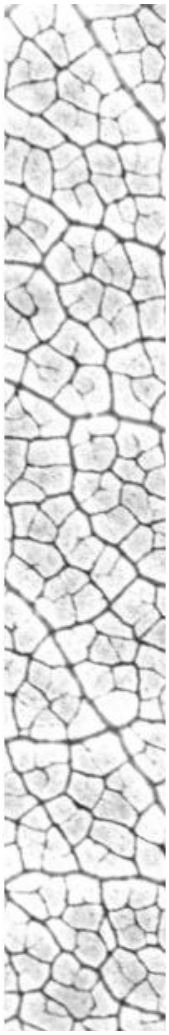

EurAsian Journal of BioSciences
Eurasia J Biosci 14, 4023-4028 (2020)

Frailty and age dynamics of separate clinical indicators in patients of therapeutic profile

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Abstract
Age-related dynamics of body homeostasis individual indicators in patients with risk of developing frailty and without frailty was studied in the research. Clinical indicators mostly associated with age were determined: muscle strength, glomerular filtration rate, total protein, potassium, hemoglobin, alanine aminotransferase activity, and blood plasma glucose. The contribution of reduced overall renal function, as well as anabolic activity of the liver in the development of age-related changes and frailty was studied. The important role of the renal function condition in the development of geriatric syndromes was noted, which must be taken into account when conducting therapeutic and rehabilitation measures for elderly and senile patients. It was noted that age-associated integral indicators, such as body weight and muscle strength, change noticeably more significantly than individual biochemical constants. This confirms the multiple nature of pathogenetic mechanisms and the role of comorbidity in the formation of geriatric syndromes, in particular, frailty.

Keywords: geriatric syndromes, frailty, sarcopenia, age related body indicators, comorbidity

Prashchayeu KI, Zubareva NN, Kuzminov OM, Gorelik SG, Voronina EA, Silyutina MV (2020) Frailty and age dynamics of separate clinical indicators in patients of therapeutic profile. Eurasia J Biosci 14: 4023-4028.

INTRODUCTION

Currently, much attention is paid to improving geriatric care for elderly and senile patients. At the same time, a wide range of specific features arises in medical and social support for this category of patients. The problem of geriatric care is multidisciplinary, requiring consideration of medical, social and psychological aspects in patient management. In the vast majority of cases, management of elderly and senile patients falls on the specialists of the therapeutic and surgical profile without special training in the area of gerontology. A specific feature of elderly and senile patients is the presence of comorbidity, polypharmacy in the picture (Lazebnik, Efremov, Konev, 2015- Prashchayeu, Ilnitski,, Pozdnyakova et al., 2016- Tkacheva, et al. 2017 Bonnefoy, Berrut,, Lesourd, et al., 2015- Gorelik et al. 2018- Koroukian, et al., 2017 Bezdenezhnykh, Sumin, 2012- Paddon-Jones, & Leidy, 2014), as well as special geriatric conditions, mostly frailty and functional deficiency syndrome (Pathak, Jain, Jaiswal, et al., 2016- Tkacheva, Runikhina, Ostapenko, et al., 2017- Tkacheva, Runikhina, Kotovskaya, et al., 2017). In general, this aggravates the condition of patients and worsens the prognosis.

According to modern concepts, frailty is characterized by a decrease in muscle strength, endurance and physical activity (Arango-Lopera, et al. 2013- Prashchayeu, et al. 2016- Boytsov, et al., 2017. Tkacheva, Pereverzev, Runikhina, et al., 2017), a decrease in body weight (Tkacheva,., 2018, Noskov, et al. 2015), development of cognitive disorders, loss of motivation and life interests, which leads to the increased risk of developing any pathology and death (Sychev, 2016, Mubang, Stoltzfus, Cohen, et al., 2015).

A specific feature of geriatric syndromes, in particular frailty, is the multiplicity of pathogenetic mechanisms of these conditions development (Raiche, Hebert, Dubois, 2008., Rymkiewicz, et al. 2016).of a syndrome as a combination of symptoms with a single pathogenesis. Moreover, in each particular case, various combinations of nosological forms can lead to the development of specific geriatric conditions.

For timely diagnosis of geriatric syndromes, it is necessary to determine those indicators of laboratory and instrumental methods of diagnosis that are most associated with age and can serve as peculiar markers of the risk of their development.

