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Lower lean mass and higher percent fat mass in patients with Alzheimer's disease

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ABSTRACT

In this study we analyzed body composition in relation to cognitive and functional status, in a cross-sectional sample of patients with Alzheimer's disease (AD).
Seventy individuals (27 men, 78.1 ± 6.5 years; 43 women, 80.4 ± 5.6 years) with mild–moderate stages of AD (clinical dementia ratings 1 and 2) were selected from the Alzheimer Center, SS. Trinità Hospital, ASL 8 of Cagliari (Italy). Cognitive and psycho-functional status was evaluated using mini-mental state examination (MMSE), activities of daily living (ADL) scale, and geriatric depression scale (GDS). Mini-nutritional assessment (MNA) was applied. Anthropometric measurements were taken and body mass index (BMI) was calculated. Body composition was assessed by means of *specific* bioelectrical impedance vector analysis (BIVA), using the references for the elderly. In comparison with the reference group, patients with AD showed similar BMI and MNA, but peculiar bioelectrical characteristics: lower phase angles and longer vectors ($p < 0.05$). According to *specific* BIVA, this bioelectrical pattern is indicative of a reduction of lean tissue mass and an increase of percent fat mass (FM%). A more accentuated lean mass reduction ($p < 0.05$) was observed in women with worse cognitive status and a FM% increase ($p < 0.01$) in women with worse functional status.
In conclusion, patients with AD had lower lean tissue mass and higher percent fat mass than healthy elderly individuals. In women, this pattern was associated with cognitive and functional decline, as indicated by MMSE and ADL values. *Specific* BIVA showed to be a suitable technique in the elderly, that could enhance BMI and MNA information in the evaluation of nutritional status.

1. Introduction

Epidemiological studies show that body composition variations are linked to both the onset and the progression of Alzheimer's disease (AD). The nature of the relationship and the underlying causal factors are not completely defined because of the phenomenological complexity of the disease, the age-related body composition variations, and the risk factor changes across the life course.

According to some authors, high levels of fat mass during mid-life are associated with late-onset AD (Luchsinger and Gustafson, 2009). However, weight loss is a typical feature of the disease, and is associated with disease severity and faster clinical progression, and can appear before the recognition of clinical symptoms of AD (Gillette-Guyonnet et al., 2000). Various causal factors, such as anorexia or neuropsychiatric disturbances, metabolic alterations, and medial temporal cortex atrophy, have been proposed for weight loss (Gillette-Guyonnet et al., 2000). On the other hand, undernutrition itself could accelerate cognitive and functional decline, via the reduction of leptin levels, due to the reduced fat mass (Soto et al., 2012), or via sarcopenia and frailty, due to the reduced lean mass (Lee, 2011).

The comprehension of such relationships requires an accurate definition of body composition variations. However, most researches use indirect techniques, such as anthropometry. Body mass index (BMI) is an anthropometric indicator of undernutrition, overweight and obesity, largely used in epidemiologic studies. However, it is sensitive to both muscular and fat mass and may be unable to disentangle their relative contribution. This limit is particularly relevant in the elderly, where frailty, sarcopenia or sarcopenic obesity syndromes are linked to body composition variations, in which the physiological decline of lean mass can be associated to an increase of fat mass, without weight changes.

Specific bioelectrical impedance vector analysis (BIVA *sp*) is a recently validated technique for assessing body composition (Buffa et al., 2013; Marini et al., 2013). It is accurate, safe, time-saving and cost-effective, and hence represents a promising tool both in routine clinical practice and in epidemiologic studies.

Abbreviations: R, resistance; Xc, reactance; Z, impedance; R*sp*, *specific* resistance; Xc*sp*, *specific* reactance; Z*sp*, *specific* impedance; BIVA, bioelectrical impedance vector analysis; FM, fat mass; DXA, dual-energy X-ray absorptiometry; MMSE, mini-mental state examination; ADL, activities of daily living; GDS, geriatric depression scale; MNA, mini-nutritional assessment; ICW, intracellular water; ECW, extracellular water.

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The aim of this study was to analyze the body composition characteristics of elderly patients with mild to moderate Alzheimer's disease in relation to their cognitive and functional status, using *specific* BIVA.

2. Subjects and methods

2.1. Subjects

The study group consisted of 70 individuals (27 men and 43 women) with mild–moderate stages of Alzheimer's disease (CDR 1 and 2), selected from the Alzheimer Center, SS. Trinità Hospital, ASL 8 of Cagliari (Italy). The mean age was 78.1 ± 6.5 years for men and 80.4 ± 5.6 years for women.

The Alzheimer's disease was diagnosed according to the NINCDS-ADRDA criteria (National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association) and the stage of dementia was assessed by the CDR scale (clinical dementia rating).

All patients had been treated with the AchE-inhibitor donepezil (5 to 10 mg per day). The mean length of therapy was 4.4 (±2.2) years in men and 4.6 (±1.8) years in women.

In accordance with the Helsinki Declaration of 1975, as revised in 2013, all patients or their tutors were informed about the research protocol and they consented to take part in the study. Exclusion criteria were: a) physical handicaps; b) uncompensated chronic diseases (uncontrolled tumoral pathology, III–IV class cardiac decompensation, chronic gastrointestinal disease, renal or hepatic insufficiency); c) nutritional support.

