-0,88	+0,08	**+1,73**	+0,24
LFnu HRV, Z	-0,028	0,126	**0,197**	+0,68	+0,51	+0,34	**+1,28**	-0,34
Baevskiy's ARS Index HRV, un	-0,000	0,032	**0,179**	2,64	3,27	2,25	**3,43**	2,62
Ps2/Ps1 ratio	0,027	-0,047	**0,150**	0,975	0,922	0,988	**1,000**	0,971
LF/HF ratio HRV, Z	currently not in the model			+0,99	+0,44	+0,88	**+1,97**	-0,22
Gench's test, Z	-0,003	-0,063	**-0,061**	+0,27	+0,05	+0,13	**+0,04**	+0,18
Pd2/Pd1 ratio	-0,032	0,089	**-0,010**	1,000	1,013	1,001	**0,970**	0,976
SIo/SIs as Autonomic Reactivity	currently not in the model			2,45	2,60	2,67	**1,95**	3,42
VLF/TP ratio HRV, Z	currently not in the model			-0,18	-0,37	-0,01	**-0,58**	-0,48
HF/TP ratio HRV, Z	currently not in the model			-0,10	0,00	-0,19	**-0,39**	+0,36
Parathyroid Activity, Z	currently not in the model			-0,05	-0,05	-0,06	**-0,12**	+0,19

The localization of the patients with AH II along the first root axis (Fig. 1) in the extreme left (negative) zone reflects combination of significantly elevated BP with maximum for sampling levels of HRV-markers of sympathetic tone and sympathetic/vagal balance as well as testosterone and cortisol plasma levels while minimum for sampling levels of HRV-markers of vagal tone as well as the entropy of HRV bands.

The extreme right zone of the axis of the first root is occupied by patients with low norm blood pressure. This reflects lower than normal or minimum for sampling levels of parameters that correlate with the root negatively and higher than normal or maximum for sampling levels of positively related parameters.

