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Phase angle as bioelectrical marker to identify elderly patients at risk of sarcopenia

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SUMMARY

Several markers have been associated with sarcopenia in the elderly, including bioelectrical indices. Phase angle (PhA) is an impedance parameter and it has been suggested as an indicator of cellular death. Thus, the relationship between PhA and muscle mass and strength was investigated in 207 consecutively elderly participants (mean age 76.2 ± 6.7 years) admitted for multidimensional geriatric evaluation. Muscle strength by grip strength using a hand-held dynamometer and muscle mass was measured by bioimpedentiometer. PhA was calculated directly with its arctangent (resistance / reactance × 180° / π). Linear relationship among muscular mass and strength and with clinical and biochemical parameters, including PhA at uni- and multivariate analysis were performed. Linear regression analysis demonstrated that lower level of PhA is associated with reduction in grip strength ($y = 3.16 + 0.08x$; $r = 0.49$; $p < 0.001$), and even more, with muscle mass ($y = 3.04 + 0.25x$; $r = 0.60$; $p < 0001$). Multivariate analysis confirms these relationships (grip strength $\beta = 0.245$, $p = 0.031$; muscular mass $\beta = 0.623$, $p < 0.01$). Thus, PhA is inversely related to muscle mass and strength in elderly subjects and it may be considered a good bioelectrical marker to identify elderly patients at risk of sarcopenia.

1. Introduction

Age-related loss of muscle mass and strength defines the "sarcopenia" (Baumgartner et al., 1988; Iannuzzi-Sucich et al., 2002). Sarcopenia is responsible for the increase in morbidity (Taekema et al., 2010) and mortality (Metter et al., 2002) in the elderly, particularly in institutionalized elderly nursing home residents (Landi et al., 2012). Etiology and pathogenesis of sarcopenia are very intricate and involve several factors including physical inactivity, hormonal, metabolic, nutritional and inflammatory state (Beenakker et al., 2010; Krabbe et al., 2004).

The suggested techniques for the assessment of sarcopenia are body-imaging techniques as computed tomography, magnetic resonance imaging (MRI) and dual energy X-ray absorptiometry (DXA) (Cesari et al., 2012; Cruz-Jentoft et al., 2010). However, bioelectrical impedance vector analysis (BIVA) is an interesting alternative approach and it is demonstratively sensitive to muscle strength variations (Norman et al., 2012). In particular, the most clinically established impedance parameter is the phase angle (PhA) considered highly predictive of impaired clinical outcome and mortality in several diseases (Norman et al., 2012). PhA expresses both the amount and quality of soft tissue and can be calculated directly as its arc tangent (resistance / reactance × 180° / π) (Norman et al., 2012). More specifically, PhA in ranges between 5° and 7° indicates higher cellularity cell membrane integrity (Bosy-Westphal et al., 2006). At muscular level, PhA definitely correlates with grip and with knee extension strength (Norman et al., 2012).

Thus, in the present study we aimed to investigate the relationship between muscle mass and strength and PhA in elderly patients who underwent multidimensional geriatric evaluation, including several clinical and biochemical parameters.

2. Methods

2.1. Study population

Two-hundred-seven elderly consecutive patients (≥65 years) admitted to Azienda Ospedaliera Universitaria Federico II (Naples, Italy) were enrolled. The study received full ethical approval from the "Research Ethics Committee". All participants signed an informed

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consent form, and the institutional review boards of all participating institutions approved the study. Anthropometric measurements including age, sex, Body Mass Index (BMI) and waist circumference (WC) were taken. Subjects with moderate-severe hepatic disease were not enrolled.

2.2. Multidimensional geriatric evaluation

Patients underwent a comprehensive geriatric multidimensional evaluation which included: cognitive function evaluation with Mini Mental State Examination (Cacciatore et al., 1997); depressive symptoms with Geriatric Depression Scale; comorbility and comorbility severity with Cumulative Illness Rating Scale (CIRS-comorbility and CIRS-severity) and drug number; disability with Basic and Instrumental Activity of Daily Living (BADL and IADL); nutritional assessment by Mini-Nutritional Assessment (MNA); equilibrium and risk of fall with Tinetti Scale; physical performance with 4-meter gait speed (m/s); physical activity with Physical Activity Scale for the Elderly (PASE); social support evaluation with Social Support Assessment scored from 4 (subjects with the lowest support) to 1 (subjects with the highest support) (SSA) (Mazzella et al., 2010).

2.3. Assessment of muscle mass, phase angle (PhA) and muscle strength

Muscle mass was measured by bioimpedentiometer (BIA) using a Quantum/S Bioelectrical Body Composition Analyzer (Akern Srl, Florence, Italy). Whole-body BIA measurements were taken between the right wrist and ankle with subject in a supine position. Muscle mass was calculated using the following BIA equation of Janssen et al. (2000): Skeletal muscle mass (kg) = ([height^2 / BIA resistance × 0.401] + [gender × 3.825] + [age × −0.71]) + 5.102 where height is measured in centimeters; BIA resistance is measured in ohms; for gender, men = 1 and women = 0; age is measured in years. Absolute skeletal muscle mass (kg) was converted to skeletal muscle index standardizing by meters squared (kg/m^2) (Lauretani et al., 2003).

