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Longitudinal and cross-sectional changes with age in selected anthropometric and physiological traits in hospitalized adults: an insight from the Polish Longitudinal Study of Aging (PLSA)

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Abstract: Longitudinal studies of aging concerning individuals with comparable lifestyle, diet, health profile, socioeconomic status, and income remain extraordinarily rare. The purposes of our ongoing project are as follows: (i) to collect extensive data on biological and medical aspects of aging in the Polish population, (ii) to determine factors affecting the rate and course of aging, (iii) to understand how aging unfolds as a dynamic and malleable process in ontogeny, and (iv) to find novel predictors of longevity. Our investigation followed 142 physically healthy asylum inmates, including 68 males and 74 females, for at least 25 years from the age of 45 years onward. Cross-sectional assessment involved 225 inmates, including 113 males and 112 females. All the patients lived for a very long time under similar and good environmental conditions at the hospital in Cibórz, Lubuskie Province. They maintained virtually the same daily schedule and lifestyle. The rate and direction of changes with age in selected anthropometric and physiological traits were determined using ANOVA, *t*-test, and regression analysis. There were sex differences in the rate and pattern of age-related changes in certain characteristics such as relative weight, red blood cell count, monocyte count, thymol turbidity value, systolic blood pressure, and body temperature. Body weight, the body mass index (BMI), and total bilirubin level increased with advancing age, while body height decreased with age in both sexes. In conclusion, the aging process was associated with many regressive alterations in biological traits in both sexes but the rate and pattern of these changes depended on biological factors such as age and sex. There were only few characteristics which did not change significantly during the period under study. On the basis of comparison between the pattern of longitudinal changes with aging and the pattern of cross-sectional changes with age in the analyzed traits, we were able to predict which pattern of changes is associated with longer lifespan.

Key words: aging, senescence, changes with age, longitudinal study, cross-sectional study, lifespan, longevity

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Introduction

Like many other developed countries, Poland is experiencing a noticeable change in the age structure of its population. Compared with previous generations, the Polish people are living significantly longer. Currently, the number of people aged 60 and above makes up a larger share of the Polish population than ever before. This number is expected to double by the year 2050. For the first time, the number of older people in European countries is close to surpass the number of children (Barbi et al. 2008). To date, few comparative studies of aging have been conducted in the Polish population. There is thus a paucity of information on the rate, pattern, and direction of age-related changes in biological traits in Polish adults of both sexes. Therefore, such long-term studies are needed.

There has been a growing interest in evaluating biological factors and mechanisms related to the aging process in humans, especially with respect to specific biomarkers of aging and reliable predictors of longer life and health expectancy (Sprott 2010; Glei et al. 2011). Despite many extensive studies, underlying mechanisms of senescence remain poorly understood and there is no single measure which could be used as a sensitive and specific biomarker of aging to date (Martin-Ruiz et al. 2011). Nevertheless, some interesting findings have emerged recently thanks to research into genetics and biology of lifespan of centenarians. For example, it was demonstrated that the offspring of the centenarians have more than a 60% reduction in the risk of dying from all causes, more than a 70% reduction in the risk of dying from malignant neoplasm, and also more than a 80% reduction in the risk of dying from ischemic heart disease in comparison to controls (Terry 2004; Sebastiani et al. 2012). Moreover, a fair percentage of individuals with exceptional longevity, such as nonagenarians, centenarians, and supercentenarians live to an advanced age and remain functionally independent at the same time, thereby escaping from cardiovascular disease, cancer, diabetes mellitus, osteoporosis, and other serious health problem which are more prevalent among older people (Kirkwood 2008a). This fact has raised hopes that longer life expectancies do not necessary mean that growing number of people will be chronically ill and functionally dependent on care in their old age. Therefore, the aging process has become one of the most important issues in current biology (gerontology) and medicine (geriatrics). Although senescence is arguably the most familiar aspect of human biology, its proximal causes as well as evolutionary explanations remain open to misinterpretation (cf. Kirkwood 2005; 2008b; 2010; Longo et al. 2005; Sanz et al. 2006; Ljubuncic and Reznick 2009; Pérez et al. 2009; Mitteldorf 2010; Blagosklonny 2010; 2012; Kirkwood and Kowald 2012; Zimniak 2012).

Numerous cross-sectional studies on aging were published worldwide. Nonetheless, longitudinal studies concerning rate, direction, and pattern of changes with age in morphological and physiological traits in individuals with comparable place of living, socioeconomic status, diet, health, income, daily schedule, physical activity, and lifestyle remain extremely rare because such undertakings are enormously costly and time-consuming (Ferruci 2008; Raina et al. 2009; Whelan et al. 2013).

The main goals of our ongoing project, which involves both longitudinal

(the Polish longitudinal study of aging, hereinafter referred to as the PLSA) and cross-sectional assessment of changes with age in numerous biological characteristics in the hospitalized population of older adults of both sexes, are as follows: (i) to collect extensive data on biological aspects of the aging process in the Polish population, (ii) to determine factors affecting the rate and course of aging, (iii) to understand how aging unfolds as a dynamic and malleable process in ontogeny, and (iv) to find novel predictors of longevity. The research was also intended to provide an extensive reference data source as well as a comparative database for future meta-analysis as well as longitudinal studies of aging in the Polish population. The results, however, should be interpreted with the utmost caution because of several specific limitations since the subjects came from the hospitalized population of asylum inmates. These methodological problems will be discussed in more detail in the Discussion.

Materials and methods

The direct access to medical files and written records that had been stored at the archives of case history at the Regional Psychiatric Hospital for People with Mental Disorders in Cibórz, Lubuskie Province, Poland, gave us a unique opportunity to study changes with age in selected morphological and physiological traits of the patients who had been treated at this medical institution in the years 1960–2000. The medical files had to be anonymized in the first instance so as not to divulge any personal or confidential information. Subsequently we collected extensive data on health profiles and biological condition of the inmates and created computerized database on the basis of the written documents. The significant part of our longitudinal and cross-sectional data on changes with age in selected anthropometric, physiological, and biochemical traits in hospitalized adults from PLSA is available online (Borysławski et al. 2015).

