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Bioimpedance vector analysis and conventional bioimpedance to assess body composition in elderly adults with dementia

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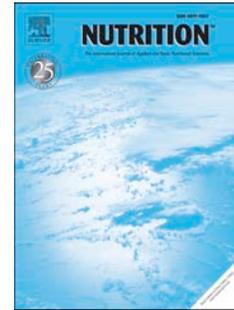
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TITLE

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ABSTRACT

Rationale: Although dementia and nutritional status have been shown to be strongly associated, differences in body composition (BC) among elderly with dementia have not yet to be firmly established.

Objective: To assess the BC through conventional and vector bioimpedance analysis (BIA and BIVA, respectively) in a sample of institutionalized elderly men with and without dementia, in order to detect dementia-related BC changes.

Methods: Forty-one institutionalized men aged 65 years or older (23 without dementia- CG- and 18 with dementia-DG-) were measured with BIA and interpreted with BIVA and predictive equations.

Results: Age (74.4 and 75.7 y) and BMI (22.5 and 23.6 kg/m²) were similar for DG and CG, respectively. Resistance and resistance/height ratio did not differ significantly between groups. Reactance and reactance/height ratio were 21.2 and 20.4% lower in DG than in CG. Phase angle was significantly lower in DG (mean: 4.0; 95% CI: 3.6-4.3 degrees) than in CG (mean: 4.7; 95% CI: 4.3-5.1 degrees). Mean fat mass index (6.0 and 7.0 kg/m²), and mean fat-free mass index (16.4 and 16.6 kg/m²) were similar in DG and CG. BIVA showed a significant downward migration of the ellipse in DG with respect to CG ($T^2=15.1$, $p<0.01$).

Conclusion: Conventional BIA showed no significant differences in BC between DG and CG, even though reactance and reactance/height were about 21% lower in DG. Nevertheless, a body cell mass depletion and an increase in the extracellular/intracellular water-ratio were identified in DG using BIVA. BIVA reflects dementia-related changes in BC better than BIA.

KEY WORDS: Body composition, bioelectrical impedance vector analysis, conventional bioimpedance analysis, elderly, dementia.

INTRODUCTION

Dementia and body composition have been shown to be strongly associated, but there are still conflicting data on the nature of this association. On the one hand, it has been recently evidenced that high values of body mass index (BMI), and hence adiposity, in adulthood are associated with an increased risk of Alzheimer's disease (AD) and vascular dementia (VD) in late life [1, 2]; on the other hand, however, it is well-known that malnutrition and specially unintentional weight loss are common clinical features in patients with dementia, which occur at the preclinical stage of the disease and are maintained at the follow-up, further aggravating the prognosis of these patients [3].

The relationship between BMI and dementia at older ages is less clear [4]. The Cardiovascular Health Study recently reported that the risk of dementia was positively associated with obesity at age 50 years, but negatively associated with BMI after the age of 65 years [5]. Several epidemiological studies have also suggested that overweight and obesity in late life are associated with reduced risk of dementia [6, 7], while others have found that a higher BMI at older ages predicts dementia [8]. Since it is widely accepted that malnutrition and unintended weight loss not only occur during the final stages of the disease, but also may be a precursor to dementia [9, 10], the term "obesity paradox" has been proposed to describe the relationship between BMI in the elderly and risk of dementia.

Despite the evidence showing a role of adiposity during adulthood in the subsequent development of dementia, data available on changes in body composition (BC) in the elderly with dementia have not yet to be firmly established. Several factors contribute to this situation. Among them, probably the most notable is the method used to measure adiposity. Both BMI and waist circumference (WC) have been employed as indicators of adiposity (overall and central adiposity, respectively) in most studies, but currently there is no

consensus on the cut-off points for obesity for the elderly [11, 12]. In addition, age-related changes in BC and loss of height alter the relation between BMI and percentage body fat [13].

