METABOLIC PROFILE AND HEART RATE VARIABILITY AS AN INDICATOR OF THE CARDIOVASCULAR SYMPATHETIC INFLUENCES IN FEMALE INDIVIDUALS OF TWO AGE GROUPS

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ABSTRACT

The positive correlation between metabolic disturbances and the prevalence of cardiovascular diseases (CVD) is well known. Elevated sympathetic outflow was shown to be an underlying factor in the pathogenesis of CVD.

The aim of our study was to examine the correlation between the sympathetic cardiovascular drive as measured by heart rate variability (HRV) and blood metabolic profile. These measurements were carried out on female individuals of two age groups.

Ten female subjects were divided in 2 groups – young (average age 20 years) and adults (average age 60 years). Five minute long electrocardiogram was recorded using the analog-to-digital converter iCardio. The iCardio software provided the major HRV indices. The total power of HRV (TP) was significantly lower in the adult individuals as marker of the elevated cardiovascular sympathetic outflow. Blood tests (total cholesterol, HDL, LDL, triglycerides and glucose) were carried out in a licensed laboratory. All blood parameters were higher in the adult group as compared to the young. Negative correlation was evidenced between the TP and total cholesterol (r = -0.76), LDL cholesterol (r = -0.80), glucose level (r = -0.99), while the correlation between TP and HDL was positive (r = 0.76) in the adult group. The young individuals showed significantly less pronounced correlation between the laboratory parameters and HRV.

Our data supported the hypothesis that elevated sympathetic drive typical for the postmenopausal women was positively correlated to their metabolic cardiovascular risk markers. The better clarification of these interactions might help in the understanding and prevention of the higher CVD incidence in this female age group.

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Key words: *Heart rate variability; Sympathetic; Blood cholesterol; Blood glucose; Cardiovascular diseases.*

Introduction.

Cardiovascular diseases (CVD) continue to be the major and global causative factor for morbidity, impaired quality of life and mortality [6]. The strategy for screening the individuals at higher cardiovascular risk and focusing primary prevention on them simply through implying lifestyle changes seems to promise optimal results. The recent introduction of numerous informative and non-invasive methods is a basis for carrying such screening studies [5].

Sympathetic influences on the cardiovascular system have been definitely shown as an underlying factor in the pathogenesis of CVD [21, 22].

Growing evidence shows that in addition to producing hemodynamic alterations, e.g. increased peripheral vascular resistance, decreased arterial compliance, and target organ damage, sympathetic overdrive might be underlying factor for the concomitant metabolic disturbances such as dyslipidemia, hyperglycemia, obesity, metabolic syndrome, type 2 diabetes [8, 11].

The relationship between metabolic disturbances and sympathetic activation is bidirectional: obesity, especially central type obesity is on its part the source of numerous humoral factors (adipokines, cytokines, bioactive molecules) that contribute to the activation of the sympathetic nervous system [12].

Gender differences in the lipid profile and in the onset of atherosclerosis and CVD have

been evidenced. Women develop CVD 7 to 10 years later than men [13]. In general LDL-C and total cholesterol is lower in pre-menopausal women as compared to males. On the contrary, by the time of menopause LDL-C starts to rise manifestly and even exceeds the level in the male individuals [7, 20].

The huge hormonal transformation that occurs with menopause in women is assumed to be the underlying factor for the changed lipid profile. Reduced estrogens are to blame through both their direct and indirect effects. Menopause causes visceral fat redistribution and alterations in energy metabolism [14]. Estrogen reduction affects lipid metabolism directly through modification of gene expression and suppression of lipoprotein lipase and up-regulation of α_2-adrenergic receptors as well [9, 18].

Glucose metabolism is also negatively affected by estrogen deficiency in older women. Estrogens were shown to participate in the maintenance of normal insulin sensitivity. Estrogen deficiency post ovariectomy and menopause contribute to the development of insulin resistance and type 2 diabetes [24].

The aim of our study was to examine the correlation between the sympathetic cardiovascular drive as measured by the heart rate variability (HRV) and blood metabolic profile in female individuals of two age groups – young premenopausal and older postmenopausal women.

Methods. Ten female subjects were divided in two groups according to their age: group 60Y/O (mean age of 60.5±3 years) and group 20Y/O (mean age 20.6±0.4 years). All examinations were non-invasive and absolutely safe for the examinees. Our protocol was approved by the University Ethics Committee. It completely adhered to the principles of the declaration of Helsinki [23]. The examined persons gave a written consent for their participation in the study.