From the total number of inmates who had stayed at the hospital in the analyzed period of time (N=3,500), we carefully selected solely data from physically healthy individuals who stayed there continuously for at least 25 years. Longitudinal data were available from 142 physically healthy inmates, including 68 males and 74 females, whose health status and aging profiles were evaluated for 25 years in five-year intervals, starting from the age of 45 onward. The longitudinal part of the investigation lasted for over 40 years. All the subjects from the first group were 45 years of age at the commencement of the study and 70 years of age at the end of the study. Cross-sectional data were available from 225 inmates, including 113 males and 112 females, who differed in lifespan. Age at death of each individual was determined on the basis of death certificate and subsequently the cross-sectional sample was divided into the following categories of lifespan: 53 years of age (N=74, including 22 males and 52 females), 63 (N=57, including 27 males and 30 females), 68 (N=89, including 49 males and 40 females), and 76+ years of age (N=43, including 13 males and 30 females). In the PLSA, numerous anthropometric, morphological, physiological, and biochemical traits were analyzed. For the purpose of the present study, however, only traits of vital biological and medical importance, which were essential for appraisal of health status of the patients, were chosen.

For several decades, the hospital in Cibórz constituted an appropriate place not only for people with severe mental problems but also for individuals who needed constant care due to mild mental and behavioural disorders. In the People's Republic of Poland (1952-1989), this medical institution functioned as long-term sheltered accommodation for people from the underclass, which was probably a socially and politically motivated decision. Therefore, the majority of the chosen group of inmates (74%) were physically and mentally healthy and the rest (26%) had mild mental disorders but were physically healthy. It should be stressed that the interindividual variation was substantially limited in the study sample because the inmates lived for many years under identical and relatively prosperous environmental conditions and maintained virtually the same daily schedule and lifestyle, including diet, nutrition, amount of sleep, leisure, and physical activity. This fact undoubtedly boosts the value of the collected data.

All measurements were performed in accordance with internationally accepted standards and requirements by the medical staff at the hospital. Research techniques and methods of the analysis were standardized. Measurements of body height were performed on the hospital premises by nurses using a standard stadiometer, graduated to the nearest 0.1 cm. Stature was measured when an individual was standing barefoot with heels together, upper extremities at the side, lower extremities and back straight, shoulders relaxed and the head adjusted to the Frankfort plane (Martin 1928; Martin and Saller 1957). Body weight was measured to the nearest 0.1 kg using calibrated digital scales. Body mass index (BMI) was calculated as body weight (kg) divided by the square of the height (m^2). Blood samples from the median cubital vein were drawn monthly by nurses. The performed examinations included complete blood count, fasting blood glucose test, total bilirubin level (TBIL), and thymol turbidity test (IPMP). Blood cell counting was carried out by medical laboratory scientists using an optical microscope and Bürker chamber or hemocytometer holding a specified volume of Giemsa stained diluted blood. Hemoglobin concentration level was determined with Sahli's hemoglobinometer method and hematocrit value was estimated using Wintrobe's method. A Folin-Malmros technique for the estimation of blood glucose was applied. TBIL was estimated in accordance with the Malloy and Evelyn procedure, whereas IPMP was assessed colorimetrically at 660 nm wavelength using the Kingsbury-Clark method. Systolic and diastolic blood pressure and heart rate were measured after short repose using a Riva-Rocci sphygmomanometer and taking pulse in the carotid artery triangle on the right side of the neck, respectively. Axillary body temperature was routinely measured once a month by a nurse.

To determine rate and patterns of changes with age in the analyzed traits and to derive mathematical formulae describing these changes, one-way ANOVA, Student's *t*-test, and regression analysis were employed. To find the best fitting regression models, the method of least squares was used. A given function was confirmed as the best fitting model of regression only when a coefficient of determination (R^2) reached the highest value and an unknown parameter (β_0) as well as a coefficient of regression (β_1) were statistically significant at $p<0.05$.

Five types of regression functions were tested: (1) linear function, $y=\beta_1 \times + \beta_0$, (2) logarithmic function, $y=\beta_1 \ln(x) + \beta_0$, (3) polynomial function, $y=\beta_1 x^2 + \beta_{2\times} + \beta_0$, (4) exponential function type I, $y=\beta_1 x^a$, (5) exponential function type II, $y=\beta_1 e^{a(x)}$, where chronological age (an independent variable) is designated by (x), (*y*) is a value of an analyzed characteristic (a dependant variable), (β_2) stands for the second coefficient of regression, (*a*) represents the exponent, and (*e*) denotes the base of the natural logarithm. Mean values of each analyzed trait were calculated for the consecutive five-year periods, starting from the age of 45 onward.

Results

The baseline statistical characteristics of the selected traits are presented in Table 1. In the studied population, males were taller than females and had lower age at death (*t*-test, $p<0.001$). Both progressive and regressive types of changes with age were observed. The rate and pattern of the age-dependent longitudinal changes in the analyzed traits are presented in Table 2. Table 3 shows the direction and patter of the cross-sectional changes in the analyzed anthropometric and physiological traits.

The total reduction in body height during the whole period under study came out at 5.6 cm, i.e. 2.2 cm/decade or 3.3% in males and 5.5 cm, i.e. 2.2 cm/decade or 3.4% in females, respectively. The best fitting regression model was logarithmic for males and linear for females in the longitudinal assessment. In males, the greatest decrease was in the first five-year period, while in females

Table 1. Traits analyzed in the PLSA: description, units of measurement and baseline characteristics (arithmetic mean ± standard deviation) at the age of 45 in both sexes

Trait	Unit	Mean ± SD		*t*-test	*p*-value
		Males (*N*=68)	Females (*N*=74)		
Body height	cm	169.7 (6.7)	157.1 (7.2)	–11.13	0.000
Body weight	kg	66.4 (8.9)	61.7 (11.6)	–2.67	0.009
BMI	kg/m^2	23.0 (2.7)	25.0 (4.4)	–3.27	0.001
Blood glucose	mg/dL	102.9 (15.8)	102.1 (23.2)	–0.23	0.816
Total bilirubin	μmol/L	0.486 (0.4)	0.456 (0.4)	–0.40	0.691
Thymol turbidity value	Maclagan units	2.13 (1.0)	2.70 (1.2)	3.06	0.003
Red blood cell count	$10^6/\mu$L	4.3 (0.3)	3.9 (0.4)	–6.46	0.000
White blood cell count	$10^3/\mu$L	6.8 (1.5)	6.3 (2.0)	–1.50	0.135
Lymphocyte count	%	30.6 (8.1)	31.8 (6.8)	1.00	0.317
Monocyte count	%	2.0 (1.7)	2.3 (2.4)	0.68	0.500
Hematocrit value	%	43.4 (3.4)	40.4 (2.9)	–5.57	0.000
Hemoglobin concentration	g/dL	13.4 (1.2)	12.2 (1.1)	–6.21	0.000
Systolic blood pressure	mmHg	121.2 (10.8)	119.8 (12.3)	–0.73	0.470
Diastolic blood pressure	mmHg	76.3 (6.8)	75.8 (7.9)	–0.38	0.702
Heart rate	bpm	82.7 (8.1)	82.1 (9.2)	–0.36	0.718
Body temperature	°C	36.6 (0.2)	36.5 (0.3)	–2.29	0.024

Statistical significances of the differences were determined by Student's *t*-test. *p*-values ≤0.05 are given in bold.

