

# Endothelial Function and Heart Rate Variability Parameters before and after Body Correction Program

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## ABSTRACT

**Background:** Obesity as a chronic polygenic condition has been a public health challenge for many years. Many scientific studies have focused on the study of the effects of excess weight on the state of the cardiovascular system (CVS). However, the effect of body composition on CVS, in particular on vascular endothelial function (EF) and heart rate variability (HRV), has not yet been clearly established.

**Methods:** Women aged 25 to 60 years went under investigation of body composition parameters identified with Tanita BC-601 analyzers. Study of endothelial function was performed using rheograph "ReoCom". HRV was studied using electrocardiograph "CardioLab".

**Results:** There was a statistically significant difference between EF parameters before and after the body composition correction program in both models. However, the statistically significant effect of body composition parameters on the EF index was only found in the first model. In addition, the first model showed noticeable influence of the parasympathetic system on the EF and significant changes in these indicators after the correction program.

**Conclusion:** Using only the BMI to examine the effect of overweight on endothelial function, it is possible to miss the significant impact of visceral fat on the state of the endothelium. Also, it is possible to overlook the effect of correcting body composition on HRV and EF. Women should be recommended to correct body composition in order to prevent risk of low parasympathetic activity resulting in CVD. Correction also serves as a therapeutic purpose in early stage correction of endothelial dysfunction linked to CVD.

**Keywords:** Fat content, heart rate variability, endothelial dysfunction, obesity, BMI.

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## INTRODUCTION

It is known that dosed exercise has a positive effect on heart function and rehabilitation after CVD. [1-3] Heart rate variability can be determined as complex fluctuations of human heartbeat dynamics and helps to assess the activity of the autonomic nervous system (ANS). HRV research leads to the best approach in understanding the development and prognosis of CVD. For practitioners, the assessment of ANS is of high interest, as there is a known correlation between the risk of sudden death and low parasympathetic activity. [4,5] Studies indicate an improvement in cardiorespiratory function in sports when participants are guided individually by daily heart rate variability measurements and the possible use of HRV measurements to assess the impact of exercise. [6,7] Another risk factor for CVD is endothelial dysfunction. The endothelium is a multifunctional organ that secretes vasoactive substances involved in inflammation of the walls of blood vessels, cellular adhesion and thromboresistance, thereby maintaining homeostasis. The functional state of the endothelium represents endothelium-dependent vasodilation. Violation of this function is manifested by an imbalance between the bioavailability of nitric oxide (NO) and endothelium-derived contracting factors and leads to endothelial dysfunction. [8,9] Every year, scientists and doctors try to find ways to correct the condition of the endothelium, as it is known that its dysfunction is associated with diseases such as hypercholesterolemia,

hypertension, vasculitis, atherosclerosis, metabolic syndrome, preeclampsia, diabetes, family history CAD, obesity, renal failure, congestive heart failure, and left ventricular hypertrophy. [10] However, neither endothelial function (EF) nor HRV studies have been widely used in clinical practice. This may be due to lack of data and limited preventive use of HRV and EF corrections. One of the possible ways to improve the state of the endothelium and the state of the ANS is to correct the parameters of body composition.

The objective of the study is to investigate the effect of body composition and parameters of HRV on endothelial function.

## MATERIALS AND METHODS

The study involved 60 healthy women aged 25 to 60 years. The study of parameters of body composition was performed using Tanita BC-601 analyzer scales (Japan). We obtained the following parameters: Fat free mass (FFM [%]), Total Fat (F [%]), Visceral fat (VF [kg]), Trunk fat (TF [%]) and Body mass index (BMI).

The heart rate variability is analyzed by constructing time series and subsequent mathematical analysis of the intervals between R-R waves on the electrocardiogram (ECG) using electrocardiograph CardioLab (KhAI-Medica). ECG recording was done for 10 minutes in the horizontal position. The blood pressure was measured and recorded before and after examination. We obtained the following data:

**Time methods:** HR (beats/minute) – heart rate; MRR – the average value of cardiointervals; SDNN (ms) – standard deviation of N - N intervals (normal intervals); RMSSD (ms) – square root of the sum of the squares of the difference between the values of successive pairs of N - N interval; pNN50 (%) – the percentage of NN50 in consecutive pairs of intervals differing by more than 50 milliseconds; CV – coefficient of variation

**Spectral methods:** TP (ms<sup>2</sup>) – total power of the spectrum; VLF (ms<sup>2</sup>) – very low frequencies in the range less than 0.04 Hz; LF (ms<sup>2</sup>) – low frequencies in the range of 0.040.15 Hz; HF (ms<sup>2</sup>) – high frequencies in the range of 0.150.4 Hz; LF / HF is the ratio of LF to HF.