Resistance (R) and reactance (Xc), measured at 50 kHz, were used to calculate the PhA by the following equation: PhA (°) = arctangent (Xc / R) × (180 / π).

Muscle strength was assessed by grip strength, measured using a hand-held dynamometer (Mecmesin Advanced Force Gauge 500N, GDM, Italy).

2.4. Biochemical parameters

Hemoglobin (normal values: 11.0–16.0 g/dL), lymphocytes (normal values: 1.0–4.8 × 10^3), albumin (normal values: 3.6–5.2 g/dL), total iron binding capacity (TIBC, normal values: 218–411 μg/dL), C-reactive protein (CRP, normal values <10 mg/L), and butyryl-cholinesterase (b-CHE, normal values: 5.400–13.200 U/L), were routinely obtained.

2.5. Statistical analysis

Continuous variables are expressed as mean ± SD. Univariate regression analysis was used to test a correlation between muscle mass and strength with PhA and other variables such as age, female sex, BMI, WC, MMSE, GDS, CIRS-comorbility, CIRS-severity, drug number, BADL, IADL MNA, Tinetti, 4-m walking speed, PASE, social support score, albumin, TIBC, lymphocytes, hemoglobin, and CRP. Statistically significant variables were included into multivariate regression model as potential confounders. All statistical analysis was performed with SPSS software (version 15.0, SPSS Inc., Chicago, IL). A value of P less than 0.05 was considered statistically significant.

3. Results

Two-hundred-seven elderly subjects with mean age 76.2 ± 6.7 years (median 75, range 65–100) were enrolled (54.1% female sex). Anthropometric, geriatric multidimensional evaluation, comorbidities and drug consumption are shown in Table 1. CIRS-comorbility and severity scores were 4.47 ± 2.09 and 1.94 ± 0.45, respectively. Mean drug consumption was 3.0 ± 1.0, MMSE score was 22.4 ± 6.0 and GDS score was 7.6 ± 4.3. Functional parameters include BADL (1.7 ± 1.8) and IADL lost (3.7 ± 2.7), 4-m walking speed (0.79 ± 0.27 m/s), and PASE score (56.1 ± 65.2). Mean values of albumin, hemoglobin, lymphocytes count and TIBC were in normal range. Inflammatory indices as bCHE (7778.9 ± 2273.2 U/L) and CRP (0.78 ± 0.53 mg/dL) are shown in Table 1. Muscle (skeletal muscle mass and grip strength) and bioelectrical parameters (resistance, reactance and angle phase) are shown. In particular, the mean value of phase angle is 5.1 ± 1.

Linear regression analysis demonstrates that several variables were "positively" correlated including age, female sex, 4-m walking speed, PASE, hemoglobin, b-CHE and phase angle. In contrast, PCR were "negatively" correlated with grip strength (Table 2). The positive linear relationship between phase angle and grip strength is shown in Fig. 1A ($y = 3.16 + 0.08x$; $r = 0.49$; $p < 0.001$). All linear relationship was confirmed at multivariate analysis, except for PASE and PCR. Also when analyzing the skeletal muscle mass (Table 2), linear regression analysis demonstrates that several variables including female sex, BMI, WC, MNA, CIRS-severity, 4-m walking speed, grip strength, PASE, b-CHE and phase angle were "positively" correlated. In contrast, age

Table 1
Baseline characteristics of the 207 patients enrolled in the study.

Characteristics	All n = 207
Antrophometric	
Age (years ± SD)	76.2 ± 6.7
Female sex, n (%)	112 (54.1%)
BMI (kg/m^2)	26.0 ± 4.3
Waist circumference (cm)	99.7 ± 13.5
Geriatric evaluation	
MMSE (score)	22.4 ± 6.0
GDS (score)	7.6 ± 4.3
CIRS-comorbility (score)	4.47 ± 2.09
CIRS-severity (score)	1.94 ± 0.45
Drug number (n)	3.0 ± 1.0
BADL (score)	1.7 ± 1.8
IADL (score)	3.7 ± 2.7
MNA (score)	21.2 ± 4.4
Tinetti (score)	18.7 ± 7.1
4-m walking speed (m/s)	0.79 ± 0.27
PASE (score)	56.1 ± 65.2
Social support (score)	8.2 ± 2.6
Muscle	
Skeletal muscle mass (kg/m^2)	8.8 ± 1.6
Grip strength (kg)	29.5 ± 8.5
Biochemical	
Albumin (g/dL)	3.9 ± 0.5
TIBC (μg/dL)	275.8 ± 99.9
Hemoglobin (g/dL)	12.5 ± 1.9
Lymphocytes (×10^3)	2.1 ± 1.7
CRP (mg/dL)	0.78 ± 0.53
b-CHE (U/L)	7778.9 ± 2273.2
Biolectrical	
Resistance (ohm)	345 ± 33
Reactance (ohm)	29.7 ± 6.4
Angle phase	5.1 ± 1.3

Legend: BMI = Body Mass Index; BADL = Basic Activity of Daily Living; IADL = Instrumental Activity of Daily Living; MNA = Mini Nutritional Assessment; CIRS = Cumulative Index Rating Scale; MMSE = Mini-Mental State Examination; GDS = Geriatric Depression Scale; PASE = Physical Activity Scale for the Elderly; TIBC = total iron binding capacity; CRP = C-reactive protein; b-CHE = butyryl-cholinesterase.