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Three types of gall-bladder motility at men with chronic cholecystitis and pyelonephritis and accompanying their parameters of kidney excretory function as well as metabolism

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Abstracts

Background. Previously it has been shown that balneotherapy in the spa Truskavets' (Ukraine) in men with chronic cholecystitis combined with pyelonephritis causes changes in gall-bladder motility. This is combined with changes in diuresis and urinary excretion of metabolites. Individual analysis revealed not only quantitative but also qualitative differences in the postprandial motility of the gall-bladder. The purpose of this study is to identify the parameters of kidney excretory function as well as metabolism under which three types of the gall-bladder motility skills differ significantly from each other. **Material and methods.** The object of observation were the same ones 22 men aged 24-70 years old, who came to the spa Truskavets' for the treatment of chronic cholecystitis combined with pyelonephritis in remission. On the tone and motility of gall-bladder judged by its fasting and postprandial volume (echocamera "Radmir"). In the daily determined content of oxalate and nitrogen metabolites: creatinine, urea and uric acid, electrolytes: phosphates, chloride, calcium, magnesium, potassium and sodium. Nitrogenous metabolites in plasma of venous blood were determined also. The survey was conducted twice, before and after balneotherapy. **Results.** The method of cluster analysis has formed three homogeneous cholekinetics groups, namely: normokinesia as well as hypertonic-hyperkinetic and hyperkinetic-hypertonic dyskinesia. The method of discriminatory analysis revealed 13 parameters of daily urine and three parameters of blood, as well as body weight and height, electrokinetic index and Kerdoe's index, in the totality of which three types of cholekinetics are clearly delineated. **Conclusion.** The type of postprandial cholekinetics is naturally associated with a number of parameters of the excretory renal function and metabolism.

Keywords. Cholekinetics, excretory renal function, electrokinetic and Kerdoe's indices.

INTRODUCTION

It has long been known that after **one-time use of bioactive water Naftusya** for an hour the volume of the gall-bladder and also gastric and pancreatic secretion, diuresis and excretion with of electrolytes changes [2,6,8,17]. Previously it has been shown that 10-12-days **course of combined balneotherapy** in the spa Truskavets' in men with chronic cholecystitis combined with pyelonephritis reduces fasting gall-bladder volume by 16% and increases its contractile response to cholekinetic by 44%. This is combined with an increase in urinary excretion of phosphate, calcium, oxalates, creatinine, uric acid, urea and magnesium with no significant changes in urinary excretion chloride, potassium and sodium. However reduces the plasma level of creatinine and urea. Ascertained as the increase electrokinetic rate of cell nuclei buccal epithelium, indicating that the "rejuvenation" of the body [14-16].

Individual analysis revealed not only quantitative but also qualitative differences in the postprandial motility of the gall-bladder, in particular, it was diagnosed as normokinesia, and hypertonic-hyperkinetic as well as hyperkinetic-hypertonic dyskinesia. The purpose of this study is to identify the parameters of kidney excretory function as well as metabolism under which three types of the gall-bladder motility skills differ significantly from each other.

MATERIAL AND METHODS

The object of observation were the same ones 22 men aged 24-70 (mean $49,1 \pm 2,5$) years old, who came to the spa Truskavets' (Ukraine) for the treatment of chronic cholecystitis combined with pyelonephritis in remission. The survey was conducted twice, before and after balneotherapy (drinking bioactive water Naftusya, ozokerite applications, mineral baths). On the tone and motility of gall-bladder judged by its volume on an empty stomach in the morning and after 5, 15 and 30 min after ingestion cholekinetic (50 ml of 40% solution of xylitol). The method echoscopy (echocamera "Radmir") applicated [1,3].

In the daily urine we determined pH level, content of oxalate and nitrogen metabolites (creatinine, urea and uric acid), electrolytes (phosphates, chloride, calcium, magnesium, potassium and sodium). Nitrogenous metabolites were determined also in plasma of venous blood. Used unified methods [7].

