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Biological age as a predictor of life expectancy in patients with ischemic heart disease

Anatoly V. Pisaruk, Irina S. Shapovalenko, Ivanna A. Antonyuk-Scheglova, Valeri B. Shatilo

D. F. Chebotarev Institute of Gerontology NAMS of Ukraine, Kyiv, Ukraine

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Correspondence: avpisaruk54@gmail.com

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Abstract. The work aimed to elucidate the relationship between the rate of ageing, determined by the criterion of biological age (BA), and the life expectancy of coronary heart disease (IHD) patients.

We analyzed 220 case histories of IHD patients aged 40–80 years. The cause of death in patients was IHD. During the observation period, patients were determined anthropometric parameters, BP, ECG, complete blood count, ESR, fasting blood glucose, lipid metabolism, urea, creatinine and prothrombin index.

The calculated BA formula was obtained on a group of 110 healthy people aged 40 to 80 years. Using stepwise multiple regression, the most informative indicators were selected and an equation was obtained linking the age of people with these indicators ($r=0.671$; $p<0.0001$). Using this formula, the BA of IHD patients and the rate of ageing of each person were calculated as the difference between their BA and chronological age. The data obtained analysis made it possible to establish a significant relationship between the rate of ageing and life expectancy in patients with IHD ($r=-0.368$; $p<0.0001$).

Keywords: biological age, life expectancy, IHD.

Age-related changes in the coronary arteries are one of the main causes of coronary heart disease (IHD). Accelerated ageing leads to the earlier development of IHD [11]. To assess the rate of ageing, the calculation of biological age (BA) is used [1-4]. The more BA compared to a person's chronological age (CA), the higher the rate of ageing, and hence the closer the end of this process - death. However, this is true only in the case when death occurs "from old age." At the same time, people with chronic cardiovascular pathology often die not from "old age", but from complications of the disease. Therefore, the answer to the question of whether BA is a predictor of life expectancy in patients with IHD is not obvious.

The calculation of BA in most works is based on the measurement of quantitative indicators called biological markers of ageing. These indicators should correlate with age, be available for measurement in a clinical setting, and be little dependent on current pathological conditions. A variety of indicators can serve as biological markers: anatomical, functional, biochemical, immunological, genetic, and epigenetic [8–10]. Currently, there is no generally accepted set of such markers.

BA can coincide with chronological age, wherein the ageing process is assessed as normal, physiological, or significantly exceed chronologically. In the latter case, ageing is estimated as accelerated [11]. The magnitude of the difference between biological and chronological age, which is considered physiological or pathological, depends on the error (error) in determining BA. If this difference exceeds the value of the standard error, then ageing can be considered accelerated. The generally accepted

mathematical method for assessing BA is the calculation of a multiple regression equation that relates chronological age and several quantitative indicators [12-13]. To determine the coefficients of this equation, survey data from a large number of practically healthy people of different ages are used. To determine the BA of the subject, a series of studies are carried out on him and his age is calculated using the resulting equation. With a significant excess of the estimated age of a person over the chronological age, a conclusion is made about accelerated ageing.

In the domestic and foreign literature, we did not find studies that studied the relationship between BA in IHD patients and their life expectancy. There are only a few works on the association of BA with mortality from various causes [5-7]. But mortality is a population characteristic. From our point of view, no less interesting is the question of the possibility of an individual life expectancy prediction, which is of not only academic but also practical interest.

This work aimed to elucidate the relationship between the rate of ageing, determined by biological age, and the life expectancy of patients with coronary heart disease.

Materials and methods

We analyzed 220 case histories of patients aged 40–80 years who were hospitalized in the Department of Cardiology of the State Institution "Institute of Gerontology named after D.F. Chebotareva" of the National Academy of Medical Sciences of Ukraine with the main diagnosis "IHD: stable angina pectoris I–IV FC". Patients were followed up for 3-25 years until their death. Only patients whose cause of death was IHD were included in the analysis. Their life expectancy was calculated according to the dates of birth and death of patients. The diagnosis of the underlying disease was established based on general clinical examinations and special instrumental and laboratory methods by current recommendations for the diagnosis of IHD at the stage of patient examination. For all patients, anthropometric parameters, BP, ECG, complete blood count, ESR, fasting blood glucose, lipid metabolism, urea, creatinine, and prothrombin index (PTI) were determined many times during the observation period.

