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INDICATORS, DISTINCTIVE FOR WOMEN WITH DIFFERENT OVARIAN STATUS AND DIFFERENT RESPONSES STRESLIMITING EFFECT OF BIOACTIVE WATER NAFTUSSYA SPA TRUSKAVETS'

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Summary

The method of discriminant analysis revealed that the group of women with different ovarian status differ not only in the absence or presence echonegative or echopositive ovarian cysts, but the ovarian and uterine volume, prolactinemia level, pH of the skin, blood levels of the subpopulation of "active" T-lymphocytes, sympathetic tone and moda HRV, as well as the severity of weakness. It is shown that changes in neuro-hormonal stress index because of balneotherapy bioactive water Naftussya accompanied by characteristic groups of women with different ovarian status changes neuroendocrine (vegetative stress index, sympathetic tone, moda HRV, autonomic reactivity, thyrotropin, triiodothyronine, aldosterone) and immune (total white blood cell count, the relative content of "active" and theophylline sensitive T-lymphocytes, B-lymphocytes, natural killer cells) parameters, systolic blood pressure, skin pH, severity of weakness, headaches, puffiness, constipation and flatulence.

Keywords: stress, ovarian, neuroendocrine, immune status, bioactive water Naftussya, Truskavets'.

INTRODUCTION

We have previously shown that at women of reproductive age with different ovarian status course of drinking bioactive water Naftussya has an multivariate effect on the level of chronic stress, measured by neuro-hormonal stress index Popovych, calculated by vegetative stress index Baevsky and content in plasma cortisol, aldosterone, triiodothyronine and estradiol [6]. In analyzing the changes of neuroendocrine, immune and clinical indicators related multivariate effects of balneotherapy on neuro-hormonal stress index was found significant (R=0,61) canonical correlation between the dynamics of neuro-hormonal stress index, on the one hand, and indicators neuroendocrine-immune complex (autonomic reactivity, plasma levels of luteinizing hormone and thyrotropin, thyroxine, immunoglobulin A, subpopulations "active", theophylline resistance and $CD3^+CD4^+$ T-lymphocytes) on the other hand. It is shown that the nature and extent of changes neuro-hormonal stress index naturally (R=0,66) conditioned its initial level and initial level vegetative stress index, sympathetic and vagal tone, triiodothyronine, T-killers and volume right ovary [7].

The purpose of this study: first, to find these initial indicators of neuroendocrine-immune status and clinical symptoms that are characteristic of previously isolated clusters of women with different ovarian status and various changes in neuroendocrine stress index after drinking bioactive water Naftussya; secondly, to identify indicators of

neuroendocrine-immune status and clinical symptoms changes of which are characteristic for reaction to balneotherapy women in each group.

MATERIALS AND METHODS

For clinical-physiological observations purposefully selected 144 women of reproductive age (20-40 years) with chronic gynecological and endocrine disorders (ovaries cystose, fibromyoma, mastopaty), but with preserved ovarian-menstrual cycle, which came to Truskavets'on 3-4 days follicular phase. At admission were recorded, primarily, gynecological status parameters: volume and echostructure ovary, uterus and breast [2,3] (applicable echokameras "Sonoline Elegra", BRD and "Acuson-128 XP/10", USA).

Endocrine status was assessed by plasma levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, thyroide stimulating hormone (TSH), estradiol, progesterone, testosterone, thyroxine, triiodothyronine, aldosterone and cortisol (ELISA used, applied analyzer "Tecan", Oesterreich, and a set of reagents for "Alkor Bio", RF).

Autonomic regulation was assessed by parameters heart rate variability (HRV) (used device "Cardio", Kyiv): moda, amplitude of moda, scale variation and autonomic (vegetative) stress index, as well as vegetative reactivity as the ratio of the stress index in standing and supine [1].

For personal indicators vegetative stress index Baevskiy (VSIB, units), cortisol (C, mg/l), aldosterone (A, ng/L), estradiol (E_2, ng/l) and triiodothyronine (T_3, nM/l) calculated neuro-hormonal stress index (NHSI) by the formula Popovych IL and Barylyak LG [11], which laid the average rates of parameters and coefficients of variability in the norm:

$$NHSI = [(VSIB/100 - 1)/0,375 + (C/165 - 1)/0,258 - (A/85 - 1)/0,441 - (E_2/115 - 1)/0,370 - (T_3/2,1 - 1)/0,238]/5$$

Immune status evaluated on a set of I and II levels recommended by the WHO, using standardized methods described in handbook [8]. For phenotyping subpopulations of lymphocytes the method of indirect immunofluorescent binding reaction monoclonal antibodies [9] from company "Sorbent" (RF) with visualization under fluorescent microscope. T-cellular immunity assessed by the following parameters: blood levels of a population of T lymphocytes (test of spontaneous rosette with sheep erythrocytes) and their subpopulations: highly active (test "active" rosette), theophylline resistance and theophylline sensitive (test sensitivity rosette to theophylline) and phenotype of $CD3^+CD4^+$(helpers/inductors). State of killer link of immunity estimated by the content of $CD3^+CD8^+$-lymphocytes (T-killers) and $CD16^+$-lymphocytes (natural killers). The state of humoral immunity judged by the content of $CD19^+$ B-lymphocytes and concentration in serum of immunoglobulins classes G, A, M (radial immunodiffusion method) and circulating immune complexes (with polyethylene glycol precipitation method).

Given the existence of weak but significantly relationships with a number of indicators of hormonal and immune status of the pH of the skin [13] it was also included in the list of tests.

In order to semi-quantitative evaluation of clinical symptoms (fatigue, headache, constipation, bloating, puffiness), as recommended Popovych IL and Barylyak LG [11] expressed their points in a scale Harrington: 0 - absence of symptoms; 0,285 - weakly expressed; 0,5 - moderate; 0,715 - strongly pronounced. Mood was assessed for severity of depression (negative points) or euphoria (positive points) for a 3-point scale [2].

After completion of drinking bioactive water Naftussya (3 ml/kg 30 minutes before meals three times a day), the duration of which corresponded to the duration of individual ovarian-menstrual cycle (21÷35 days) conducted retest. Reference values obtained when examining 30 healthy women of similar age Truskavets' residents.

RESULTS AND DISCUSSION

Based on the lifting of the provisional analysis was formed 6 groups of women, based on indicators of ovarian status and neuro-hormonal stress index and its dynamics under the influence of balneotherapy (Table 1).

Table 1. Features of the initial level chronic stress and the influence of bioactive water Naftussya in women with different ovarian status

Ovarial-gyneco-logycal status and Stress Index before/after	n	Para-meters	D/S - index	Volume of ovarium, cm^3		Cystose of ovarium, points			Neurohormonal Stress Index (SI)		
				Right	Left	Right	Left	Total	Initial	Final	Effect (difference)
D^0S^0An	21	X	1,39	7,4	5,3	0	0	0	0,53	0,06	-0,47
SI +/0		m	0,01	0,2*	0,2				0,11*	0,16	0,09#
D^0S^0A	65	X	1,12	6,3	5,8	0	0	0	0,81	0,38	-0,43

SI ++/+		m	0,05*	0,3*	0,2				0,08*	0,10	0,10#
D^-S^0Ad	17	X	7,1	36,6	5,5	-4	0	-4	0,78	0,74	-0,03
SI ++/++		m	1,1*	4,1*	0,3	0*		0*	0,08*	0,15*	0,14
D^-S^-As	22	X	0,87	10,4	17,6	-2,2	-3,3	-5,5	0,95	0,66	-0,29
SI ++/+		m	0,09*	1,1	3,3*	0,4*	0,3*	0,5*	0,11*	0,09*	0,12#
D^+S^+An	8	X	1,54	7,2	4,8	+1,4	+1,3	+2,7	0,81	0,99	+0,18
SI ++/++		m	0,09	0,5*	0,4	0,3*	0,3*	0,3*	0,12*	0,17*	0,08#
D^+S^+As	11	X	0,97	5,5	6,6	+1,3	+1,2	+2,5	0,63	0,15	-0,48
SI +/0		m	0,08*	0,6*	1,4	0,2*	0,2*	0,2*	0,13*	0,12	0,09#
Norm	30	X	1,40	9,1	6,5	0	0	0	0		
		m	0,01	0,8	0,8						
		Min	1,3	3,7	2,7				-0,5		
		Max	1,5	14,4	10,3				0,5		

Foot-notes. Significantes deviations from norm marked*, significantes changes after course rehabilitation marked#.

