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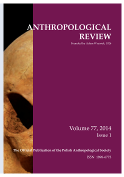

Body composition of Slovak midlife women with cardiovascular complications

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ABSTRACT: The aim of this study was to analyse differences in body composition of women with and without cardiovascular complications. Bioelectrical parameters were measured with bioimpedance monofrequency analyser (BIA 101) and tissue electric properties were analysed by bioelectric impedance vector analysis (BIVA). The clinical sample (with CVD) consisted of 254 women ranging in age between 39 and 65 years. The sample of women without CVD consisted of 318 women in the same age range and was created from database of our previous studies. Statistical analysis adjusted for age showed significant differences in body composition characteristics of the studied samples. The results of vector analysis showed significantly different tissue electric properties of women in studied groups, what was confirmed by the Hotelling T^2-test (p=0.0000). More women with CVD attained risky mean values of obesity indices of BMI and WHR than their "healthy" counterparts. Among women with CVD 80.2% had higher value of the BMI index than optimal one (>24.9 kg/m^2) and 74.4% of women had higher value of the WHR index than optimal (>0.80). From the BIA parameters strong correlation coefficient was found between BMI and FM in both groups (r=0.962 for women with CVD; r=0.968 for relatively healthy women). Our data confirmed that cardiovascular disease complications are strongly linked in body composition changes. The cross-sectional nature of our study makes it difficult to draw conclusions regarding causal pathways, though variables of obesity are in line with unhealthy conditions.

KEY WORDS: Bioelectrical impedance analysis, body fat mass, obesity indices, BIVA

Introduction

The global burden of cardiovascular diseases (CVD) is rapidly increasing around the world. Among women, cardiovascular disease risk increases particularly after menopause which may be related to metabolic and hormonal changes (Zárate et al. 2007). Especially, in women who have undergone natural or surgical menopause oestrogen deficiency was linked to rapid increase in CVD (Giardina 2000). The menopause compounds many traditional CVD risk factors, including changes in body fat distribution from a gynoid to an android pattern, reduced glucose tolerance, abnormal plasma lipids, increased blood pressure, increased sympathetic tone, endothelial dysfunction and vascular inflammation (Rosano et al. 2007).

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Body composition data can provide the basis for a wide variety of therapeutic, health and fitness programs (Amir and Rakhshanda 2009). In epidemiological studies, surrogate measures of body fatness such as body mass index (BMI), waist circumference and waist-hip ratio (WHR) have been used extensively. However, these techniques do not precisely characterize persons by body composition (percentage of body fat or muscle mass), and there is substantial variation across age, sex and ethnic groups (Womersley 1977; Wang et al. 2000; Dagenais et al. 2005). One of the methods that command more accurate information in estimation of CVD risk in comparison with BMI is bioelectrical impedance analysis (BIA). It is a practical method that is widely available, relatively simple, quick (takes only a few minutes), user friendly and foremost is a non-invasive technique which gives reliable measurements of body composition with minimal intra-and inter-observer variability. The results are available immediately and reproducible with <1% error on repeated measurements (Diaz et al. 1989; Guo et al. 1999; Dehghan and Merchant 2008).

Bioimpedance is a complex quantity composed of resistance (R, Ohm) which is related to quantity of fluids and reactance (X_C, Ohm) which has relation to capacitance of the cell membrane (Kyle et al. 2004). Several number of BIA parameters (PA, phase angle; FM, fat mass; FFM, fat free mass; MM, muscle mass; BCM, body cell mass; TBW, total body water; ECW, extra cellular water; ICW, intra cellular water; BMR, basal metabolic rate; Na/K, exchange Na/K) can be estimated by using the Bodygram program, Version 1.3 (Akern, S.r.l). From the above mentioned, phase angle (PA) has been suggested to be an indicator of cellular health, where higher values reflect higher cellularity, cell membrane integrity and better cell function (Mattar 1996). In healthy subjects PA usually ranges between values 5 and 7; low PA values suggest cell death or decreased cell integrity, whereas higher PA values suggest a large amount of intact cell membranes (Selberg and Selberg 2002). Observation of body compartment fluctuations like fat mass (FM), fat free mass (FFM) and total body water (TBW) from normal limits are considered as key factors to be used in bioimpedance analysis in healthcare applications. In healthy subjects the value of FM ranges between 20 and 30%; higher values of FM are associated with obesity. The amount of FFM reflects health, fitness and good shape since this compartment, in addition to the internal organs, is constituted mainly by muscles. The human body with regular values of muscle and fat mass content has 73–75% (for women) to 80% (for men) of lean tissues, depending on age and sex (Talluri 1998; Guo et al. 1999; Kyle et al. 2004). The body cell mass (BCM), which represents the metabolically active component of FFM, is the single best predictor of a subject's nutritional status. The standard range of BCM is set at 40% of the healthy body weight. The loss of BCM is often associated with higher disease activity (Kehayias et al. 1997; Wiliams et al. 2003). The human body is formed by at least two thirds of water and a normal hydration state is of paramount importance for the maximum normal content of body water ranges between 60 and 70% of body weight. The average amount of extracellular water (ECW) is about 45%, and it defines also the normal proportion between intra and extracellular spaces. When ECW is expanded (i.e. ECW >45%) the expansion can be attributed to overhydration or malnutrition or both (Talluri 1998; Khalil, Mohktar and Ibrahim 2014).