Table 2. The rate and direction of changes with age in the traits analyzed during the longitudinal assessment (all patients aged 45 to 70, $N=142$), expressed as the best fitting regression models: a value of a given characteristic is a dependant variable (y), whereas age is an independent variable (x)

Trait	Regression model and coefficient of determination (R^2)	
	Males ($N=68$)	Females ($N=74$)
Body height	logarithmic $y=-12.5279 \ln(x) + 217.3984$ $R^2=0.999$	linear $y=-0.2082x + 166.4192$ $R^2=0.995$
Body weight	logarithmic $y=6.0347 \ln(x) + 43.9329$ $R^2=0.852$	logarithmic $y=12.5756 \ln(x) + 13.87$ $R^2=0.975$
BMI	exponential type I $y=9.1929\ x^{0.2432}$ $R^2=0.978$	exponential type I $y=9.1929\ x^{0.347}$ $R^2=0.996$
Blood glucose	polynomial $y=0.0303x^2 - 3.7377x + 209.8392$ $R^2=0.911$	exponential type I $y=128.1311\ x^{-0.0596}$ $R^2=0.536$
Total bilirubin	exponential type II $y=0.3038e^{0.093x}$ $R^2=0.667$	exponential type II $y=0.1838e^{0.0187x}$ $R^2=0.950$
Thymol turbidity value	exponential type II $y=2.0435e^{0.0015x}$ $R^2=0.114$	exponential type II $y=2.6153e^{0.0009x}$ $R^2=0.048$
Red blood cell count	polynomial $y=-0.0004x^2 + 0.0504x + 2.8291$ $R^2=0.680$	logarithmic $y=0.4129 \ln(x) + 2.3394$ $R^2=0.693$
White blood cell count	polynomial $y=0.0026x^2 - 0.2866x + 14.4374$ $R^2=0.852$	polynomial $y=0.0048x^2 - 0.5386x + 20.922$ $R^2=0.939$
Lymphocyte count	polynomial $y=-0.0144x^2 + 1.6325x - 14.1607$ $R^2=0.887$	polynomial $y=-0.0148x^2 + 1.599x - 10.5286$ $R^2=0.870$
Monocyte count	exponential type II $y=0.5739e^{0.0251x}$ $R^2=0.874$	polynomial $y=0.0032x^2 - 0.3097x + 9.8247$ $R^2=0.974$
Hematocrit value	polynomial $y=-0.0142x^2 + 1.5917x$ $R^2=0.857$	polynomial $y=-0.0134x^2 + 1.4897x$ $R^2=0.594$
Hemoglobin concentration	linear $y=-0.0091x + 13.8588$ $R^2=0.287$	polynomial $y=-0.0014x^2 + 0.1618x + 7.6632$ $R^2=0.702$
Systolic blood pressure	polynomial $y=-0.005x^2 + 0.6717x + 100.5333$ $R^2=0.585$	logarithmic $y=20.9224 \ln(x) + 40.04$ $R^2=0.953$
Diastolic blood pressure	polynomial $y=-0.0088x^2 + 1.0364x + 47.5758$ $R^2=0.954$	polynomial $y=-0.0168x^2 + 1.9296x + 23.26$ $R^2=0.738$
Heart rate	polynomial $y=0.0036x^2 - 0.3426x + 91.3526$ $R^2=0.427$	polynomial $y=0.0059x^2 - 0.6638x + 100.0405$ $R^2=0.677$
Body temperature	linear $y=0.0008x + 36.5345$ $R^2=0.249$	linear $y=0.0064x + 36.192$ $R^2=0.955$

Table 3. The rate and direction of changes with age in the traits analyzed during the cross-sectional assessment of patients who differed in lifespan (N=225), expressed as the best fitting regression models: a value of a given characteristic is a dependant variable (y), whereas age is an independent variable (x)

Trait	Regression model and coefficient of determination (R^2)	
	Males (N=113)	Females (N=112)
Body height	polynomial $y=0.0074x^2-0.8226x+191.0143$ $R^2=0.998$	exponential type II $y=152.3382e^{0.0003x}$ $R^2=0.836$
Body weight	polynomial $y=-0.0202x^2+2.3872x$ $R^2=0.536$	exponential type I $y=126.6221x^{-0.1666}$ $R^2=0.981$
BMI	polynomial $y=-0.0076x^2+0.873x$ $R^2=0.801$	linear $y=-0.0884x+31.9729$ $R^2=0.995$
Blood glucose	linear $y=-0.5020x+127.0633$ $R^2=0.966$	polynomial $y=0.0109x^2-1.3117x+135.9569$ $R^2=0.144$
Total bilirubin	polynomial $y=0.001x^2-0.1263x+4.4524$ $R^2=0.999$	polynomial $y=-0.0006x^2+0.072x-1.6924$ $R^2=0.195$
Thymol turbidity value	polynomial $y=-0.0018x^2+0.235x-5.635$ $R^2=0.829$	polynomial $y=-0.0039x^2+0.5123x-14.0375$ $R^2=0.995$
Red blood cell count	polynomial $y=-0.001x^2+0.132x$ $R^2=0.625$	polynomial $y=0.0004x^2-0.0525x+5.7418$ $R^2=0.631$
White blood cell count	polynomial $y=-0.0021x^2+0.2421x$ $R^2=0.417$	polynomial $y=-0.0017x^2+0.2061x$ $R^2=0.888$
Lymphocyte count	polynomial $y=-0.0283x^2+3.8734x-98.542$ $R^2=0.798$	polynomial $y=-0.0062x^2+0.9062x$ $R^2=0.565$
Monocyte count	polynomial $y=0.0057x^2-0.7375x+25.411$ $R^2=0.855$	logarithmic $y=-4.8112\ln(x)+22.0117$ $R^2=0.935$
Hematocrit value	polynomial $y=-0.0095x^2+1.2996x$ $R^2=0.766$	exponential type II $y=37.6929e^{0.0013x}$ $R^2=0.592$
Hemoglobin concentration	polynomial $y=-0.003x^2+0.4059x$ $R^2=0.5982$	polynomial $y=0.0016x^2-0.1895x+17.7732$ $R^2=0.999$
Systolic blood pressure	polynomial $y=-0.0319x^2+4.0096x$ $R^2=0.390$	polynomial $y=-0.0310x^2+3.9812x$ $R^2=0.482$
Diastolic blood pressure	polynomial $y=-0.0189x^2+2.435x$ $R^2=0.529$	polynomial $y=-0.0057x^2+0.7065x+57.5934$ $R^2=0.390$
Heart rate	polynomial $y=-0.0074x^2+0.9291x+56.1727$ $R^2=0.425$	polynomial $y=0.0072x^2-1.0641x+120.232$ $R^2=0.662$
Body temperature	linear $y=-0.0052x+36.8828$ $R^2=0.983$	exponential type II $y=36.7952e^{-0.00009x}$ $R^2=0.800$

