Comparison of potential markers of the biological age of healthy male adults and paraplegics

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Abstract

The actual level of the true aging of an organism is characterized by its biological age. By the means of measuring the function ability of its physiological systems, it is possible to evaluate the biological age and use it as an indicator of premature aging. Inclusion of the biological age screening among the basic health precautions should offer yet another viewpoint on how to objectively measure the changes in an organism corresponding to aging.

The article presents a comparison of age dependency of selected biomarkers between groups of healthy men and paraplegics. The measurement of the battery of biomarkers was run in a group of 25 healthy male adults between 36 and 54 years of age. The second group was formed by 20 paraplegics – men between 33 and 50 years of age. In spite of small size of the groups, significant differences were found in 4 of 6 biomarkers.

Abbreviations

BA – biological age
CA – chronological age
MLR – multiple linear regression
BM – biomarker

INTRODUCTION

Aging is a natural process which is manifested in changes of many properties of living organism. The speed of the process is markedly different for various species and in much more limited extent, also for individuals of the same species including human race.

The concept of biological age (BA) can be found in scientific papers throughout last 40 years. Unfortunately, the concept based on formulations as "the true physiological state of the organism" lacks precise and generally accepted definition. An alternative access defines BA as age corresponding better to "true life expectancy" of the individual than his or her chronological age (CA).

Aging is from the strictly academic point of view perceived as an ongoing and natural change of the physiological functions of the examined mature organism – their functional decline caused by the age gradation, not by a diseased state. The evaluation of the aging of an organism and of its overall health and functional condition is in general rather complicated and diverse. Aging is a process presettled for each biological species. Each life span is of a certain length that enables the individual

ORIGINAL ARTICLE

specimen members to fully mature, reproduce and bring up the offspring. There is no universal cause of aging; however, there are certain ways of sustaining the physical and mental health despite the advancing age – ways of affecting one's health condition. Disease, involution and deconditional limitations as well as various psychosocial factors contribute to the functionally healthy state of any organism. The concept of successful aging should be based on improvement of the functional state of the organism and the old-age phenotype. Multiplicity, individual causality and manifestation of the aging of an individual are entities examined by gerontologists who attempt to precisely, yet with difficulty, limit and diversify the old-age.

Calendar old-age (chronological age) can be precisely defined for any individual being. The reason why the current gerontology does not blindly accept this figure is that it does not cover all individual differences. The age limits of the entire population are shifting, the health and functional conditions of the currently aging generations are improving. The age 65 is considered the beginning of the old-age; at the age of 75, which is referred to as the ontogenetic nodal point, begins the actual old-age. In 1960s Neugarten suggested the use of terms "young seniors" for senior of ages between 55 and 74 and "old seniors" for seniors of ages of 75 and more (Kalvach *et al*., 2004).

Social old-age reflects the change of the so called life roles, individual needs, change of life style and above all the economic stability resources left after one retires from his/her job. Majority of respondents indicated the decreased level of their life style and the loss of the economic resources as a significant negative factor characteristic of this life stage. Passive "retirement hood" will be in the future considered a socio-pathological occurrence and a proof of the unsuccessful aging.

Biological old-age is linked with stating the level of specific involution changes of any individual. Neither the biological old-age nor its specific markers that play the most important role in the actual aging have been precisely defined. Individual involution could be measured by molecular or cellular markers that would show the actual functionality of the individual systems in the tested volumes. Changes of the aging markers belong among the verification criteria when evaluating the theories of aging. These very sets of markers have lately become the main source for stating the so called biological age. Biological age characterizes the state of an organism, sets the level of its aging and enables to more sufficiently calculate the actual individual age. Stating the BA has a great application potential as an indicator of the early aging. From the medical perspective, its importance lies in the option to verify the methods and means for decelerating the aging process (Ďoubal, Klemera, 2000). As opposed to the verification method based on evaluating the relations between the mortality or survival curves, this criterion has the advantage of the relative speed of assessment. On the other hand, it is not a direct verification method as such. There still remains the dispute concerning the existence of a universal "clock" – of a pacemaker that hypothetically rules the aging of the entire organism. Some gerontologists presume that the process of aging has a multifactorial background (Olson, 1987). Analyses of the mortality course changes of large groups of organisms in relation to the age and environment support the pacemaker theory (Ďoubal, 1990). Had we accepted the pacemaker hypothesis, we have to note that the changes of the aging markers could not strictly be resulting from the pacemaker's activity, but could also possibly be effected by other than aging factors. Therefore, practically measurable entities, changes of which would literally correlate with the level of aging of an organism, are being searched. The current state of methodology development of stating the biological age enables, to a certain level, advancing in the choice of methodology when designating the formulas for calculating the biological age (Voitenko, 1983, Dean, 1988, Nakamura, 1988, 1991, Hofecker, 1991).In spite of intermittent critism (Ingram, 1983, 1988, Wilson, 1988, Lindsay and Kaplan, 1994, McClearn, 1997, Azbel, 1998), the common access to BA determination is as follows: a set of age – dependent variables – biomarkers (BMs) and an algorithm (statistical method) of evaluating values of these markers are chosen. The resulting quantity is interpreted as BA (e.g., Voitenko and Tokar, 1983, Steen at al., 1998, Kroll and Saxtrup, 2000, Guéguen, 2002, Duggirala *et al*., 2002).In fact, every set or "battery" of BMs together with a method of computation represent an implicit hidden definition of BA, so that resulting BAs obtained by various authors are hardly comparable and interpretable.