Also recorded Kerdoe's vegetative index [4] as well as electrokinetic index of buccal epithelial cell nuclei (by microelectrophoresis device "Biotest", Kharkiv), which is considered a marker of biological age [5,9,10,18].

Results processed by methods of cluster and canonical analyses, using the software package "Statistica 5.5".

RESULTS AND DISCUSSION

Initially, we counted the actual postprandial volumes of the gall-bladder relative to the resting, and then created cholecystovolumograms. Then they were subjected to cluster analysis (method k-means clustering). Three clusters are selected (Table 1). Judging by the η^2 -criterion, the maximum contribution to the distribution to the clusters gives a relative volume 30 minutes after the use of cholekinetic, and minimal - in 5 minutes, which is quite anticipated.

Table 1. Cluster Analysis Gall-bladder Postprandial Volumes. Analysis of Variance

Gall-bladder Volume	Between SS	Degree freedom	Within SS	Degree freedom	η^2	R	F	signif. p
5 min Pp, %	67	2	91	41	0,424	0,651	15,2	$<10^{-4}$
15 min Pp, %	1722	2	578	41	0,749	0,865	61,1	$<10^{-6}$
30 min Pp, %	3871	2	751	41	0,838	0,915	105,6	$<10^{-6}$

Euclidean Distances between Clusters make up: N1 vs N2 11,2; N1 vs N3 16,6; N2 vs N3 6,3.

Taking into account the existing criteria [1,11-13], the second cluster of cholecystovolumograms is considered as normokinesia, first as hypertonic-hyperkinetic dyskinesia and the third as hyperkinetic-hypertonic dyskinesia (Table 2 and Fig. 1).

Table 2. Cluster Analysis Gall-bladder Postprandial Volumes. Cluster Means

Postprandial Gall-bladder Volume, % Initial	Cl No.1 T ⁺ K ⁺ (n=11)	Cl No.2 Norm (n=17)	Cl No.3 K ⁺ T ⁺ (n=16)
After 5 min	97,9±0,5	96,8±0,3	94,8±0,4
After 15 min	86,1±1,5	79,4±0,6	70,2±1,0
After 30 min	76,5±1,3	58,2±1,2	52,7±0,9

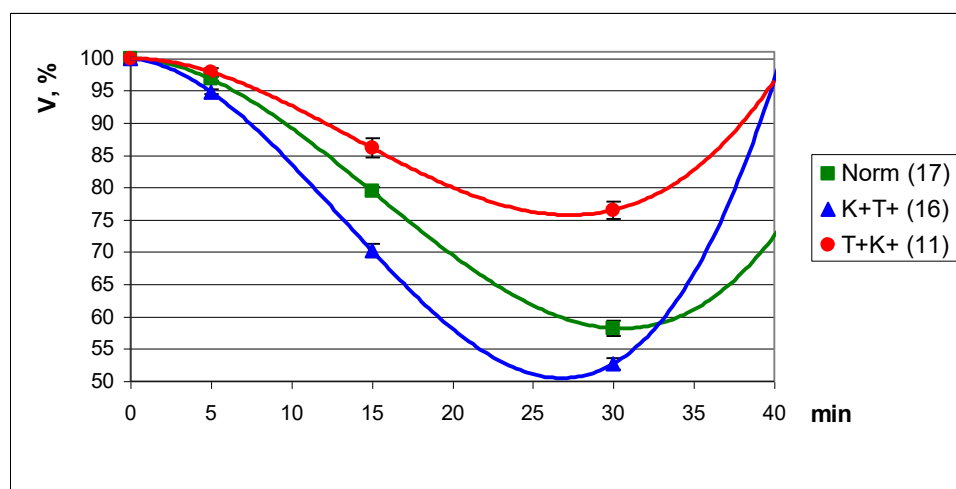


Fig. 3. Three types of postprandial cholecystovolumograms

On the summary of the method forward stepwise, the program includes only relative volumes in the model, whereas the actual volumes were beyond the model (Table 3).