the greatest rate of reduction occurred in the last five-year period. The smallest decrease in height occurred in the third age category 55–60 in both sexes and amounted to 0.9 cm, which was equivalent to 16% of the total reduction in males and 16.7% in females. The rate of decline in stature increased in older age groups.

In males and females, body weight, BMI, and TBIL increased significantly with age over the whole period under study, whereas body height decreased with increasing age (Fig. 1). Although body weight was constantly greater in males compared with females, males had lower BMI, thus they were relatively slimmer and females were stouter. Compared with females, males experienced a smaller rise in relative body weight, i.e. from 23.0 kg/m^2 when they were 45 years of age to 25.9 when they were 70 years of age vs. 25.0 to 29.9 kg/m^2 for females, respectively. The highest rate of increase occurred in the first age category in males (0.9 kg/m^2 within five years) and the third age category in females (over 1 kg/m^2 within five years). The best fitting regression function was exponential in both sexes. Fasting blood glucose level fluctuated between 68.0 and 150.0 mg/dL in males and 60.0 and 233.3 mg/dL in females. It reached the highest value at the age of 45 in males (102.9 mg/dL) and at the age of 50 in females (102.7 mg/dL). The lowest level occurred at the age of 55 in males (94.3 mg/dL) and females (99.6 mg/dL). The greatest sex difference in blood glucose level was observed at the age of 55 and amounted to 5.2 mg/dL (t=–1.80, p=0.07). The curve of regression assumed a U-shaped pattern in males with the trough at the age of 55, whereas a decrease in blood glucose was observed in females. In longitudinal part of the study, the model of regression was polynomial in males and exponential type I in females. The highest level of TBIL occurred at the age of 70 in both sexes (0.593 in males and 0.686 μmol/L in females). No significant sex differences in TBIL were found. The best fitting models were the same for both sexes, i.e. exponential type II. Males had constantly lower level of thymol turbidity value compared with females. There were no significant age-related changes in thymol turbidity test value in both sexes. The best fitting regression models were identical for both sexes, i.e. exponential type II.

The age-related changes in red blood cell count (RBC) were not significant in males. In females, there was an increase with age in RBC and the regression function was logarithmic. Males had higher RBC compared with females in each age category (Fig. 2). The changes with age in white blood cell count (WBC) were significant in males and females and the regression models were always polynomial. The pattern of changes was U-shaped as the lowest WBC count was observed at the ages of 50–60 in both sexes. In the period between age 50 and 65, males had significantly higher number of WBC compared with females (t-test, $p<0.05$). Similarly, the best fitting regression models of changes with age in lymphocyte count were always polynomial. The regression lines, however, assumed an inverted U-shaped pattern as the highest level of lymphocyte count was observed at the age of 60 in both sexes. There were no significant sex differences in any age category. A steady increase with age in monocyte count in males and females was found. The model of regression was exponential type II in males and polynomial in females in

