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Bioelectrical Impedance Vector Analysis (BIVA) in Slovak population: application in a clinical sample

Research Article

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Abstract: The purpose of this study is to provide new data on body composition in the Slovak population, particularly impedance vector components according to sex and age, relevant for bioelectrical impedance vector analysis (BIVA) in a clinical sample. The reference sample consisted of 1543 apparently healthy individuals (1007 females and 536 males), aged from 18 to 92 years and of 60 patients with Parkinson´s disease (PD) (26 females and 34 males), aged from 40 to 81 years. Bioelectrical parameters of resistance (R) and reactance (Xc) were measured with a monofrequency analyser (BIA 101). BIVA was used to analyse tissue electric properties in control subjects and patients with PD. The mean vector position differed significantly between PD patients and healthy controls in males of age subgroups 60-69 years and 70-79 years, respectively. These results were conterminous with significant Hotelling's T^2-test; 60-69 y $T^2=7.8$, $P=0.024$ and 70-79 y $T^2=7.6$, $P=0.026$. In the RXc-score graph three patients had values outside the 95% ellipse. Altered tissue electric properties were present in 23.5% of males and 15.4% of females. Distribution of impedance vector components in different age categories of healthy Slovak subjects are relevant to comparative population studies and to clinical practice.

Keywords: *Bioelectric impedance • Resistance • Reactance • Parkinson´s disease*

1. Introduction

Anthropometry was, for decades, the only method available for quantifying body size and proportions since Matiegka [1] developed an equation for predicting body fat from measurements of skinfold thickness. In Slovakia, anthropometry is still the most widely used method due to the fact that it is simple, inexpensive, and portable. The disadvantage is lack of standardization in methodology. During the past two decades, several reliable new techniques, such as dual-energy X-ray absorptiometry (DXA), magnetic resonance imaging (MRI), computerized tomography (CT) and bioelectrical impedance analysis (BIA) were developed and validated for measuring body composition [2-5]. The last method measures body composition by sending a low, safe electrical current through the body to determine the electric impedance (Z). The whole body impedance consists of two components, resistance (R, ohm) and reactance (Xc, ohm). These variables are displayed directly by the analyser; R is a measure of total body water and Xc a measure of body cell mass. From the determined impedance and by using the Bodygram program, Version 1.3 (Akern, S.r.l.) several number of BIA parameters can be estimated (FM, Fat Mass; FFM, Fat-Free Mass; BCM, Body Cell Mass; PA, Phase Angle, TBW, Total Body Water; ECW, Extra Cellular Water; ICW, Intra Cellular Water; MM, Muscle Mass; BMR, Basal Metabolic Rate; Na/K, Exchange Na/K) using the Bodygram program (Akern, S.r.l.).

The BIA can be further enhanced by combining it with bioelectrical impedance vector analysis (BIVA) [6] that offers clinical benefits [7]. This method has been shown to be effective to assess hydration status [8] and identify patients with a critical fluid overload [9]. Walter-Kroker *et al*. [10] using both the BIA and BIVA

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methods revealed altered nutritional and fluid status in chronic obstructive pulmonary disease patients (e.g. malnutrition in obese and underweight patients and water retention). Marini *et al*. [11] in their study investigated the suitability of BIVA for the assessment of sarcopenia and detected muscle-mass variations in sarcopenic individuals. Buffa *et al*. [12] in their study detected low body cell mass and dehydration in patients with Alzheimer´s disease. Norman *et al*. [13] who conducted a comprehensive literature search relevant to studies on the use of phase angle and/or BIVA, came to conclusion that phase angle could be used as a screening tool for the identification of patients with impaired functional and nutritional status. The BIVA is then recommended for further nutritional assessment and monitoring, in particular when calculation of body composition is not feasible. Only a few reports provide objective measures of weights in patients with Parkinson´s disease either by anthropometric [14] or bioelectrical impedance [15].

Because no data is available on impedance vector components in the Slovak population, this study was conducted to investigate body composition assessed with bioelectrical impedance in adult female and male subjects and Parkinson´s disease (PD) patients who were matched for age and gender. We compared the distribution of impedance vectors in a reference population with those from PD patients in order to examine altered tissue electric properties in a clinical sample. We have applied this concept to assess the possible utilization of Slovak reference data in clinical practice.