Table 3. Discriminant Analysis of Gall-bladder Postprandial Volumes. Wilks' Statistics

Parameters

Step 3, N of variables in model: 3; Grouping: 3 groups

Wilks' Lambda: 0,082; approx. $F_{(6,8)}=32,3$; $p < 10^{-6}$

Variables (Volumes) currently in model	Wilks' Λ	Partial Λ	F-remove (2,4)	p-level	Tolerance
After 30 min, % Initial	,250	,330	39,6	10^{-6}	,912
After 15 min, % Initial	,136	,608	12,6	10^{-4}	,752
After 5 min, % Initial	,089	,929	1,5	,240	,695

Variables (Volumes) currently not in model	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerance
Initial, ml	,080	,975	,483	,621	,855
After 5 min, ml	,080	,975	,496	,613	,827
After 15 min, ml	,080	,966	,679	,513	,745
After 30 min, ml	,078	,952	,959	,393	,680

Information on relative volumes is condensed in two discriminant roots, but the lion's share of recognition capabilities falls to the major root ($r^*=0,940$; Wilk's $\Lambda=0,082$; $\chi^2_{(6)}=99,9$; $p < 10^{-6}$), while the minor root remains only 5,3% ($r^*=0,545$; Wilk's $\Lambda=0,703$; $\chi^2_{(2)}=14,1$; $p < 10^{-3}$).

Table 4. Discriminant Analysis of Gall-bladder Postprandial Volumes. Standardized, Structural and Raw Coefficients and Constants for Canonical Variables

Coefficients	Standardized		Structural		Raw	
	Root 1	Root 2	Root 1	Root 2	Root 1	Root 2
Variables (Volumes) currently in model						
After 30 min, %	-,838	-,623	-0,82	-0,46	-,196	-,146
After 15 min, %	-,657	,688	-0,60	0,79	-,175	,183
After 5 min, %	,277	,337	-0,29	0,50	,187	,226
Cumulated Properties	,947	1,000	Constants		7,499	-27,22

The calculation of individual scores of discriminant roots of cholecystovolumograms by summing the products of individual variables into Raw coefficients and Constants (Table 4) makes it possible to visualize all cholecystovolumograms on the plane of the two roots (Fig. 2).

The localization of representative points of the **first** cluster along the first root axis in its extreme left region (centroide: -4,25) reflects the maximal relative postprandial volumes (see Fig. 1). The shift of the **second** cluster to the right (centroide: +0,29) reflects more pronounced contraction of gall-bladder, while the extreme right of localization of the members of the **third** cluster (centroide: +2,61) reflects the minimal relative postprandial volumes. Less distances between clusters reflect the smaller difference between their cholecystovolumograms.