As we mentioned earlier, biological age is pre-settled for each biological species. Nevertheless, this setting represents the rough framework only. The real live span as well as the dynamics of process of aging depends potentially on many other factors.

It is generally accepted that biological age may be modified by on physical and intellectual activities, stresses, nutrition and more generally by life style. Elucidation of these "non genetic" factors is particularly important from practical point of view.

Comparison of biological age development between healthy and paraplegic groups may provide relevant information and may be excellent source for verification of theories of aging.

The aim of this study is to compare selected BMs in groups of healthy and paraplegic adult males.

The actual measuring of the biological age was based on selection of such biomarkers that have high correlation with chronological age. Next criterion was the feasibility of practical measurements, namely with respect to minimisation of discomfort for persons under test. The selected biomarkers for the individual measuring were systolic blood pressure, diastolic blood pressure, forced vital capacity forced expiratory volume (1 s), body mass index and revised near point of eye. These selected mark-

ers are among the most frequently used ones (Dean, 1988). These markers could also be measured without using a special laboratory.

MATERIAL AND METHODS

Hypothesis on correspondence among BA, CA and BMs.

Differences in BA, as far as people of mutually equal CA are concerned, correspond to the differences in their individual degree of aging. In accordance with (Klemera, Ďoubal 2006), the relation between BA and CA can be expressed by equation: $BA=CA+R(0, s^2)$, where $R(0, s^2)$ is a random variable with zero mean and variance s^2.The variance and even the type of the distribution of R might be dependent on CA. Any measurable property of human organism that changes systematically with CA might be affected by the individual degree of aging and used then as BM. With few exceptions, most authors still use multiple linear regression (MLR) as a basic tool for computation of quantity they call BA. Nevertheless, the MLR method is unsuitable for computation of BA as was found recently. The following formula was proved as an optimum method (Klemera, Ďoubal 2006):

$$BA = \frac{\sum_{j=1}^{m}(x_j - q_j)\,k_j/s_j^2 + CA/s_B^2}{\sum_{j=1}^{m} k_j/s_j^2 + 1/s_B^2}$$

Variables $x_1, \ldots, x_m$ represent the individual values of the markers of BA. Value k_j is slope, q_j intercept and s_j^2 residual dispersion of linear regression of the dependence of marker x_j on CA. Symbol s_B^2 represents an estimate of variance of differences (BA–CA) for the population under study.

Experimental groups and methodology of measurements

Two groups were selected for the measuring – a group of 25 healthy adult males (age 36 to 54) and a group of 20 paraplegics (age 33 to 50) with impaired locomotion due to accident in adulthood. It was expected that BMs in the group of healthy individuals might be influenced by their sedentary job, limited amount of exercise and greater consumption of energetically rich nutrients. In the group of paraplegics, wheel chair confinement together with consequent changes in life style was expected to be the main factor that influences BMs.

The group of paraplegics was chosen intentionally, as we were interested in the aging trends of the two groups of almost identical age range. Unfortunately, finding suitable volunteers was very difficult.

Sight change is a very prominent and easily measured aging marker; therefore, the changes reflecting the accommodative ability of the eye lens. Accommodative ability can be evaluated based on the changes of the near point. The measuring of the near point cannot generally be used for individuals with errors of refraction. In the test file, the parameter corresponding to the amplitude accommodation is so called revised near point that is the reciprocal value to accommodation range. The measurement was performed using optical bench. The systolic and diastolic blood pressures were measured using a digital sphygmomanometer. Both parameters were included as they are age dependent and because we suspected that a limited physical activity of both groups as well as the unhealthy life style of the first group should have an impact even within the chosen age group. The weight was taken on the personal weighing scale, the height by the anthropometric gauge, for the lung vital capacity evaluation was used a personal spirometer MSP1 and the BMI was calculated by standard. The results of the measurements were analyzed by methods of linear regression and correlation analysis.