On the other hand, we and other authors have shown that a few isolated anthropometric measurements, such as calf circumference, are good indicators of BC in the elderly. [14]. Nevertheless, the applicability of the anthropometry to estimate BC in this population also presents a number of challenges and constraints. We recently evidenced that the predictive equations based on anthropometric measurements leads to significant underestimation of FM in elderly individuals with dementia. [14]

Bioelectrical impedance analysis (BIA) has shown to be valid for BC analysis in the elderly when using the specific equations developed and validated in this population [15]. Nevertheless, age-related changes in the amount (hypo- or hyper-hydration) and distribution (intra-/extra-cellular) of body water are relatively common in elderly institutionalized individuals [16] and may lead to significant errors in estimating body compartments [17] because of assumptions of a constant hydration of the FFM [18].

In the vectorial approach of BIA, called Bioelectrical Impedance Vector Analysis (BIVA), the individual components of the impedance vector, resistance (R) and reactance (Xc), are normalized by the height of the subject (R/H and Xc/H) and represented in the R-Xc graph (abscissa, R/H; ordinate, Xc/H) [19]. R is inversely related to the intra- and extracellular water (ICW and ECW), whereas Xc is directly related to the amount of soft tissue structures (mass). Therefore, vector length is influenced by tissue hydration (shortening indicates over-hydration, and lengthening suggests dehydration), and vector direction (i.e. phase angle or PA) is influenced by the amount of cell mass contained in soft tissues (a small PA indicates malnutrition-cachexia-anorexia; a large PA may be observed in both obese and athletic individuals). The vector derived for an individual is compared against the normal interval of the healthy, reference population, and is expressed in percentiles of the normal

distribution of a bivariate, probabilistic graph. Therefore, BIVA does not yield any absolute estimates of body compartment [20], but it allows assessing changes in both BC and the hydration status. BIVA is simpler and more affordable than dual-energy x-ray absorptiometry (DXA; a commonly used reference method) and, in contrast to anthropometric measurements or conventional BIA, is unaffected by regression adjustments that may introduce clinically relevant bias [20].

Recent studies also emphasise in the role of phase angle (PA), calculated as arc tan reactance/resistance and expressed in degrees, as a practical indicator of functional and nutritional status in the elderly [21]. It also provides information about the clinical outcome and mortality, which is another important advantage of BIVA [22, 23].

The objective of this study was to assess the body composition through conventional through conventional and vector bioimpedance analysis (BIA and BIVA, respectively) in a sample of institutionalized elderly men, including a group of no-demented men and a group of demented men, in order to detect dementia-related BC changes.

We sought to overcome the limitations of BMI as a general indicator of adiposity by using BIA to estimate body composition and BIVA to categorize soft tissue mass and hydration.

MATERIALS AND METHODS

Subjects and design

This was a cross-sectional study carried out on a sample of elderly men institutionalized in the Psychogeriatric Area of the Residential Care Centre San Juan de Dios (Palencia, Spain). Inclusion criteria were being Caucasian, male, aged ≥ 65 y, and at risk of

malnutrition or having normal weight on the basis of the BMI cutoffs established for the elderly (18.5-21.9 kg/m² and 22-26.9 kg/m², respectively) [24]. Individuals were excluded if they showed clinical signs of hydration imbalance, had ongoing acute illness, or had pacemakers or metal implants.

The sample consisted of 41 institutionalized elderly men aged 65-96 y; 18 (43.9%) with dementia according to DSM IV criteria [25] (dementia group, DG), and 23 (56.1%) without dementia (control group, CG). All men with dementia were in moderately severe to very severe stages, corresponding to stages 5 to 7 on the Global Deterioration Scale (GDS) [25], and the subtypes of dementia were AD, VD and MD (Alzheimer's disease and cerebrovascular disease). The CG consisted of institutionalized men without dementia, matched for age, BMI and comorbidities.

Anthropometric and recumbent hand-to-food bioelectrical impedance measurements were performed by the same trained person, first thing in the morning, following an overnight fast. This study was conducted in accordance with the Declaration of Helsinki and all procedures involving human participants were approved by the Ethics Committee of the Residential Care Centre San Juan de Dios on April 2010. Written informed consent was obtained from the legal guardians of all subjects included in the study.