After 10 minutes resting supine position continuous 5 minute electrocardiogram (ECG) was recorded using the analog-to-digital converter iCardio (IT Innovations). The ECG signal was analysed for evaluation of the short-term parameters of HRV in the frequency domain using the software packet iCardio. The total power (TP) of HRV in the range of 0.04-0.4 Hz was measured.

The important laboratory markers of cardiovascular risk such as total cholesterol, HDL and LDL cholesterol, triglycerides and glucose level were analysed in a licensed laboratory.

The data were presented as means ± SEM. Statistical analysis was performed using the Data Analysis ToolPak of the Excell software. The Student-Fisher t test and regression analysis were applied. The level of significance for p was assumed to be at least 0.05.

Results. The general characteristics and the studied parameters are presented in Table 1.

Table 1. General characteristics, total power of HRV and laboratory markers of cardiovascular risk. Data are presented as means ± SEM. * $p < 0.005$; ** $p < 0.0002$ vs. 20Y/O. BMI – Body mass index; TP – Total power of HRV; T Chol – Total cholesterol; LDL – Low density lipoprotein cholesterol; HDL-C – High density lipoprotein cholesterol; TG – Triglycerides.

	Age (years)	BMI (kg/m^2)	TP (ms^2)	T Chol (mmol/l)	LDL-C (mmol/l)	HDL-C (mmol/l)	TG (mmol/l)	Glucose (mmol/l)
60Y/O	59.2±3	26±0.6*	1466±372	6.6±0.3**	3.7±0.6	2.1±0.5	2.2±1.1	5.5±0.2
20Y/O	21±0.4	21±1.3	3592±1173	4.4±0.3	2.6±0.2	1.3±0.1	1±0.1	5.2±0.2

Body mass index (BMI) was significantly higher in the 60Y/O group ($p < 0.005$). The absolute total power (TP) of HRV in the older females was markedly lower as compared to the young persons (Table 1, Fig. 1). The laboratory data showed essential differences

between the levels of the major cardiovascular risk markers in the two groups. Total cholesterol was elevated and significantly higher and the females of the 60Y/O group as compared to the young. LDL-C and triglycerides were elevated and higher in the 60Y/O as well although the difference did not reach statistical significance.

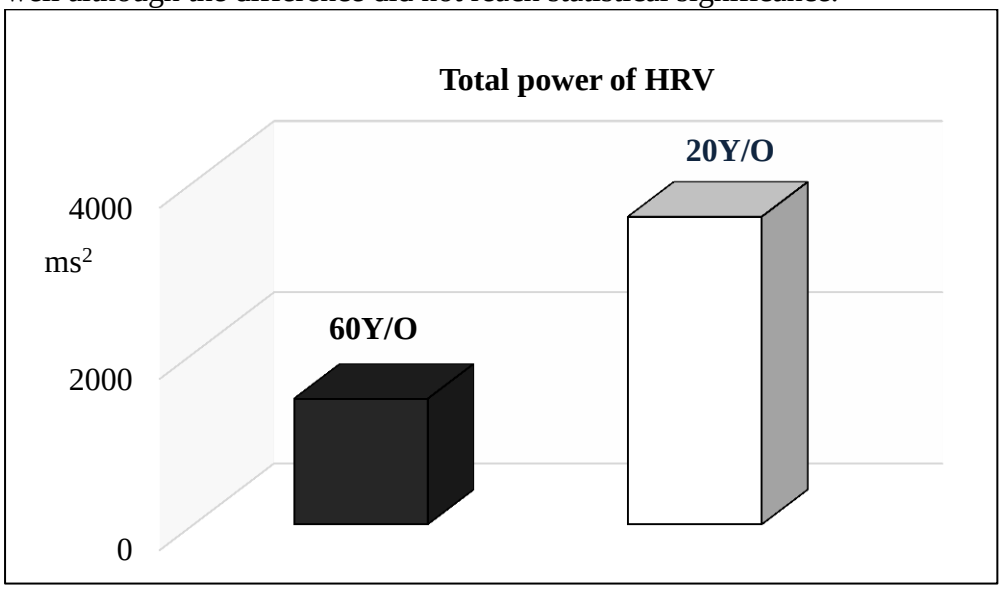

Fig. 1. Total power of HRV.

We performed regression analysis and we evidenced several important dissimilarities between the two studied groups.