The BIA can be further enhanced by combining it with bioelectrical impedance vector analysis (BIVA) that offers clinical benefits (Barbosa-Silva and Baross 2005). BIVA approach developed by Piccoli et al. (1994) uses the plot of the impedance parameters resistance (R) and reactance (Xc) normalized per height as a bivariate vector in the RXc graph. The position and length of the vector provides information about hydration status, body cell mass and cell integrity (Norman et al. 2012). This method has been shown to be effective to identify patients with a critical fluid overload (Nescolarde et al. 2004). Toso et al. (2000) using both the BIA and BIVA methods detected that reactance components decrease in pulmonary disease patients. Atilano et al. (2012) in their study investigated the suitability of BIVA for the assessment of renal system diseases and detected differences in post dialysed patients. Buffa et al. (2010) in their study identified low body cell mass and dehydration in patients with Alzheimer's disease. Haas et al. (2012) discovered that the body cell mass significantly changed between patients with anorexia nervosa and control subjects. In Slovakia, Siváková et al. (2013) analysed differences between patients with Parkinson disease and control subjects using BIA and BIVA methods.

Because no data are available about the bioimpedance components in patients with cardiovascular disease (CVD), including those from Slovakia, the purpose of this study was to examine differences in body composition characteristics between women creating a "clinical" sample and relative healthy Slovak women of the same age. In addition, we determined correlation between indicators of obesity like BMI and WHR and waist circumference and selected BIA parameters in both samples of Slovak midlife women.

Materials and methods

The investigated clinical sample (women with CVD) consisted of 254 women ranging in age between 39 and 65 years. These women suffered at least from one of the following diseases like hypertension, ischemic heart disease, diabetes mellitus, atherosclerosis or high blood cholesterol. They were mostly married (69.7%), and the place of birth in towns (51.9%) prevailed. Additional baseline description of the study sample is presented in Table 1. The compared sample (women without CVD) consisted of 318 women in the same age range was created from database of our previous studies carried in different localities in Slovakia.

Table 1. Distribution of baseline characteristics of women suffering from cardiovascular disease (with CVD).

Variable		n	%
Menopausal status	Premenopause	75	29.5
n = 254	Perimenopause	19	7.5
	Postmenopause	160	63.0
Physical exercises	No	54	21.3
n = 254	Occasionally	172	67.7
	Regularly	28	11.0
Smoking	No	178	70.0
n = 254	Occasionally	38	15.0
	Regularly	38	15.0
Education	Primary	51	20.1
n = 254	Secondary	161	63.4
	Academic	42	16.5

Those women at the time of investigation did not use any hormone therapy; they had not experienced gynaecological surgery or other serious illness (based on the questionnaire), they did not suffer from hypertension and have not high level of serum cholesterol. Among them there were 186 (58.5%) women in premenopause, 22 (6.9%) in perimenopause and 110 (34.6%) women in postmenopause. The both samples were recruited via cooperation with local medical doctors. The women were interviewed during their routine medical check-ups and investigated with respect to their health, anthropometrical, biochemical and lifestyle aspects. However, for the purpose of this study only anthropometry and body composition parameters were analysed. All women considered for this study have signed "Informed Consent".