In this regard, the analysis and interpretation of traditional clinical data obtained during treatment and

Received: February 2020
Accepted: April 2020
Printed: October 2020

Table 1. Individual indicators of the body state in different age groups (M±m)

Indicator	Young and Mature Age	Elderly Age	Senile Age	Correlation coefficient between the indicator and the age for the whole group
Main Group (n=200)				
Number of patients	57	88	55	–
Age, years	51.6±0.89	66.7±0.38	80.3±0.62	–
Body mass index, kg/m^2	30.6±0.85	29.8±0.51	28.1±0.84*	-0.17
Total protein, g/l	75±1.75	73±1.33	67.3±0.90*	-0.37*
Glucose, mmol/l	6.3±0.27	6.9±0.27	7.5±0.47*	0.20*
Total cholesterol, mmol/l	5.3±0.59	5.1±0.25	5.5±0.29	0.09
Bilirubin, mcmol/l	14.4±1.47	13.4±0.88	17.2±2.36	0.06
Alanine aminotransferase, u/l	28.4±1.93	25.8±1.36	16.9±1.12*	-0.35*
Aspartate aminotransferase, u/l	26.6±1.95	27.1±1.80	23.8±1.41	-0.21*
Potassium, mmolln	4.1±0.05	4.2±0.05	4.7±0.09*	0.48*
Urea, mol/l	6.9±0.47	7.1±0.57	7.3±0.55	0.21*
Creatinine, mcmol/l	92.4±4.73	94.3±3.50	100.6±3.42	0.06
Glomerular filtration rate (Cockcroft-Gault), ml/min	105±3.51	84±2.78*	53±2.41*	-0.66*
Hemoglobin, g/l	141±1.96	135±1.7*	122±2.34*	-0.36*

The sign "*" marks the indicators in the groups of the elderly and senile age, reliably different from the indicators in the groups of adult and young age ($p < 0.05$) and reliable correlation coefficients in the combined group ($p < 0.01$).

diagnostic measures indicating the possible development of specific geriatric conditions in patients is of great importance. It is relevant to identify the age-associated indicators of the body and assess their relationship with geriatric syndromes, which will allow us to form a more complete picture of the disease and differentially plan treatment, diagnostic and rehabilitation measures in elderly and senile patients.

The purpose of this work is to study age-related dynamics of clinical indicators that reflect the basic vital systems of the body and assess their impact on the development of frailty.

MATERIAL AND METHODS

The study included clinically compensated patients undergoing inpatient treatment in therapeutic departments in connection with the exacerbation of chronic diseases of the cardiovascular and bronchopulmonary systems of the City Clinical Hospital and the hospital for war veterans in the city of Belgorod. Severe patients, cancer patients, and patients with decompensated therapeutic pathology were excluded from the study.

All patients from the main group (n = 200) underwent anthropometric measurements and laboratory examinations standard for therapeutic pathology. In some patients (additional group (n = 84), the risk of developing senile asthenia was assessed using the questionnaires "PRISMA-7" and "Questionnaire for citizens aged 75 years and older", which includes the scale "Age is not a hindrance" [2, 4, 11, 20], echocardiography, wrist dynamometry was performed, the peak expiratory flow rate was examined.

The data obtained was processed using parametric statistics methods (estimation of the average value (M), the average error of the arithmetic mean (m), the significance of differences using Student's t-test), in addition, correlation and regression analysis of the data was performed. During the correlation analysis, the hypothesis of the normality of the parameter distribution in the combined age group was checked, then the Pearson correlation coefficient (r) was calculated. The correlation was considered weak with a modulus of *r* less than 3, moderate with a value of r more than or equal to 3, but less than 7, strong - with r greater than or equal to 7.

RESULTS AND DISCUSSION

Hemostatic profiles at different ages of the main group are presented in **Table 1**.

Analysis of **Table 1** allows to determine the parameters of the body, which reliably unidirectionally change with patients' age rising. A decrease in anabolic processes in the liver (a decrease in total protein, alanine aminotransferase activity, an increase in blood glucose), a deterioration in total kidney function (a decrease in glomerular filtration rate, hemoglobin, an increase in potassium in the blood plasma) are observed. **Fig. 1** presents a diagram of unidirectional dynamics of changes in the studied parameters in the groups of elderly and senile patients compared to the group of patients of mature and young age, the average value of which is accepted as equaling one.

Table 2 presents data obtained from studying the risk of developing frailty and associated sarcopenia using the "PRISMA-7" questionnaire and the "Questionnaire for citizens aged 75 years and older", wrist dynamometry, peak inspiratory flow rate, echocardiography.