2. Experimental Procedures

2.1 Study samples

The reference sample was based on data collected during cross-sectional surveys in Slovakia between 2004 and 2011 within projects carried by the Department of Anthropology, Comenius University in Bratislava and supported by the Scientific Grant Agency of the Ministry of Education, Science, Research and Sport of the Slovak Republic and the Slovak Academy of Sciences. A total of 1543 subjects; 1007 women and 536 men were divided into the following age categories: 18-28 years, 29-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and 80-92 years. Subjects were recruited from different localities in the western and middle parts of Slovakia *via* an invitation letter regarding the study, circulated and distributed prior to data collection with the help of local medical doctors. Participants were then interviewed during a medical examination in the morning, and they were investigated with respect to their health, anthropometrical and lifestyle aspects at local Health Centres. However, only selected variables were considered for the purpose of this paper. All participants were considered as being free from serious physical handicaps or illnesses (Alzheimer disease, Parkinson´s disease, cancer) at the time of the recruitment. Subjects recovering from acute disorders such as cancer, myocardial infarction, or stroke were excluded from the survey. None of elderly men and women had been admitted to hospital in the three months before the survey, they were also not bed-ridden or mentally impaired. In the whole sample, average values of BMI ranged from 20.5 to 30.25 (kg/m²), *i.e.* participants cover three BMI classes (19-24.9, 25-29.9, and 30-34.9). All subjects gave written Informed Consent for participation in the study.

The sample with Parkinson's disease (PD) patients consisted of 26 females and 34 males diagnosed and followed up at the 2nd Department of Neurology, Faculty of Medicine, Comenius University in Bratislava. Patients were free-living. Data was collected in 2010 by anthropologists and was obtained with the same type of impedance analyser as in the reference sample. Ages of the patients fall in five age categories (40-49 years, 50-59 years, 60-69 years, 70-79 years and more than 80 years). Distribution of age categories in male and female patients is in Table 1. The PD patients did not differ significantly from their reference counterparts in

Females			Males		
Age categories	N	mean ± SD	Age categories	N	mean ± SD
-	-		40–49 y	2	47.00 ± 0.00
50–59 y	5	56.80 ± 2.39	50–59 y	10	55.00 ± 3.43
60–69 y	12	65.42 ± 2.15	60–69 y	10	64.70 ± 3.20
70–79 y	7	73.14 ± 3.13	70–79 y	10	74.70 ± 3.20
80 y >	2	81.00 ± 0.00	80 y >	2	80.00 ± 0.00

Table 1. Distribution of age categories in patients with Parkinson´s disease.

the mean values of body weight. These values ranged in patients from 63.90 to 92.55 (kg). In the whole clinical sample, average values of BMI ranged from 25.55 to 31.30 (kg/m²), *i.e.* patients cover the category between overweight to obese. Duration of the disease, taken as time from original diagnosis, ranged from 3 to 15 years. Standard supportive care was given to all patients. Written Informed Consent was obtained from PD patients for participation in this study.

2.2 Anthropometric analysis

Anthropometric and bioimpedance measurements were collected by trained anthropologists. The body height was measured with a Sieber and Hegner anthropometer at the head level with the participant standing barefoot and with feet together, with 0.5 cm accuracy.

2.3 Bioelectric Impedance Analysis (BIA)

The body composition variables were obtained using a bioelectric impedance analyser (BIA 101, Akern, S.r.l.). This apparatus generates a constant excitation current at 800 mA at a signal frequency of 50 kHz with a four-electrode arrangement. Original disposable electrodes for impedance analysis were used (Biatrodes™, Akern, S.r.l.). The BIA measurements were carried out in the morning, with the subjects supine on a bed after overnight fasting and at least 12 hours after physical training or vigorous exercise, and adhering to all defined pre-test conditions [16,17]. The BIA method is based principally on the greater electrolyte content and conductivity of body water and fat-free mass and on the low electrical conductivity and high impedance of fat mass [17]. Vector BIA was conducted on direct impedance measurements of resistance (R, Ohm) and reactance (Xc, Ohm) in males and females in both the reference and clinical samples. Clinical utility of BIA can be achieved using vector analysis as a stand-alone procedure based on patterns of direct impedance measurements [18].