The reference population consisted of 560 healthy individuals (265 men and 295 women) aged 65 to 100 years (women: 76.0 ± 7.1 years; men: 77.0 ± 7.2 years), all born in Italy and recruited on a voluntary basis. The *specific* bioelectrical characteristics of the reference, and their interpretation, have been described elsewhere (Saragat et al., 2014). Detailed information on cognitive (based on mini-mental state examination, MMSE), psychological (geriatric depression scale, GDS), functional (activities of daily living, ADL) and nutritional (mini-nutritional assessment, MNA) status is available for a sub-sample of the reference population (collectively, 130 men and 120 women) (Buffa et al., 2010a; Saragat et al., 2012). This sub-sample shows, in average, a normal functional (ADL; men: 5.3 ± 0.5; women: 5.8 ± 0.6), psychological (GDS; men: 2.4 ± 1.9; women: 3.6 ± 3.3), and nutritional status (near the threshold for malnutrition risk, in women) (MNA; men: 25.5 ± 2.6; women: 24.2 ± 2.8), and a quite normal cognitive condition (MMSE; men: 25.3 ± 2.8; women: 23.0 ± 4.1).

2.2. Measurements

The cognitive and psycho-functional status was assessed at the moment of the survey, using mini-mental state examination (Folstein et al., 1975), activities of daily living scale (Katz et al., 1963), and 15 item geriatric depression scale (Sheikh and Yesavage, 1986). The mini-nutritional assessment (Guigoz et al., 1994) was applied. Anthropometric (stature, weight, upper arm, waist, and calf circumferences) and bioelectrical impedance measurements (50 kHz and 0.8 A, with a single-frequency impedance analyzer; BIA 101, Akern, Firenze, Italy) were taken according to standard procedures by a single experienced operator (RB).

2.3. Statistical analyses

According to the procedure described by Marini et al. (2013) and by Buffa et al. (2013), the *specific* bioelectrical impedance vector analysis was applied. The method has been recently proposed as an extension of the classic BIVA, conceived by Piccoli et al. (1994), and its efficacy has been verified by comparison with dual-energy X-ray absorptiometry (DXA).

In order to eliminate the effect of "conductor" length (L) and cross-sectional area (A) on bioelectrical values, R and Xc are multiplied by a correction factor A/L (in meters), where A (m^2) = 0.45 arm area + 0.10 waist area + 0.45 calf area, and L (m) = 1.1 height. Cross-sectional areas are estimated as $C^2/4\pi$ (m^2), where C (m) refers to segmental circumference. *Specific* bioelectrical values, rescaled multiplying by 100 (resistivity, R*sp*, and reactivity, Xc*sp*, Ohm·cm), can be analyzed with the same statistical procedure of classic BIVA. The phase angle (degrees) is calculated as arctan (Xc/R); the impedivity vector (Z*sp*) as $(Rsp^2 + Xcsp^2)^{0.5}$.

The major axis of *specific* tolerance ellipses refers to bioelectrical variations associated with changes of the relative quantity of fat mass (individuals with a higher FM% toward the upper pole). The minor axis refers to changes of the lean tissue mass (left side: more lean mass; right side: less lean mass) and of extracellular/intracellular water ratio (ECW/ICW; with higher values on the right side).

Anthropometric and bioelectric variables of patients were compared with the reference by means of two-way ANOVA, considering sex and health status effects.

For each psycho-functional variable, and for length of therapy, the sample of patients with AD was divided into two groups (below and above the median) and bioelectrical and anthropometric variables were compared by means of the Student t-test. The difference between the mean *specific* impedance vectors was assessed by means of Hotelling's T^2 test.

Statistical analysis was performed by means of Systat package (13.1) and of the newly-assembled *specific* BIVA software (open access version under a Creative Commons Attribution-NonCommercial-ShareAlike License, on the website http://specificbiva.unica.it/).

3. Results

Patients with Alzheimer's disease showed mild-to-moderate cognitive impairment (MMSE, men: 19.4 ± 5.6; women: 19.0 ± 4.9), and psychological (GDS, men: 3.3 ± 2.9; women: 4.2 ± 3.5) and functional declines (ADL, men: 4.3 ± 1.3; women: 3.7 ± 1.6). MNA mean value was equal to 25.5 (±3.1) in men (81.5% of well-nourished individuals) and to 24.3 (±4.1) in women (64.4% of well-nourished individuals), almost the same levels as the reference.

A significant sexual dimorphism was observed for height, weight, and bioelectrical variables, with higher phase angle and lower *specific* resistance and impedance in men (Table 1).

In comparison with the Italian reference sample, patients of both sexes showed lower height and weight values, but a similar BMI (Table 1). Bioelectrical vectors of patients (both sexes) were characterized by low phase angles and high *specific* impedance values, and were almost entirely (95.7%) located on the right side of the *specific* tolerance ellipses of the Italian elderly (Saragat et al., 2014) (Table 1).

In women, bioelectrical characteristics changed according to cognitive and functional status, but not to the GDS scale of depression. Women with worse conditions, i.e. with MMSE and ADL values below the median, showed lower phase ($p = 0.010$) and higher *specific* vector length ($p = 0.024$), respectively (Fig. 1). These bioelectrical characteristics can be related to a low fat mass and high ECW/ICW (as indicated by the lower phase), and high FM% (as indicated by the longer vector). BMI values were higher in the groups with worse cognitive and functional status, significantly in the case of ADL ($p = 0.002$). In men the pattern was similar but the differences were not significant.

MNA values were not significantly different in patients with different cognitive and functional statuses.

In both sexes, no bioelectrical difference was observed between patients with a different length of therapy ($T^2 = 3.5$; $p = 0.202$).

4. Discussion

In this study, patients with mild to moderate stage Alzheimer's disease had lower body weight, different body compositions, but similar BMI and MNA, with respect to the reference. According to *specific*