In addition, the presented results of commonly used in therapeutic practice biochemical analysis and echocardiography reflect the integral function of liver, kidneys, and heart. Also, correlation coefficients calculated for the studied indicators in the combined age group (young and mature age, elderly age, senile age) are included in the tables.

As we can see in **Table 2**, the risk of frailty developing (test "PRISMA-7" and "Questionnaire for is sufficiently high (r = 0.6 and r = 0.61, respectively). No significant differences between the data from the two

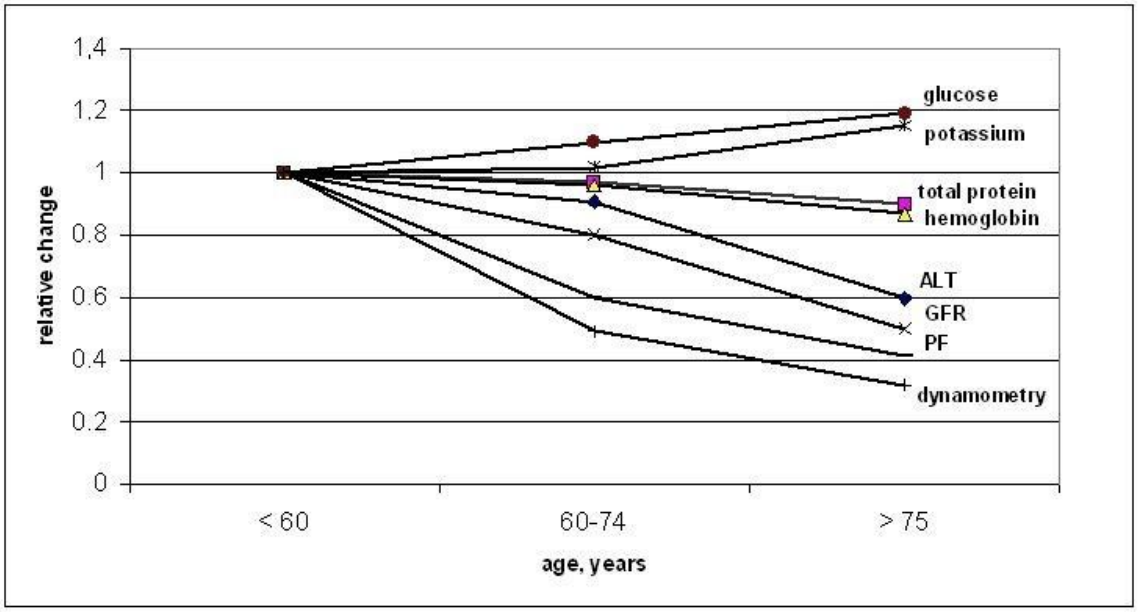

Fig. 1. The relative decrease in individual indicators of the body in different age groups

Table 2. Individual indicators of the body state at different ages of the additional group (M±m)

Indicator	Young and Adult Age	Elder Age	Senile Age	Correlation coefficient between the indicator and the age for the whole group
Additional Group (n=84)				
Number of patients	13	27	43	–
Age, years	51±2.19	66±0.71	82±0.89	–
"PRISMA-7" test, scores	0.9±0.23	2.1±0.16*	3.2±0.27*	0.60*
Questionnaire for citizens aged 75 years and older, scores	1.9±0.31	2.6±0.22	4.2±0.35*	0,61*
Wrist dynamometry, daN	37±3.68	18±2.08*	12± 0.88*	-0.71*
Peak expiratory flow rate, l/min	422±35.80	254±22.65*	173±16.02*	-0.61*
Left ventricle end-diastolic dimension, cm	5.2±0.20	5.2±0.09	4.7±0.09*	-0.46*
Left ventricle end-systolic dimension, cm	3.6±0.24	3.6±0.14	3.3±0.07	-0.24
Interventricular septum thickness, cm	1.4±0.04	1.5±0.03	1.5±0.03	0.08
Left ventricle posterior wall thickness, cm	1.3±0.03	1.4±0.02*	1.4±0.03*	0.09
Myocardial mass, g	381±27.73	401±15.12	342±13.58	-0.29*
Left ventricular myocardium mass index, g/ m^2	186±9.97	196±7.15	197±7.21	0.01
Left ventricle ejection fraction, %	55±2.58	57±2.08	59±1.27	0.13

The sign "*" marks the indicators in the groups of the elderly and senile age, reliably different from the indicators in the groups of adult and young age ($p < 0.05$) and reliable correlation coefficients in the combined group ($p < 0.01$)

tests were noted. The dynamics of changes are presented in **Fig. 2**.