Anthropometric measurements were taken using standard anthropometric technique by trained anthropologists. Body mass index (BMI) was calculated as body weight divided by height squared and values below 24.9 kg/m^2 were considered as optimal. Waist-to-hip ratio (WHR) was calculated as the circumference of the waist divided by the circumference of the hips. Values of WHR below 0.80 were considered as optimal. Body cell mass index (BCMI) was calculated as BCM (body cell mass) divided by height squared (kg/m^2) and values above 8.0 were considered as optimal.

Body composition measurements were carried out in the morning. The Body composition was obtained using a bioelectric impedance analyzer (BIA 101, Akern S.r.l.) at a signal frequency of 50 kHz, with constant excitation current at 800 μA and four-electrode arrangement. Individual variables of body composition were obtained by the software Bodygram programme (Version 1.21, Akern S.r.l). Reference values were used for the age and sex specific group given by the programme (Talluri 1998).

The bioelectric impedance vector analysis (BIVA method) was used to allow graphic comparison of variability in the corresponding groups. This method uses a sex- and age-specific diagram (RXc graphs) with three tolerance ellipses 50%, 75%, and 95% which are also known in literature as prediction ellipses of a reference population projected in a Cartesian plane defined by the value of R/H (Ohm/m) and Xc/H (Ohm/m). The specific resistivity and reactivity plotted on a nomogram showing the normal or abnormal states of hydration and nutrition. This overlay combined with the patients measured vector shows how the patients hydration level (and nutrition level) compares with those of normal subjects of the same sex and height. Heterogeneity of the files in BIVA diagram was tested by Hotelling T^2-test (Piccoli et al. 2002).

Data analysis

All analyses were carried out using the statistical program SPSS for Windows (Version 19.0, Chicago, IL). Kolmogorov–Smirnov test was used for checking for the normality of data distribution. A simple comparison of the data between the subgroups was analyzed using the Mann-Whitney U-test, used for data with non-normal distribution. General linear model (GLM) was used for comparison of arithmetic means with age as the covariate. To assess correlation between the variables the Pearson's chi-square test was used in case of normally distributed variable and Spearman non-parametric test for data with non-normal distribution. Binary logistic regression was performed; health condition as dependent variable and menopausal status, physical exercises, smoking, education and FM (kg) as covariates. Differences of $p<0.05$ were considered statistically significant.

Results

The basic anthropometric parameters and indices of women suffering from CVD and without CVD are summarized in Table 2. Mean values of studied variables, except for the body height, differed significantly between compared groups even after adjustment for age.

The women with CVD attained mean values of all investigated parameters higher than the women without CVD except for mean value of BCMI index. The BCMI was higher, and thus optimal, in women without CVD. This result suggests that more obese women in the sample "with CVD" may be malnourished as highlighted by significantly low value of BCMI. Among women "with CVD" we have observed 80.2% subjects with the BMI higher than optimal (i.e. BMI>24.9 kg/m^2) and 74.4% of women with higher values of the WHR index than optimal (i.e. WHR>0.80). On the other hand, in the sample of women without CVD there were only 42.1% of subjects with higher value of BMI than optimal and 47.3% women with higher value of WHR index than optimal. These differences in distribution of indices categorisation were statistically significant ($p<0.001$). Those figures show that women with CVD have more fat mass and less body cell mass due to their health complications.

The mean values of bioelectric impedance variables are shown in the Table 3. After adjustment for age we found statistically significant differences between the women of both samples practically in all examined parameters except for phase angel (PA, $p=0.461$) and percentage of BCM ($p=0.387$). The main imped-

Table 2. Anthropometric characteristic and obesity indices in women suffering from cardiovascular disease (with CVD) and relatively healthy women (without CVD).