Selected BMs and their abbreviations.

body mass index	BMI
systolic blood pressure	SBP
diastolic blood pressure	DBP
forced expiratory volume (1 s)	FEV1
forced vital capacity of lung	FVC
revised near point of eye	RNP

RESULTS

In most cases, regression analysis proved significant differences between parameters for healthy men and paraplegics, as illustrated in Figures 1 to 6 and Tables 1 to 3. No significant differences were found only for systolic and diastolic blood pressure. BMI was significantly lower for paraplegics, but its age dependence was not significant. Vital capacity of lung was significantly lower for paraplegics while the near point of eyes was higher. Unlike the vital capacity, differences for revised near point occur for younger individuals only.

Significant correlations between various pairs of parameters were proved only for couples (DBP, SBP) and (FVC, FEV1) as expected.

DISCUSSION

An interesting finding is that the differences between the line gradients (slopes) for healthy men and paraplegics were not significant, while significant differences in "shifts" (intercepts) of the lines were found for all BMs except bloody pressures. We do not know what the lung

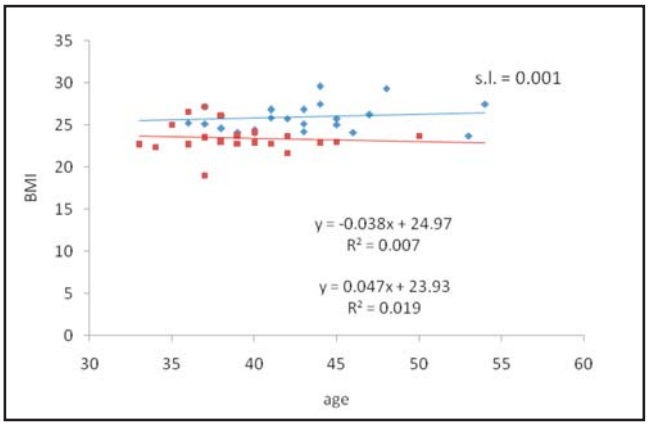

Figure 1. Comparison of the dependence of BMI on age in tested groups of healthy men (◆) and paraplegics (■).

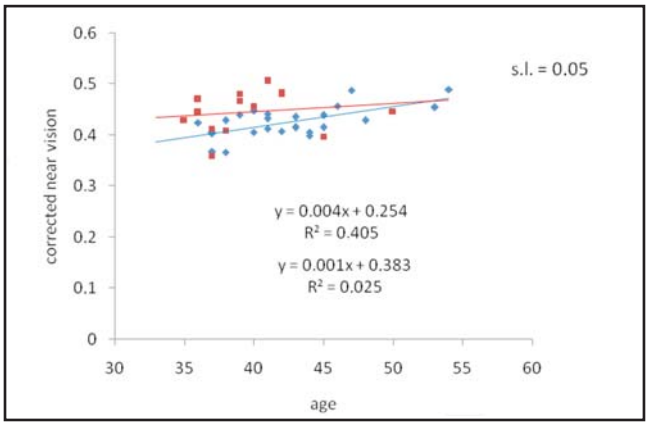

Figure 2. Measuring of the revised near point (◆ healthy men, ■ paraplegics).

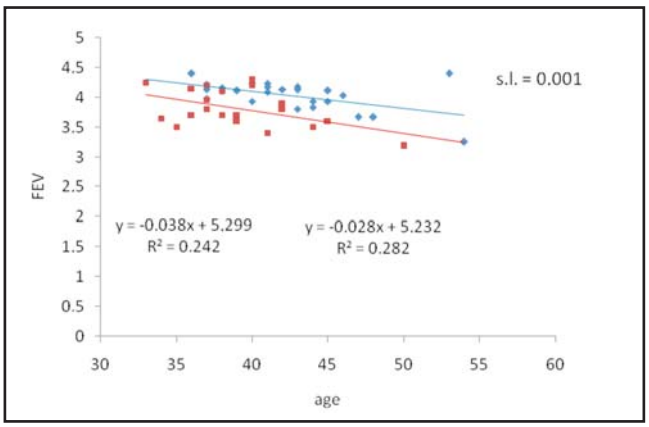

Figure 3. Measuring of the lung vital capacity FEV1 (◆ healthy men, ■ paraplegics).