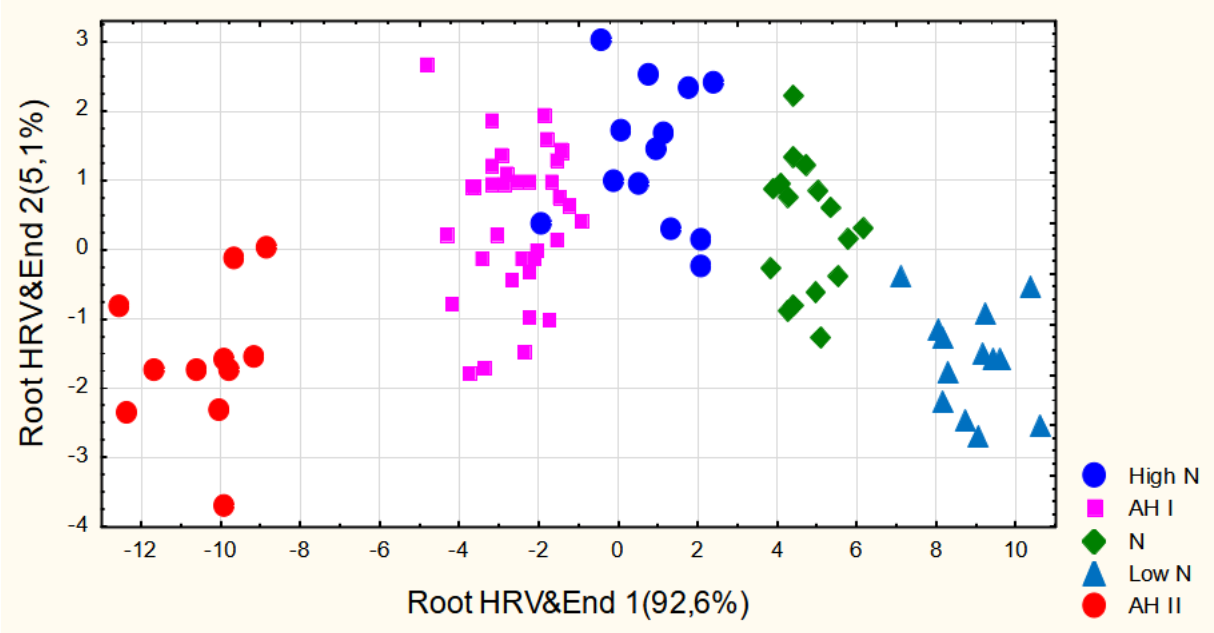

Fig. 1. Scattering of individual values of the first and second discriminant autonomic-endocrine roots of patients of different blood pressure clusters

Contrary to expectations, among the constellation of vagal markers was Kerdoe's vegetative index, the negative level of which is considered to reflect the vagal shift of the vegetative balance. In a special study, we showed that Kerdoe's vegetative index correlates with a number of EEGs parameters, but not HRVs [6]. However, we confirmed the relevance of the $(Cap/Kp)^{0,5}$ ratio as a marker of sympathetic/vagal balance [7].

Intermediate positions of members of other blood pressure clusters usually reflect intermediate levels of their autonomic and endocrine parameters.

Additional differentiation of patients with High Norm BP occurs along the axis of the second root. The upper position of the cluster members reflects their maximum reduced levels of calcitonin, triiodothyronine and Mode HRV (indicating the maximum sampling level of circulating catecholamines and other positive chronotropic factors [1,9]) in combination with the maximum sampling levels of aldosterone and ULF band HRV spectral power. Interestingly, the gender composition of the cluster is represented exclusively by men (Sex index = 1).

Along the axis of the third root (Fig. 2), the top position is occupied by patients with the optimal level of BP, which is accompanied by the highest (compensatory?) normalized (relative) parameters of LF band HRV and Baevskiy's Activity Regulatory Systems index in combination with the minimum for sampling relative parameters of VLF and HF bands HRV as well as Autonomic Reactivity, Gench's test and parathyroid activity.