Anthropometry

Anthropometric measurements were performed according to the protocol of the Spanish Society for Parenteral and Enteral Nutrition (SENPE) and the Spanish Society of Geriatric Medicine and Gerontology (SEGG) [24]. Body weight (W, kg) was measured to the nearest 100 g, using a SECA 954 chair scale with the subject in underwear; and height (H, m) was estimated from a knee height measurement using the equation of Chumlea et al. [27].

Waist and calf circumferences were measured with a flexible, inelastic measuring tape (to the nearest 1 cm).

Body composition analysis

Bioimpedance measurements

Whole body impedance measurements were made using a standard protocol [28]. A 50 kHz, tetra-polar, phase-sensitive BIA (BIA-101; AKERN-Srl, Florence, Italy) introduced a sinusoidal, alternating current of 400 μ A RMS to measure R, Xc and PA. Measurement errors of the system, determined with a precision resistor and capacitor, were <1% for R and <2% for capacitance.

BIA

The amount of fat-free mass (FFM, kg) was estimated with the prediction equation for BIA in adults aged 20-94 y [29]. Previous studies that we have performed evidenced that this equation was accurate in our sample of elderly individuals [14]. Fat mass and fat-free mass indices (FFMI and FMI, respectively) were calculated as $FMI (kg/m^2) = FM/H^2$, and $FFMI (kg/m^2) = FFM/H^2$. These indices were used to compare the BC data obtained in this study with the reference BC data for Caucasians [30].

BIVA

In this study, the reference bivariate tolerance ellipses (50, 75 and 95% of the distribution of the values in general population) for the adult and elderly men [31] were used for the qualitative and semi-quantitative assessment of BC and hydration status in each individual subject. The 95% confidence ellipses for mean vectors of the DG and the CG were drawn to compare these groups.

Statistical Analysis

Statistical analysis was carried out using the SPSS® version 18.0 (SPSS, Chicago, IL, USA). All data are presented as mean (95 % CI). The normality of the distribution of the variables was checked by the Shapiro-Wilk test and the homogeneity of variances by Levene's test. T-tests were used for pair-wise comparisons. The level of significance was set at $p < 0.05$.

In BIVA analysis, statistically significant differences between the mean vectors were determined with the Hotelling's T^2 test for vector analysis, which is a multivariate extension of the Student's test for unpaired data in comparison of mean vectors from two groups. Two mean vectors have a significantly different ($p < 0.05$) position in the RXc graph if their 95% confidence ellipses are separated according to Hotelling's T^2 test [32]. Overlapping ellipses are not a significantly different ($p > 0.05$).

RESULTS

The DG consisted of 18 men aged 74.4 y (range: 65-92 y), whose mean BMI was 22.5 kg/m² (95% CI: 20.7-24.2 kg/m²). In the CG (n=23), the mean age was 75.7 years (range: 66-96 y) and the mean BMI was 23.6 kg/m² (95% CI: 22.7 - 24.4 kg/m²). Age and BMI between the groups were not significantly different. Anthropometric measurements also were similar between the groups, except in the calf circumference (CC), which was significantly higher in the CG (Table 1).

Table 2 shows the differences in the BIA measurements and estimated body composition variables between the groups. The DG had significantly lower values of Xc, Xc/H and PA with no significant differences in R and R/H compared to CG. The impedance-

predicted relative measures of fat mass and fat-free mass (FM%, FFM%, FMI and FFMI) and FFMI were similar between the groups.

The mean impedance vectors and 95% confidence ellipses were significantly different ($T^2=15.1$, $p<0.01$) between the two groups (Figure 1). The ellipse of the DG was shifted downward.

The position of the individual vectors of all of men was to the right of the major axis of the reference population (Figure 2). The individual vectors of men in the DG group were in the lower right quadrant and most of those for the CG (60.8%) in the upper right quadrant. Furthermore, 66.7% of the vectors of the men included in the DG and 56.5% of the included in CG fell outside the 75% tolerance ellipse.