Our data showed (**Table 2**) that there were no univocal age-related changes in the state of the myocardium. In patients of senile age, the final diastolic volume is significantly lower than in elderly and adult patients. There is a reliable moderate correlation between age and final diastolic volume of the left ventricle, as well as a weak, negative correlation between age and myocardial mass. In general, it can be noted that according to the data of echocardiography the heart condition in senile patients is somewhat better than in elderly patients. The latter fact requires further research and, possibly, is associated with the fact that patients with better indicators of myocardial condition have longer life span.

The latter indicator depends not only on bronchial passability, but also on the strength of the intercostal muscles. The degree of correlation between these indicators is comparable with the indicators of screening tests for assessing the risk of frailty development, which reflects their close pathogenetic relationship. The greatest ("strong", r=-0.71) correlation with age was found for the indicator of muscle strength assessment during wrist dynamometry, which reasonably finds its application in screening of geriatric syndromes such as sarcopenia and frailty (**Fig. 3**).

In general, it is clear that the greatest age-related deviations are observed in such indicators as muscle strength, glomerular filtration rate, and risk of frailty developing. Total protein, potassium, hemoglobin, the activity of alanine aminotransferase and blood plasma glucose noticeably change with age. The results of our study show that the age-associated integral indicators, such as the risk of frailty development, muscle strength, weight loss, change more significantly than individual biochemical parameters. This confirms the multiple

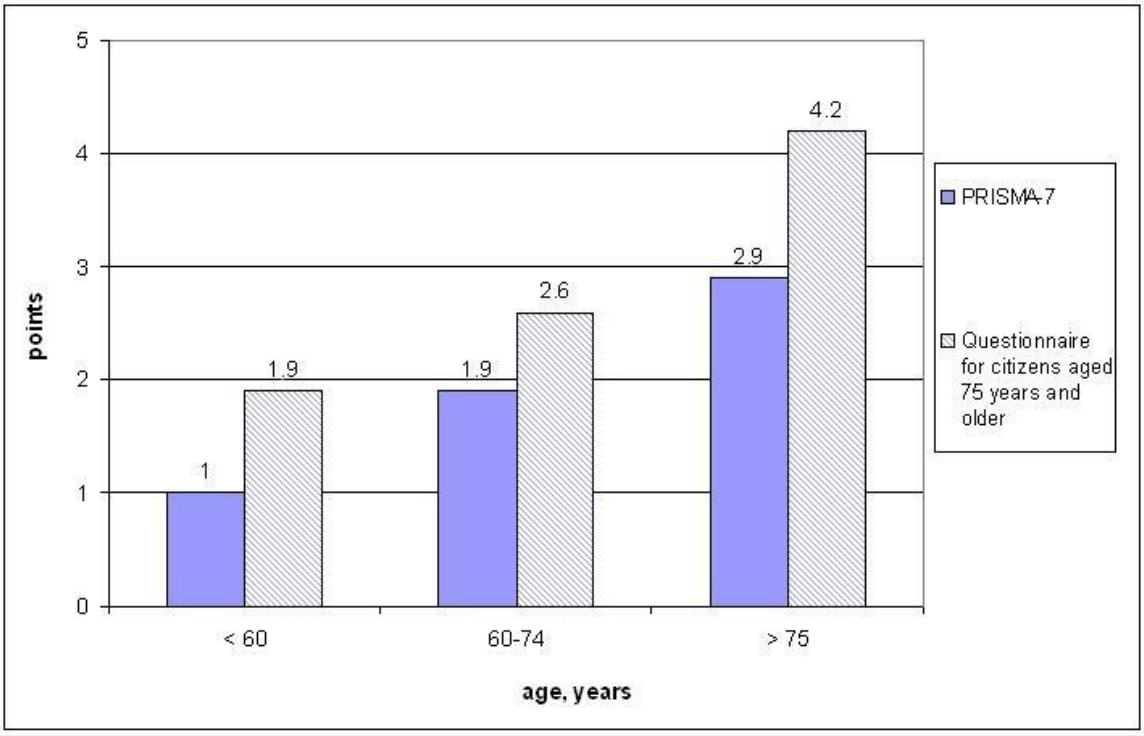

Fig. 2. Results of tests “PRISMA-7” and “Questionnaire for citizens aged 75 years and older “ in patients of different age groups