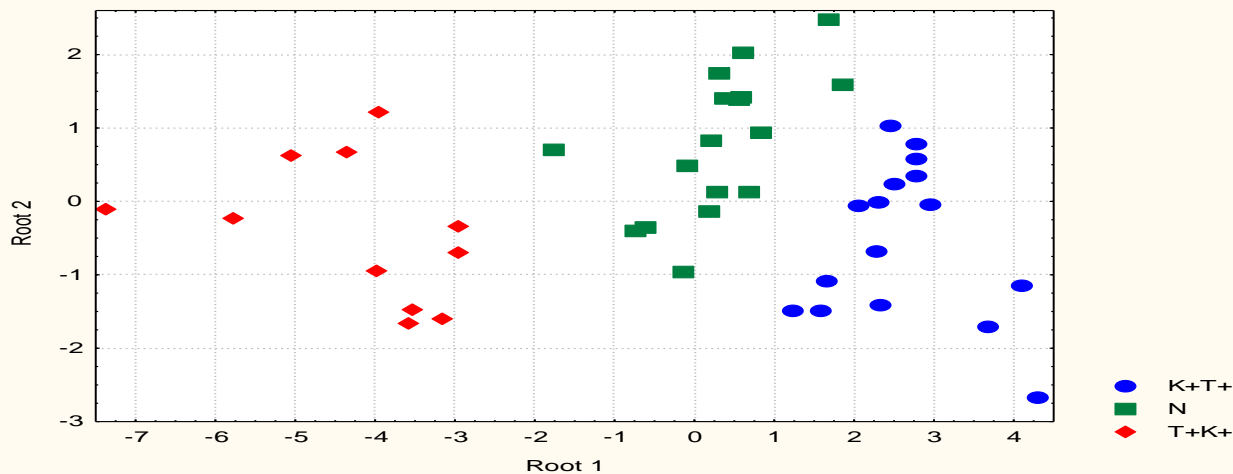


Fig. 2. Individual scores of discriminant roots of cholecystovolumograms of different clusters

Squared Mahalanobis Distance between first and second clusters make up 23,6 ($F=46$; $p<10^{-6}$), between first and third 50,5 ($F=96$; $p<10^{-6}$), while between second and third only 7,7 ($F=19$; $p<10^{-6}$).

If we place individual roots in pairs (before and after balneotherapy), it becomes possible to visualize the orientation and severity of the effect of balneotherapy on cholekinetics.

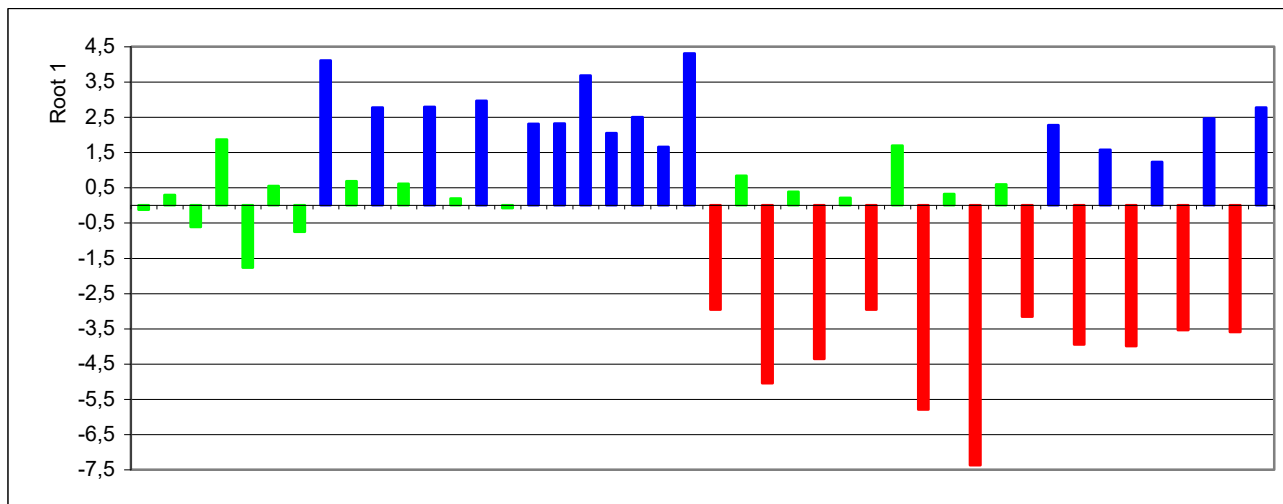


Fig. 3. Doubtful individual scores of major root of cholecystovolumograms (first in each pair – before balneotherapy, second – after balneotherapy)

It is seen that in the first patient, normal cholekinetics does not respond to balneotherapy. In two subsequent patients, there is a cholecystokinetic effect within the limits of normokinesia; in five, normokinesia passes into hyperkinetic-hypertonic dyskinesia, while in the other three, the severity of dyskinesia increases. Among 11 patients with hypertonic-hyperkinetic dyskinesia in six, the normalization of cholekinetics occurs, and in five it is confirmed its transformation into hyperkinetic-hypertonic dyskinesia. In general, five variants of the effect of balneotherapy on cholekinetics can be distinguished (Fig. 4).