DISCUSSION

Several epidemiological studies have reported an association between high levels of adiposity in adulthood and an increased risk of developing both AD and VD in old age [1, 2]. Thus, we hypothesized that individuals in the DC would have a higher FM than those in the CG. However, the findings of the present study did not support this hypothesis. The BIA predictions of FM or FFM found no differences between the groups. However, use of BIVA identified a significant depletion in body cell mass (BCM) in the DG compared to the CG group.

Body compartment volumes were not estimated from the anthropometric parameters because this method has been found to have a low level of accuracy in populations aged > 60 years [33, 34]. Nevertheless, some specific anthropometric measurements, such as WC and CC, deserve special attention in the elderly because of their correlation with fat and muscle mass, respectively. In this regard, no significant differences were found between the groups in

WC, but the CC was significantly lower in the DG (Table 1), which may suggest a higher level of muscle-related disability in these individuals [35].

With regard to the conventional BIA, contrary to expectations, we found no significant differences in the mean values of the relative FM and FFM measures (i.e., percentages and indexes) estimated through predictive equations (Table 2). According to the reference percentiles in Caucasians [30], the mean values of the FMI were around the 50th percentile (6.4 kg/m^2) in both groups, while the mean values of the FFMI were around the 5th percentile (16.6 kg/m^2) (Table 2). This could be consequence of the shortcomings of using conventional BIA in the elderly, mainly because of assumptions of a constant composition of the fat-free body (e.g., hydration of the FFM and constant protein to bone ratio).

When using the confidence ellipses (BIVA) to compare the groups, the mean value of the PA was found to be lower in the DG (Figure 1). It must be emphasized that this was due to a smaller X_c/H component with a comparable R/H (Table 2). In this context it should be pointed out that X_c and X_c/H for the DG were a 20.4% and a 21% lower than for the CG, respectively. In contrast, insignificant percentages changes in R and R/H (5.5% and 4.4%, respectively) were found between both groups. Given that X_c is directly related to the amount of soft tissue structures, and that R is inversely related to the ICW and ECW, this findings clearly indicates an alteration in BCM with a comparable amount of total body water (TBW) in the groups, as can be observed in Figure 1. Our findings are in agreement with previous studies performed with BIVA, in which patterns in patients with AD were also characterized by a reduction in X_c/H values with preserved R/H [36,37].

The results obtained through the two methods of BC analysis (BIVA and BIA) are not incompatible; actually we are referring to two different levels of BC analysis: the cellular and molecular models. Through the BIA approach, we employed a predictive equation of FFM (kg), and the FM (kg) was calculated as body mass (in kg) minus FFM (kg). Hence, we

analyzed the BC on the basis of the two-compartment model, and therefore at the molecular level [38]. In contrast, the R-Xc graphs (i.e., BIVA) allow a semi-quantitative assessment of the hydration status and the BCM of an individual. Considering BCM, we are actually analysing the BC at the cellular level on the basis of the four compartment model, in which the BM is the sum of the FM, BCM, extra-cellular fluids and extra-cellular solids [38]. The BCM comprises the cellular components of muscles and viscera, including the ICW but not the stored fat lipids within them. Therefore, the BCM can also be defined as the FFM minus the extra-cellular mass (i.e., the bone mineral, and ECW), and consequently, a depleted level of BCM in the DG with respect to the CG is plausible even without significant differences in FFM between the groups.

These findings suggest, in turn, a change in the FFM composition in the DG with respect to the CG, characterized by a relative increase in ECW with respect to ICW that can be interpreted as a low number of cells per unit volume [36], which in turn could be compatible with an higher loss of skeletal muscle mass (SMM) since the decrease in SMM has shown to be greater than that of the non-muscle lean (organ) mass in older-adults [39, 40]. Figure 1 clearly indicates a BCM (and not FFM) depletion and a higher ECW/ICW ratio in the DG, considering that 1) a high R is correlated to small amounts of FFM; 2) for the same body mass, a low Xc indicates a decrease in the amount of BCM; and 3) a decrease in PA may be due both to a worsening in the hydration of the FFM and a decrease in the amount of the BCM relative to the amount of the FFM. An increase in the ECW/ICW ratio is expected as a result of the decrease in BCM, which, in turn, may be attributed to protein-energy malnutrition [41], fast weight loss [42], or catabolic stress [43], as well as to elevated adiposity levels [44-46]. It has been suggested that under these circumstances, the assessment of BCM is especially important, since its depletion (as well as that of the skeletal muscle

mass -SMM-) may be masked by normal values of FFM [47], as was observed in our sample comparing the DG with the CG.