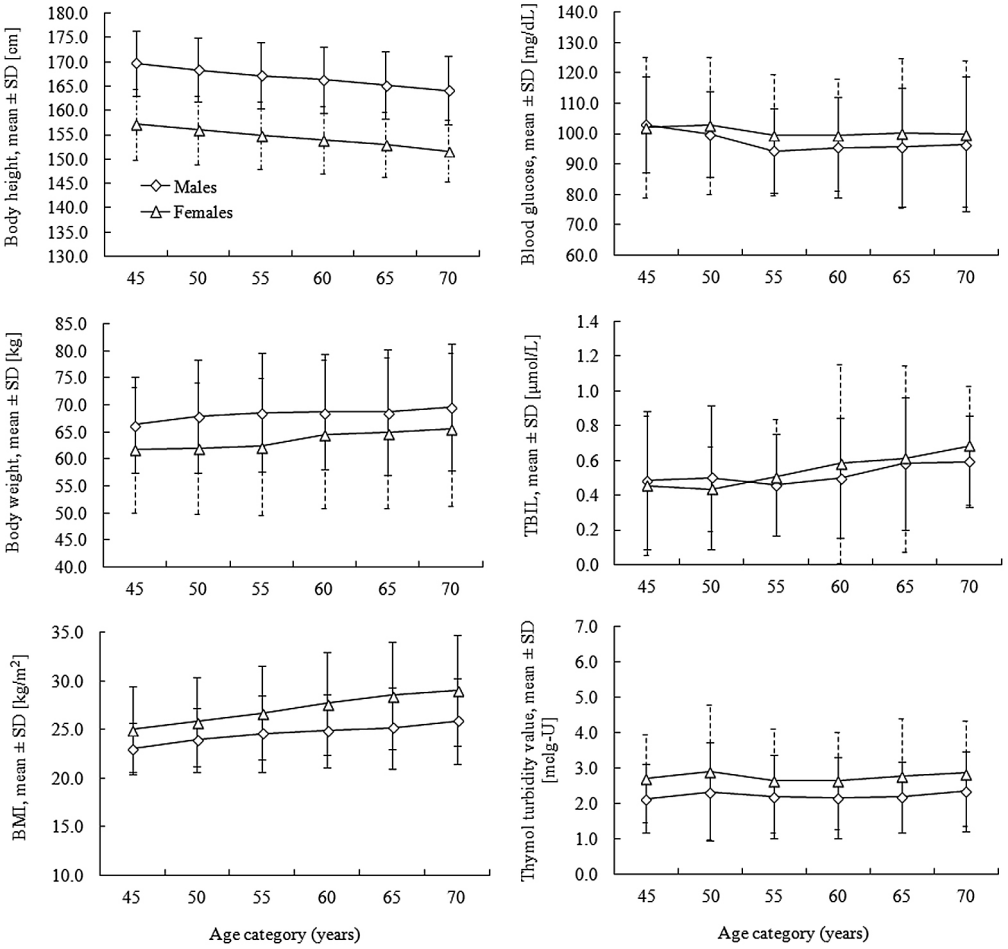

Fig. 1 Changes with age in the anthropometric, hematological and biochemical traits analyzed longitudinally in the consecutive age categories – data from the PLSA (N=142, including 68 males and 74 females; arithmetic means ± standard deviations)

longitudinal assessment. There were significant changes with age in hematocrit value and the curves assumed an inverted U-shaped pattern in both sexes with the highest values at age 55-60 in males and age 50-55 in females. The lowest level of hematocrit was observed at the age of 70 in both sexes. The models of regression were always polynomial. In males, blood hemoglobin concentration decreased slightly with age but these changes proved to be non-significant. Likewise, there were no statistically significant changes in hemoglobin concentration in females. Males had constantly higher hemoglobin concentration in comparison with females. The regression models were always polynomial, except for the case of changes with age in males in the longitudinal assessment when it was linear.

Systolic blood pressure (SBP) in males increased in the first three age categories but decreased thereafter (Fig.

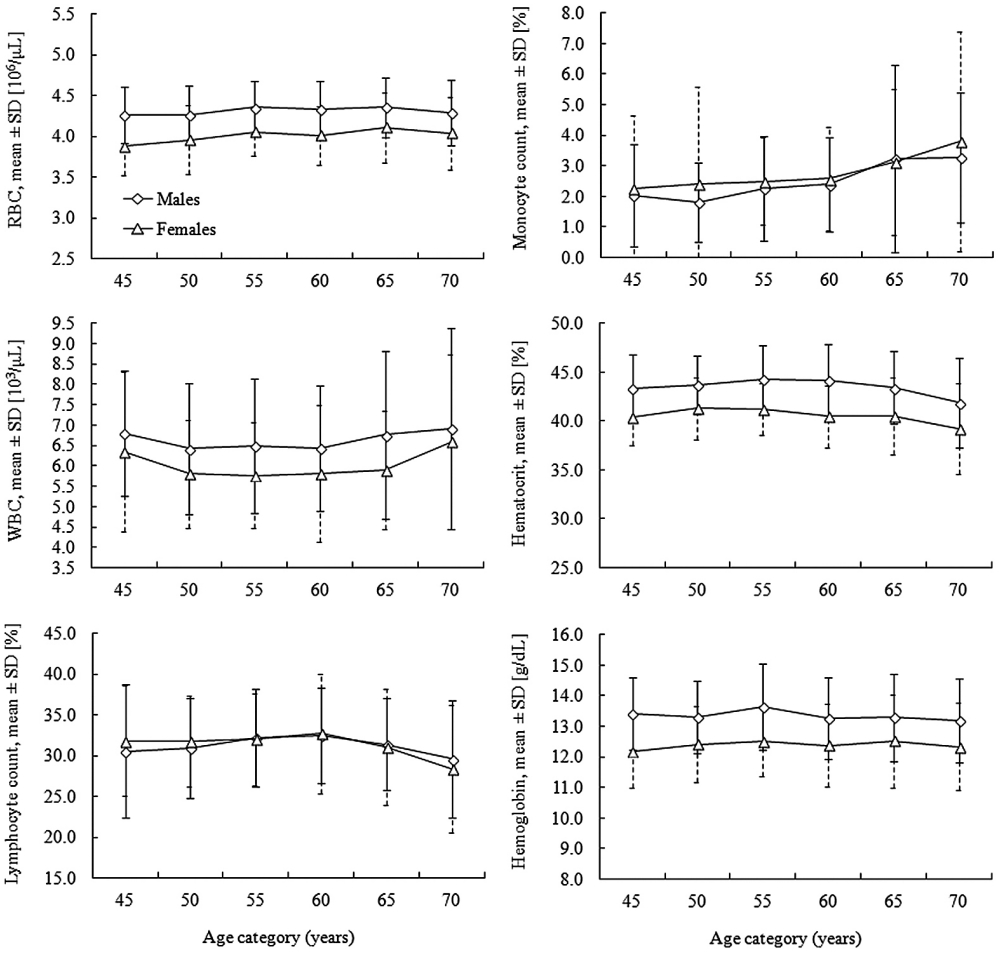

Fig. 2 Changes with age in the blood cell counts analyzed longitudinally in the consecutive age categories – data from the PLSA (N=142, including 68 males and 74 females; arithmetic means ± standard deviations)

3). The peak in SBP occurred at the age of 60. The model of regression was polynomial and the curve of regression assumed an inverted U-shaped pattern. In females, there was a steady increase with age in SBP and the regression model was logarithmic. Males had significantly lower SBP than females at the age of 55 (t=–1.99, p=0.048) and 70 (t=–2.10, p=0.037). The changes with age in diastolic blood pressure (DBP) were significant in both sexes and models of regression were polynomial in each case. The curves of regression assumed an inverted U-shaped pattern. The highest value of DBP occurred at the age of 60 in males (78.1 mmHg) and at the age of 55 in females (79.6 mmHg). The lowest value was observed in the first age category, i.e. at the age of 45 in both sexes, 76.3 and 75.8 mmHg, respectively. No significant sex differences in DBP were found. There were no statistically significant changes with age in heart rate (HR) in both sex-