The endothelial function was performed using non-invasive method of reactive hyperemia on the REOCOM complex (KhAI-Medica). The electrodes of the RVG-1 remote block were placed on the right and left arms at specific distances from each other. A cuff was applied to the left arm to inflate the pressure. Recording was performed on both arms for 2.5 minutes before occlusion, 5 minutes during occlusion (created by injecting cuff pressure up to 50 mm Hg above the previously measured systolic pressure), and 2.5 minutes after occlusion. Thus, we obtained a test of reactive hyperemia in the brachial artery and avoided the influence of central regulation of vascular tone on endothelial function<sup>11</sup>.

Women did not use any medications or stimulants (e.g., coffee) on the day of examination before the procedure.

After receiving the results, we asked these women to undergo a body composition correction program to find out how the EF, HRV, visceral and total fat content in the groups would change. Of the 60 women, 20 did not agree to participate and another 10 did not meet the exclusion criteria (acute and chronic diseases, menopause, lactation or pregnancy). All of the remaining 30 women reviewed the program and agreed to further research, but another 4 women were excluded from the study because they did not follow the instructions. The program included dietary adjustments according to WHO recommendations (sufficient consumption of fresh fruits and vegetables; restriction of salt, high-calorie foods, sweeteners, alcohol; inclusion of whole grains; sufficient amount of water). All women were advised to take a minimum of 6,000 steps per day, increasing the number each day if possible. The subjects also practiced individually in the gym under supervision of a coach, using both aerobic and anaerobic exercises. The Helsinki Declaration of the World Medical Association "Ethical Principles of Human-Based Medical Research as an Object of Research" was followed during the examinations. We examined the parameters of body composition, EF and heart rate variability again after 45 days.

All types of analysis were processed using the statistical program STATISTICA 10.0 (StatSoftInc, USA).

## RESULTS

In formulating the hypothesis, we chose two models for statistical analysis. The first model included Puo (parameter of endothelial function) and parameters of body composition: FFM, F, VF and TF. Another model included BMI, Puo, FFM, F, VF, and TF. Accordingly, women were divided into groups depending on the total fat content expressed as a percentage and measured by the bioimpedance method (in the first model), and relative to the body mass index (in the second model): N, n – normal weight; OW, ow – overweight; O, o – obesity. These models were statistically unreliable. Based on the data about influence of body composition on the state of the endothelium we decided to remove the FFM from both models, since existing studies mostly focus on the effects of obesity and the substances secreted by adipose tissue, which are associated with increased circulating lipids, hyperglycemia, oxidative stress, inadequate vasodilation or paradoxical vasoconstriction. [12,13] In this formulation (influence of fat content on EF) we used multifactor regression analysis. The first model (Puo, F, VF, TF) had statistically significant importance (F(3.48) =3.38; p<0.03). Moreover, the endothelial function (EF) was statistically significantly influenced by the content of visceral fat, which had a negative correlation to Puo. (When increasing the content of visceral fat per unit, the endothelial function will increase by

b= -0.94 (p<0,03). The model with BMI (Puo, BMI, F, VF, TF) had no statistical significance (F [3.48] =2.45; p<0.07). Based on the data obtained, we can assume that by measuring only the body mass index, it is possible to omit the implicit effect of body fat on the endothelium, and underestimate the effect of internal fat on the state of the CVS.

To determine whether the EF changed after a 45-day body composition correction program, we used repeated measures analysis. In the model with group division by percentage of fat using the bioimpedance method, the Puo index changed statistically significantly after the end of the program (F=16.37; p<0.00) (Graph 1).

In the model with the distribution of fat according to BMI, the EF index differed between groups in fat content (F=4.21, p<0.03), and then statistically significantly differed after the correction program (F=12.75, p<0,00) (Graph 1).

Puo parameter in both models was the lowest in the obesity groups and only in these groups were there indicators of endothelial dysfunction (<9). The mean value of EF in the obesity group in the BMI model was 7.04 ± 1.94 before, and 16.54±1.33 after correction of body composition. In the first model the EF in obesity group before the start of the program was 7.82±1.83, and 17.16±1.26 after. The mean values are given in table №1.