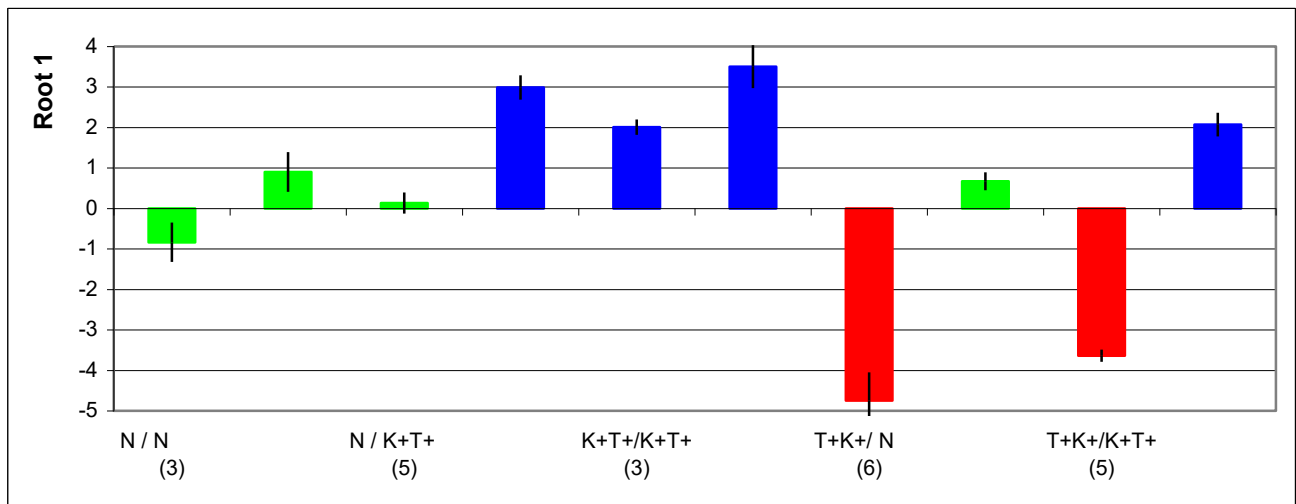


Fig. 4. Means of doubted scores of major root of cholecystovolumograms (first in each pair – before balneotherapy, second – after balneotherapy)

The method of discriminatory analysis revealed 20 recognizable metabolic parameters: 13 of daily urine and 3 parameters of blood, as well as body weight and height, electrokinetic index and Kerdoe's vegetative index (Table5).

Table 5. Discriminant Analysis of Metabolic Accompaniments Gall-bladder Motility Types.

Step 20, N of variables in model: 20; Grouping: 3 groups.
Wilks' Lambda: 0,071; approx. $F_{(40)}=3,0$; $p=0,0002$

Variables currently in model	Wilks' Λ	Partial Λ	F-rem (2,22)	p-level	Tolerance	F to enter	p-level	Λ	F-value	p-level
Oxaluria	,116	,610	7,02	,004	,025	6,75	,003	,752	6,75	,003
Body Mass	,126	,562	8,59	,002	,099	2,78	,074	,661	4,61	,002
Creatinin Plasma	,118	,601	7,29	,004	,078	3,93	,028	,550	4,53	10^{-3}
Diuresis	,083	,852	1,90	,173	,031	2,93	,066	,476	4,26	10^{-3}
Oxalates Urine	,128	,551	8,95	,001	,025	2,90	,068	,412	4,13	10^{-3}
Body Height	,142	,499	11,0	,000	,208	2,57	,090	,360	3,99	10^{-4}
Uricaciduria	,087	,814	2,51	,104	,016	2,46	,100	,316	3,89	10^{-4}
Electrokinetic Index	,109	,648	5,97	,008	,203	3,54	,040	,262	4,06	10^{-4}
Calcium Urine	,096	,739	3,88	,036	,387	2,16	,132	,231	3,96	10^{-4}
Kerdoe's Index	,095	,744	3,79	,038	,501	1,55	,229	,211	3,77	10^{-4}
Glomerular Filtration	,082	,864	1,73	,200	,089	1,47	,247	,193	3,60	10^{-4}
Uric acid Plasma	,091	,776	3,18	,061	,475	1,46	,249	,176	3,46	10^{-4}
Kaliumuria	,091	,777	3,15	,062	,018	1,60	,220	,158	3,38	10^{-4}
Uric acid Urine	,093	,763	3,41	,051	,018	1,47	,246	,143	3,29	10^{-4}
Potassium Urine	,085	,834	2,19	,135	,017	1,89	,170	,126	3,28	10^{-4}
Urea Plasma	,088	,809	2,60	,097	,152	2,28	,123	,107	3,35	10^{-4}
pH Urine	,085	,835	2,18	,137	,450	1,06	,360	,098	3,22	10^{-4}
Natriumuria	,087	,815	2,50	,105	,015	1,04	,370	,091	3,10	10^{-3}
Sodium Urine	,083	,850	1,94	,168	,018	1,74	,199	,079	3,10	10^{-3}
Phosphaturia	,079	,899	1,24	,310	,307	1,24	,310	,071	3,03	10^{-3}