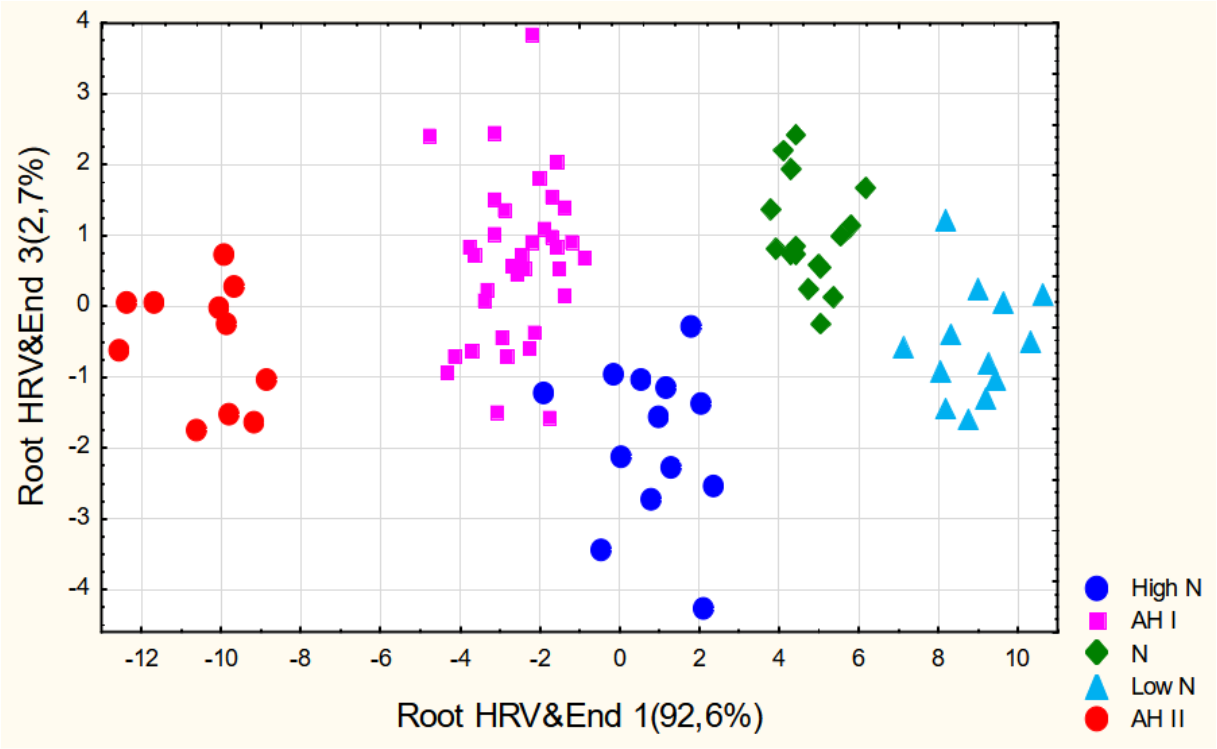

Fig. 2. Scattering of individual values of the first and third discriminant autonomic-endocrine roots of patients of different blood pressure clusters

In our opinion, the patterns of BP parameters recorded three times in a row deserve special attention. Returning to the table. 4, we see that the level of Pd3/Pd1 ratio in patients with AH I is greater than 1 and the maximum for the sample. This is combined with an elevated level (+0,50 Z) of general peripheral resistance of vessels (GPRV) [see: 14]. In contrast, patients with Low Norm BP have a Pd3/Pd1 ratio less than 1 and are associated with low GPRV (-0,54 Z). Patients in the other three clusters are characterized by almost identical close to 1 Pd3/Pd1 ratio and quasi-zero GPRV levels.

Hence, it is suggested that in patients with AH I in response to triple occlusion of the shoulder arteries with a tonometer cuff, their endothelium increases the release of vasoconstrictors and/or reduces the release of vasodilators while in patients with Low Norm BP a similar procedure causes increase the release of vasodilators and/or decrease the release of vasoconstrictors. It seems that vasodilation has a cholinergic nature and realizes by M_2-receptors [8]. In patients of other clusters, the balance of vasoconstrictors/vasodilators remains stable.

Patients with AH I also had the highest level of Pd2/Pd1 ratio, while the lowest level was found in patients with Norm BP, combined with maximum levels of sympathetic markers. This suggests the realization of vasodilation through β_2-adrenoceptors [8].

Maximal level of Ps3/Ps1 ratio in patients with High Norm BP indicates the minimum for the sample reduction of systolic BP in the third consecutive measurement, which we interpret as the minimum release of vasodilators and/or maximum release of vasoconstrictors in response to occlusion.

We dare to assume that vasodilators/vasoconstrictors balance is in some way related to both the aldosterone-renin-angiotensin system and the ULF band HRV, the physiological nature of which is still unknown.

In general, all clusters on the planes of three roots are 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=29,6; $p<10^{-5}$ - 10^{-6})

Blood Pressure Clusters	High Norm	AH I	Norm	Low Norm	AH II
High Norm	0	**19,1**	**26,2**	**77,2**	**137**
AH I	**4,15**	0	**56,7**	**136**	**69,5**
Norm	**4,29**	**14,2**	0	**26,5**	**237**
Low Norm	**11,5**	**29,6**	**4,35**	0	**376**
AH II	**18,7**	**13,3**	**35,2**	**51,2**	0

The same discriminant parameters can be used to identify the belonging of one or another person to one or another cluster (Table 6).