On the other hand, it is necessary to note that over half of the individual impedance vectors (66.7% of the vectors of the DG and 56.5% of the vectors of the CG) fell outside the 75% tolerance ellipse (Figure 2), indicating abnormal tissue impedance in these subjects [31]. This condition may contribute to large prediction errors in estimating the volumes of body compartments through the conventional BIA approach. In fact, Vilaça et al. recently found that the agreement between BIA and DXA was less strong when applied in undernourished elderly subjects [48]. Further, this might explain the discrepancies found in previous studies focused on dementia-related changes in BC using BIA [49, 50].

Finally, as we said above, BIVA allows a semi-quantitative assessment of BC, and hence we cannot check the accuracy of the predictive equations based on BIA in our sample. Nevertheless, the assumed bias is the same in both groups and, independently of the accuracy of the predictions of FM and FFM, the BIVA patterns are consistent with the results showed by the conventional BIA approach.

The main limitation of this study are the sample size. However, the selection criteria established were strict in order to control all the potential confounding variables. Specifically, the main determinants of BC (ethnicity, sex, age and degree of mobility) were controlled in the study design (data not shown). The BMI was also considered in the study design, since it is necessary for the correct interpretation of both the vector distribution patterns and the FMI and FFMI. All this ensures the comparability between the two study groups.

CONCLUSION

Conventional BIA showed no significant differences in BC between DG and CG, even though X_c and X_c/H were about 21% lower in DG with respect to CG. BCM depletion and an

increase in ECW/ICW-ratio were evidenced in DG using BIVA. BIVA reflects the dementia-related changes in BC better than BIA.

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CONFLICT OF INTEREST

Authors declare not having any financial conflict of interest.

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TABLES

| Table 1. Descriptive statistics of the anthropometric measurements | | |
|---|---------------------|-------------------------|
| | Demented men (n=18) | Non-demented men (n=23) |
| Weight (kg) | 60.7 (54.6 - 66.7) | 64.1 (60.8 - 67.4) |
| Height (m) | 1.64 (1.57 - 1.71) | 1.65 (1.62 - 1.68) |
| BMI (kg/m ²) | 22.5 (20.7 - 24.2) | 23.6 (22.7 - 24.4) |
| Waist circumference (cm) | 90.1 (85.6 - 94.5) | 93.2 (89.9 - 96.5) |
| Calf circumference (cm) | 34.0 (30.7 - 37.3)* | 36.0 (34.6 - 37.2) |
| Results are expressed as mean (95% CI). *p<0.05. | | |

Table 2. Bioelectrical and body composition variables

| | Demented men (n=18) | Non-demented men (n=23) |
|---------------------------|-----------------------|-------------------------|
| R (ohm) | 568.1 (530.2 - 605.9) | 601.0 (571.6 - 630.5) |
| Xc (ohm) | 38.9 (35.4 - 42.5)*** | 49.4 (45.8 - 53.1) |
| PA (degrees) | 4.0 (3.6 - 4.3)** | 4.7 (4.3 - 5.1) |
| R/H (ohm/m) | 349.6 (323.5 - 375.6) | 365.8 (345.9 - 385.8) |
| Xc/H (ohm/m) | 23.9 (21.7 - 26.2)*** | 30.1 (27.7 - 32.5) |
| FM (kg) | 15.8 (13.6 - 18.0)* | 19.0 (17.0 - 21.1) |
| FM (%) | 26.4 (23.6 - 29.2) | 29.4 (27.1 - 31.6) |
| FMI (kg/m ²) | 6.0 (5.2 - 6.8) | 7.0 (6.3 - 7.7) |
| FFM (kg) | 43.7 (40.9 - 46.6) | 45.1 (43.0 - 47.2) |
| FFM (%) | 73.6 (70.8 - 76.4) | 70.7 (68.4 - 72.9) |
| FFMI (kg/m ²) | 16.4 (15.7 - 17.1) | 16.6 (16.1 - 17.1) |