The first group included 21 women with absence (0) ovarian cysts and normal (right-hand) asymmetry (An), evaluated by an index Dexter/Sinister, in which moderately (+) expressed SI coming down to nothing. The second group consisted of 65 women with ovarian cysts absence, but the left-hand or ultra right-hand asymmetry, in which initially expressed (++) SI decreased to moderate (+). The third group formed 17 women with severe echonegative (-) cystose of right (D) ovarian that created ultra right-hand asymmetry (Ad), which was accompanied by a marked (++) SI, without influence of balneotherapy. 22 women fourth group were characterized by moderate bilateral ovarian echonegative cystose with their left-sided asymmetry (As), in which initially expressed (++) SI decreased to moderate (+). In 8 women with normal ovarian volume ratios were found echopositive (+) bilateral cystose, accompanied by a pronounced (++) SI, without influence of balneotherapy, even with a tendency to increase SI. Finally, in 11 women diagnosed bilateral ovarian echopositive cystose with left-sided asymmetry, in which moderate SI after balneotherapy coming down to nothing.

Related gynecological status parameters are shown in Table 2.

Table 2. Features gynecological status in women with different reaction of chronic stress on water balneotherapy

Ovarial-gyneco-logycal status and Stress Index before/after	n	Para-meters	Ovarial-menstrual cycle, days	Uterus		Cystose of breast, points		Mastopathy, points	
				volume, cm^3	myoma, points	Right	Left	Right	Left
D^0S^0An	21	X	29,4	88	0,67	+0,24	+0,29	-0,24	-0,33
SI +/0		m	0,7	7*	0,27*	0,27	0,29	0,27	0,27
D^0S^0A	65	X	28,1	72	0,25	+0,15	+0,14	-0,38	-0,54
SI ++/+		m	0,5	3*	0,09*	0,12	0,12	0,13*	0,15*
D^-S^0Ad	17	X	26,9	68	0,24	+0,41	+0,41	-0,47	-0,53
SI ++/++		m	1,3	5*	0,16	0,19*	0,19*	0,21*	0,24*
D^-S^-As	22	X	32,2	76	0,36	+0,45	+0,53	-0,73	-0,86
SI ++/+		m	1,5*	9*	0,18*	0,22*	0,23*	0,31*	0,32*
D^+S^+An	8	X	24,8	119	0,75	+0,38	+0,38	-0,25	-0,63
SI ++/++		m	1,0*	32*	0,41	0,26	0,26	0,25	0,42
D^+S^+As	11	X	28,8	84	0,40	+0,10	-0,27	-0,20	+0,09
SI +/0		m	1,5	16	0,25	0,10	0,38	0,19	0,09
Нормативи	30	X	28	53	0	0	0	0	0
		m	0,5	4					
		Min	21	32					
		Max	32	74					

To achieve the declared purpose used discriminant analysis method (forward stepwise) [4] using the software package "Statistica 5.5" and algorithm science school Truskavets' SPA [5,10].

Table 3. Discriminant Function Analysis Summary. Options statistics Wilks'

Step 10, N of variables in model: 10; Grouping: 6 groups;
Wilks' Lambda: 0,0127; approx. $F_{(51)}=19,0$; $p<10^{-6}$

Variables currently in model	Wilks' Λ	Partial Λ	F-rem (5,1)	p-level	Tole-rancy	F to enter	p-level	Λ	F-value	p-level

Ovarium Left Cystose	,067	,191	109,5	10^{-6}	,805	132	10^{-6}	,173	132,3	$<10^{-6}$
Ovarium Right Cystose	,042	,299	60,4	10^{-6}	,860	93,2	10^{-6}	,039	111,0	$<10^{-6}$
Ovaria Total Volume	,021	,604	16,9	10^{-6}	,860	16,1	10^{-6}	,025	70,8	$<10^{-6}$
Skin pH	,015	,840	4,9	10^{-3}	,878	4,78	10^{-3}	,021	49,6	$<10^{-6}$
Uterus Volume	,014	,880	3,5	,005	,912	2,75	,021	,019	38,1	$<10^{-6}$
Weakness	,014	,910	2,6	,031	,896	2,50	,034	,017	31,3	$<10^{-6}$
Sympathetic tone HRV	,014	,893	3,1	,011	,863	2,27	,051	,016	26,7	$<10^{-6}$
Prolactin plasma level	,014	,908	2,6	,027	,858	2,03	,079	,015	23,4	$<10^{-6}$
“Active” T-Lymphocytes	,014	,923	2,1	,064	,875	2,03	,079	,014	20,9	$<10^{-6}$
Moda HRV	,014	,924	2,1	,067	,926	2,12	,067	,013	19,0	$<10^{-6}$

The program includes in model 10 initial parameters (Table. 3), which reflect expected, above all, that of ovarian and gynecological status (4 indicators). It seems natural to include in the discriminant model of plasma prolactin and pH of the skin as a marker dependent on hormones secretion of the sebaceous glands [13], and two parameters vegetative status as markers of stress. Identification was also blood levels of the subpopulation of "active" T-lymphocytes as a representative of the neuroendocrine-immune complex. Finally, on the face of unexpected inclusion in the model of severity of weakness (fatigue) is understandable, when viewed as a marker of neuroendocrine and immune disfunction [12,14].

In the next stage of analysis 10-dimensional space discriminant variables were transformed in 6-dimensional space of canonical discriminant functions (canonical variables or roots), each of which is a linear combination of discriminant variables (tab. 4). The real usefulness of discriminant function given by the canonical correlation coefficient R - reliance among groups and discriminant function.

Table 4. Chi-Square Tests with Successive Roots Removed

Roots Removed	Eigen-value	Canonicl R	Wilks' Λ	χ^2	Degree freedom	p-level
0	8,189	0,944	0,013	589	50	$<10^{-6}$
1	4,395	0,903	0,117	290	36	$<10^{-6}$
2	0,397	0,533	0,630	62	24	$<10^{-4}$
3	0,092	0,290	0,880	17	14	0,24
4	0,041	0,198	0,961	5	6	0,49

According to the theory of discriminant analysis [4], instead of checking statistical significance of the discriminant function is considered residual discriminant ability of the system to determine the function. Residual discriminant ability - the ability to distinguish between groups of variables, excluding information obtained using previously calculated functions. Inverse measure of the differences between the groups in several discriminant variables are Λ-statistics Wilks'. What size smaller Wilks' Λ, the higher the distinction is clearer separation center cluster groups among themselves concerning the degree of scatter within clusters. It turned out that there are significant first three roots. Thus the first two roots contain 96% discriminant capacity calculated by the quota of the eigenvalues (tab. 5).