Discriminant information is condensed in two roots. First root have 69,5% of recognition capabilities ($r^*=0,896$; Wilk's $\Lambda=0,071$; $\chi^2_{(40)}=83,4$; $p<10^{-4}$), while the minor root remains 30,5% ($r^*=0,801$; Wilk's $\Lambda=0,359$; $\chi^2_{(19)}=32,3$; $p=0,029$).

Applying the already mentioned algorithm and Raw coefficients (Table 6), we visualized each patient on the plane of two discriminatory roots (Fig. 5).

Table 6. Standardized, Structural and Raw Coefficients and Constants for Canonical Variables

Variables currently in model	Standardized		Structural		Raw	
	Root 1	Root 2	Root 1	Root 2	Root 1	Root 2
Oxaluria	-1,961	4,389	0,28	0,07	-,0032	,0073
Diurese	1,416	-2,242	0,26	-0,08	3,041	-4,816
Phosphaturia	-,031	,715	0,21	0,09	-,0019	,0443
Oxalates Urine	3,480	-3,633	0,19	0,08	,0168	-,0165
Body Mass	2,345	,072	0,12	0,10	,169	,005
Calcium Urine	,236	-,991	0,08	-0,02	,194	-,814
Uricaciduria	3,188	2,340	0,08	0,17	2,125	1,560
Potassium Urine	3,489	-,168	-0,12	-0,17	,195	-,009
Electrokinetic Index	-1,313	,741	-0,12	-0,02	-,166	,094
Sodium Urine	,153	3,611	-0,10	-0,06	,0042	,0991
Urea Plasma	1,221	-,302	-0,09	-0,02	,981	-,243
Creatinine Plasma	-2,508	-,328	-0,08	-0,12	-,206	-,027
Body Height	-1,613	,703	-0,06	0,01	-,288	,126
Uric acid Urine	-4,039	-,399	-0,07	0,25	-7,116	-,704
Glomerular Filtration	-1,365	-,243	-0,01	0,19	-,058	-,010
pH Urine	-,158	,736	0,03	0,07	-,406	1,896
Uric acid Plasma	,716	,305	0,00	0,03	,0074	,0032
Kaliuria	-3,860	-,475	-0,02	-0,22	-,099	-,012
Natriuria	,298	-4,370	0,01	-0,10	,0031	-,0457
Kerdoe Vegetat. Index	,649	-,520	0,02	-0,05	,047	-,038
Discr. Properties, %	69,5	30,5	Constants		52,98	-24,60

The localization of representative points of patients with **hypertonic-hyperkinetic** dyskinesia along the first root axis in its extreme left region (centroide: -3,28) reflects the **minimal** values in cohorts of metabolic parameters (Table 7) that correlate with the root **positively** (Table 6) while the **maximal** levels of **negatively** correlating with it parameters. The shift of two others clusters to the right reflects the increase or decrease of the respectively parameters, herewith the representative points of patients with both **normokinesia** and **hyperkinetic-hypertonic** dyskinesia are partially mixed despite the statistically significant distance between the clusters (centroids: +0,57 and +1,65).

