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Estimating the functional age of the respiratory system

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Abstract. The work aimed to develop a mathematical model of the functional age of the respiratory system. 95 practically healthy people aged 29 to 80 were examined. Spirograph parameters were determined on the device "Spirometer MIR Spirobank II" (manufacturer MIR S.r.l., Italy). The most informative indicators of age-related changes in the respiratory system were selected and a formula was obtained that allows to estimate the functional age of this system quite accurately. The average absolute error is 5.28 years.

Keywords: functional age; respiratory system

There are regular changes in the functions of external respiration, which lead to significant violations of ventilation during ageing [1]. The preconditions for the development of pulmonary pathology are created in the elderly. Age-related changes lead to a decrease in the adaptive capacity of the respiratory system. Obstructive disorders in the bronchial tree in old age, which are due to a combination of organic and functional changes, deepen ventilation disorders, cause hypoventilation of various parts of the lungs, leading to decreased oxygen partial pressure in alveolar air, aerial hypoxemia, and tissue hypoxia [2].

A lot of research has been devoted to the study of age-related changes in the respiratory system. But they did not have the task of integrated assessment of age-related changes in the external respiratory system in each individual. At the same time, determining the functional age of the external respiratory system is important for identifying people with accelerated ageing of this system (determining the "pulmonary" type of ageing).

Biological age - a model concept, is a measure of compliance of individual morphofunctional level to a certain average norm of the population, reflects the uneven development, maturity, and ageing of different physiological systems and the rate of age-related adaptive capacity of the organism [3].

When choosing indicators for the assessment of biological age from a huge number of possible biomarkers, those that meet several requirements deserve attention, which significantly increases the informativeness and quality of assessment. These requirements differ slightly from one author to another [4].

Some authors believe that the results of forced spirometry can serve as an indicator of the speed of involutional processes in the human body as its biological ageing [5]. So according to Belozerova LM biological age of the person can be defined on indicators of spirometry and allocate persons with a slowed-down average and accelerated rate of ageing [6].

In previous works of the D.F. Chebotarev Institute of Gerontology NAMS of Ukraine, the criterion for accelerated ageing was an increase in the functional age of the respiratory system compared to the calendar (passport) age by more than 7 years. [7].

The work aimed to develop a mathematical model of the functional age of the respiratory system.

Materials and methods

We surveyed 95 healthy people aged 29 to 80 years. The type and severity of disorders of ventilatory function of the lungs and bronchial patency were determined by spirography on the device "Spirometer MIR Spirobank II" (manufacturer MIR S.r.l., Italy). The analysis of the "flow-volume" curve of forced exhalation was used to assess bronchial patency. Forced expiration flow-volume curves were also recorded by a device and processed by a computer. It is known that the "flow-volume" curve of forced exhalation is the relationship between exhaled air volume and the corresponding airflow during forced exhalation in the biaxial coordinate system, where the abscissa shows the volume, and the ordinate - respiratory flow [8].

The use of the "flow-volume" curve of forced exhalation is based on the fact that after reaching the maximum flow with forced exhalation, the number of airflow decreases. This is due to the compression of the airways by increasing transpulmonary pressure. The localization of compression is determined by points of equal pressure, ie points where the external pressure is equal to the pressure in the lumen of the bronchi. During exhalation, the point of equal pressure moves from the large bronchi to the small ones by peripheral airways. Therefore, the magnitude of the exhaled airflow at the level of different lung volumes can be judged on the patency of the respective segments of the bronchial tree. The following indicators of pulmonary ventilation function and forced expiratory flow-volume curve were calculated:

1. VC – vital capacity of the lungs, l;
2. FVC – forced vital capacity of the lungs;
3. FEV_1 – volumetric exhalation rate, 1 s;
4. PEF – maximum speed of forced exhalation;
5. FEV_1/ FVC % - Tiffno index;
6. FEF $_{25\% - 75\%}$ – moderate exhalation flow.

Inhalation and expiration respiratory arrest were also determined.

Statistical processing of the obtained data was carried out with the help of Excel 2007 and Statistica 7 programs. Standard statistical procedures, including variation and regression analyses, were used.

Results and discussion

Our results showed that in healthy people aged 60-69 and 70-79 years, compared with young people (30-39 years), there is a decrease in many indicators of respiratory function of the respiratory system (Tab. 1). There are statistically significant differences in the average values of indicators in different age groups (F = 4.07, p< 0.001).