2.4 Bioelectric Impedance Vector Analysis (BIVA)

Impedance (Z vector) is a combination of Resistance (R) and Reactance (Xc) across ionic solutions of soft tissue interface and cell membranes. Z can be considered as a bivariate random vector. The R and Xc were standardized by each subject´s height in metres (R/H and Xc/H), to eliminate the effect of conductor length on the bioelectrical parameters, in order to define the impedance vector (Z/H). The BIVA 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). By plotting the two components R/H and Xc/H measured in an individual subject as an individual impedance vector (a point) on the RXc graph, one can directly rank its distance from the reference mean vector through the tolerance ellipses (RXc point graph). It is possible to interpret the bioelectrical data in terms of variations of body composition characteristics; in fact, the long axis of the tolerance ellipses indicates tissue dehydration (upper area) or fluid overloading (lower area), while the short axis indicates more (left side) or less cell mass (right side) contained in soft tissues [6].

The BIVA method also allows graphic representation of the mean impedance vectors of groups by means of the 95% probability confidence ellipses as well as with statistic evaluation by Hotelling T²-test. This is useful for clinical research studies aimed to identify disorders in body composition.

After the transformation of measured vector components of the RXc graphs into bivariate Z-scores (*i.e.* R/H and Xc/H minus the mean and divided by the standard deviation of R/H and Xc/H calculated in the reference population), the RXc-scores graph allows utilization of standard reference intervals for impedance vectors in practice [5]. Therefore we projected values of the Z-score of impedance vectors of the clinical sample (patients´ age categories) on the RXc-score graph of the reference population.

2.5 Statistical analysis

Statistical analysis was carried out using SPSS software (version 17.0 for Windows). A p value less than 0.05 was considered statistically significant. The vector analysis of bioelectrical impedance was performed with BIVA software [6]. Inter-group differences in the mean impedance vectors between age groups of the reference population as well as between reference and clinical sample (in our case 95% confidence limits for mean impedance vectors of reference and clinical subjects matched by sex and age) were assessed with the Hotelling´s T²-test. The significance level was defined as $P<0.05$.

3. Results

Table 2 shows mean values of impedance vector components in Slovak subjects stratified by sex and age. Table 3 shows corresponding values in subjects with Parkinson's disease. Both tables show all the parameters necessary for calculation of the respective confidence or tolerance ellipses in particular age subgroups of females and males.

Age categories	Females						
	N	Height	R	Xc	R/H	Xc/H	r
		mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
18-28 y	202	167.22 ± 6.79	633.33 ± 63.44	71.86 ± 9.00	378.18 ± 40.35	42.93 ± 5.78	0.67
29-39 y	55	167.38 ± 6.00	588.47 ± 48.49	71.02 ± 9.66	352.02 ± 31.29	42.51 ± 6.20	0.73
40-49 y	256	164.17 ± 5.70	551.43 ± 65.63	62.52 ±10.23	336.37 ± 42.41	38.17 ± 6.60	0.63
50-59 y	215	162.82 ± 5.57	545.28 ± 66.20	61.05 ± 9.60	335.38 ± 43.33	37.56 ± 6.12	0.65
60-69 y	102	158.19 ± 6.57	521.60 ± 73.22	52.41 ± 11.66	330.66 ± 50.46	33.10 ± 7.40	0.44
70-79 y	125	154.47 ± 6.86	523.07 ± 69.13	48.55 ± 12.49	339.71 ± 51.36	31.55 ± 8.57	0.54
80-92 y	52	152.33 ± 6.19	532.98 ± 74.58	49.67 ± 18.71	349.52 ± 47.15	32.57 ± 12.16	0.51
	Males						
	N	Height	R	Xc	R/H	Xc/H	r
		mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
18-28 y	193	180.99 ± 6.88	476.88 ± 52.48	64.28 ± 11.18	263.76 ± 30.00	35.58 ± 6.40	0.53
29-39 y	45	179.73 ± 6.49	458.09 ± 56.38	64.24 ± 9.22	255.38 ± 34.30	35.82 ± 5.48	0.73
40-49 y	22	178.86 ± 5.18	448.95 ± 50.45	55.32 ± 6.34	251.42 ± 30.73	31.00 ± 3.98	0.86
50-59 y	32	174.40 ± 5.85	440.34 ± 44.06	53.91 ± 11.08	252.60 ± 24.75	30.92 ± 6.27	0.47
60-69 y	104	171.35 ± 6.95	462.88 ± 69.22	49.90 ± 13.75	270.68 ± 42.47	29.16 ± 8.37	0.59
70-79 y	110	167.65 ± 7.10	468.40 ± 78.65	44.65 ± 11.66	279.48 ± 51.13	26.66 ± 7.23	0.71
80-92 y	30	163.16 ± 5.87	464.40 ± 84.60	40.77 ± 13.04	285.62 ± 56.46	25.12 ± 8.60	0.65