On the other hand, along the axis of the second root, the second (**normokinetic**) cluster occupies an extreme bottom position (centroide: -1,58), while the other two are placed at approximately the same level (centroids: +0,53 and +1,31 for **hypertonic-hyperkinetic** and **hyperkinetic-hypertonic** clusters respectively). Such a disposition reflects the **minimal** values in cohorts of metabolic parameters that correlate with the second root **positively** while the **maximal** levels of **negatively** correlating with it parameters.

In general, all three clusters are quite clearly delineated. Squared Mahalanobis Distance between normokinetic and hyperkinetic-hypertonic clusters make up 10,2 (F=2,12; p=0,04), between normokinetic and hypertonic-hyperkinetic 20,7 (F=3,41; p=0,003), between the two dyskinetic 26,6 (F=4,29; p<10⁻³).

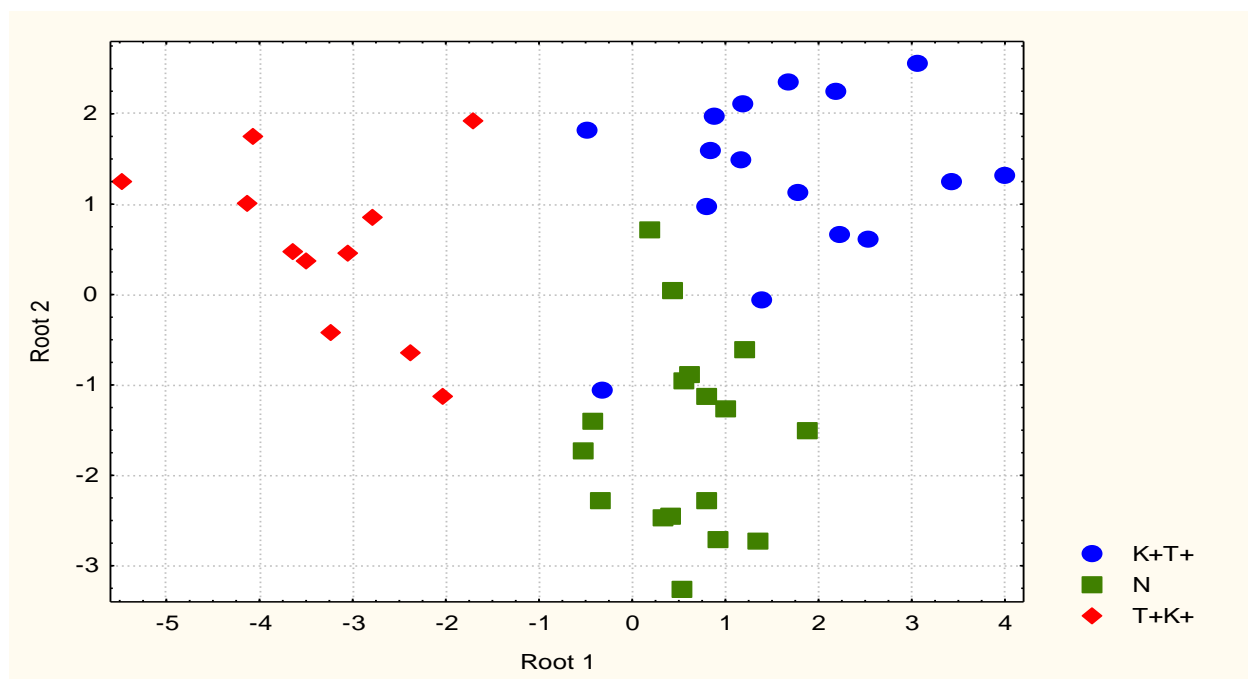


Fig. 5. Individual scores of discriminant roots of metabolic parameters of different clusters