Table 5. Standardized and Raw Coefficients for Canonical Variables

	Standardized Coefficients					Raw Coefficients				
Variables currently in model	Root 1	Root 2	Root 3	Root 4	Root 5	Root 1	Root 2	Root 3	Root 4	Root 5
Ovarium Left Cystose	-,434	-1,013	,045	,032	-,045	-,711	-1,659	,073	,052	-,073
Ovarium Right Cystose	-,825	,496	-,129	-,199	-,029	-1,094	,657	-,172	-,264	-,039
Ovaria Total Volume	,400	-,585	-,326	-,314	-,089	,045	-,066	-,037	-,035	-,010
Skin pH	-,226	-,101	-,658	,020	-,352	-,711	-,318	-2,073	,062	-1,109
Uterus Volume	-,043	-,160	-,601	,246	,197	-,001	-,004	-,016	,006	,005
Weakness	,100	,236	-,385	-,120	,259	,296	,699	-1,138	-,354	,765
Sympathotone HRV	-,095	,292	,305	-,315	,555	-,015	,044	,046	-,048	,084
Prolactin plasma	,176	-,244	,040	-,606	-,093	,019	-,026	,004	-,065	-,010
“Active” T-Lymphocyt.	,098	-,227	-,211	-,341	,610	,010	-,022	-,021	-,033	,060
Moda HRV	-,141	,185	,217	-,467	-,342	-0,0014	0,0019	0,0022	-0,0048	-0,0035
					Constant	**3,332**	**1,406**	**11,517**	**6,805**	**5,666**
					Discriminant Properties, %	62,4	33,6	3,0	0,7	0,003

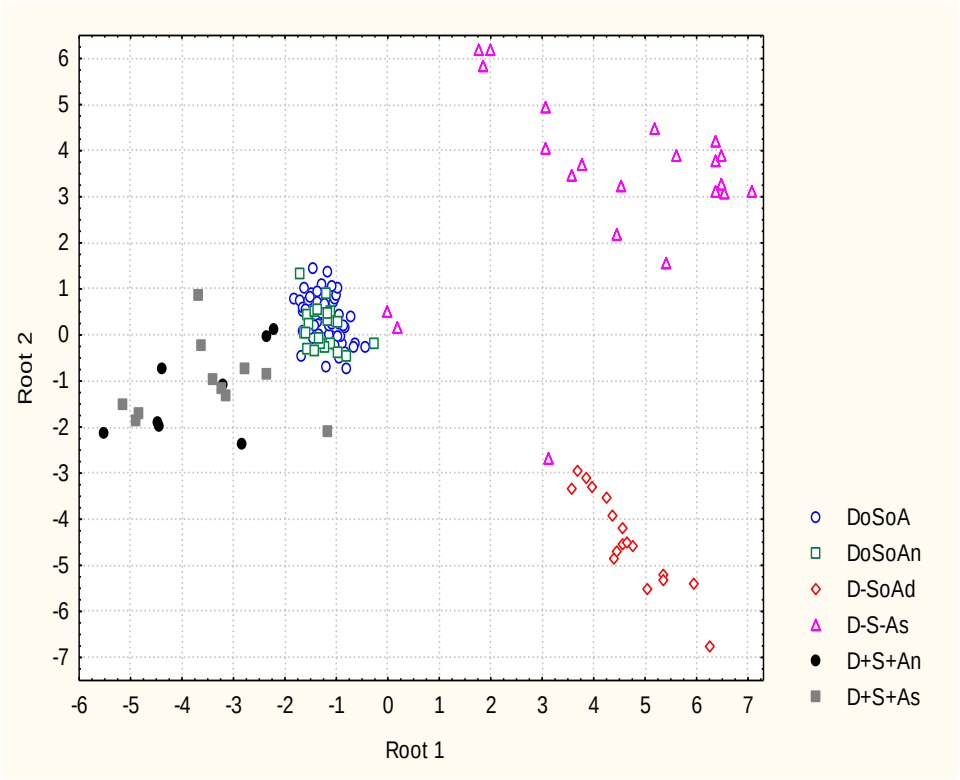
Table 6. Factor Structure Matrix (Correlations Variables - Canonical Roots) and Means of Variables in model

Variables currently in model	Root 1	Root 2	Root 3	Root 4	D^+S^+ An	D^+S^+ As	D^0S^0 An	D^0S^0 A	D^-S^- As	D^-S^0 Ad
Ovarium Right Cystose, point	**-0,72**	0,24	-0,18	-0,27	+1,4	+1,3	0	0	-2,2	-4
Ovaria Total Volume, cm^3	**0,38**	-0,21	-0,28	-0,36	12,1	12,1	12,8	12,1	28,0	42,1
Ovarium Left Cystose, points	-0,56	**-0,71**	0,22	0,09	+1,3	+1,2	0	0	**-3,3**	0
"Active" T-Lymphocytes, %	-0,03	**-0,09**	-0,10	-0,28	35,6	31,1	26,0	28,7	**24,9**	31,2
Skin pH	-0,02	0,05	**-0,58**	-0,14	**6,02**	5,87	5,78	5,57	5,81	5,55
Uterus Volume, cm^3	-0,05	0,00	**-0,43**	0,23	**119**	84	88	72	76	68
Weakness, points	-0,01	0,03	**-0,37**	-0,09	**0,50**	0,34	0,29	0,21	0,25	0,21
Moda HRV, msec	-0,02	0,02	**0,17**	-0,44	**846**	938	879	905	893	883
Prolactin plasma level, µg/l	0,01	0,00	-0,05	**-0,63**	12,6	18,7	**10,9**	13,3	15,2	14,2
Sympathetic tone (AMo), %	0,02	0,05	0,13	**-0,27**	20,0	19,0	**17,8**	21,2	21,7	19,5

The **relative** contribution of each variable (independent of units of measurement) in the value of discriminant function **standardized** coefficients reflect, whereas **non-standardized** coefficients provide information on the **overall** contribution of the variable (Table 5).

Complete structural coefficients - the coefficients correlation between the discriminant function and variable - show how closely related variables and discriminant function, that is what share information discriminant function built into this variable (tab. 6).

Sum of products of non-standardized discriminant coefficients on the values of variables with constant given values discriminant function for each individual. The value of discriminant functions define a point in their information space, which makes it possible to visualize each person or group.