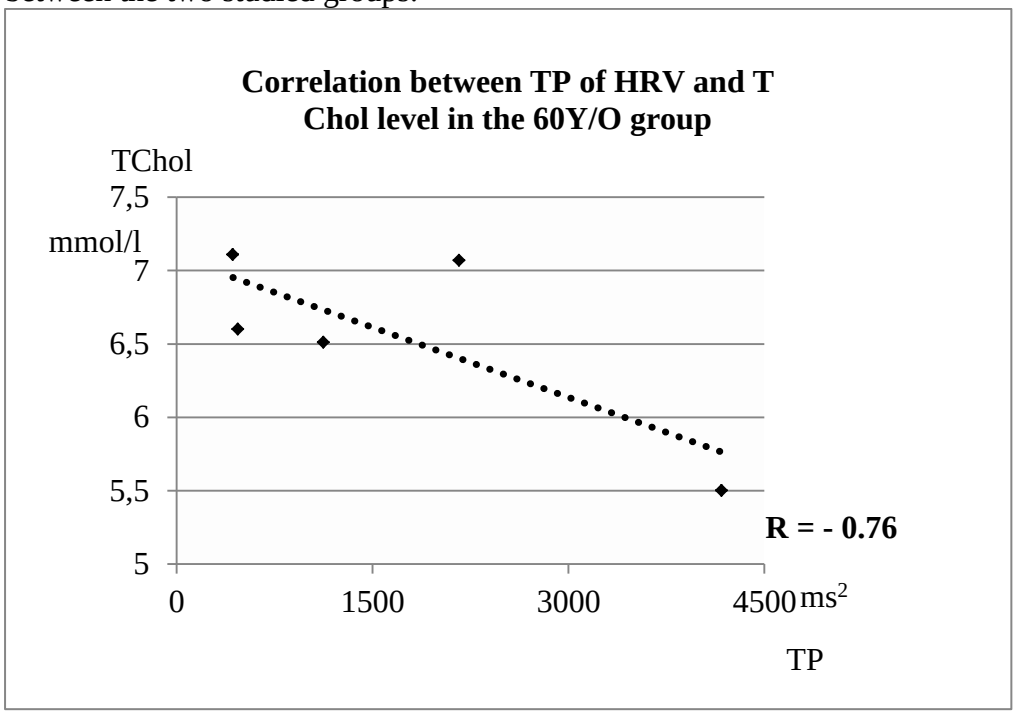

Fig. 2. Negative correlation between total cholesterol and total power of HRV in the 60Y/O group. T Chol - Total cholesterol; TP - Total power. R = - 0.76

Negative correlation was shown to exist between the levels of total cholesterol and HRV (Fig. 2 and 3). However, this correlation was more pronounced for the older female persons as shown by the Pearson's coefficients – R = - 0.76 in the 60Y/0 and R = - 0.53 for the 20Y/O individuals.