Table 1

Spirometry in healthy people of different ages

Age, years	**30-39 (n = 9)**	**40-49 (n = 27)**	**50-59 (n = 18)**	**60-69 (n = 27)**	**70-79 (n = 14)**	**ANOVA, p**
VC, l	3.93 ± 0.87	3.96 ± 1.03	3.36 ± 0.94	2.99 ± 0.89	2.74 ± 1.04	p< 0.001
FVC, l	4.40 ± 1.02	4.33 ± 1.17	3.68 ± 1.03	3.21 ± 0.87	3.02 ± 1.14	p< 0.001
FEV_1, l	3.41 ± 0.61	3.29 ± 0.79	2.80 ± 0.67	2.42 ± 0.62	2.35 ± 0.80	p< 0.001
PEF, l/s	6.77 ± 1.54	6.54 ± 2.08	5.40 ± 1.89	4.77 ± 1.75	4.63 ± 2.13	P = 0.001
FEV_1/FVC, %	78.62 ± 8.65	76.63 ± 5.90	77.07 ± 7.77	76.37 ± 9.29	79.68 ± 14.16	P = 0,801
FEF 25-75%, l/s	3.21 ± 0.87	2.89 ± 0.93	2.33 ± 0.88	2.04 ± 0.80	2.14 ± 0.80	p< 0,001

Thus, the obtained data indicate changes in the indicators of respiratory function in the elderly, which is associated with age-dependent changes in the external respiratory system. Spirometry indicators can be markers of determining the biological age of man and were used by us in the formulas for calculating the functional age of the respiratory system.

The change in these indicators is associated with morphofunctional changes in the respiratory system, in particular, an increase in residual lung capacity, decreased lung elasticity, and weakening of the respiratory muscles. This is also confirmed by a statistically significant correlation between chronological age and most spirographic indicators (Tab. 2).

Table 2

Correlation coefficients between chronological age and biomarkers (Marked correlations are significant at $p < 0.05$)

Biological markers	R
Vital capacity of the lungs (VC), l	**-0.44**
Forced VC (FVC), l	**-0.49**
The volume of forced expiratory for 1 s (FEV1), l	**-0.53**
Peak expiratory flow (PEF), l/s	**-0.42**
FEV1/FVC, %	0.05
Forced expiratory flow 25-75% (FEF25-75), l/s	**-0.44**
Respiratory delay time on inspiration (Ti), s	**-0.35**
Respiratory delay time on expiration (Te), s	-0.14

Table 3 shows the correlations between the indicators of the respiratory system. It can be seen that many of these correlations are very high. When selecting indicators for the multiple regression equation, those were selected that had a weaker correlation with each other and a higher correlation with age.

Table 3

Correlations matrix biological markers (Marked correlations are significant at $p < 0.05$)

	VC	FVC	FEV1	PEF	FEV1/FVC	FEF25-75	Ti	Te
VC	1.00	**0.85**	**0.86**	**0.62**	-0.17	**0.54**	**0.40**	0.14
FVC	**0.85**	1.00	**0.95**	**0.73**	**-0.37**	**0.53**	**0.41**	0.15
FEV1	**0.86**	**0.95**	1.00	0.80	-0.08	**0.72**	**0.44**	0.15
PEF	**0.62**	**0.73**	**0.80**	1.00	-0.03	**0.64**	**0.37**	0.05
FEV1/FVC	-0.17	**-0.37**	-0.08	-0.03	1.00	**0.34**	-0.00	-0.05
FEF25-75	**0.54**	**0.53**	**0.72**	**0.64**	**0.34**	1.00	**0.28**	-0.01
Ti	**0.40**	**0.41**	**0.44**	**0.37**	-0.00	0.28	1.00	**0.44**
Te	0.14	0.15	0.15	0.05	-0.05	-0.01	**0.44**	1.00

The use of stepwise multiple regression made it possible to select the most informative indicators and obtain an equation linking the age of the examined people with several respiration indicators (Tab. 4).

Table 4

Regression summary for dependent variable: Age (Marked correlations are significant at $p < 0.05$)

Regression Summary for Dependent Variable: Age. R=0.702; R^2= 0.492; Adjusted R^2=0.470; F (4,95) = 22.51 p< 0,000001; SE of estimate: 9.303						
	Beta	Std. Err. of Beta	B	Std. Err. of B	t(109)	p-level
Intercept			128.0050	8.9414	14.3160	0.0000
Gender (1 - male, 2 - female)	-0.5519	0.1034	-14.7688	2.7669	-5.3376	0.0000
FEF25-75, l/s	-0.3334	0.0903	-4.4581	1.2073	-3.6927	0.0004
Respiratory delay time on inspiration, s	-0.2513	0.0838	-0.1879	0.0627	-2.9980	0.0035
FVC/Growth, l/m	-0.6078	0.1030	-12.8154	2.1711	-5.9026	0.0000

Note: R – correlation coefficient of indicators with the model; R^2 – coefficient of model determination; Adjusted R^2 – adjusted R-square (taking into account the number of predictors in the model); F – Fisher's test; t – Student's test; p – assessment of the significance of the model; SE of the estimate – standard error of estimation; Intercept – a free member of the equation; Beta – standardized regression coefficient; B – regression coefficient.

$$Y = 128 - 14.77\ X1 - 4.46\ X2 - 0.19\ X3 - 12.82\ X4,$$

Y – Predicted age, years;
X1 – Gender (1 - male, 2 - female);
X2 – FEF25-75/Growth, liter/m
X3 – Respiratory delay time on inspiration, s;
X4 – FVC/Growth, liter/m.