Variable	Women				p*
	with CVD		without CVD		
	n = 254		n = 318		
	Mean	SD	Mean	SD	
Age (y)	52.41	6.11	47.60	5.32	<0.001
Body Height (cm)	162.97	6.05	163.74	5.66	n.s
Body Weight (kg)	79.29	16.30	68.44	12.20	<0.001
Waist circumfer. (cm)	93.15	14.46	81.11	11.23	<0.001
Hip circumfer. (cm)	108.43	11.84	101.31	8.81	<0.001
BMI (kg/m^2)	29.86	6.06	25.52	4.28	<0.001
WHR	0.86	0.08	0.79	0.07	<0.001
BCMI (kg/m^2)	7.69	0.63	8.22	1.06	<0.001
FMI (kg/m^2)	12.63	4.88	9.20	3.50	<0.001

Notes: SD – standard deviation, BMI – body mass index, WHR – waist to hip ratio, BCMI – body cell mass index, FMI – fat mass index, FFMI – fat free mass index, * – adjusted for age stands for variables except for age, ns – the difference was not statistically significant.

ance characteristics (resistance, R; and reactance, Xc) of women suffering from CVD were significantly lower than those without CVD. These differences were also graphically displayed below, in Fig. 1, when R and Xc values were standardized by the body height. The women with CVD attained significantly higher absolute values of the following variables: TBW (l), ECW (l), ICW (l), FM (kg), FFM (kg), MM (kg) than the women without CVD (Table 2).

Table 4 shows correlation coefficient between indicators of obesity, i.e. BMI index, WHR index and waist circumference, and selected BIA parameters examined in two samples of women. The highest positive correlation coefficients for women suffering from CVD were observed between BMI and FM values (r=0.962; p< 0.000); waist circumference and FM (r=0.867; *p*<0.000); BMI and waist circumference values (r=0.858; p< 0.000); BMI and TBW (r=0.740; *p*<0.000) and

Table 3. Body composition characteristics of women suffering from CVD and without CVD.

Variable	Women				p*
	with CVD		without CVD		
	n = 254		n = 318		
	Mean	SD	Mean	SD	
Rz (ohm)	522.53	70.70	560.52	61.95	<0.001
Xc (ohm)	58.72	10.68	63.24	9.90	<0.001
PA	6.41	0.89	6.44	0.87	n.s
Na_K	0.89	0.11	0.93	0.12	<0.001
BCM (kg)	21.84	3.12	20.65	2.26	<0.001
BCM (%)	47.64	3.58	47.14	2.14	n.s
TBW (l)	37.63	23.38	33.77	3.78	<0.001
TBW (%)	46.50	5.06	49.97	4.82	<0.001
ECW (l)	16.57	2.88	14.94	2.14	<0.001
ECW (%)	45.60	3.08	44.17	2.63	<0.001
ICW (l)	19.64	2.35	18.83	2.03	<0.001
ICW (%)	54.40	3.08	55.84	2.63	<0.001
FM (kg)	33.47	12.68	24.65	9.41	<0.001
FM (%)	40.83	8.07	34.87	7.58	<0.001
FFM (kg)	45.81	5.13	43.79	4.14	<0.001
FFM (%)	59.17	8.07	65.10	7.59	<0.001
MM (kg)	28.26	15.64	25.71	2.79	<0.01
MM (%)	35.21	5.10	38.16	4.36	<0.001
BMR (kcal)	1421.33	118.25	1396.69	107.64	<0.001

Notes: Rz – resistance, Xc – reactance, PA – phase angle, Na/K – sodium – potassium exchange, BCM – body cell mass, TBW – total body water, ECW – extra cellular water, ICW – intracellular water, FM – fat mass, FFM – fat free mass, MM – muscle mass, BMR – basal metabolic rate, SD – standard deviation, * – adjusted for age, ns – the difference was not statistically significant.

Table 4. Correlation coefficient between obesity indicators and selected BIA parameters of women suffering from CVD and without CVD

Women with CVD		BMI	Rz	Xc	Pa	FM	MM	TBW
BMI	r	—	–0.669***	–0.547***	–0.037 n.s	0.962***	0.591***	0.740***
WHR	r	0.433***	–0.300***	–0.230***	–0.033 n.s	0.454***	0.279***	0.319***
waist circumference	r	0.858***	–0.564***	–0.473***	0.102 n.s	0.867***	0.591***	0.707***
Women without CVD		BMI	Rz	Xc	Pa	FM	MM	TBW
BMI	r	—	–0.586***	–0.325***	0.147**	0.968***	0.465***	0.590***
WHR	r	0.492***	–0.316***	–0.170**	0.66 n.s	0.489***	0.321***	0.362***
waist circumference	r	0.828***	–0.531***	–0.316***	0.089 n.s	0.835***	0.579***	0.673***

Notes: BMI – body mass index, WHR – waist to hip ratio, Rz – resistance, Xc – reactance, PA – phase angle, FM – fat mass, MM – muscle mass TBW – total body water,r – correlation coefficient , ** – < 0.01, *** – ≤ 0.001 n.s – the difference was not statistically significant

Table 5. Binary logistic regression of selected independent variables influencing the health condition in Slovak women.