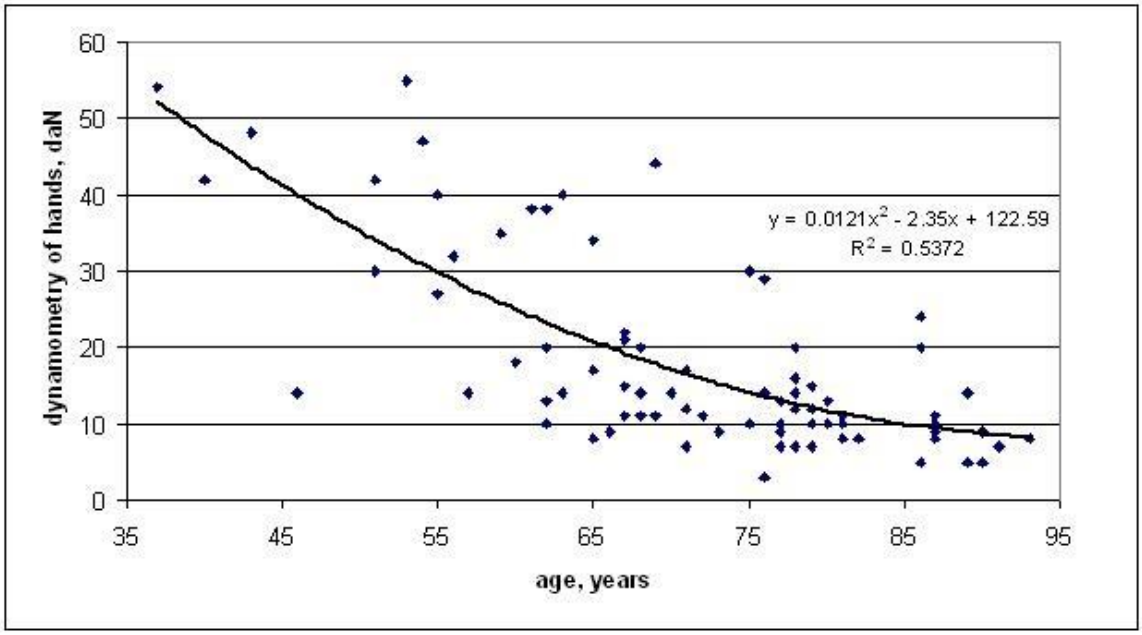

Fig. 3. Age-related dynamics of the patients’ muscular strength according to wrists dynamometry

nature of pathogenetic mechanisms and the role of comorbidity in the development of geriatric syndromes.

A correlation analysis was performed to study the influence of individual indicators on each other. Correlation coefficients were calculated not only between age and those indicators, but also between the indicators themselves. The main results are presented in **Table 3**.

A strong negative correlation (r=-0.71) was found between muscle strength according to the wrist dynamometry and age. In addition, a fairly high correlation was found between age and the likelihood of frailty development according to the “PRISMA-7” test (r=0.60). The strong positive correlation between the wrist dynamometry and the peak expiratory flow rate (r=0.81) reflects the fact that both indicators are related to the muscle strength – hands and chest, respectively.

Table 3. Correlation coefficients between individual indicators of the body in patients of different ages (correlation matrix)

	«PRISMA-7»	Body Mass	Wrists Dynamometry	Peak expiratory Flow Rate	Left Ventricle Ejection Fraction	Myocardial Mass	Total Protein	Potassium	Hemoglobin	Glomerular Filtration Rate
Age	0,60	-0.51*	-0.71*	-0.61*	0.13	-0.29*	-0.37*	0.48*	-0.36*	-0.66*
«PRISMA-7»		-0.08	-0.26*	-0.21*	0.02	-0.05	-0.15	0.14	-0.12	-0.22*
Body mass			0.37*	0.36*	-0.35*	0.52*	0.31*	-0.38*	0.32*	0.47*
Wrist dynamometry				0.81*	-0.10	0.04	0.25	-0.30*	0.39*	0.62*
Peak expiratory Flow Rate					0.03	0.05	0.31*	-0.31*	0.37*	0.46*
Left Ventricle Ejection Fraction						-0.35*	-0.06	-0.41*	0.22	0.25
Myocardial Mass							0.13	-0.34*	0.06	0.22