The formula for calculating BA was obtained on a group of 108 healthy people aged 40 to 80 years. With the help of stepwise multiple regression, the most informative indicators were selected and an equation was obtained that relates the age of people with these indicators. Using this formula, the BA of IHD patients and the rate of ageing of each person were calculated as the difference between their BA and chronological age.

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

Results and discussion

Table 1 shows the correlation coefficients of indicators with age in practically healthy people examined by us. A check was made for the normality of the distribution of the studied indicators. As it turned out, the ESR distribution is very different from the normal one. After a logarithmic transformation, it became normal. As can be seen from Table 1, of the 18 studied indicators, only 6 significantly correlate with age. As it turned out, body weight and, accordingly, body mass index (BMI) do not have a significant linear relationship with age. This is because body weight first grows, up to about 60-70 years, and then begins to decline. A similar situation occurs with the concentration of both total cholesterols in the blood and LDL cholesterol (LDL). At the same time, the atherogenic index, as the ratio of LDL cholesterol to HDL, significantly increases with age. Systolic blood pressure (SBP) also significantly increases due to a decrease in the elasticity of large arteries. Due to the deterioration of kidney function in old age, the level of creatinine in the blood increases slightly, but significantly. A decrease in protein synthesis in the liver during ageing causes a decrease in the prothrombin index (PTI). There is a fairly high positive correlation of ESR with age, which is due to an increase in the fraction of blood globulins.

Table 1

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

Biomarkers	R
Weight	0.12
Growth	-0.08
BMI	0.14
SBP	**0.16**
DBP	-0,13
SBP- DBP	**0.17**
Heart rate	-0.11
Erythrocytes	0.02
Haemoglobin	0.04
Leukocytes	0.06
Log ESR	**0.41**
Blood glucose	0.12
Cholesterol, blood chemistry	0.15
HDL cholesterol	0.08
LDL cholesterol	**0.16**
Atherogenic index	**0.21**
Urea	**0.17**
Creatinine	**0.37**

The use of stepwise multiple regression made it possible to select the most informative indicators and obtain an equation relating to the age of the examined people with these indicators (Tab. 2).

Table 2

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

Regression Summary for Dependent Variable: Age. R=0.671; R^2= 0.450; Adjusted R^2= 0.423; F(5,102)=16.71; p<0.00001; Std. The error of estimate: 4.656.						
	Beta	SE of Beta	B	SE of B	t(214)	p-level
Intercept			75,9946	8,7479	8,6871	0,00001
SBP-DBP, mm Hg	0,1768	0,0755	0,0775	0,0331	2,3427	0,0211
Log(ESR), mm/h	0,3075	0,0767	6,8964	1,7203	4,0088	0,0001
Atherogenic index	0,1583	0,0747	0,6467	0,3050	2,1199	0,0364
Creatinine, mkmol/l	0,2703	0,0740	0,1140	0,0312	3,6534	0,0004
PTI, %	-0,3258	0,0758	-0,3644	0,0848	-4,2957	0,00001

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; B – regression coefficient; SE of B – standardized error of the coefficient B; Beta – standardized regression coefficient; SE of Beta – standardized error of the coefficient Beta.

$$Y = 0.0775\ X1 + 6.896\ X2 + 0.6467\ X3 + 0.114\ X4 - 0.364\ X5 + 75.99$$

где:

Y – Biological age, years;
X1 – SBP-DBP, mm Hg;
X2 – Log(ESR), mm/h;
X3 – Atherogenic index;
X4 – Creatinine, mkmol/l;
X5 – PTI, %

The standard error of age determination using this equation is 4.61 years, which indicates good accuracy of the model. The age of a person calculated according to the multiple regression equation is considered to be his biological age. Based on the obtained formula, to calculate BA, the values of the indicators of a particular person were summed up, multiplied by the corresponding coefficients, and a constant was added to the resulting amount.