Independent variables	OR	CI (95%)		p
		Lower Bound	Upper Bound	
Menopausal status				
Premenopause	0.338	0.226	0.505	<0.001
Perimenopause	0.639	0.303	1.348	0.240
Postmenopause	1.000			<0.001
Physical exercises				
No	1.000			<0.001
Occasionally	0.258	0.132	0.504	<0.001
Regularly	0.458	0.198	1.058	0.068
Smoking				
No	1.222	0.725	2.062	0.452
Occasionally	1.761	0.888	3.490	0.105
Regularly	1.000			0.255
Education				
Primary	1.000			0.077
Secondary	0.573	0.317	1.035	0.065
Academic	0.449	0.223	0.904	0.025
FM (kg)	1.066	1.046	1.086	<0.001

Notes: OR – Odds Ratio, CI – Confidence Interval, FM – fat mass.

between values of waist circumference and TBW (r=0.707; p<0.000). Among the women without CVD the same pairs of variables showed also the highest positive correlation coefficients as follows: between BMI and FM values (r=0.968; *p*<0.000); waist circumference and FM (r=0.835; *p*<0.000) and between values of BMI and waist circumference (r=0.828; *p*<0.000). The correlation coefficient between BMI and PA showed negative value (r= –0.037; p=0,552) and not significant in women with CVD, however in women without CVD the value was positive (r=0.147; *p*<0.01).

The results of binary logistic regression are displayed in Table 5. Health condition (in our case cardiovascular complication) represents a dependent variable and menopausal status, physical exercises, smoking, education and FM (kg) are considered as covariates contributing to CVD risk. We found that statistically significant lower risk of CVD had premenopausal women (OR=0.338, *p*<0.001) in comparison with postmenopausal women. Statistically significant lower risk of CVD was observed also among women with occasionally physical activity (OR=0.258, *p*<0.001) and women with academic education (OR=0.449, *p*=0.025). Binary logistic regression also showed the increasing risk of CVD difficulties with increased proportion of fat mass (OR=1.046, *p*<0.001). We have considered the effect of FM (kg) only, because other parameters connected with obesity and CVD risk (BMI and WHR index) were in correlation with fat mass (Table 4), what is not suitable for binary logistic regression.

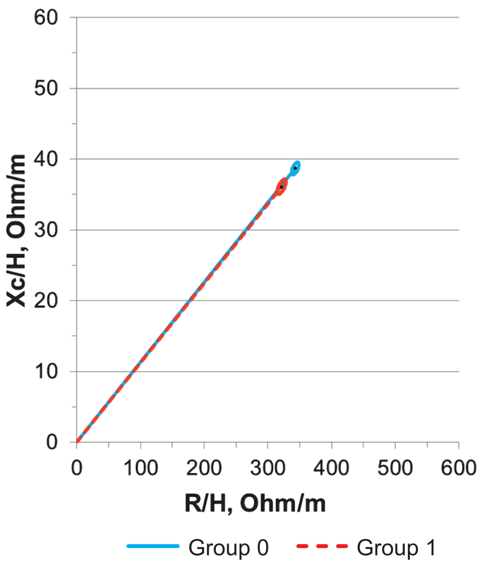

Fig. 1. Mean impedance vectors with 95% confidence ellipses from women with and without CVD.

Notes: Group 0 – women with CVD, Group 1 – women without CVD;
R/H – rezistance standardized by the body height;
Xc/H – reactance standardized by the body height.

Figure 1 shows mean impedance vectors with 95% confidence ellipses of women suffering from CVD (group 0) and relatively healthy women without CVD (group 1). Size of the confidence ellipse is affected by the variability of vector components and the sample size (smaller ellipse of a greater number of individuals with similar SD). As shown in Figure 1, there was a significant displacement of the average impedance vector in women with CVD and without CVD. Not overlapping 95% confidence ellipses indicate statistically significant differences between mean vectors of the compared groups. This heterogeneity of samples was confirmed by value of the Hotelling T^2 test (*p*=0.000).