Sign "*" marks reliable correlation coefficients (p <0.01)

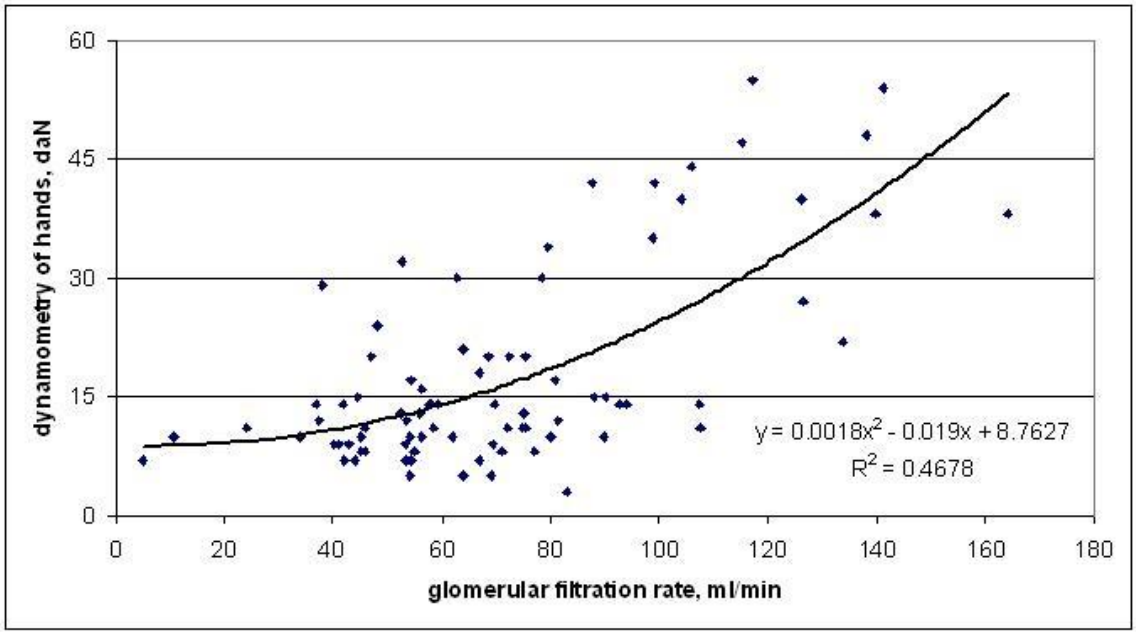

Fig. 4. Muscle strength of hands depending on the glomerular filtration rate in patients of different ages

The patient's body weight shows a moderate correlation with muscle strength, heart condition (ejection fraction, myocardial mass), kidneys condition (glomerular filtration rate, potassium, hemoglobin), which reflects the natural anatomical and physiological relations. Muscle strength (dynamometry, peak expiratory flow rate) is most strongly related to glomerular filtration rate (r=0.62 and r=0.46, respectively). **Fig. 4** illustrates the relationship between the muscle strength of hands and glomerular filtration rate in patients of different ages.

Myocardial mass and ejection fraction of the left ventricle show a moderate negative relationship with the potassium content in blood plasma (r=-0.34 and r=-0.41, respectively). A reliable but weak correlation was found between the risk of frailty development according to the "PRISMA-7" test, muscle strength and glomerular filtration rate (r=-0.26 and r=-0.22, respectively).

CONCLUSION

Clinical parameters of the body, such as muscle strength, glomerular filtration rate, some biochemical indicators (total protein, potassium, hemoglobin, alanine aminotransferase activity and blood plasma glucose), which are most closely associated with age, were determined. Changes in these parameters must be taken into account when assessing the condition of elderly and senile patients, as well as in predicting the development of geriatric syndromes for them.

The study revealed a significant contribution of decreased total renal function (a decrease in glomerular filtration and blood hemoglobin rate and increase in potassium) and anabolic liver activity (a decrease in total protein, alanine aminotransferase activity) in the development of age-related changes in the body and in the risk of frailty development. Management and correction of these systems must be taken into account when developing therapeutic treatment and rehabilitation programs for elderly and senile patients.

The analysis of age-related body indicators dynamics showed that integral indicators, such as the risk of frailty development, body weight and muscle strength, change significantly more over time than individual indicators of homeostasis, which reflects the multiple nature of pathogenetic mechanisms and the

role of comorbidity in the development of geriatric syndromes, particularly in the development of asthenia.

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