Based on a previous regression analysis, we determined whether the visceral fat rate changed after the 45 days of the program. Visceral fat had a statistically significant difference between groups in fat content % (F= 9,13, p<0,00) and as a result of

correction of body composition ( $F=18,45$   $p<0,00$ ), and also between-groups and within-groups difference in total ( $F=3,51$ ,  $p<0,05$ ). Graph №3

Looking retrospectively at – available research in the scientific community, we were interested in whether heart rate variability affects the EF and whether this data will change after the body composition correction program. Studies indicate that MSSD and RMSSD provide an index of parasympathetic reactivation after exercise. [14] However, other data suggest an insufficient correlation of variability indicators, namely indicators of parasympathetic activity and vagal effects on heart rate. [15]

We applied multiple regression analyses for the following indicators: time methods – HR, MRR, SDNN, RMSSD, pNN50, CV; spectral methods – HF, LF, VLF, TP, LF / HF, as in the vastness of scientific works there are many studies about the impact of the functional state of the heart on EF. For example, Pooja Bhati et al [16] reported a pathophysiological link between endothelial dysfunction and cardiac autonomic dysfunction. Another study reported a higher risk of CVD in women with endothelial dysfunction and sympathetic activation, regardless of the presence or absence of obesity and metabolic syndrome. [17]

HR, MRR, RMSSD and pNN50 had a statistically significant effect on EF. ( $F(11,34)=2.51$ ,  $p<0.02$ ) (Table №2)

RMSSD as well as pNN50 characterize the effect of autonomic regulation of the heart. HF – high-frequency interval of HRV is responsible for vagal control. Therefore, we can say that the EF is affected by the state of the parasympathetic nervous system. In addition, heart rate and mean values of cardiointervals were negatively correlated with Puo. The parasympathetic part of ANS has a trophotropic effect on the heart, reduces heart rate and heart contractility and restores homeostasis. [18]

The mean values in the group before correction of body composition were: HR ( $70,39 \pm 8,97$ ); MRR ( $866,57 \pm 107,91$ ); RMSSD ( $35,61 \pm 21,67$ ); pNN50 ( $13,09 \pm 14,34$ ). After a 45-day program, these indicators were: HR ( $65,87 \pm 6,38$ ); MRR ( $918,87 \pm 89,78$ ); RMSSD ( $44,57 \pm 21,21$ ); pNN50 ( $22,35 \pm 18,32$ ). (Graph №4)

To identify the presence or absence of a significant difference between HRV parameters that affect the EF,

we conducted repeated measures analyses in two models. In the model with grouping by percentage of fat content, the following indicators statistically significantly differed: RMSDD differed between groups arranged by fat content ( $F=4,74$ ;  $p<0,02$ ), but had no within-group difference ( $F=3,75$ ;  $p<0,07$ ); pNN50 differed both between fat groups ( $F=5,01$ ;  $p<0,02$ ) and before and after the correction program ( $F=5,86$ ;  $p<0,03$ ); HR was statistically significantly different after the 45 day program ( $F=6,8$ ;  $p<0,02$ ). In the model where women were grouped by fat content according to BMI, no indicator had a statistically significant difference.

Table 1:

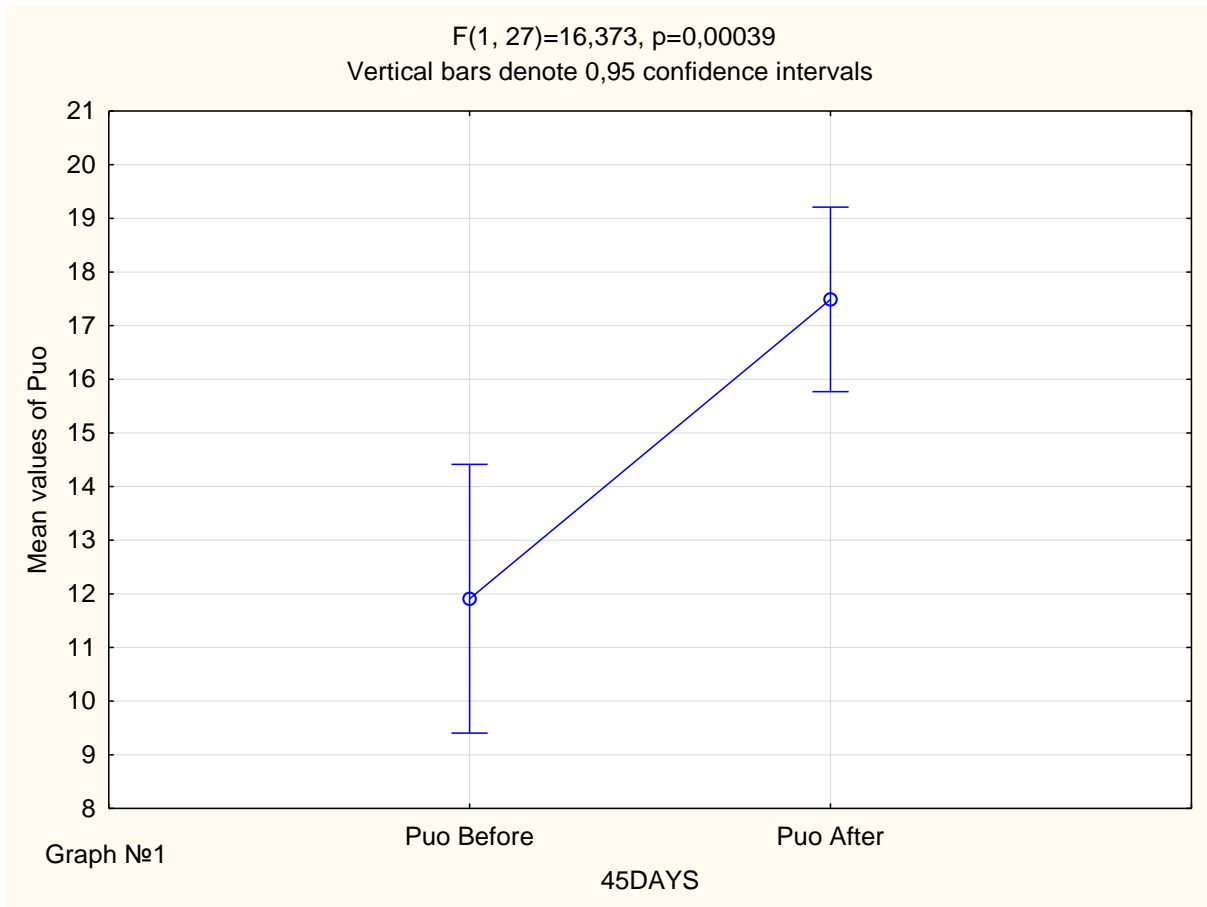
Cell No	Mean values of Puo in BMI groups			
	BMI Group	45 days	Mean	Std. Err
1	n	Puo Before	14,30000	4,348570
2	n	Puo After	22,80000	2,983957
3	ow	Puo Before	14,52000	1,643605
4	ow	Puo After	17,10000	1,127830
5	o	Puo Before	7,04400	1,944739
6	o	Puo After	16,54000	1,334466
Mean values of Puo in BMI groups				
	Fat Group	45 days	Mean	Std. Err
1	n	Puo Before	14,66333	2,590806
2	n	Puo After	16,81667	1,777998
3	ow	Puo Before	13,24167	1,831976
4	ow	Puo After	18,49167	1,257234
5	o	Puo Before	7,82167	1,831976
6	o	Puo After	17,15833	1,257234

Table 2: The influence of HRV parameters on Puo.  $R=0,66922125$ ;  $R^2= 0,44785708$ ;  $Ra^2=0,26922261$ ;  $F(11,34)=2,5071$ ;  $p<0,01973$