R, resistance (Ω); Xc, reactance (Ω); R/H, reactance standardized by height (Ω/m); Xc/H, reactance standardized by height (Ω/m); FM, fat mass; FMI, fat mass index; FFM, fat-free mass; FFMI, fat-free mass index (kg/m²).

Results are expressed as mean (95 % CI).

*p<0.05, **p<0.01, *** p<0.001.

Figure 1. Mean impedance vectors and confidence ellipses for men with dementia (n=18) and without dementia (n=23).

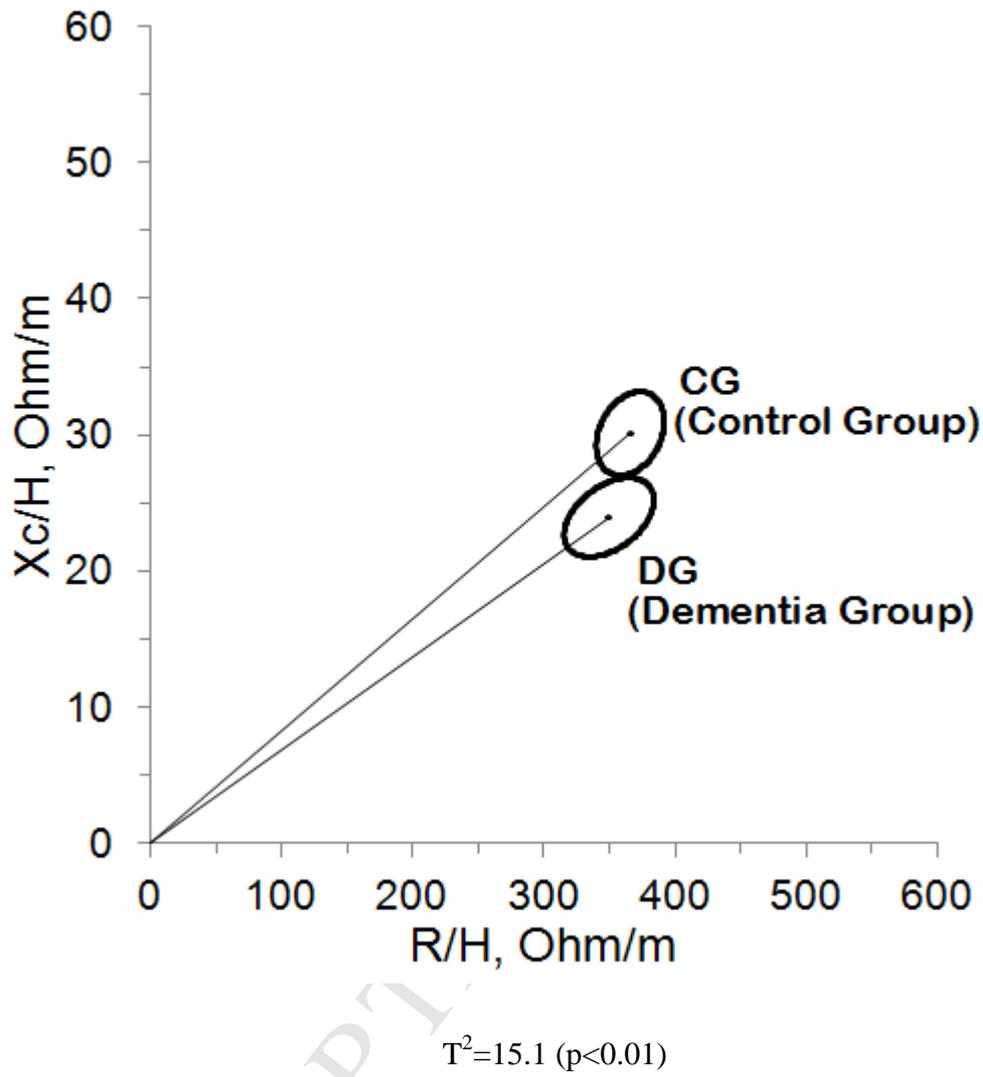
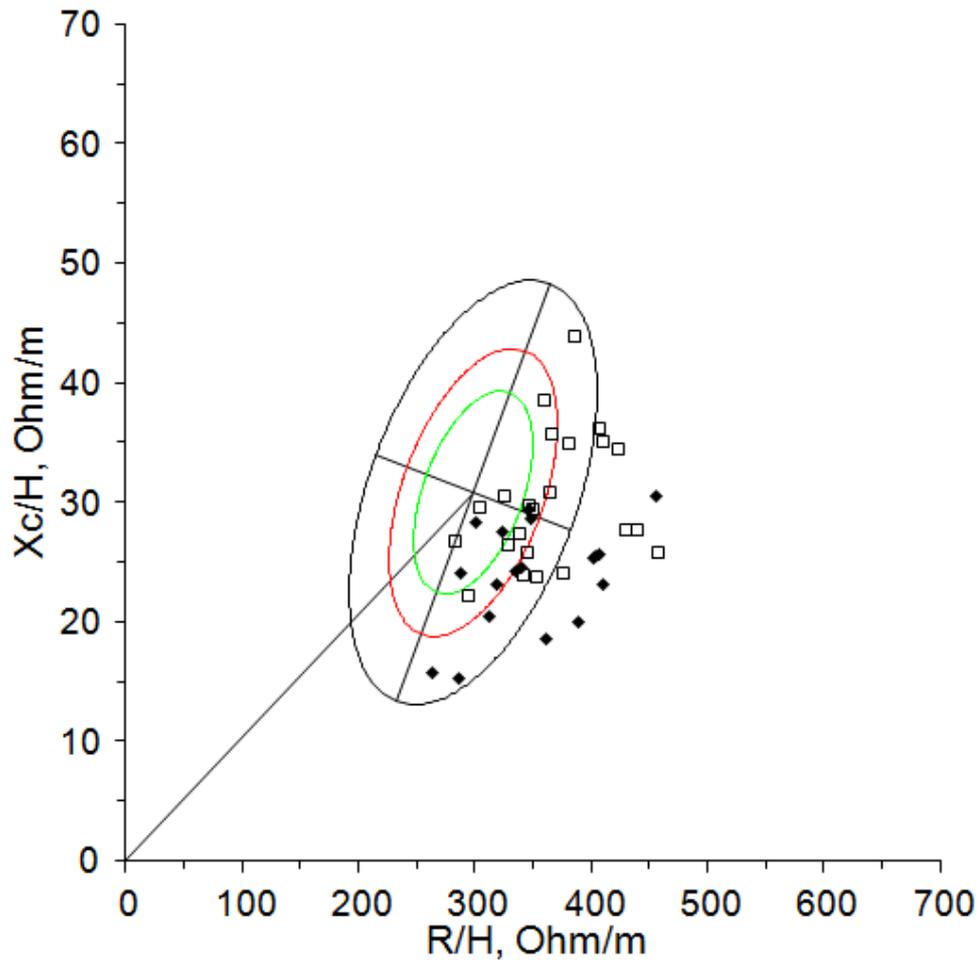


Figure 2. Individual impedance vectors from men with dementia (n=18) and without dementia (n=23).



Dementia Group (DG), dark points; Control Group (CG), white points.

HIGHLIGHTS

Dementia-related changes in body composition are detected with bioimpedance vector analysis but not with conventional bioimpedance analysis

Dementia-related changes in body composition were identified despite the absence of differences in anthropometrics with respect a comparable group of patients without dementia

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