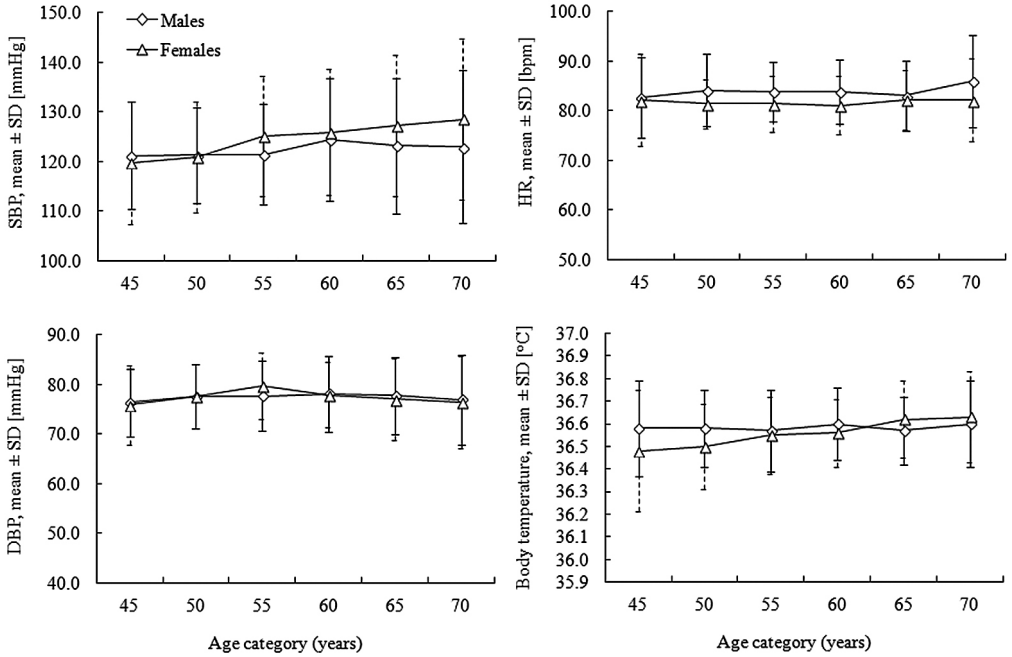

Fig. 3 Changes with age in the hematological parameters and body temperature analyzed longitudinally in the consecutive age categories – data from the PLSA (N=142, including 68 males and 74 females; arithmetic means ± standard deviations)

es. The best fitting models were polynomial in each case. Males had higher HR than females at the age of 50 (t=2.70, p=0.008), 55 (t=2.50, p=0.014), 60 (t=2.75, p=0.007), and 70 (t=2.56, p=0.012). The changes with age in body temperature were non-significant in males. In females, however, there was a steady increase in body temperature and thus the peak occurred at the age of 70 (36.6 °C) and the trough at the age of 45 (36.5 °C). Interestingly, males had higher body temperature than females at the age of 45 (t=2.29, p=0.024) and 50 (t=2.49, p=0.014). The regression models were linear in each case.

The analysis of longitudinal data revealed that body height and blood color index were negatively correlated with chronological age, while body weight, BMI, bilirubin level, and erythrocyte sedimentation rate (ESR) were positively correlated with chronological age in both sexes. In males, monocyte count increased with advancing age, while RBC count, SBP, and body temperature increased significantly with age only in females. The analysis of cross-sectional data showed that there was a gradual and steady increase in body height (on the border of statistical significance, p=0.078) and there was an age-related decrease in body weight, BMI, fasting blood glucose level, and body temperature in males. The curve of regression of changes in TBIL assumed a U-shaped pattern, while the regression line of changes in RBC count, hemoglobin level, hematocrit value, SBP, and DPB assumed an inverted U-shaped pattern. In females, there was an age-related increase in body height in each consecutive age category of lifespan

(on the border of statistical significance, $p=0.085$). Similarly, hemoglobin level, blood color index, eosinophil count, and lymphocyte count increased in females, whereas an age-related decrease in body weight was observed. BMI and monocyte count decreased with age as well. On the other hand, WBC count, thymol turbidity value, and SBP increased with advancing age in females.

On the basis of comparison between the pattern of longitudinal changes and the pattern of cross-sectional changes with age in the analyzed traits (Tables 2 and 3), we were able to predict which pattern of changes is associated with longer lifespan. Taller and slimmer individuals from the PLSA tended to live longer compared with shorter and stouter ones. Subjects with lower SBP and lower body temperature had higher age at death. Lower blood glucose level and higher bilirubin values were genuine predictors of longevity only for males, whereas higher hemoglobin concentration, higher values of color index, increased absolute granulocyte count (AGC), slighlty elevated lymphocyte count, lower monocyte count as well as WBC count, lower ESR, and lower thymol turbidity test values were all associated with extended lifespan solely in females. Interestingly, body weight, BMI, bilirubin level, and ESR significantly increased with age in both sexes. Monocyte count rose only in males, whilst RBC count, SBP, and body temperature increased only in females. Body height and color index decreased with age in males and females, whilst urine specific gravity diminished with age only in females. There were significant U-shaped changes with age in WBC count and AGC in both sexes. The same pattern of changes with age was observed for blood glucose level in males as well as band cell count and monocyte count in females. The inverted U-shaped pattern of changes with aging was found for hematocrit value in both sexes, whereas this model proved fitting for DBP only in males.

Discussion

Age is considered to be a major risk factor for many medical conditions. The aging process itself consists in a progressive dysfunction in homeostatic mechanisms since they tend to falter in later ontogeny and eventually allow entropy in biological systems. Consequently, this dynamic state endangers compensatory strategies of the metabolism and many important cell functions gradually become disrupted (Johnson et al. 1999; de Magelhães and Faragher 2008; Guarente et al. 2008). Thus aging at later stages of ontogeny (senescence) is intrinsically associated with innumerable age-related changes in morphological and physiological traits of the organism. However, the onset and the rate of these age-dependent alterations depend on environmental factors, socioeconomic status, availability of medical care, diseases, diet, nutritional status, stress level, physical activity, and other components of lifestyle. It is important to understand that much as the regressive changes are part of the normal development of the organism, they are not simply reversal of progressive changes during the growth. Therefore, they represent the regressive development of the organism.

It has been established that virtually all morphological and physiological traits change significantly with increasing age. There are only few biological characteristics which remain relatively constant throughout adult ontogeny. For exam-

ple, total blood volume per unit of body weight, blood pH, fasting blood glucose level, the total amount of protein in the blood, RBC count and body temperature in males, hemoglobin concentration in females, and thymol turbidity test values in both sexes, remain relatively constant. In repose, the intraindividual variation in these characteristics is normally strictly regulated by homeostatic mechanisms to stay within a narrow range. However, an older individual needs more time to restore the normal level of these characteristics after the action of a disturbing factor such as physical exercise, excessive calorie intake, or the administration of xenobiotics (Wolański 2012).