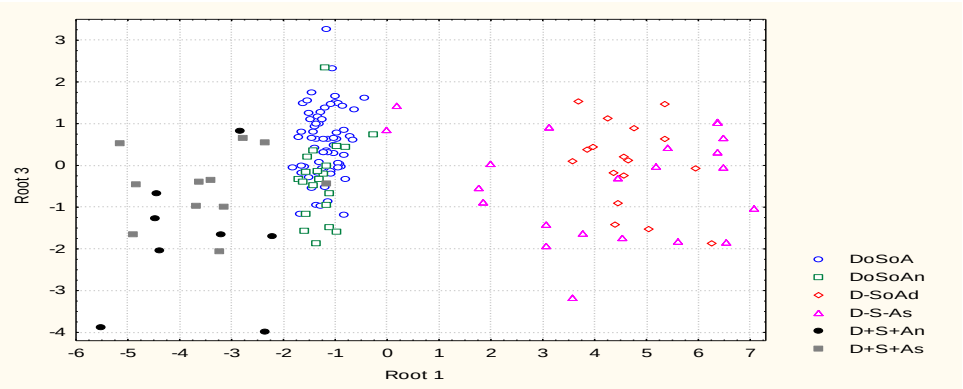
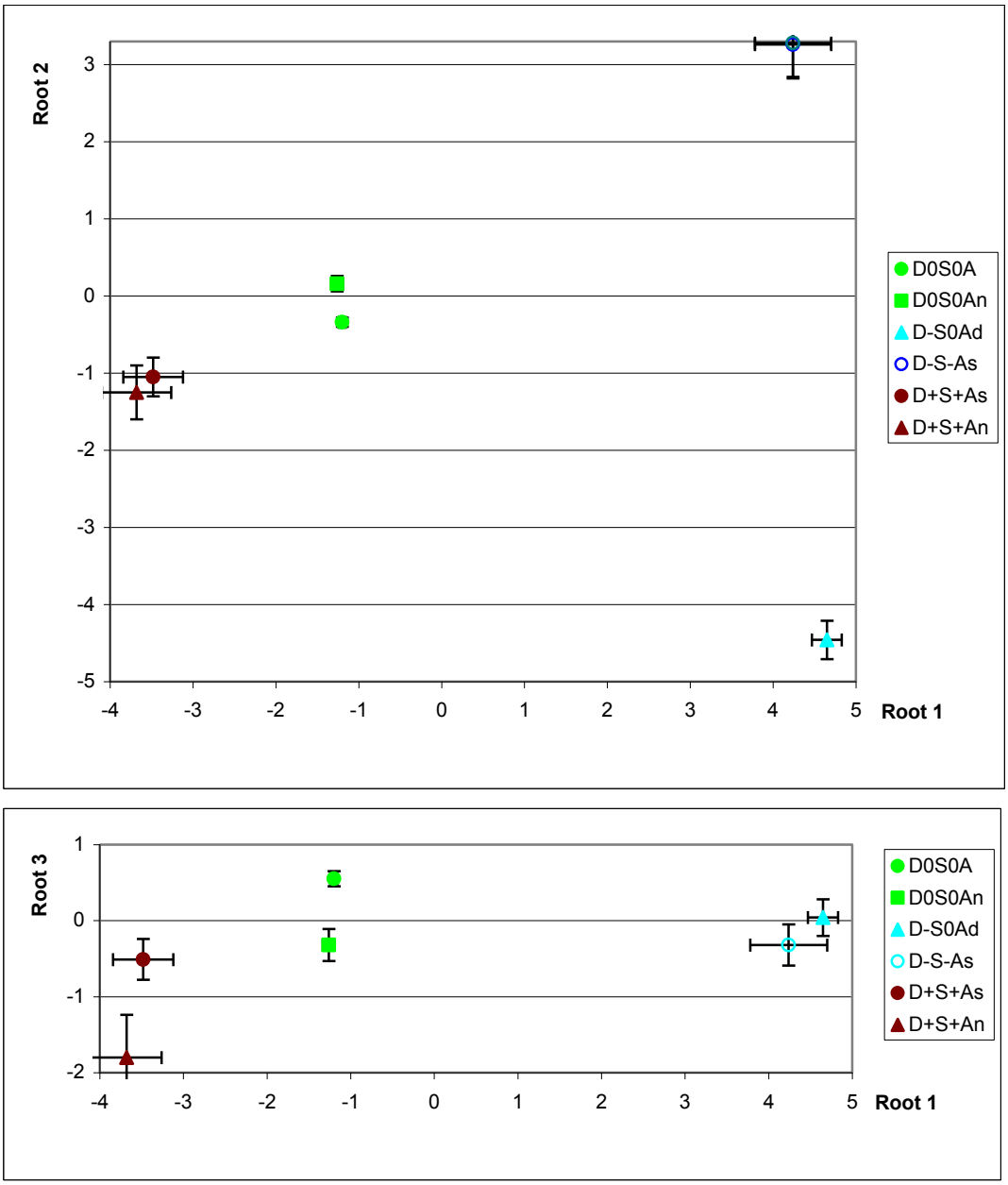


Fig. 1. Personal non-standardized canonical value of the first three roots of the information field of women with different ovarian-gynecological status

As can be seen (Fig. 1) along the axis of the first root zone of negative values taken by women with ovarian statuses D^+S^+An and D^+S^+As, and both clusters are not separated, that documented the calculation of averages (centroids) canonical roots (Table. 7, Fig. 2). Quasizero zone of axis of first root occupy the women with statuses D^oS^oAn and D^oS^oA, not separated too. Finally, women with ovarian statuses DS^-As and D^-S^oAd located in the area of positive values of the axis of the first root. The location of clusters displayed as a negative correlation first root with the echogenicity just right (D) ovaries and positive correlation with the total volume of both ovaries, resulting virtual route cystose right ovary echogenicity pattern for $D^+S^+An \approx D^+S^+As < D^oS^oAn \approx D^oS^oA < D^-S^-As \approx D^-S^oAd$ and total volume of both ovaries at the opposite pattern $D^+S^+An \approx D^+S^+As > D^oS^oAn \approx D^oS^oA > D^-S^-As \approx D^-S^oAd$ (Table. 6 and 7, Fig. 1 and 2).



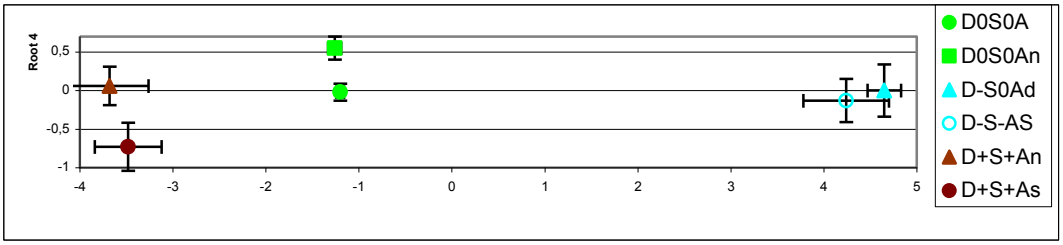


Fig. 2. The non-standardized canonical value centroids first four roots of the information field of women with different ovarian-gynecological status

Table 7. Means of Canonical Variables

Groups	Root 1	Root 2	Root 3	Root 4	Root 5
DoSoA	-1,20±0,04	+0,34±0,06	+0,55±0,10	-0,02±0,11	+0,09±0,12
DoSoAn	-1,26±0,07	+0,16±0,10	-0,32±0,21	+0,55±0,15	-0,27±0,18
D-SoAd	+4,65±0,18	-4,46±0,25	+0,04±0,24	0,00±0,34	0,00±0,24
D-S-As	+4,24±0,46	+3,28±0,44	-0,44±0,27	-0,13±0,28	0,00±0,22
D+S+An	-3,68±0,42	-1,25±0,35	-1,80±0,56	+0,06±0,25	+0,50±0,50
D+S+As	-3,48±0,36	-1,05±0,25	-0,51±0,27	-0,73±0,31	-0,38±0,34

Along the axis of the second root clusters D^+S^+An and D^+S^+As also not delineated, while between centroids of clusters D^oS^oAn and D^oS^oA already appears negligible "gap" and clusters D^-S^-As and D^-S^oAd fully delineated. The location of clusters along the axis of the second root reflects its strong negative correlation with echogenicity just left (S) ovarian and weak - with blood level of "active" T-lymphocytes described pattern $D^-S^oAd»D^-S^-As<D^oS^o\approx Ad^oS^oAn< D^+S^+As<D^+S^+An$.

Only along the axis of the third root centroids clusters D^+S^+An and D^+S^+As as well as D^oS^oAn and D^oS^oA delineated clearly, while the disengagement clusters D^-S^-As and D^-S^oAd unclear. This reflects the pairwise differences between clusters at pH skin, uterine volume, severity of weakness and to a lesser extent, the largest of moda HRV. Virtual route centroids of clusters along axis of the third root described by pattern $D^+S^+An>D^+S^+As\approx D^-S^-As\approx D^oS^oAn>D^-S^oAd>D^oS^oA$ (regarding moda HRV direction is opposite).

Mirror placement centroids of clusters D^+S^+An and D^+S^+As as well as D^oS^oAn and D^oS^oA along the axis of the fourth root reflect the reverse way prolactinemia, the minimum of which ascertained women cluster D^oS^oAn. Pattern looks like: $D^+S^+As>D^+S^+An>D^oS^oAn<D^oS^oA<D^-S^-As\approx D^-S^oAd$. Women cluster D^oS^oAn identified as the minimum level of sympathetic tone, but it correlates directly with the fifth root.

In total set of 10 discriminant variables all clusters significant (with one exception) are different from each other, as evidenced by the squared Mahalanobis distances between them (Table. 8).