Table 7. Metabolic Accompaniments of Gall-bladder Motility Types

Variables currently in model	T⁺K⁺ (n=11)	Norm (n=17)	K⁺T⁺ (n=16)
Oxaluria, μM/24 h	118±14	186±14	216±17
Diurese, l/24 h	1,94±0,39	2,47±0,12	2,49±0,12
Phosphaturia, mM/24 h	19,2±1,5	31,3±3,6	39,0±5,3
Oxalates Urine, μM/l	62±6	77±6	87±6
Body Mass, kg	76,6±5,5	80,3±3,5	87,1±3,6
Calcium Urine, mM/l	2,26±0,30	2,75±0,34	2,80±0,30
Uricaciduria, mM/24 h	3,93±0,48	3,93±0,35	4,78±0,40
Potassium Urine, mM/l	43,0±5,3	40,4±5,9	29,3±2,2
Electrokinetic Ind. Epitheliocytes, %	46,8±3,1	41,3±2,6	40,5±2,4
Sodium Urine, mM/l	116±10	104±9	94±9
Urea Plasma, mM/l	7,0±0,5	6,5±0,2	6,3±0,3
Creatinine Plasma, μM/l	97±3	96±4	90±2
Body Height, cm	175,2±1,5	173,5±1,3	173,3±
Uric acid Urine, mM/l	2,07±0,23	1,58±0,11	1,94±0,15
Glomerular Filtration, ml/min	103±9	88±5	105±8
pH Urine	5,11±0,10	5,09±0,07	5,21±0,14
Uric acid Plasma, μM/l	353±23	346±29	356±22
Kaliumuria, mM/24 h	81±10	97±13	71±5
Natriumuria, mM/24 h	231±32	256±25	230±22
Kerdoe Vegetative Index, units	-13±3	-9±5	-12±3

Selected 20 metabolic parameters can be used to identify the belongings of a particular patient to one or another cholekinetic cluster. This purpose of discriminant analysis is realized with the help of classifying functions (Table 8).

These functions are special linear combinations that maximize differences between groups and minimize dispersion within groups. The coefficients of the classifying functions are not standardized, therefore they are not interpreted. An object belongs to a group with the maximum value of a function

calculated by summing the values of the variables by the coefficients of the classifying functions plus the constant.

Table 8. Coefficients and Constants of Classification Functions for Gall-bladder Motility Types

Variables currently in model	K ⁺ T ⁺	Norm	T ⁺ K ⁺
Oxaluria	3,04	2,86	3,14
Body Mass	-12,89	-13,09	-13,73
Creatinin Plasma	14,52	14,82	15,56
Diuresis	93,09	103,76	81,88
Oxalates Urine	-11,54	-11,23	-12,19
Body Height	25,34	25,29	26,66
Uricuria	-169,3	-176,1	-180,9
Electrokinetic Index	13,98	13,89	14,72
Calcium Urine	-27,05	-24,91	-27,38
Kerdoe's Index	-4,55	-4,49	-4,75
Glomerular Filtration	4,74	4,83	5,03
Uric acid Plasma	-0,418	-0,436	-0,457
Kaliumuria	6,45	6,59	6,95
Uric acid Urine	615,1	624,8	650,7
Potassium Urine	-14,19	-14,37	-15,14
Urea Plasma	-66,41	-66,76	-71,05
pH Urine	128,4	123,4	128,9
Natriumuria	-2,79	-2,66	-2,77
Sodium Urine	5,66	5,37	5,57
Phosphaturia	0,98	0,85	0,95
Constants	-3056	-3040	-3301

In this case, we can retrospectively recognize the belonging to normokinetic cluster with an accuracy of 94,1% (one error of 17 cases), hyperkinetic-hypertonic – of 93,8% (one error of 15 cases) while to hypertonic-hyperkinetic cluster unmistakably.

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ACCORDANCE TO ETHICS STANDARDS

This study was approved by the local ethical committee of Truskavets’ Scientists Assotiation. 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 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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