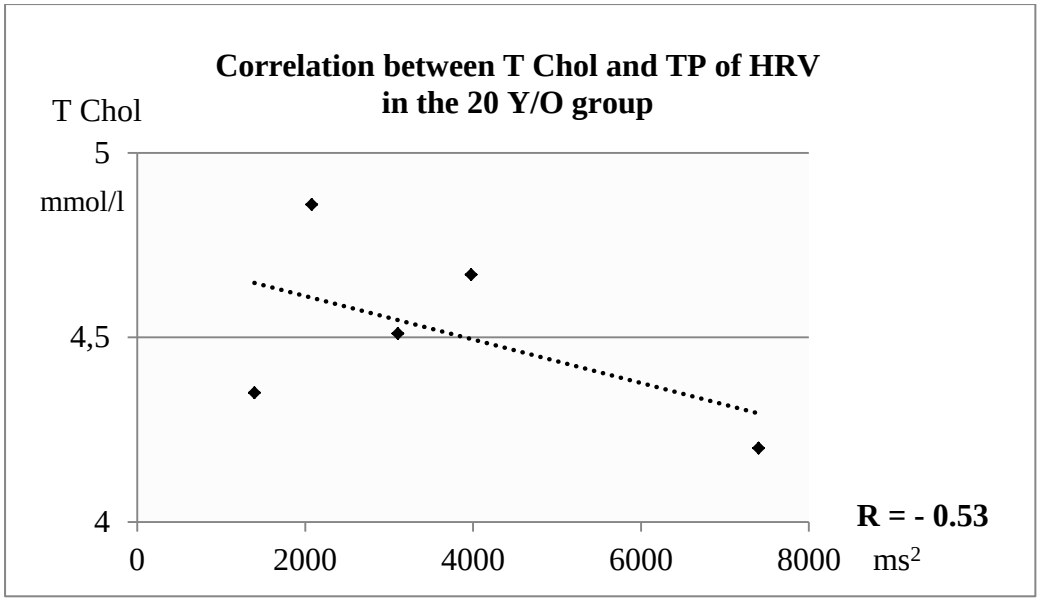

Fig. 3. Negative correlation between total cholesterol and total power of HRV in the 20Y/O group. T Chol - Total cholesterol; TP- Total power. R = - 0.53.

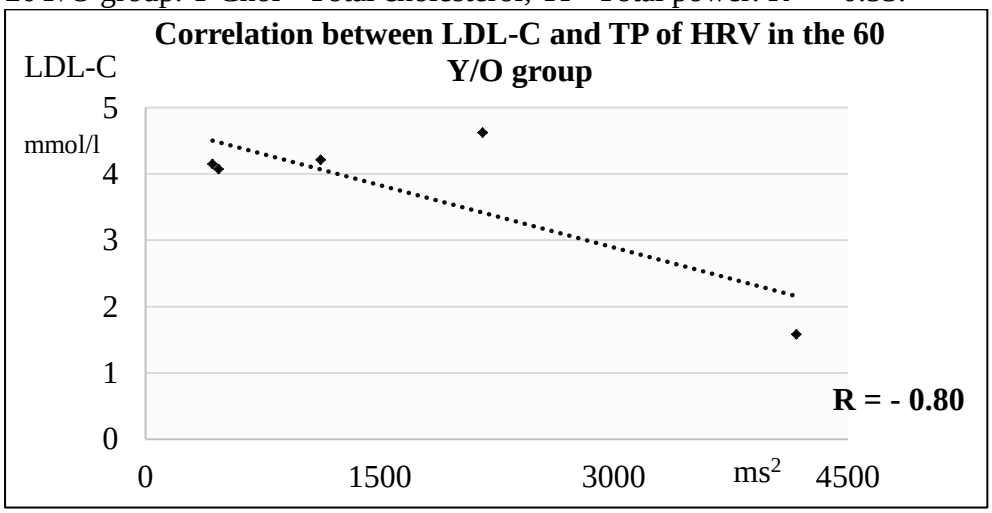

Fig. 4. Negative correlation between LDL-C and total power of HRV in the 60Y/O group. T Chol - Total cholesterol; TP - Total power. R = - 0.80.

Similar were the data for relationship between LDL-C levels and the TP of HRV. (Figs. 4 and 5) The correlation was negative; yet, the regression analysis showed R = - 0.53 for the 60Y/O group as compared to R = - 0.25 for the younger females. Regression analysis evidenced highly positive correlation between HDL-C level and TP of HRV (Fig. 6, R = 0.77). The correlation between HDL-C and TP of HRV was negative (Fig. 6, R = - 0.76).