Table 8. Squared Mahalanobis Distances between groups (over bisector) and values F (df=10,1) and p (under bisector)

Groups	DoSoA	DoSoAn	D-SoAd	D-S-As	D+S+An	D+S+As
DoSoA	0	1,0	60	41	15	9
DoSoAn	**2** ($p=0,05$)	0	59	42	11	8
D-SoAd	**72** ($p<10^{-6}$)	**49** ($p<10^{-6}$)	0	63	87	82
D-S-As	**60** ($p<10^{-6}$)	**40** ($p<10^{-6}$)	**53** ($p<10^{-6}$)	0	89	82
D+S+An	**9** ($p<10^{-6}$)	**5** ($p<10^{-5}$)	**40** ($p<10^{-6}$)	**44** ($p<10^{-6}$)	0	3
D+S+As	**8** ($p<10^{-6}$)	**5** ($p<10^{-5}$)	**47** ($p<10^{-6}$)	**52** ($p<10^{-6}$)	**1,3** ($p=0,26$)	0

Fees discriminant variables enable retrospectively identify persons belonging to a particular cluster. This is achieved by classification (discriminant) functions - special linear combinations for each group to maximize differences between groups and minimize the variance within groups (Table. 9).

Table 9. Classification Functions and Constants for groups

Variables in model	DoSoA	DoSoAn	D-SoAd	D-S-As	D+S+An	D+S+As
Ovarium Left Cystose	6,082	6,421	9,851	-2,726	10,291	9,929
Ovarium Right Cystose	4,247	4,207	-5,215	0,434	6,278	6,214
Ovaria Total Volume	0,189	0,214	0,789	0,282	0,261	0,246
Skin pH	61,39	63,74	59,91	58,74	68,08	66,12
Uterus Volume	0,104	0,120	0,125	0,100	0,153	0,122

Weakness	-0,798	-0,428	-1,909	3,966	0,308	-1,351
Sympathetic tone HRV	0,364	0,258	0,034	0,367	0,251	0,281
Prolactin plasma level	-0,248	-0,281	-0,016	-0,218	-0,272	-0,209
"Active" T-Lymphocytes	0,074	0,055	0,242	0,080	0,156	0,101
Moda HRV	0,104	0,100	0,086	0,100	0,098	0,107
Constants	**-227,6**	**-237,6**	**-242,3**	**-232,7**	**-272,7**	**-264,7**

Odds classification functions are not standardized, so be not interpreted. The person belongs to a group of maximum value function computed by summation of the quantities of products at variable rates of classification functions plus constants.

Discovered (tab. 10) that all 17 women with ovarian status D^-S^oAd identified accurately, fairly high accuracy of identification of women with ovarian statuses D^oS^oA and D^-S^-As, moderate - on status D^+S^+An and D^+S^+As, but low - for women with ovarian status D^-S^oAs, but in this case, the accuracy of discrimination twice as high as the probability of random assignment of individuals to this cluster (100%/6=16,7%). Overall accuracy identification is 78,8%.

Table 10. Classification Matrix. Rows: Observed classifications; Columns: Predicted classifications

Groups	Percent Correct	DoSoA p=0,451	DoSoAn p=0,146	D-SoAd p=0,118	D-S-As p=0,153	D+S+An p=0,056	D+S+As p=0,076
DoSoA	90,8	59	6	0	0	0	0
DoSoAn	33,3	14	7	0	0	0	0
D-SoAd	100	0	0	17	0	0	0
D-S-As	86,4	2	0	1	19	0	0
D+S+An	62,5	1	0	0	0	5	2
D+S+As	54,5	3	0	0	0	2	6
Total	**78,5**	79	13	18	19	7	8

Thus, the groups of women with different ovarian status differ not only in the absence or presence echonegative or echopositive ovarian cysts, but the volume ovarian and uterine, prolactin plasma level, pH of the skin, blood levels of the subpopulation of "active" T-lymphocytes, sympathetic tone and moda HRV, as well as the severity of weakness.

The next step discriminant analysis were subjected to changes in rates of neuroendocrine-immune status and severity of clinical symptoms to identify those changes which groups of women with different ovarian status differ. Such indicators revealed 19 (tab. 11).

Table 11. Discriminant Function Analysis Summary. Options statistics Wilks'

Step 19, N of vars in model: 19; Grouping: 6 groups

Wilks' Lambda: 0,287; approx. $F_{(96)}=1,81$; $p<10^{-4}$

Variables which changes currently in model	Wilks' Λ	Partial Λ	F-rem (5,12)	p-level	Tole-rancy	F to enter	p-level	Λ	F-value	p-level
Triiodthyronine level	,330	,871	3,56	,005	,738	3,48	,005	,888	3,48	,005
$CD16^+$ Lymphocytes	,307	,935	1,67	,147	,806	2,65	,025	,810	3,05	,001
Sympathetic tone HRV	,308	,931	1,77	,124	,144	2,60	,028	,739	2,90	10^{-3}
$CD19^+$ B-Lymphocytes	,311	,924	1,96	,089	,882	2,16	,062	,684	2,72	10^{-3}
Moda HRV	,307	,933	1,71	,137	,692	2,11	,068	,634	2,60	10^{-4}
Puffiness	,320	,897	2,76	,021	,803	1,97	,087	,590	2,51	10^{-4}
Theophyllinsens. T-Lym.	,312	,921	2,07	,074	,918	2,07	,073	,547	2,45	10^{-4}
Headache	,311	,922	2,03	,080	,789	1,66	,148	,515	2,36	10^{-5}
Constipation	,308	,932	1,76	,125	,785	1,56	,176	,486	2,28	10^{-5}
Meteorism	,301	,955	1,14	,343	,792	1,56	,177	,458	2,21	10^{-5}
Vegetative Reactivity	,314	,915	2,22	,056	,833	1,52	,190	,432	2,15	10^{-5}
Aldosterone plasma level	,306	,937	1,60	,164	,831	1,74	,130	,405	2,13	10^{-5}
Weakness	,305	,942	1,48	,201	,814	1,40	,228	,383	2,07	10^{-5}
Systolic Blood Pressure	,303	,948	1,33	,257	,924	1,38	,238	,363	2,03	10^{-5}
Skin pH	,306	,937	1,62	,160	,844	1,28	,278	,346	1,98	10^{-5}

“Active” T-Lymphocytes	,302	,952	1,21	,308	,822	1,40	,227	,327	1,95	10^{-5}
Stress Index HRV	,302	,950	1,25	,288	,142	1,03	,401	,314	1,89	10^{-4}
Leucocytes blood level	,301	,952	1,20	,312	,851	1,16	,332	,299	1,86	10^{-4}
TTH plasma level	,299	,959	1,02	,406	,823	1,02	,406	,287	1,81	10^{-4}

Firstly, this performance, which was calculated neuro-hormonal stress index: vegetative stress index, sympathetic tone, moda HRV, triiodothyronine and aldosterone.

Secondly, this other neuro-hormonal parameters: autonomic reactivity, thyroid-stimulating hormone, and subordinates neuro-hormonal regulation of systolic blood pressure and pH of the skin.

The third group consists of immune parameters: total blood levels of white blood cells, the relative level of "active" and theophyllin sensitive T-lymphocytes, B-lymphocytes and natural killer cells.

The fourth group consisted of clinical symptoms: fatigue, puffiness, headaches, constipation and flatulence.

Identification information contained in the 19 indicators condensed into 5 canonical roots, but only three of them play a significant role in discrimination, accounting for 81,4% of inter-group variance (tab. 12).

Table 12. Chi-Square Tests with Successive Roots Removed

Roots Removed	Eigen-value	Canoni-cal R	Wilks' Lambda	Chi-Sqr.	df	p-level
0	,621	,619	,287	163	95	10^{-4}
1	,306	,484	,465	100	72	0,02
2	,272	,462	,608	65	51	0,09
3	,153	,365	,773	34	32	0,39
4	,121	,329	,892	15	15	0,45

This first root contains 42,1% of distinctive features, the second – 20,8%, the third – 18,5% (tab. 13).