Table 2. Impedance vector components in healthy Slovak subjects by sex and age.

R, resistance; Xc, reactance; H, subjects´ height; r, correlation coefficient between Rz/H and Xc/H

Age categories	Females						
	N	Height	R	Xc	R/H	Xc/H	r
		mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
50-59 y	5	163.12 ± 7.81	484.00* ± 19.77	54.40 ± 15.58	297.06 ± 15.31	33.59 ± 10.92	0.86
60-69 y	12	161.78 ± 6.27	525.08 ± 59.26	52.00 ± 5.66	325.37 ± 41.29	32.24 ± 4.17	0.14
70-79 y	7	158.70 ± 3.61	562.26 ± 80.00	57.43 ± 7.80	353.78 ± 45.77	36.22 ± 5.17	0.44
80 y >	2	152.80 ± 0.28	475.00 ± 91.92	44.50 ± 3.54	310.92 ± 60.74	29.13 ± 2.37	1.00
	Males						
	N	Height	R	Xc	R/H	Xc/H	r
		mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
40-49 y	2	172.40 ± 2.05	392.50 ± 44.55	53.00 ± 2.83	227.47 ± 23.13	30.73 ± 1.28	1.00
50-59 y	10	177.63 ± 8.24	445.22 ± 66.54	56.11 ± 10.70	251.38 ± 40.80	31.69 ± 6.37	0.78
60-69 y	10	171.28 ± 5.54	420.80 ± 50.63	52.70 ± 10.70	245.70 ± 28.74	30.76 ± 6.09	0.90
70-79 y	10	173.04 ± 7.24	418.70 ± 73.89	44.20 ± 10.34	242.44 ± 44.41	25.59 ± 6.04	0.80
80 y >	2	164.35 ± 0.21	423.00 ± 43.84	43.00 ± 5.66	257.36 ± 26.35	26.17 ± 3.41	1.00

Table 3. Impedance vector components in Slovak subjects with Parkinson's disease by sex and age.

*R, resistance; Xc, reactance; H, subjects´ height; r, correlation coefficient between Rz/H and Xc/H; *P<0.05 comparison with healty females of the same age category*

The mean values of R and Xc in PD patients of particular age subgroups did not differ significantly from values of their counterparts from the reference sample (P>0.05), except for R value in females of 50-59 years (P=0.040), (results not shown).

The confidence ellipses of particular age subgroups of the reference Slovak population were compared with each other, too. The Hotelling´s T^2 used to compare females' age subgroups was significant between the age subgroups 18-28 and 29-30 (T^2=31.80, P<0.001), 29-39 and 40-49 (T^2=20.10, P<0.001), 50-59 and 60-69 (T^2=39.70, P<0.001) and 60-69 and 70-79 (T^2=7.60, P<0.05). The comparison of males´ age subgroups showed significant difference in bioelectrical vectors between the age subgroups 18-28 and 29-39 (T^2=6.80, P<0.05), 29-39 and 40-49 (T^2=241.40, P<0.001) and 60-69 and 70-79 (T^2=19.70, P<0.001).

Observed differences could be attributed to aging process.