The natural process of height loss during aging and its causes have been the subject of many studies. Although numerous epidemiological and gerontological studies of these interrelationships have been conducted worldwide, comprehensive longitudinal investigations concerning individuals with similar diet, lifestyle, health, income, and socioeconomic status are exceptionally rare. The phenomenon of age-related reduction in adult body height has been well documented in the anthropological literature (Sorkin et al. 1999; Bagga 2013). After reaching a peak in the development in the third decade of life, height declines approximately 1–2 cm/decade due to the compression of the intervertebral fibrocartilages, which are interposed between the adjacent surfaces of the bodies of the vertebrae, growing deficits in bone mass of the vertebral bodies, aging-associated alterations in muscles and joints, loss of muscle tone, and certain postural deformities, including a decrease in femoral neck-shaft angle, deeper location of the head of the femur in the hip joint, excessive curvature of the thoracic spine, and platypodia (Rossman 1979; Malinowski and Strzałko 1985). Most authors concur that age-related reduction in stature is a result of diminution in the heights of the vertebral bodies and cartilaginous intervertebral discs (Rossman 1979; Schulz 2006; Spirduso et al. 2005). The former is related to changes in bone mineral density, whereas the latter is attributable to aging-associated alterations in fibrocartilage quality of an outer fibrous ring (anulus fibrosus) and an inner gel-like center (nucleus pulposus) of each intervertebral disc. Other significant causes include gradual loss of muscle tone and certain postural changes such as an aging-related decrease in femoral neck-shaft angle (coxa vara), deeper location of the head of the femur in the hip joint, excessive curvature of the thoracic spine (hyperkyphosis), and platypodia (flat feet). Therefore, age-related reduction in stature proves to be an ineluctable process when changes with age are evaluated over an extensive duration of time such as several decades. Postmenopausal females experienced a more rapid loss of height at later stages of ontogeny compared with older males.

The patients from the PLSA had a slightly higher rate of height loss in comparison with healthy individuals from the general population, which indicates that their health status was lower than expected (Chmielewski et al. 2015). However, it is quite obvious that the lengthy stay at the hospital must have been disadvantageous to their physical and psychological health. The inmates were held in custody permanently after all. Moreover, they lived among patients with severe mental problems and were not able to choose freely their diet and lifestyle. It is worth mentioning that living in hospital is often associated with

high level of psychological stress, hospital-acquired infections, sedentarism, and hypokinesis.

We found that taller individuals of both sexes lived significantly longer than shorter ones. Interestingly, the link between adult stature and longevity in humans involves conflicting findings and the results remain mixed. According to some authors, taller height can be a weak and nonspecific predictor, which means that this relationship is not causal but coincidental, of longer life expectancy (Kemkes-Grottenthaler 2005; Borysławski and Chmielowiec 2010). On the other hand, the longevity benefits of smaller body size are currently supported by considerable evidence and a variety of different types of investigations (Bartke 2012; He et al. 2014; Samaras 2014; Chmielewski 2015). Samaras (2014) claims that numerous studies demonstrated that shorter height or smaller body size is generally related to greater longevity in humans. Additional papers supporting this position include Holzenberger et al. (1991) and Salaris et al. (2012). Nevertheless, it is conceivable that both these opposing relationships are in fact spurious and result from different types of artifacts.

For example, taller people are expected to have longer life expectancies compared with shorter ones, if they belong to younger birth cohorts since there was the dramatic increase in average life expectancy during the twentieth century. Similarly, shorter people are expected to have greater longevity than taller ones, if they are recruited from older birth cohorts and the study uses mortality data or consists in a cross-sectional analysis in lieu of a longitudinal assessment because the secular trend in body height is an important confounding factor. After elimination of the cohort effect concerning the positive secular changes in body height, the relationship between adult stature and lifespan usually diminishes or even disappears in some cohorts, especially in women (Chmielewski 2015).

It is worth noting that increasing body weight with age in the present study is at variance with centenarian studies which show that centenarians as well as supercentenarians tend to be relatively short and slim. Since body height is estimated to be only 10% of the longevity picture (Samaras 2014), it is easy to see why longevity studies often conflict with mortality data, especially with investigations which do not track the entire cohort to death. Shorter stature may not be an advantage until advanced ages. In addition, taller and leaner cohorts are often compared to shorter and stouter ones, which gives taller people a longevity advantage. As stated above, another very important confounder is year of birth. People born in later cohorts tend to be significantly taller and have considerably longer life expectancies simply due to advances in medical care and substantial improvements in education, sanitation, and prophylaxis (Borysławski and Chmielowiec 2010). Moreover, people within a given cohort who were poor in their youth have significantly higher mortality and are also shorter independently of their current socioeconomic status.

It is noteworthy, however, that the inmates from the PLSA lived on a diet prescribed by nutritionists at the hospital and thus the food portions were very similar in terms of their energy content. Therefore, it is theoretically possible that taller inmates had constantly lower daily caloric intake compared with shorter ones, which brings to mind the tentative explanation for greater longevity in taller subjects from the PLSA. Many authors

agree that there is a link between lower caloric intake and oxidative damage associated with rate of aging and longevity in many species (Weindruch and Sohal 1997). In rats, mice, and other short-lived species, the aging process can be retarded by caloric restriction.

While proof is not available that caloric restriction increases maximum longevity or helps to postpone aging in humans, a number of studies have demonstrated a relation between low energy intake and reduced mortality or even increased life expectancy. For example, a study that tracked 1915 healthy men aged 45–68 for 36 years found that all-cause mortality declined with decreasing caloric intake (Willcox et al. 2004). These findings held true down to 50% of the group mean energy intake. Below 50%, mortality started increasing. Likewise, Okinawans consume about 17% fewer calories than the mainland Japanese people and have 40% lower risk of cancer and cardiovascular disease (Willcox et al. 2004). Moreover, Okinawans, as opposed to mainland Japanese people, are also significantly shorter and have longer life expectancies. Other studies found that numerous biological parameters improve with reduced caloric intake and dietary restriction has, by and large, "a powerful protective effect" against type 2 diabetes, cardiovascular disease, inflammation, and cancer (Fontana 2009; Cava and Fontana 2013). Therefore, it is reasonable to predict that reduced risk of heart disease, cancer, and diabetes mellitus can increase longevity since over 75% of the causes of deaths after the age of 65 are due to these chronic diseases. For instance, the Framingham Heart Study showed that when the risk of cardiovascular disease is low, the average lifespan increases from 29 to over 39 years (Cava and Fontana 2013). On the other hand, there is currently no evidence that dietary restriction increases lifespan or health span in humans, primates, or other long-lived species (Austad 2012). The positive effect of calorie restriction on human health is still a matter of controversy. Furthermore, some researchers argue that calorie restriction is in fact a double-edged sword and "there are very good grounds to believe that any such positive effect in humans is likely to be extremely modest, if it exists at all" (Shanley and Kirkwood 2006; Kirkwood, personal communication).