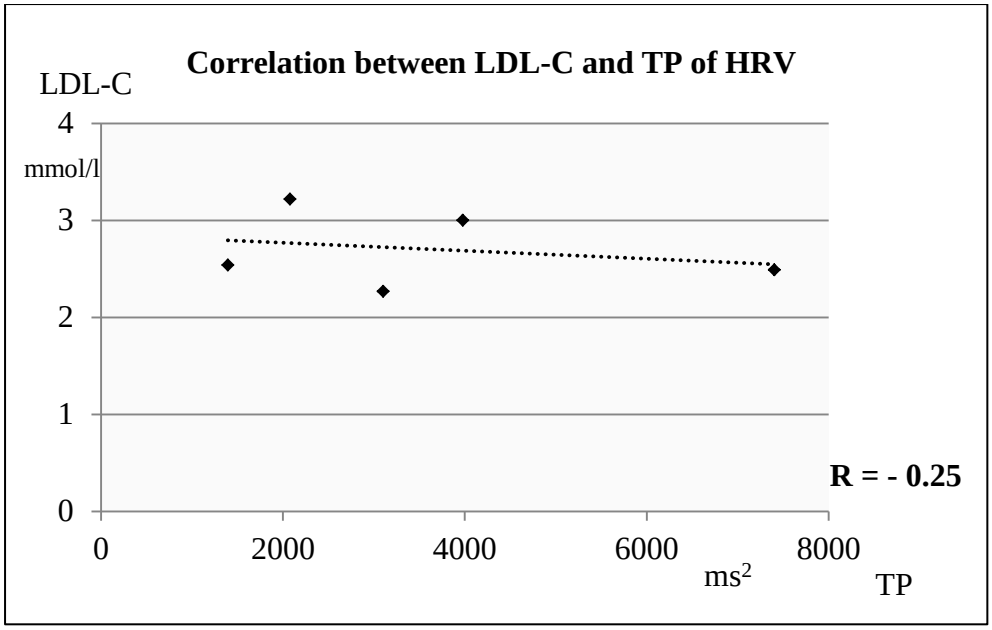

Fig. 5. Negative correlation between LDL-C and total power of HRV in the 20Y/O group. LDL-C – Low density lipoprotein cholesterol; TP Total power. R = - 0.25.

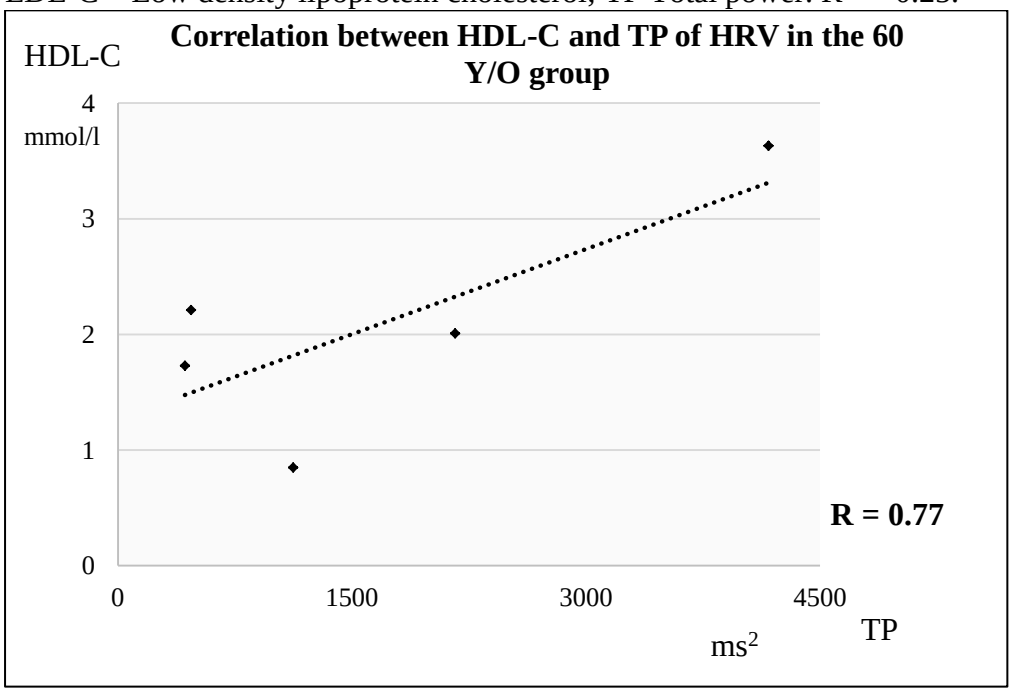

Fig. 6. Positive correlation between HDL-C and total power of HRV in the 60Y/O group. HDL-C - High density lipoprotein cholesterol; TP Total power. R = 0.77.

Regression analysis evidenced exclusively high negative correlation between blood glucose level and TP of HRV in the 60Y/O group – R = - 0.99. Negative correlation between these parameters was observed in the 20Y/O individuals as well. Yet, it was less pronounced – R = - 0.50.