Discussion

The results of the present study showed that women with CVD (that means women suffering from one or more of the following health problems like hypertension, ischemic heart disease, Diabetes Mellitus, atherosclerosis or high blood cholesterol), attained significant weight gain and increased fat mass in comparison with women without this burden. The fact that weight gain and higher levels of BMI index (>24.9 kg/m^2) appear to increase risk of heart disease in middle-aged women was observed also by Willett et al. (1995) in middle-aged women from United States.

The body mass index is widely used in different type of studies despite objection of several authors that the BMI is of little diagnostic value, because this index is a poor approach for the measurement of muscle mass, protein status or lean tissues (Kyle et al. 2003; Kalvach et al. 2004; Amir and Rakhshanda 2009; Gába, Přidalová and Zajac-Gawlak 2014). The BCMI has been shown to be more sensitive to changes in protein status and lean tissue compared to BMI (Talluri et al. 2003). Further, it has been observed that for subjects with normal or high BMI values (i.e. between 20 and 30), there is a great variability in BCMI (i.e. between 5 and 19 kg/m^2), which means that these subjects may appear overweight on the basis of BMI, but in fact those who have lower BCMI values are malnourished (Talluri et al. 2003). This observation agrees with our study as the women with CVD had significantly higher BMI values and significantly lower BCMI values in comparison with women without CVD. The significant correlations between BMI, WHR and FM observed in our study correspond to results published by Van Pelt et al. (2001) that found the BMI and WHR strongly and significantly correlated with percentage of body fat (r=0.91 and 0.85, respectively). Further, Dalton et al. (2003) found significant correlations between each of anthropometric measures of obesity (BMI, WHR) and cardiovascular disease in a predominantly Caucasian population. In our study significant correlation between above mentioned variables were recorded not only among women with CVD but also in the compared sample of women without CVD. On the other hand, the correlation coefficient between phase angel and BMI was week in both samples and reached opposite values; it was equal to r=–0.037 in women with CVD, but equal to r=0.147 in the compared sample. We can only speculate having in mind that higher values of PA reflect higher cellularity, cell membrane integrity and better cell function (Mattar 1996); the lower PA values in women with CVD than in women without CVD (though not significant) may suggest cell death or decreased cell integrity in these women.

The changes in body composition of women with CVD in our study embrace 17 variables from the whole 19 examined ones (except of phase angle and BCM in percentage). Due to lack of data on body composition variables of patients suffering from any CVD, it is difficult to discuss magnitude of observed changes between studied samples. However, some studies identified, for example, change of phase angle in overweight and obese hemodialyzed patients with higher BMI (Guida et al. 2001). Therein patients had lower phase angle than patients with normal weight. According to (Barbosa-Silva et al. 2005) the reference values of phase angle from a healthy population offer the possibility of assessing individual deviations of patients at risk of impaired functional and nutritional status and increased mortality. Unfortunately, in our study we did not record such differences.

In summary, the used bioimpedance method provide wider spectrum of variables useful for estimation of CVD risk between women with and without CVD, except for classical variables of obesity. The cross-sectional nature of our study makes it difficult to draw conclusions regarding causal pathways, though variables of obesity are in line with unhealthy cardio-metabolic conditions. The risk of CVD is associated with metabolic variables, menopausal complaints /symptoms, a sympathetic nervous system activity and life style of the subjects and some others. Therefore, our findings should trigger further studies that should consider also some of the above mentioned variables and genetic markers.

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Authors' contributions

All authors participated on the data collection and subject's measurements. DD, DS and VC organized the investigations. ZD, DS, DD designed the paper structure. The statistical analysis was done by ZD, DD and VC. DD drafted and finalized manuscript. All authors read and approved the final version of the paper.

Conflict of interest

The authors declare that there is no conflict of interests.

Abbreviations: CVD – cardiovascular disease, BMI – body mass index, WHR – waist to hip ratio, BIA – bioelectrical impedance analysis, BIVA – bioelectric impedance vector analyses, BIA – bioelectric impedance analyses, R – resistance, Xc – reactance, FM – fat mass, FFM – fat free mass, MM – muscle mass, TBW – total body water, ECW – extracellular water, ICW – intracellular water, BCM – body cell mass, BCMI – body cell mass index, BMR – basal metabolic rate, PA – phase angle

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