The age-related increase in relative body weight expressed as the body mass index (BMI) was probably a consequence of the fat accumulation process throughout late adulthood. The main causes of this alteration in body weight and composition are aging-associated changes in metabolism like leptin resistance along with decreased physical activity, sedentary lifestyle, and height loss (Cornoni-Huntley et al. 1991; Rolland-Cacher et al. 1991; Guo et al. 1999). Moreover, there is a common and inevitable process of loss of height with normal aging which can contribute to the increase in relative weight. Some proposals of best weight for height suggested that a modest increase in relative weight with age was related to optimum survival but the suggested magnitude of the BMI increase was in part a result of the artifact of height loss on the BMI (Sorkin et al. 1999). In advanced age, however, a decrease in relative weight is frequently observed in elderly people. This process results from bone and muscles loss, and dehydration of the organism. In the PLSA, an age-related decrease in body weight has not been observed because this process occurs at later phases of senescence which have not been studied here.

Blood glucose is derived from the diet, gluconeogenesis and glycogenolysis but its level in the blood is strictly regulated within a narrow range (60–100 mg/dL). It increases after the ingestion and decreases in starvation. Many epidemiological studies have shown that older people have a higher blood glucose level compared with younger people, which results from the lower rate of glucose metabolism and insulin resistance (Stout 1994; Chang and Halter 2003). However, individuals with exceptional longevity maintain normal values of glucose level even in their old age because they are less likely to develop diabetes mellitus than control groups (Davey et al. 2012; Garagnani et al. 2013).

There are several groups of factors involved in the control of blood pressure, such as various anatomical characteristics, e.g. structure and elasticity of blood vessels, physiological and biochemical agents, e.g. heart work, proper function of baroreceptors, function of parasympathetic and sympathetic nervous system, nitric oxide, lipids and hormones profiles, etc., genetic factors, lifestyle along with diet, physical activity, and psychological stress level (Black and William 2013). Elderly people have generally higher blood pressure compared with younger ones due to age-related structural and functional changes in the circulatory system (Whelton 1994; Houston 2009). The age-related loss of elasticity of blood vessels is linked to elevated SBP, while higher peripheral vascular resistance is the main cause of elevated DBP. Interestingly, increased arterial stiffness and elevated blood pressure are probably mutually causally related. The strength of this relationship is likely to increase with elevated BP, even in healthy subjects who do not suffer from hypertension (Yambe et al. 2007). Before the menopause, females tend to have lower BP than males because of the higher activity of nitric oxide synthase (NOS) and higher level of NO, which is also associated with the higher level of estrogens. After the menopause, females tend to have higher BP than males at the same age and thus they are also more prone to CVD. In the PLSA, individuals attaining lifespan of 76 or greater, were more likely to have lower BP compared with those who had lower age at death. This observation supports earlier findings from epidemiological studies in the Polish population (Zyczkowska et al. 2004).

We recognize that the present study has a number of limitations that should be noted. First, the patients constituted a rather specific group of subjects because they lived for a very long time at the psychiatric hospital and had mental disorders. Some of them were treated with psychoactive drugs every now and then. The individuals who underwent such treatment more often were excluded from the study sample. No statistically significant differences were found between the group of the treated subjects and those who took psychopharmaceuticals occasionally (ANOVA, $p>0.05$), except for higher number of eosinophils in the treated group of inmates. Further, we analyzed long-term trends in rapidly reacting parameters and established patterns and directions of changes with aging (longitudinal data) and with age (cross-sectional data), yet significant changes in some hematological and cardiovascular parameters can occur within hours, minutes, or even within seconds. However, the fact that the measurements were taken relatively often by generally the same nurses for many years increases the reliability of our data. Moreover,

we were able to calculate means with standard deviations and standard errors and, therefore, different types of variations were under control. Nonetheless, we have no firm evidence that these short-term changes in hematological and cardiovascular parameters did not interfere with the observed long-term trends, which is another important limitation of our study. The probability that these short-term changes had an impact on the final results of the long-lasting analysis at the population level is, however, extremely low and negligible. It is noteworthy that the baseline WBC count was comparatively high at the beginning of the study and averaged $>6.0\times10^3$ cells/μL, which may be attributed to poor health status of the subjects. Likewise, WBC count was slightly higher in individuals from the PLSA, as opposed to average parameters for healthy individuals from the general population. Thus, the U-shaped pattern was observed instead of a gradual age-related decline in total leukocyte count, which is a more typical pattern of changes with aging in leukocyte count in healthy older individuals.

Conclusions

The aging process is linked to regressive changes in virtually all morphological and physiological traits. There are only few biological characteristics which do not change significantly with advancing age in humans. Although taller and slimmer individuals from the PLSA lived longer than shorter and stouter ones, the relationship between body size and lifespan remains unclear. Lower SBP, DBP, and body temperature are associated with greater longevity in both sexes. In males, higher level of TBIL and lower level of fasting blood glucose level are genuine predictors of longer lifespan. Lower level of WBC and monocyte count, higher level of thymol turbidity test, higher level of lymphocyte count, and higher level of blood hemoglobin concentration are related to longer lifespan in females. In general, the regressive changes are destructive and can be linked to some disorders at older ages. The rate and pattern of numerous regressive changes depend on sex and other biological factors. More longitudinal and cross-sectional studies of aging in the Polish population are needed.

Authors' contributions

PC conducted the data analysis, interpreted the results, prepared the first draft of the manuscript and all subsequent versions, and also approved the final version of the manuscript. KB supervised the research and reviewed the article for scientific content. KC and JC collected the data and performed the initial analysis. All authors were involved in developing the design, strategy, and analysis plan for the study.

Conflict of interest

Authors declare that there is no conflict of interest regarding publication of this paper.

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