Table 13. Standardized and Raw Coefficients for Canonical Variables

	Standardized Coefficients					Raw Coefficients				
Variables which changes currently in model	Root 1	Root 2	Root 3	Root 4	Root 5	Root 1	Root 2	Root 3	Root 4	Root 5
Triiodthyronine level	-,259	-,523	,568	,121	,363	-,522	-1,06	1,146	,243	,732
$CD16^+$ Lymphocytes	-,145	,346	-,342	-,180	,378	-,097	,232	-,229	-,120	,253
Sympathotone HRV	,624	,949	-,079	-,919	,131	,089	,135	-,011	-,130	,019
$CD19^+$ B-Lymphocytes	-,441	,142	,149	,026	-,132	-,180	,058	,061	,011	-,054
Moda HRV	,281	-,460	,202	-,233	-,058	2,663	-4,36	1,915	-2,20	-,545
Puffiness	-,448	,078	,212	-,320	-,500	-2,33	,407	1,102	-1,67	-2,60
Theophyllinsens. T-Lym.	,349	-,061	,005	,539	,053	,043	-,007	,001	,066	,006
Headache	-,226	-,314	-,495	-,122	,124	-,804	-1,12	-1,76	-,433	,442
Constipation	,374	,300	,189	-,104	-,178	2,935	2,354	1,479	-,817	-1,39
Meteorism	,039	-,246	-,418	-,074	,204	,312	-1,96	-3,33	-,588	1,626
Vegetative Reactivity	,233	-,523	-,065	-,158	-,341	,185	-,414	-,051	-,125	-,270
Aldosterone plasma level	-,381	,038	,153	,275	,204	-,011	,001	,005	,008	,006
Weakness	-,086	-,006	,515	-,136	,294	-,330	-,023	1,976	-,520	1,129
Systolic Blood Pressure	,328	-,168	-,197	,060	,014	,038	-,020	-,023	,007	,002
Skin pH	-,394	-,180	-,123	-,182	,010	-1,39	-,633	-,434	-,640	,037
“Active” T-Lymphocytes	-,158	-,283	-,232	-,348	-,154	-,018	-,033	-,027	-,040	-,018
Stress Index HRV	-,317	-1,089	,247	,375	,148	-,004	-,012	,003	,004	,002
Leucocytes blood level	-,250	-,235	-,186	,297	-,001	-,223	-,210	-,166	,264	-,001
TTH plasma level	-,044	-,165	-,405	,207	-,130	-,025	-,095	-,234	,119	-,075
					Constants	**,437**	**,157**	**-,600**	**-,423**	**,369**
					Discriminant Properties, %	**42,1**	**20,8**	**18,5**	**10,4**	**8,2**

Table 14. Factor Structure Matrix. Correlations Variables - Canonical Roots (Pooled-within-groups correlations)

Variables which changes currently in model	R 1	R 2	R 3	R 4	R 5	D^0S^0 A	D^-S^- As	D^-S^0 Ad	D^+S^+ As	D^0S^0 An	D^+S^+ An
$CD19^+$ B-Lymphocytes, %	**-0,35**	,15	,12	-,13	-,05	**+0,3**	-0,6	+0,1	+0,2	-0,9	**-2,5**
Skin pH	**-0,24**	-,02	-,18	-,11	,08	**+0,05**	+0,01	+0,02	-0,17	-0,15	**-0,23**
Puffiness, points	**-0,23**	-,01	,07	-,19	-,63	**+0,07**	+0,12	+0,11	+0,15	+0,04	**-0,12**
$CD16^+$ Lymphocytes, %	**-0,16**	,27	-,16	-,21	,48	**+0,1**	-0,7	+0,1	-0,9	-0,8	-0,3
Aldosterone plasma, ng/l	**-0,15**	,04	,09	,18	,14	**+18**	+9	+5	+15	+12	**+4**
Headache, points	**-0,16**	-,13	-,36	-,27	,08	**-0,14**	-0,09	-0,08	-0,14	-0,17	**-0,27**
Weakness, points	**-0,13**	-,11	,18	-,17	,26	**-0,12**	-0,11	-0,13	-0,17	-0,08	**-0,26**
Sympathotone (AMo), %	**0,29**	-,07	,07	-,43	,31	-2,3	-3,1	+1,9	-2,3	+1,3	**+3,7**
Theophyllinsensit. T-Lym, %	**0,28**	-,09	,03	,39	,05	-0,5	+1,2	-2,7	+1,5	+2,4	**+7,4**
Systol. Blood Pressure, mmHg	**0,25**	-,09	-,24	,06	-,08	**-3**	+2	-1	-3	0	**+5**
Moda HRV, sec	**0,24**	-,20	,18	-,30	,07	**-0,07**	-0,06	-0,02	-0,04	+0,01	-0,01
Constipation, points	**0,20**	,26	-,04	-,17	-,23	**-0,06**	-0,04	0,00	-0,01	-0,08	**+0,03**
Stress Index HRV, units	**0,17**	-,09	,02	-,35	,25	-17	-24	+22	-27	+16	**+26**
Triiodthyronine level, nM/l	-,10	**-0,41**	,44	,12	,34	+0,33	+0,14	+0,12	+0,33	**+0,67**	+0,04
Vegetative Reactivity, units	,06	**-0,40**	,11	-,05	-,35	+0,19	+0,77	+0,40	+0,62	**+1,07**	+0,05
“Active” T-Lymphocytes, %	-,07	**-0,24**	-,07	-,24	-,00	+0,7	+1,9	+2,6	-1,7	**+3,0**	-2,6
Leucocytes blood level, 10^9/l	-,09	**-0,23**	-,14	,19	-,10	-0,23	-0,10	-0,54	-0,52	**-0,11**	-0,61
Meteorism, points	,01	-,17	**-0,39**	-,10	,11	-0,07	**-0,03**	-0,05	**-0,16**	-0,06	-0,06
TTH plasma level, mIU/l	,01	-,21	**-0,20**	,20	,03	+0,03	**+0,51**	-0,33	**-0,56**	+0,29	+0,14

Analysis of the factor structure matrix (tab. 14) shows that the first root of the inverse way reflects changes in blood level B-lymphocytes and NK- lymphocytes, pH of skin, aldosteronemiai and severity of puffiness, headaches and weakness, while directly - changes in sympathetic tone, systolic blood pressure, moda HRV and autonomic stress index and theophyllin sensitive T-lymphocytes and severity of constipation.

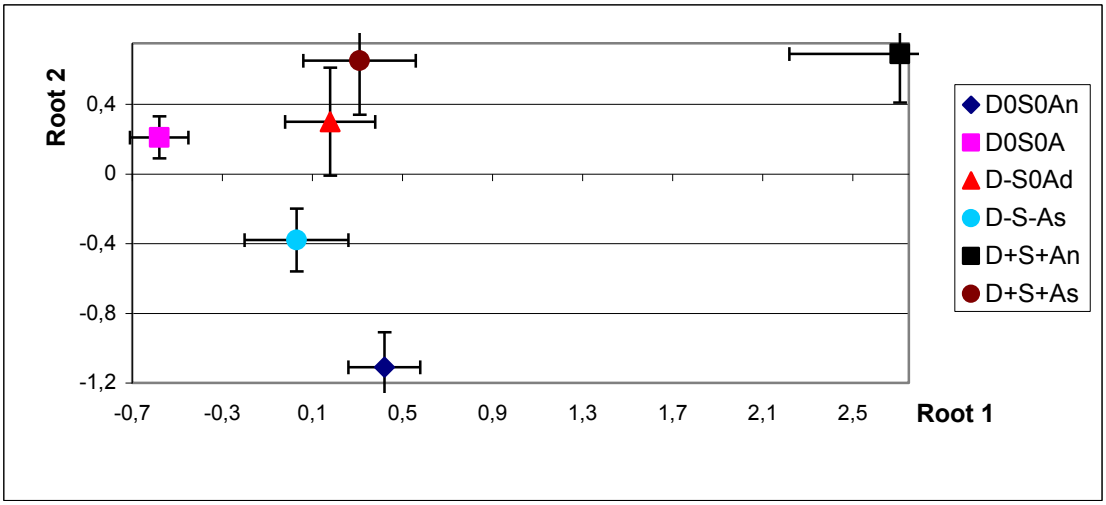
The second root is also the reverse way reflects the dynamics of autonomic reactivity and levels triiodothyronine, "active" T-lymphocytes and total leukocytes.