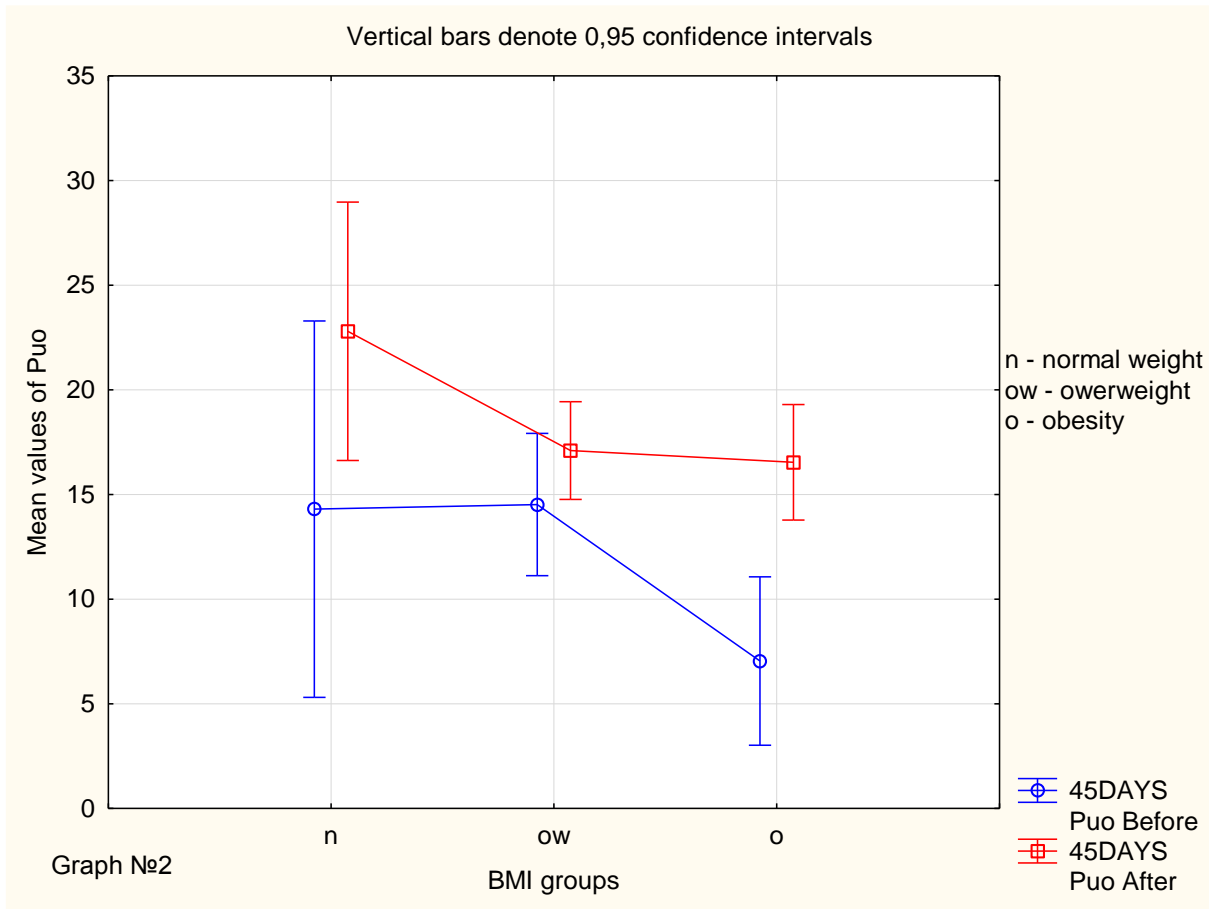
	b	Std.Err.-of b	p-value
LF/HF	-0,6872	1,0516	0,517843
HR	-2,3702	0,8562	0,009057
MRR	-0,1564	0,0673	0,026247
SDNN	-0,2244	0,4331	0,607678
RMSSD	-0,5806	0,2579	0,030959
pNN50	0,7767	0,2694	0,006788
CV	1,0890	2,9596	0,715189
TP	0,0034	0,0104	0,748686
VLF	-0,0011	0,0115	0,926023
LF	-0,0001	0,0096	0,995448
HF	-0,0077	0,0113	0,500901

$R^2$  – coefficient of determination;  $Ra^2$  – adjusted coefficient of determination ; F – Fisher test; p – the significance level.