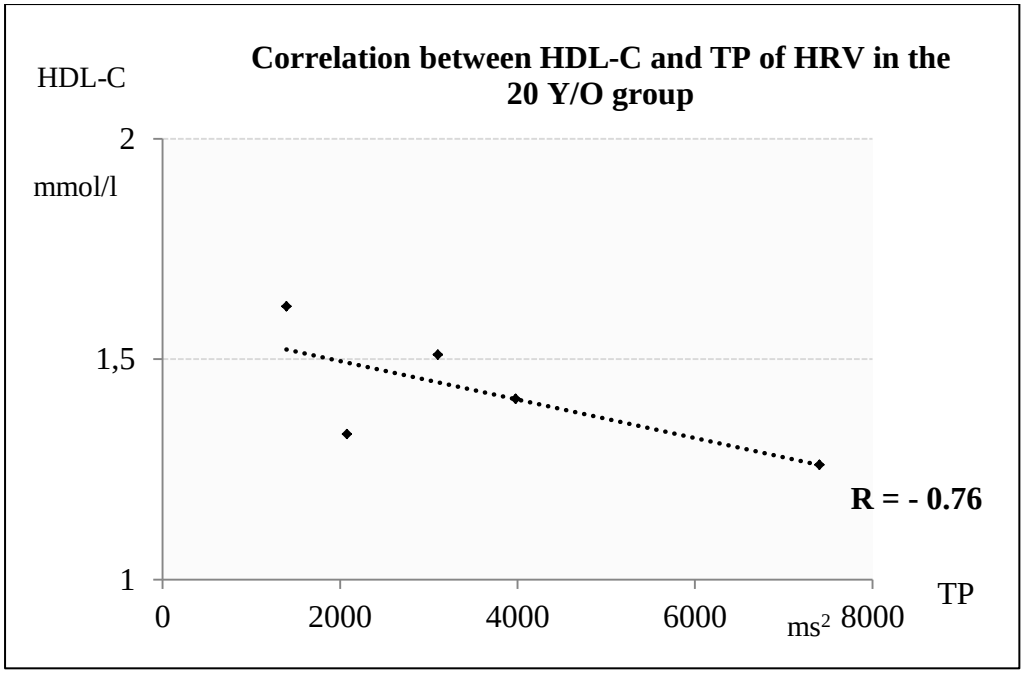

Fig. 7. Negative correlation between HDL-C and total power of HRV in the 20Y/O group. HDL-C - High density lipoprotein cholesterol; TP Total power. R = - 0.76.

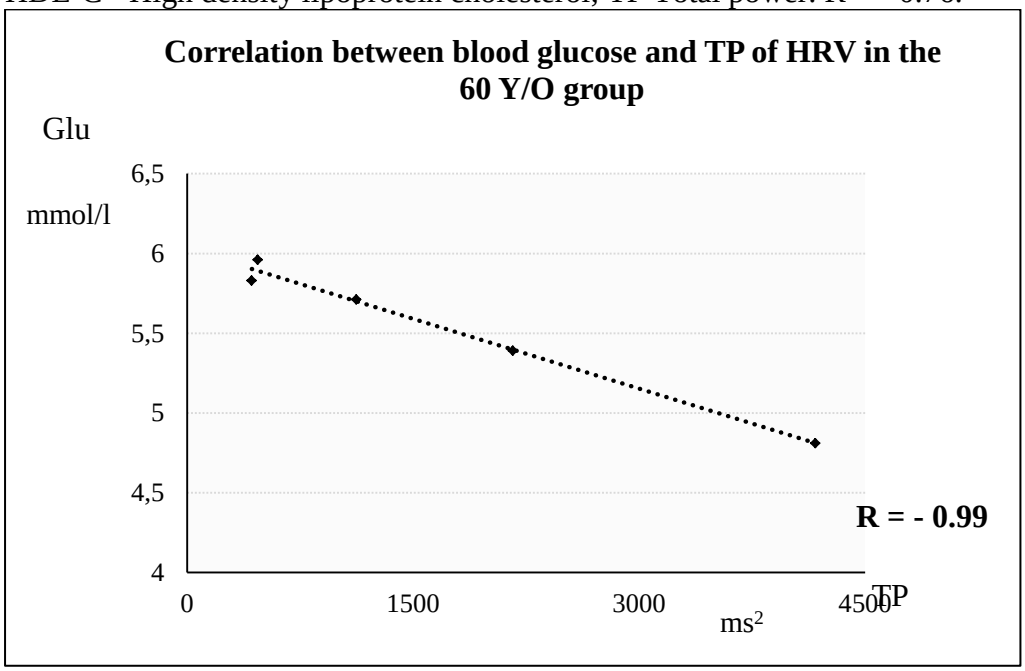

Fig. 8. Negative correlation between blood glucose and total power of HRV in the 60Y/O group. Glu - Glucose; TP Total power. R = - 0.99.

The correlation between TG and TP of HRV was weaker. R was – 0.38 for the 60Y/O group. For the 20Y/O group the correlation was positive and R = 0.30.