The third root is also negatively associated with severity of bloating and changes in plasma levels of thyroid-stimulating hormone.

Calculations according to Table. 13 averages canonical roots (tab. 15) with subsequent visualization (Fig. 3 and 4) shows a fairly clear distinction between groups of women for their reactions to the use of bioactive water Naftussya.

Table 15. Means of Canonical Variables

Groups	Root 1	Root 2	Root 3	Root 4	Root 5
DoSoA	-0,58±0,13	+0,21±0,12	-0,03±0,11	+0,13±0,13	+0,21±0,12
DoSoAn	+0,42±0,16	-1,11±0,20	+0,51±0,21	-0,07±0,19	+0,19±0,23
D-SoAd	+0,18±0,20	+0,30±0,31	-0,17±0,20	-1,01±0,23	-0,10±0,20
D-S-As	+0,03±0,23	-0,38±0,18	-0,75±0,21	+0,23±0,20	-0,54±0,22
D+S+An	+2,71±0,49	+0,69±0,28	-0,42±0,51	+0,36±0,27	+0,42±0,31
D+S+As	+0,31±0,25	+0,65±0,31	+1,27±0,49	+0,23±0,33	-0,68±0,37



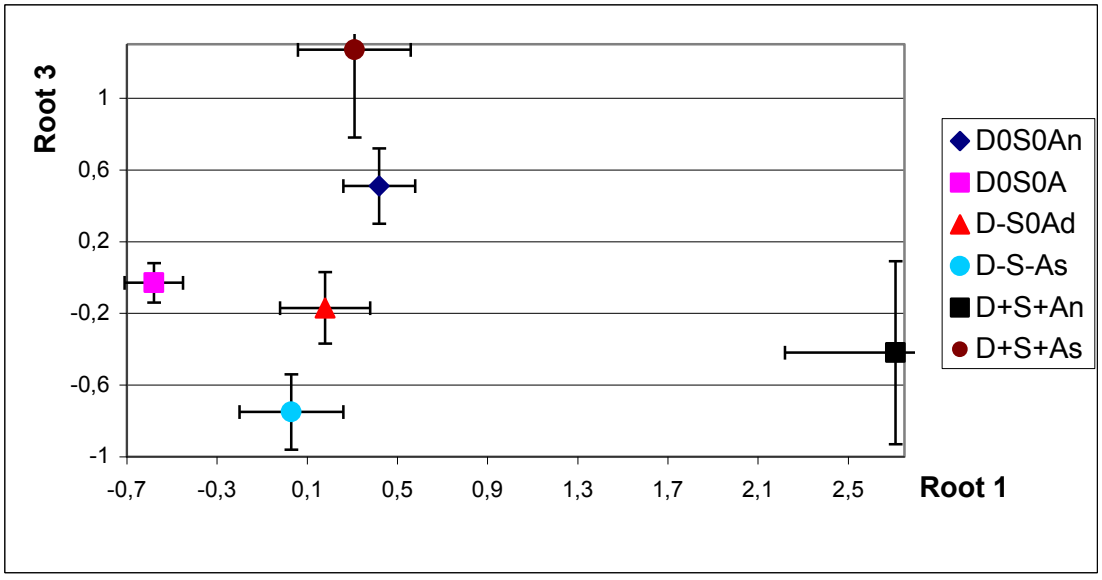
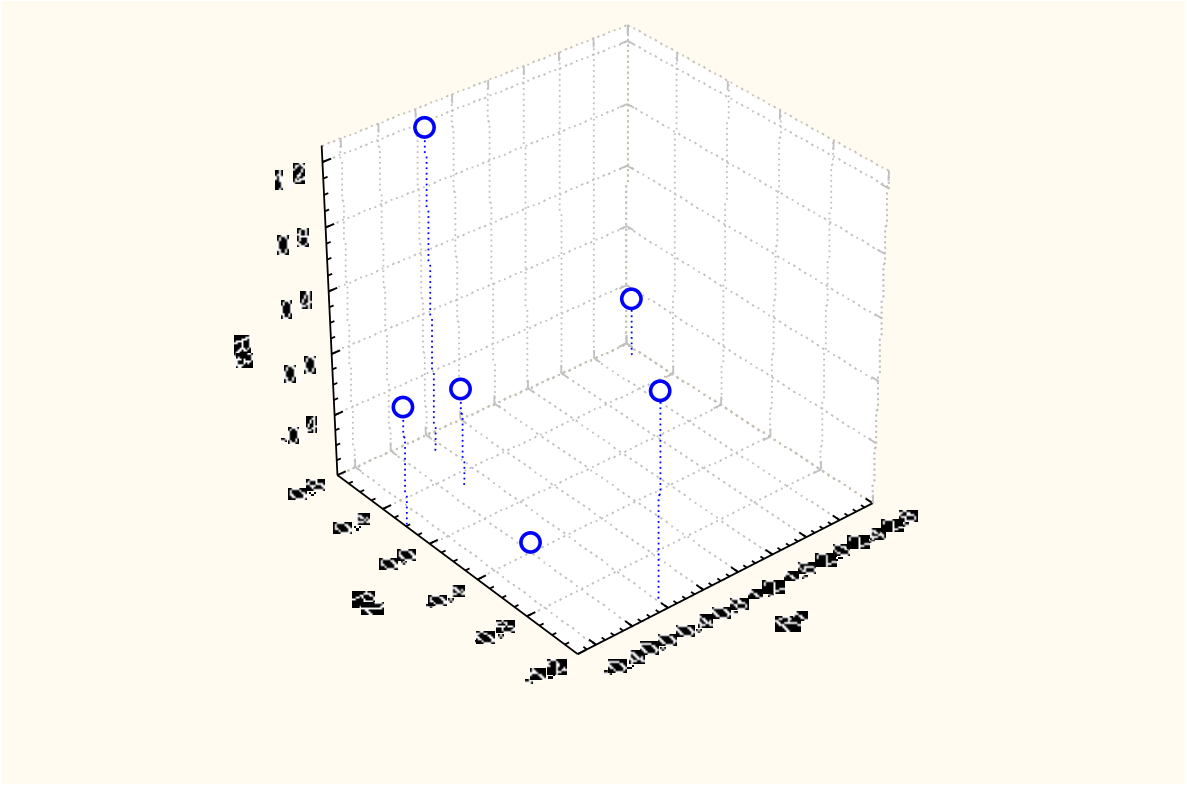


Figure 3. Nonstandardized canonical value centroids first three roots of the information field of women with different ovarian gynecological statuses and reactions to streslimiting effect of balneotherapy