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	165,4	165,4	164,7	163,5	165,9
Sex Index (M=1; F=2)	-28,88	-27,08	-28,67	-26,14	-20,42
LF band HRV, %	0,338	0,396	0,799	0,727	0,097
Blood Pressure Systolic 2, mmHg	-91,28	-90,75	-94,06	-96,38	-86,29
Pd3/Pd1 ratio	2918	2881	2847	2783	2931
$(Cap/Kp)^{0.5}$ as Sympathetic/Vagal balance	-813,8	-757,1	-804,3	-831,9	-729,2
ULF band HRV, %	7,450	6,913	8,160	8,390	5,826
Ps3/Ps1 ratio	10220	10121	9843	9520	10459
AMo/MxDMn as Sympatho/Vagal balance	-0,471	-0,508	-0,396	-0,375	-0,651
100(1-Pd/HR) as Kerdö Vegetative Index	1,874	1,846	1,867	1,966	1,974
Pd2/Pd1 ratio	-759,5	-720,7	-800,1	-820,5	-654,0
Ps2/Ps1 ratio	13384	13307	13759	14053	12751
Testosterone standardized by Sex&Age, Z	-3,129	-2,991	-4,369	-4,268	-2,093
Cortisol Plasma, nM/L	0,0197	0,0208	0,0134	0,0134	0,0343
Blood Pressure Systolic 3, mmHg	-70,60	-70,14	-68,29	-65,85	-72,71
Calcitonin standardized by Sex&Age, Z	-78,46	-77,92	-75,43	-74,09	-80,15
Mode HRV, msec	0,403	0,411	0,409	0,410	0,445
(VLF+LF)/HF as Centralization Index	2,897	2,810	2,996	3,038	2,851
LFnu HRV, %	-1,127	-1,067	-1,114	-1,295	-1,063
HF band HRV, $msec^2$	0,166	0,164	0,190	0,189	0,132
Baevskiy's Activity Regulatory Systems Ind	-41,61	-42,11	-40,37	-38,84	-44,46
Triangular Index HRV, units	16,75	15,33	17,92	19,59	12,78
VLF band HRV, $msec^2$	0,132	0,134	0,160	0,161	0,100
SDNN HRV, msec	-16,13	-15,85	-15,21	-14,58	-16,61
Total Power HRV, $msec^2$	0,0739	0,0748	0,0428	0,0321	0,1138
AMo HRV, %	3,136	3,244	3,587	3,914	3,017
Gench's Expiration Test, sec	0,0267	0,1566	-0,0285	-0,0702	0,3409
Baevskiy's Stress Index HRV, units	1,089	1,144	0,987	0,934	1,347
LF band HRV, $msec^2$	-0,0078	-0,0094	0,0108	0,0182	-0,0352
Constants	-12988	-13015	-12820	-12594	-13292

In this case, we can retrospectively recognize patients with high norm BP with one mistake and others patients **unmistakably**. Overall classification accuracy is 98,9% (Table 7).

Table 6. Classification Matrix for Blood Pressure Clusters

Group	Rows: Observed classifications Columns: Predicted classifications Percent Correct	High N p=,14773	AH I p=,39773	N p=,18182	Low N p=,14773	AH II p=,12500
High N	92,3	12	1	0	0	0
AH I	100,0	0	35	0	0	0
N	100,0	0	0	16	0	0
Low N	100,0	0	0	0	13	0
AH II	100,0	0	0	0	0	11
Total	98,9	12	36	16	13	11

CONCLUSION

Thus, a wide range of blood pressure in Truskavets' spa patients is accompanied by an equally wide range of HRV parameters and adaptive hormones. The most informative among them are HRV-markers of sympathetic tone and sympathetic/vagal balance as well as testosterone and cortisol, whose levels are maximal in patients with hypertension II, while minimal in patients with low norm BP, on the one hand, and markers of vagal tone and Kerdö's vegetative index, the levels of which are polar, on the other hand. Autonomic and endocrine accompaniments of quantitative-qualitative blood pressure clusters corresponding to the existing ideas about the regulation of heart and blood pressure [8].

The following articles, already prepared for publication, will provide data on EEGs, metabolic and immune accompaniments of quantitative-qualitative blood pressure clusters.

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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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