Discussion.

Heart rate variability is a widely accepted non-invasive parameter used for assessment of the autonomic influences on the cardiovascular system [3, 21]. The TP of HRV in our study was more than twice lower in the group of postmenopausal women as

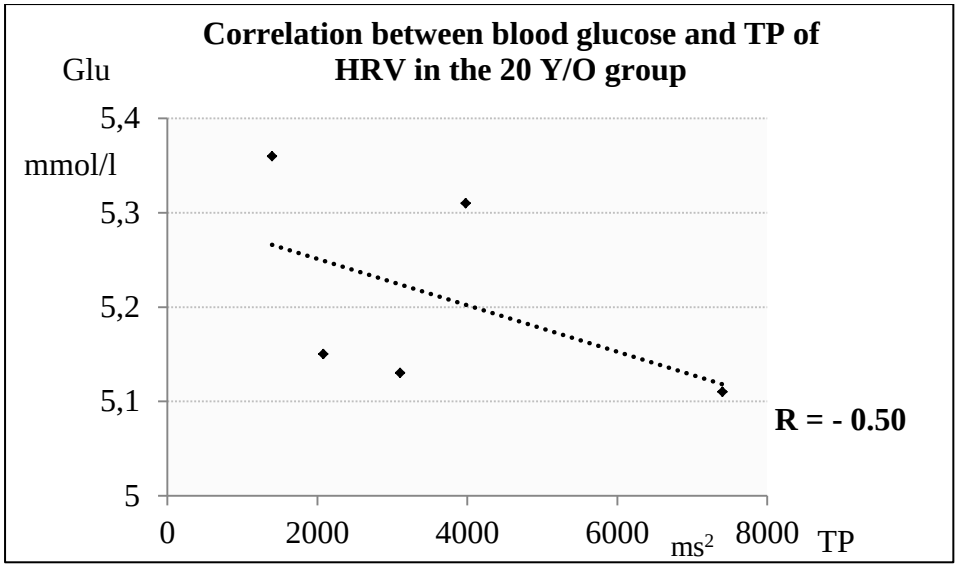

Fig. 9. Negative correlation between blood glucose and total power of HRV in the 20Y/O group. Glu - Glucose; TP Total power. R = - 0.50.

compared to the 20Y/O group. It is generally believed that the alterations of HRV with aging result from altered autonomic function with growing predominance of the sympathetic nervous system [4]. We presume the lack of statistical significance between our HRV values is due to the well-known large interindividual variance typical for HRV and the relatively small number of examined persons [16]. Our findings are supported by numerous studies showing the gradual reduction of HRV with aging independent of pathological conditions or medication [1, 2, 10]. In addition, the lower HRV was linked to elevated risk of coronary arterial disease, CVD and poor prognosis in case of myocardial infarction [3, 17, 21].

We find of interest the significant negative correlation between the markers of dyslipidemia total cholesterol and LDL-C and HRV in the postmenopausal women; similar is the relationship with plasma glucose (showing the highest R = - 0.99). On the other hand, the correlation with the so-called 'good' cholesterol (HDL-C) is positive. In the young individuals these correlations are less pronounced.

Our interpretation of the differences between the two experimental groups is based on the estrogen deficiency in the postmenopausal women. We believe our data show a strong link between the higher sympathetic efferent activity and the level of the unfavourable markers of cardiovascular risk (total cholesterol, LDL-C, glucose) in the 60Y/O group where the estrogen protection is lacking. These data definitely demonstrate that the higher is sympathetic efferent activity (lower TP of HRV) the higher are the levels of the metabolic risk markers.

In the 20Y/O group both the sympathetic activity and the metabolic cardiovascular risk markers are lower. The correlation between them is less manifested. We may speculate that in the young females the protective role of estrogens blunts the negative sympathetic impact on metabolism.

We believe our results are a further evidence for the diverse estrogen defence: direct and indirect protective effects on lipid and carbohydrate metabolism as well as on vascular health through stimulation of endothelial vasodilatory mechanisms (primarily nitric oxide) and through interaction with the impairing sympathetic influences [15, 19].

In conclusion, primary prevention of cardiovascular diseases in females of postmenopausal age should be directed towards reduction of the metabolic disorders based on proper diet, modified lifestyle with adequate physical activity and management of stress.

The evaluation of cardiovascular risk should be grounded on the assessment of sympathetic cardiovascular influences as well.

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