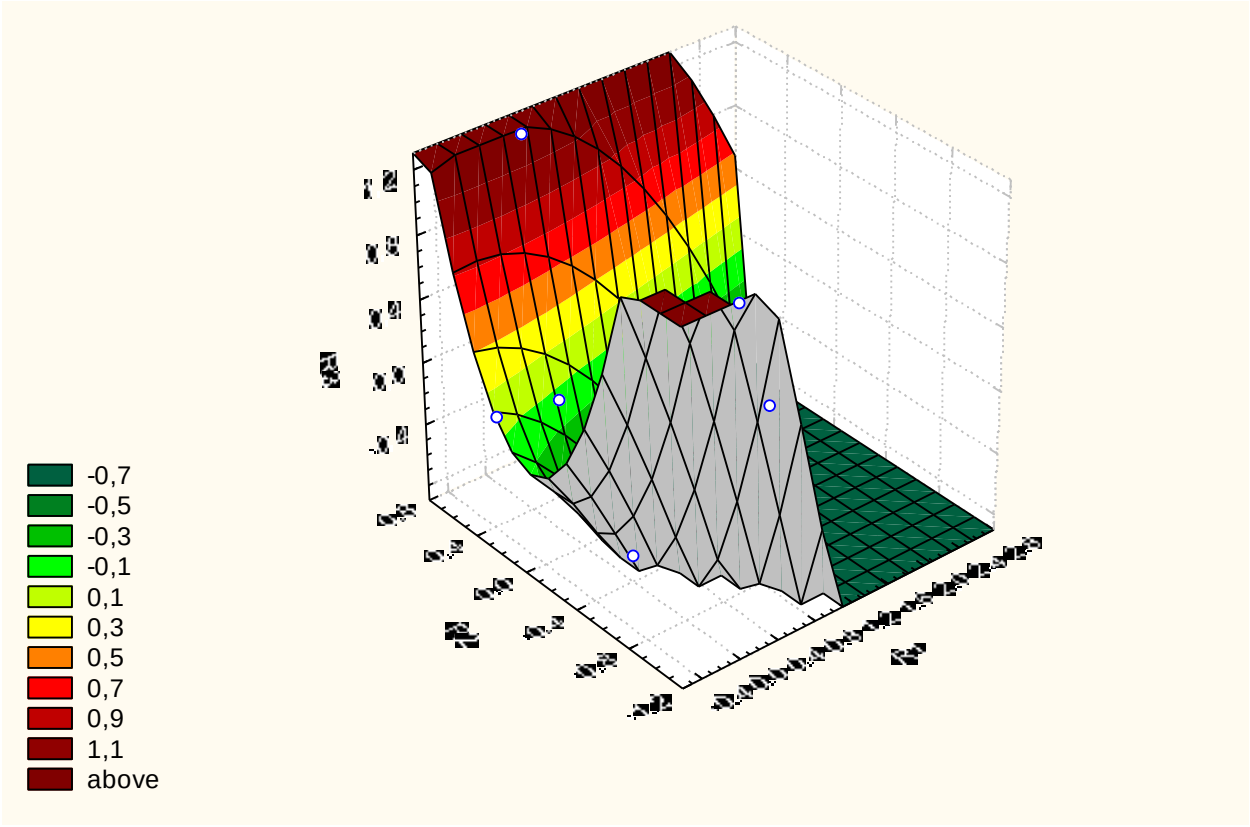


Figure 4. Localization in 3D-space centroids groups of women with different ovarian gynecological statuses and reactions to streslimiting effect bioactive water Naftussya

It is seen that among the axis of the first root of extreme negative position taken by the changes in women cluster D^0S^0A, but in the opposite positive zone of axis is cluster D^+S^+An, while other clusters are located in the quasizero area and not delineated. This illustrates the fact (tab. 14) that changes the first 5 indicators, negatively correlated with the first root, the most positive in the cluster D^0S^0A and/or maximum negative in cluster D^+S^+An, while the dynamics of these indicators in women of other clusters severity intermediate and approximately the same.

A somewhat different situation with the severity of headaches and weakness, that most decreases in women cluster D^+S^+An. Conversely, 6 indicators, positively correlated with the first root, most grow in cluster D^+S^+An and/or maximum fall in the cluster D^0S^0A, while the dynamics of these indicators in women of other clusters intermediate severity and again about the same.

More or less clear assignment of clusters is performed along the axis of the second radical, negatively correlated with changes in indicators, most pronounced in women cluster D^0S^0An. However, the sharpest distinction between clusters is performed along the axis of the third radical, negatively correlated with the severity of bloating and changes in plasma levels of TSH. At most pronounced negative changes in women cluster D^+S^+As, and minimum or maximum negative positive in women cluster D^-S^-As (tab. 14, fig. 3).

More or less clear assignment of clusters is performed along the axis of the second radical, negatively correlated with changes in indicators, most pronounced in women cluster D^0S^0An. However, the sharpest distinction between clusters is performed along the axis of the third radical, negatively correlated with the severity of bloating and changes in plasma levels of TSH. At most pronounced negative changes in women cluster D^+S^+As, and minimum or maximum negative positive in women cluster D^-S^-As (tab. 14, fig. 3).

Most clearly delineation of 6 clusters visible in 3D-space first three roots (Fig. 4).

Yet the accuracy of identification of clusters by their changes performance appeared very high only for clusters D^oS^oA and D^+S^+An, moderatein cluster D^oS^oAn, as well as for the entire sample (tab. 16 and 17).

Table 16. Classification Matrix. Rows: Observed classifications; Columns: Predicted classifications

Groups	% Correct	DoSoA	DoSoAn	D-SoAd	D-S-As	D+S+An	D+S+As
DoSoA	86,2	**56**	2	3	3	0	1
DoSoAn	57,1	7	**12**	1	1	0	0
D-SoAd	29,4	11	1	**5**	0	0	0

D-S-As	31,8	10	2	2	**7**	0	1
D+S+An	75,0	1	0	0	1	**6**	0
D+S+As	36,4	6	0	0	1	0	**4**
Total	**62,5**	91	17	11	13	6	6

Table 17. Coefficients and Constants for Classification Functions

Variables which changes currently in model	DoSoA	DoSoAn	D-SoAd	D-S-As	D+S+An	D+S+As
Triiodthyronine level	1,578	3,010	,425	,542	-,873	1,512
$CD16^+$ Lymphocytes	,046	-,463	,081	-,188	-,046	-,473
Sympathotone HRV	-,127	-,197	,096	-,173	,207	-,033
$CD19^+$ B-Lymphocytes	,101	-,124	-,035	-,045	-,494	,094
Moda HRV	-5,177	4,765	-1,110	-2,157	,120	-1,976
Puffiness	3,652	1,757	4,466	2,985	-5,171	5,344
Theophyllinsensitive T-Lymph	-,022	,017	-,067	,010	,131	,014
Headache	-,759	-,955	-,872	,325	-3,258	-4,683
Constipation	-3,373	-2,567	,229	-3,122	6,340	3,337
Meteorism	-3,596	-2,395	-2,910	-1,103	-2,013	-10,0
Vegetative Reactivity	-,189	,548	,150	,397	,152	-,045
Aldosterone plasma level	,024	,012	,004	,010	-,011	,016
Weakness	-1,092	-,243	-1,382	-3,608	-2,826	,112
Systolic Blood Pressure	-,043	,007	-,021	,008	,084	-,049
Skin pH	,859	,201	,520	,621	-3,980	-1,309
"Active" T-Lymphocytes	,012	,031	,051	,049	-,065	-,041
Stress Index HRV	,005	,018	-,005	,007	-,013	-,001
Leucocytes blood level	-,001	-,088	-,466	,138	-,709	-,478
TTH plasma level	-,044	-,092	-,151	,235	-,072	-,332
Constants	**-2,089**	**-3,874**	**-3,004**	**-3,198**	**-6,380**	**-5,657**

This provision is documented by calculating Mahalanobis distances between groups (tab. 18).

Table 18. Mahalanobis distances squares between groups (over bisector) and values F (df=19,1) and p (under bisector)

	DoSoA	DoSoAn	D-SoAd	D-S-As	D+S+An	D+S+As
DoSoA	0	3,23	2,08	1,90	11,75	3,61
DoSoAn	**2,25** ($p<10^{-3}$)	0	3,62	3,04	9,98	4,74
D-SoAd	**1,22** (p=0,25)	**1,47** (p=0,11)	0	2,67	9,09	4,23
D-S-As	**1,38** (p=0,15)	**1,42** (p=0,13)	**1,11** (p=0,35)	0	9,81	5,49
D+S+An	**3,39** ($p<10^{-3}$)	**2,37** ($p<10^{-3}$)	**2,03** (p=0,01)	**2,36** ($p<10^{-3}$)	0	10,24
D+S+As	**1,43** (p=0,13)	**1,45** (p=0,12)	**1,19** (p=0,28)	**1,70** (p=0,04)	**1,93** (p=0,02)	0

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