To estimate the rate of ageing, we calculated the difference between the biological and chronological age of each person (BA-CA). It was found that the difference between BA and CA, exceeding 5 years (accelerated ageing), occurs in 50.9% of patients with IHD and only in 12.9% of healthy people. The correlation coefficient between the differences in BA-CA (ageing rate) and the life expectancy of the examined people (Figure) turned out to be negative and significant ($r=-0.368$; $p<0.0001$). The higher the rate of ageing, the shorter the life. From this, we can conclude that BA is a predictor of life expectancy. However, the predictive power of this predictor is not high. This can be explained as follows. On the one hand, the higher the rate of ageing, the greater the risk of developing cardiovascular pathology, its severity, and hence the risk of death from complications of this pathology. This should lead to a reduction in the life expectancy of sick people. On the other hand, the development of the disease motivates people to lead a healthy lifestyle, give up bad habits, and conduct medical examinations more often, which has a positive effect on their life expectancy.

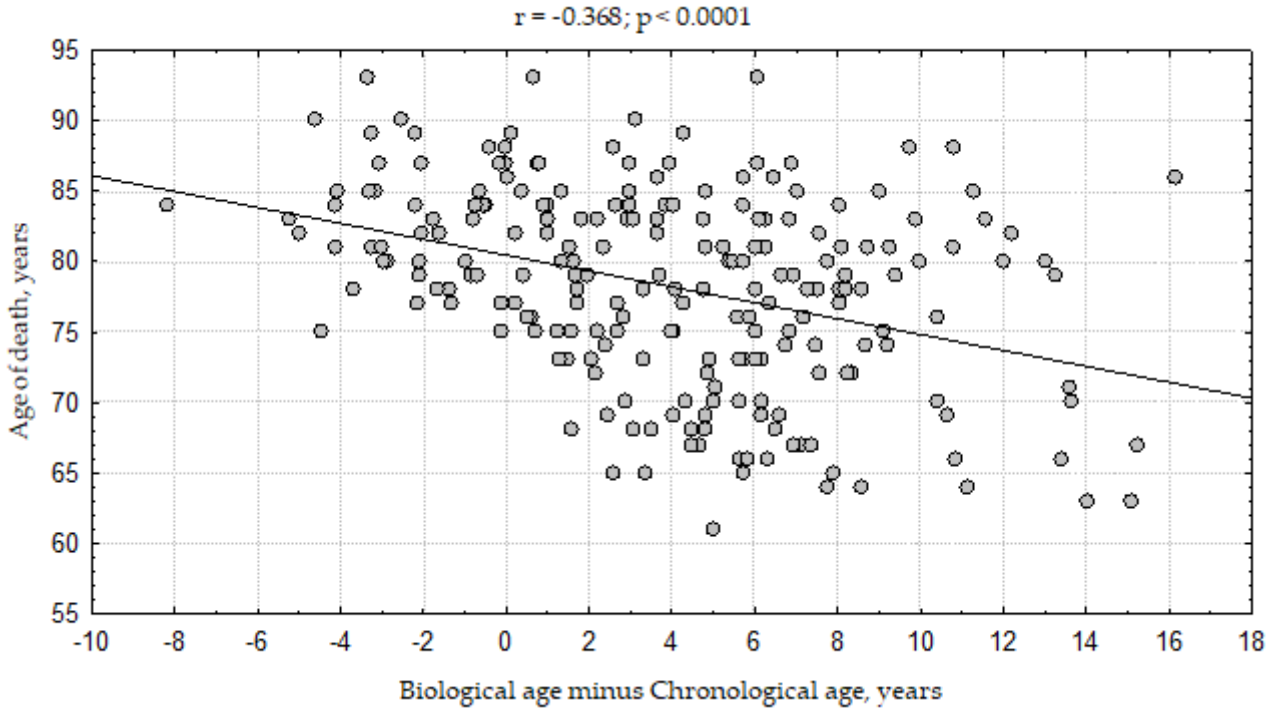

Figure. Correlation age of death with the ageing rate (BA-CA) in patients with IHD.

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

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