In Figure 1 mean impedance vectors with 95% confidence ellipses from healthy subjects and PD patient´s stratified by sex and age are as follows: females 50-59 y, 60-69 y and 70-79 years; males 50-59 y, 60-69 y and 70-79 years. The size of the confidence ellipses was influenced by variability of the vector components and the sample size (smaller ellipses from a greater number of subjects). The shape of both the tolerance and the confidence ellipses was determined by the correlation coefficient between R/H and Xc/H (more flat and elongated shape with a higher correlation). As shown in Figure 1, there was a significant displacement of the average impedance vector in PD males´ patients aged 60 to 69 y and 70 to 79 years, respectively, compared with healthy controls, as indicated by the non-overlapping 95% confidence ellipses and significant values of the Hotelling´s T^2-test (60-69 y T^2=7.8, P=0.024 and 70-79 y T^2=7.6, P=0.026), respectively. The vector position of the male patients 50-59 years and female patients of 50-59 y, 60-69 y and 70-79 years, respectively, did not differ significantly from healthy controls as indicated by the values of the Hotelling´s T^2-test (males 50-59 y T^2=0.2, P=0.909; females 50-59 y T^2=3.9, P=0.14; 60-69 y T^2=0.2, P=0.907; 70-79 y T^2=2.0, P=0.37). Similar vector distribution patterns/graphs and Hotelling´s T^2-test within/in age groups for females 80-92 y and males 40-49 y and 80-92 years, respectively, could not be done because of an insufficient number of PD individuals in those particular age categories.

Figure 2 shows the reference RXc-score graph with 95%, 75% and 50% tolerance ellipses. Besides both dimensionless Z scores, *i.e.* resistance score Z (R) and reactance score Z (Xc), there are bioimpedance vectors from clinical sample plotted on the RXc-score graph. These values were obtained after transformation of impedance

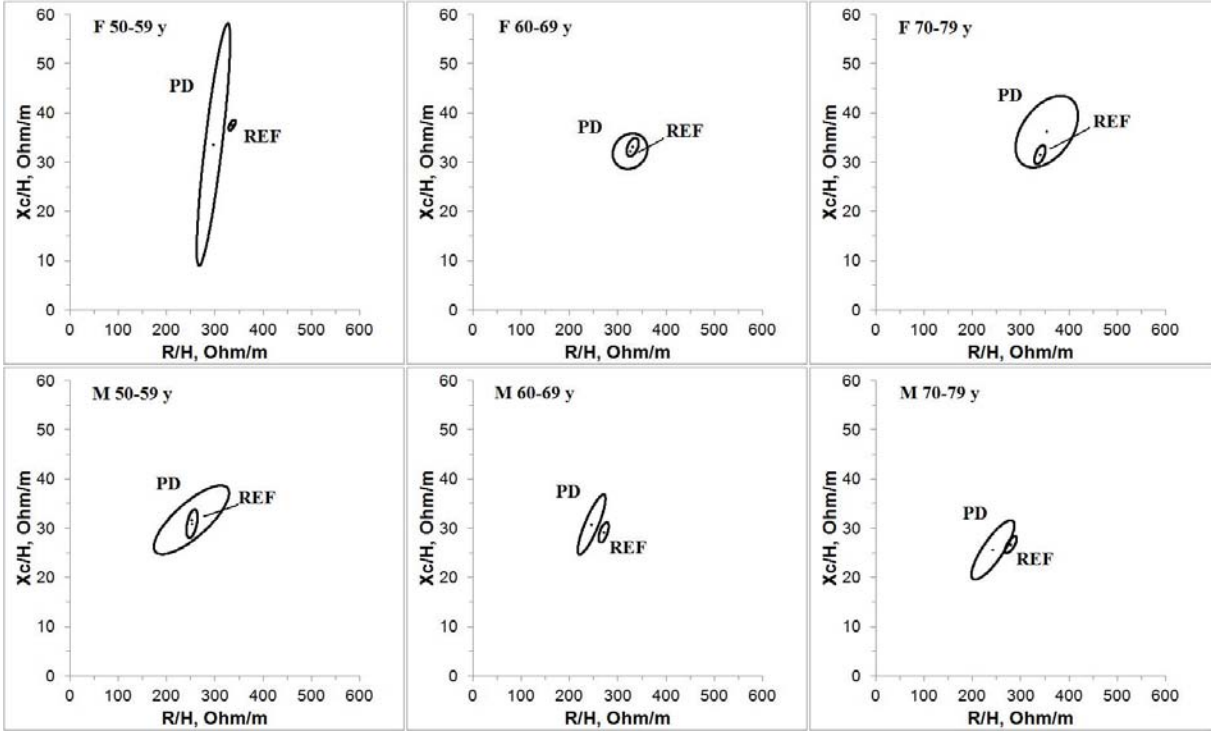

Figure 1. Mean impedance vectors with 95% confidence ellipses from healty subjects and PD patients stratified by sex and age.
R= resistance; Xc= reaktance; H= subject's height; F= females; M= males; PD= Parkinson´s disease; REF= reference population.