When calculating the BV formula, the ratio of FVC to human growth was used. This is because the amount of lung volume strongly depends on growth ($r = 0.8$). Therefore, human growth is used to calculate the appropriate values. A man of small stature is a small VC. That is, if you do not take into account the growth, you could make the wrong conclusion about the functional state of the lungs based on small lung volume.

The systematic error in calculating the age, associated with the peculiarities of constructing the multiple regression equation is calculated using the regression equation: prognosticated age - chronological age [9]. For our data, this error is calculated by the formula:

$$\text{Age predicted error} = 28.79 - 0.508\ \text{CA}\ (r = -0.707;\ p = 0.0001).$$

In turn, BA is calculated as the difference between the predicted age and the error in its calculation.

$$\text{BA} = \text{Predicted age} - \text{Age predicted error}.$$

The average absolute value of the error of BA calculation, in this case, is 5.28 years.
Figure 1 shows a graph of the correlation between BA after error correction and CA. It can be seen that the dispersion of points around the regression line is small and the multiple correlation coefficient is high ($r = 0.895$; $p < 0.00001$).

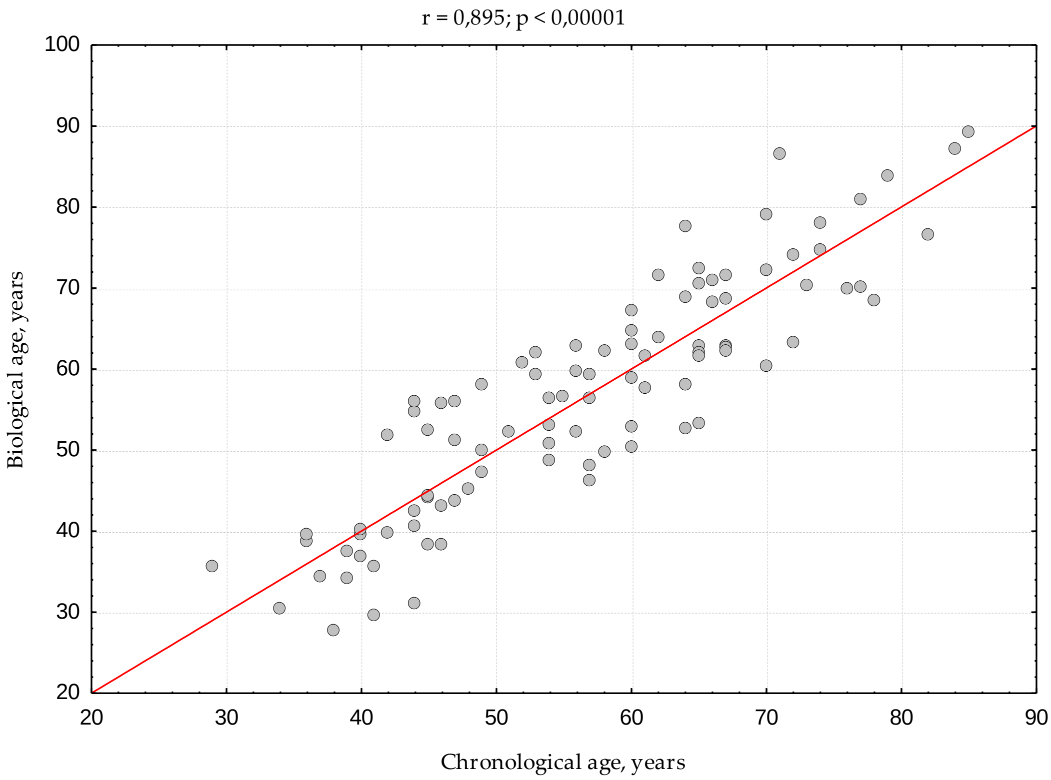

Figure 1. Correlation between biological and chronological age of people.

Thus, the formula for calculating the functional age is quite accurate and can be used to assess the risk of age-dependent pathology of the respiratory system.

Accelerated ageing was considered people whose functional age exceeded the chronological age by 7 years or more [7]. Table 5 shows the proportions of rapidly ageing people in different age groups. We see that starting from the age of 40, the share of people with accelerated ageing is naturally decreasing. This is because rapidly ageing people have a shorter life expectancy.

Table 5

The proportion of people with accelerated ageing in different age groups, %

Age, years	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**
The proportion of people with accelerated ageing, %	11.1	23.1	16.7	14.3	13.3

The method of determining the functional age of the respiratory system is indicative, but given the widespread use of spirography in medicine, it may be recommended for screening studies to diagnose the rate of biological ageing.

Conclusions

1. Spirometry indicators can be markers of determining the biological age of a man.
2. The formula which allows estimating rather accurately the functional age of this system on the most informative indicators of age changes in the respiratory system is received.

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Conflicts of Interest: The authors declare no conflict of interest.

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