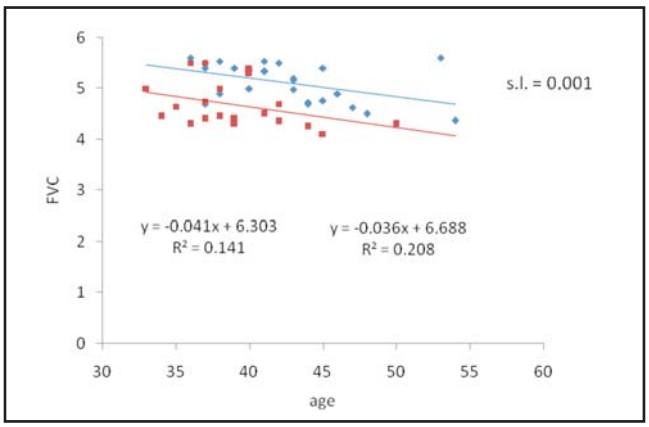

Figure 4. Measuring of the lung vital capacity FVC (◆ healthy men, ■ paraplegics).

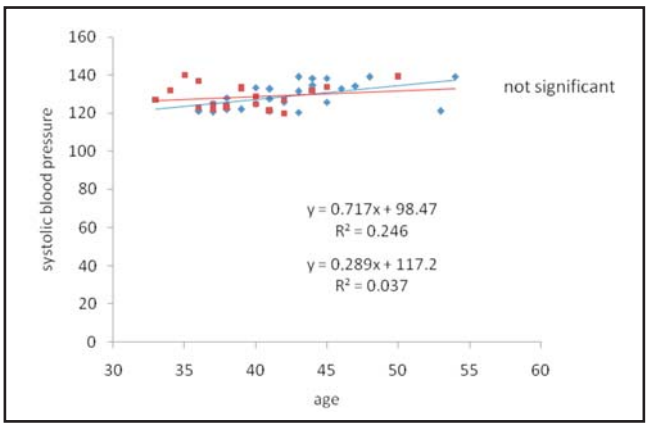

Figure 5. Measuring of the systolic blood pressure (◆ healthy men, ■ paraplegics).

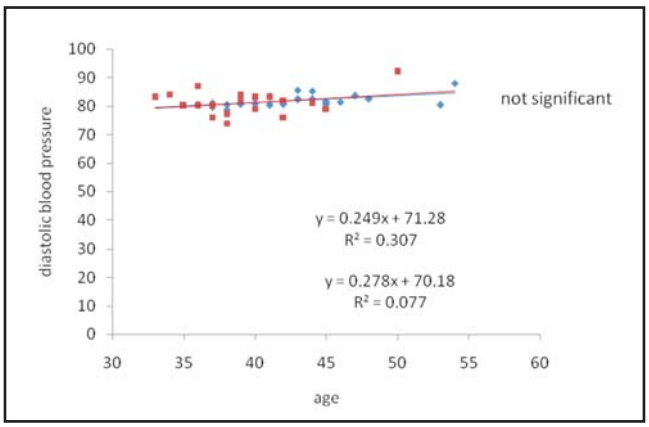

Figure 6. Measuring of the diastolic blood pressure (◆ healthy men, ■ paraplegics).

Table 1. Results of tests of differences between regression lines for healthy men and paraplegics.

Significance levels for differences of:	BMI	SBP	DBP	FEV1	FVC	RNP
regressioin lines as whole	0.001	NO	NO	0.01	0.01	NO
intercept of regression lines	0.001	NO	NO	0.001	0.001	0.05
slope of regression lines	NO	NO	NO	NO	NO	NO

Table 2. Significance levels between the markers.

	BMI	SBP	DBP	FEV1	FVC
BMI					
SBP	NO				
DBP	NO	0.01			
FEV1	NO	NO	NO		
FVC	NO	NO	NO	0.001	
RNP	NO	NO	NO	NO	NO

NO means that it was not possible to prove the correlation even in the level of 0.05.

Table 3. Correlation coefficients of dependence between markers.

	BMI	SBP	DBP	FEV1	FVC	RNP
BMI	1					
SBP	0.261	1				
DBP	0.170	0.620	1			
FEV1	0.111	–0.520	–0.303	1		
FVC	0.298	–0.423	–0.132	0.802	1	
RNP	0.176	0.061	0.133	–0.036	0.0492	1

vital capacities were before the injuries and whether the measured values are a result of the mobility limitation or not.

The causes in the changes of the measured vital capacity markers are probably connected with impaired locomotion and changes in biomechanics in paraplegics. Changes in vision may be connected with aye trophic, also as the consequence of impaired locomotion.

Except couples (DBP, SBP) and (FVC, FEV1), whose correlation is known and natural, the week correlation among BMs supports the suitability of their use in batteries of BMs.

CONCLUSION

At least some important BMs proved to have different dependence on age for healthy men and for paraplegics. It is not clear whether it is result of differences in BV or more profound changes in "pre-setting" of aging process. In the second case, the biological age of paraplegics should be evaluated separately: the computation of their BA should not be generally based on parameters corresponding to healthy people. The results of the present paper stress the necessity of further study of the problem.

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