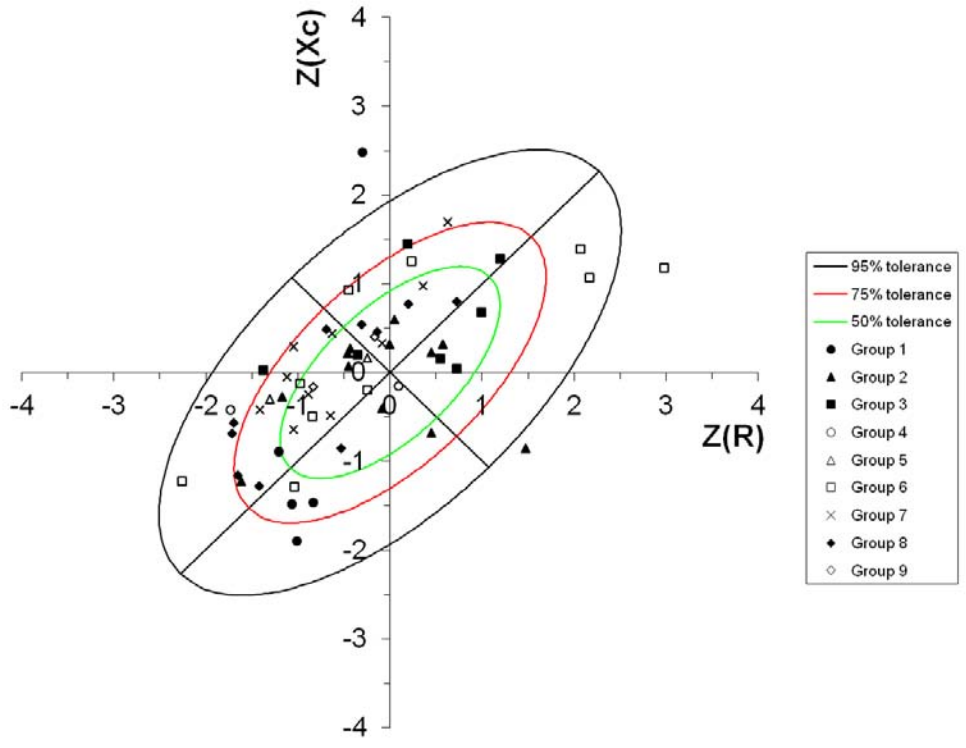

Figure 2. RXc-score graph from PD patients.
Z(R) – Z-score rezistancie, Z(Xc) – Z-score reaktancie, three tolerance ellipses of reference population are distinguished, corresponding to the 50%, 75% and 95% percentiles, Group 1 – female PD patients 50 – 59 y, Group 2 – female PD patients 60 – 69 y, Group 3 – female PD patients 70 – 79 y, Group 4 – female PD patients over 80 y, Group 5 – male PD patients 40 – 49 y, Group 6 – male PD patients 50 – 59 y, Group 7 – male PD patients 60 – 6 y, Group 8 – male PD patients 70 – 79 y, Group 9 – male PD patients over 80 y.