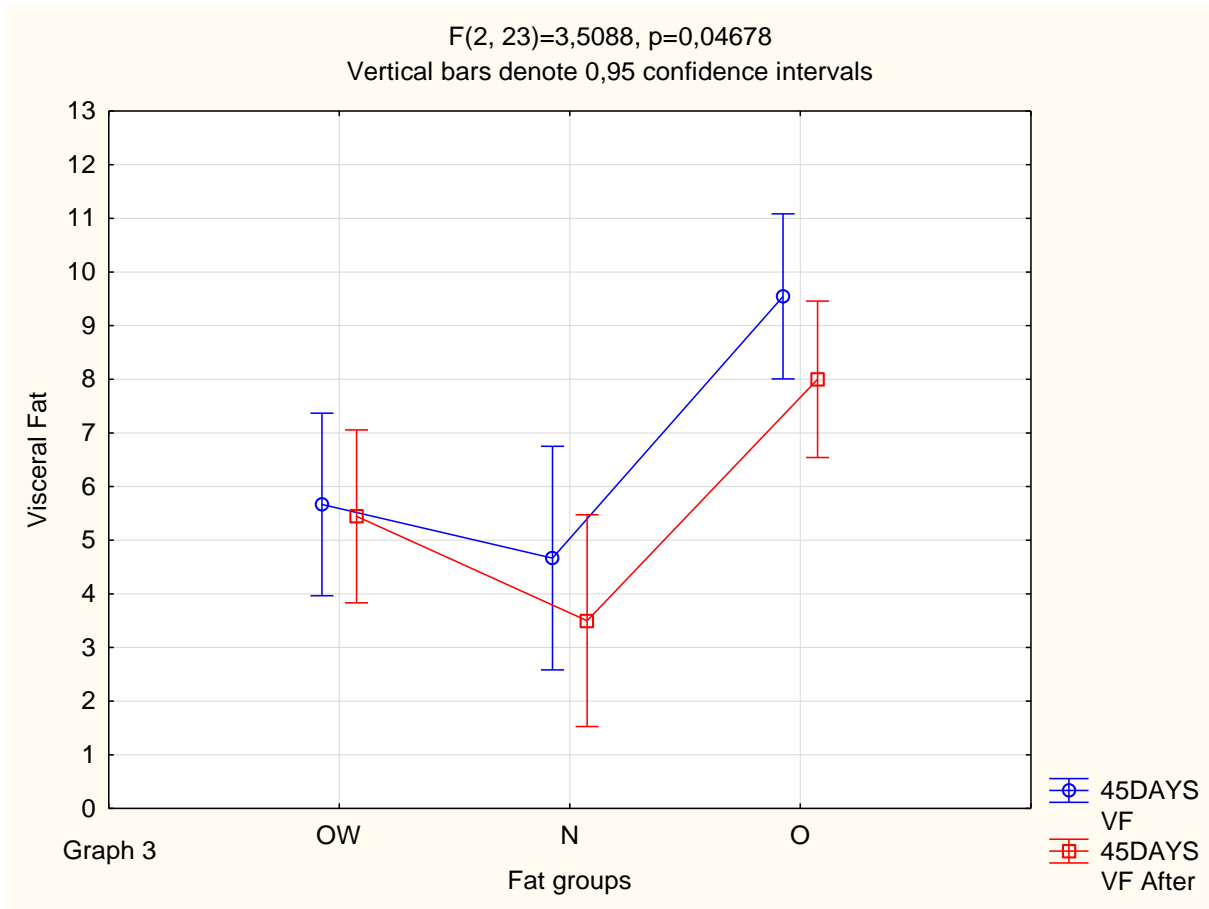
Graph 1: Values of endothelial function (Puo) before and after the completion of a 45-day body composition correction program