measurements from PD patients´ into bivariate Z scores (with respect to the Slovak reference population). The PD patients belonging to different age groups are indicated by different marks (solid and open). Interpretation of individual vector position on the RXc graph is as follows: Displacement of vectors above the long axis (/) indicates an increase in soft tissue mass, vectors below the long axis a decrease in soft tissue mass. Vectors located above the short axis (\) indicate dehydration status and vectors below the short axis indicate more fluids, *i.e.* increased water retention. Values falling outside the reference intervals (95%) in the four quadrants point to the following conditions: in the right lower quadrant malnutrition – in our case a female patient of the age group 2 (60-69 y), position of the point in the BIVA nomogram below the line of normal cell mass in soft tissue (long axis) and above the line of normal hydration value (short axis) points to cachexia; right upper quadrant exsiccosis - in our case a male patient of the age group 6 (50-59 y), position of the measurement point below the line of normal body cell mass value (long axis) and above the line of normal hydration (short axis) points to bodily dehydration; left upper quadrant good training status – in our case female patient of the age group 1 (50-59 y), position of the measurement point far above the long axis indicates increased soft tissue along with a position above the line with normal hydration suggests decrease of fluids; left lower quadrant oedema – in our study no value is located here, outside the 95%.

From clinical validation studies in adults, vectors falling out of the 75% tolerance ellipse indicate abnormal tissue impedance. Table 4 reports the distribution of the impedance vectors of the PD patients´ with respect to the 50%, 75%, and 95% tolerance ellipses of the reference population. The percentage of cases falling out of the 75% tolerance ellipse, but within the 95% tolerance ellipse varies between 7.69% for females to 20.58% for males. Three patients had values outside the 95% ellipse; two females aged over 50 and 60 years (7.69%) and one man aged over 50 years (2.94%).

4. Discussion

The patterns of bioelectrical impedance vector distribution from the Slovak population have not been

Sex	N	50%	75%	95%	out 95%
Females (50-81 y)	26	61.50%	23.10%	7.69%	7.69%
Males (40-80 y)	34	50.00%	26.47%	20.58%	2.94%

Table 4. Distribution of impedance vectors in a clinical sample with respect to the tolerance ellipses (50%, 75% and 95%) of the Slovak reference population.

published as yet. Data of impedance measurements of whole-body were obtained during cross-sectional studies in Slovakia and only the opportunity/possibility of evaluating the Parkinson´s disease patients with the same analyser, prompted us to report this data in normal individuals and in disease state. In our study we were not able to stratify subjects by BMI along with age and sex as it has been done in the large NHANES database in the United States [5] and Germany [19], due to a small number of subjects in the particular age categories. Our data also give the first information about the bioelectrical characteristics of the PD patients in Slovakia. Parkinson´s disease (PD) is a common neurodegenerative disease, leading to primary degeneration of the nigrostriatal system [20]. Except for motor features of PD subjects, the non-motor symptoms, in some cases, can dominate the clinical picture. Among the most seen non-motor feature is gastrointestinal dysfunction which manifests in many ways and pose many problems [21]. PD patients due to their disease tend to have lower levels of body weight, fat mass and circumferential measures than the matched control subjects. Beyer *et al*. [15] reported that patients with PD were four times more likely to report weight loss (greater than 10 lb) than the control subjects. These patients also attained significantly lower values of body mass index (BMI), percentage of body fat (determined by BIA method), and other measures of body composition. Weight loss, malnutrition and associated factors in Chinese PD patients were reported by Wang *et al*. [22]. Among our Parkinson´s disease patients no subject had malnutrition by BMI (BMI<19) and mean values of this index in the whole sample ranged from BMI=25.55 to 31.30 (kg/m²), which places subjects in the overweight to obese category. In patients we did not follow body weight changes over some time before the study, thus we are not able to discuss frequency of body weight loss as it has been reported in other clinical samples as mentioned above. Also the distribution of impedance vectors in our PD patients listed in Table 4 shows that 50% of males and 61.5% of females lie within the 50% tolerance ellipse and are within the normal range. However, approximately 23.5% of males and 15.4% of females were out of the 75% ellipse. According to Kyle *et al*. [23] the BIVA method by providing detailed information on hydration and cell mass integrity may be more predictive of prognosis than weight loss. This assumption is supported with results by Toso *et al*. [24], the altered tissue electric properties in lung cancer patients were more predictive of prognosis than weight loss.

5. Conclusions

We have aimed to provide an example of using the BIA/BIVA analysis results in evaluating altered electric properties of tissue in primary care of PD patients. The follow-up of a larger sample is required which monitors medical and nutritional care and establishes the relation between body impedance and identifies the prognosis of PD. In our opinion, BIVA should be considered as an assessment and monitoring tool.

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