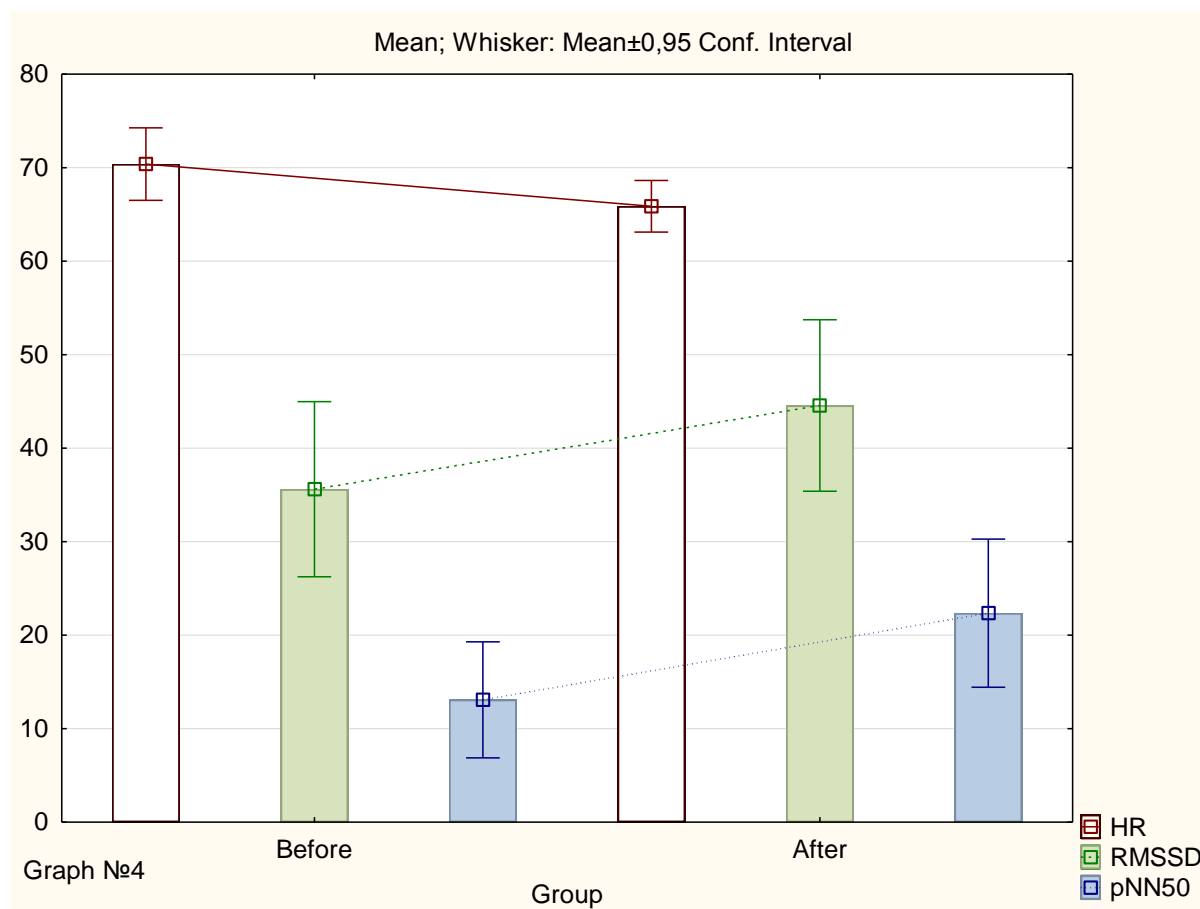
Graph 2: Values of endothelial function (Puo) before and after the completion of a 45-day body composition correction program in the BMI groups



Graph 3: Values of visceral fat (VF) before and after the completion of a 45-day body composition correction program in groups divided by fat content



Graph 4: Values of HRV in groups before and after 45 day correction program



## DISCUSSION

In an effort to avoid the so-called "obesity paradox", which is characterized by better prognostic data in people with CVD and overweight, we have created two models for statistical analysis. We tried to count the effect of body composition parameters in the models according to both BMI and fat and muscle content using bioimpedance method. Endothelial dysfunction is one of the first risk factors for CVD. For example, development of atherosclerosis is influenced by the condition of the endothelium and risk of its development increases with increasing fat content in the body<sup>19</sup>. As found in our study, visceral fat, which cannot be calculated using BMI alone, had a statistically significant effect on EF. In addition, we were interested not so much in BMI calculated from total weight as in the effect of body composition and its correction on EF. Given the data on impact of HRV on heart function and the risk of CVD, we decided to study the interaction between HRV and EF. Our results showed a possible effect of the parasympathetic system on EF. Interestingly, HRV values changed statistically significantly after the 45-day program only in the first model. Endothelial dysfunction was present only in the obesity groups and returned to normal after the program.

## CONCLUSION

To study the fat content and its effect on the state of body health, using both BMI and bioimpedance method rather than BMI alone may provide better statistical results. Correction of body composition parameters in women can lead to improved parasympathetic activity of ANS, which in turn leads to improved EF. In addition, a decrease in visceral fat content statistically significantly leads to increase in P<sub>uo</sub>. Regardless of which fat group women are in, preventing development of cardiovascular disease may require improving parasympathetic activity by switching to a healthy diet, regular exercises and daily dosed walking. In addition, to improve endothelial function resulting in prevention of CVD, women with obesity are recommended to correct their body composition (particularly decreasing visceral fat content).

**Conflict of interest:** The authors state that there are no conflicts of interest regarding the publication of this article. None declared.

**Declaration:** The manuscript has been read and approved by all the authors each author believes that the manuscript represents honest work.

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