

Cross-sectional study on the relation between the Phase Angle and the Musculoskeletal Mass: Discriminating phenotypes of body composition addressed to precision nutrition.

Fernando Rojo⁽¹⁾, Ramón de Cangas⁽¹⁾, Guillermo Nicieza⁽²⁾, David Zamarreño⁽³⁾.

1. Dpto. de Investigación en Nutrición de Precisión. Centro Salud Nutricional. Gijón (Asturias). 2. Hospital Universitario Central de Asturias (HUCA)-Fundación Hospital del Jove. Gijón (Asturias). 3. Dpto. Urgencias. Hospital de Cabueñes. Gijón (Asturias).

Summary:

The precision nutrition integrates genotypic and phenotypic information in order to implement personalized nutrition. The segmental octopolar multifrequency BIA (Bioelectric impedance analysis) has been validated against a 3C model (DXA) [Dual-energy X-ray absorptiometry] to estimate the Skeletal-Muscle-Mass (SMM). The phase angle (ϕ) is an indicator of the integrity of the cell membranes and water distribution between extra and intracellular compartments and; it has been related to the prognosis of certain clinical outcomes.

The goal is to evaluate the values of ϕ and the SMM ($\bar{x} \pm SD$) in a sample of patients and their possible association, magnitude and direction.

Cross-sectional study on a sample (n = 83 subjects: 56 women and 27 men) aged 19-79 years and (Body mass index) the BMI = 28.18 ± 4.76 Kg / m². ϕ (50 kHz) and SMM were recorded using InBody 770. The non-parametric Spearman Rho relation test was applied.

An average value of $\phi = 5.65 \pm 0.74$ was found (men = 6.37 ± 0.61 , women = 5.3 ± 0.51) and SMM = 27.61 ± 6.18 Kg (men = 34.99 ± 4.19 , women = 24.06 ± 3.01). The Rho = 0.628 (p = 0.00), suggests the existence of an association, not necessarily linear, moderate-strong, positive, between ϕ and SMM, in both genders. The phase angle is able to discriminate subjects according to gender and quantity of SMM, so it stands as a useful parameter to monitor the SMM.

Introduction

The precision nutrition requires the compilation of genotypic and phenotypic information in order to implement a personalized dietary strategy (1).

The estimation of the body composition is a valuable tool to discriminate body biotypes, as it is an expression of nutritional status and the pattern of physical activity, two dynamic variables integrated in the exposome with the greatest impact on health and disease (2).

The body composition is a division of biological anthropology that studies the composition and relationship of the components of the human body, according to different methods (Magnetic Resonance Imaging -MRI-, Dual Energy X-ray Absorptiometry -DXA-, etc.) that differ at the level of analysis (atomic, molecular, cellular, tissue, organ, whole body) and model (2C, 3C ...) on which it stands.

Everything starts from a biophysical modeling of the human body, which assumes certain assumptions and the constancy of certain parameters a priori, to make the method viable (3).

The two most commonly used methods in clinical practice are dispersion and the Bioelectric Impedance Analysis (BIA).

The broad dispersion of the BIA, is that it is a fast, non-invasive method, that there are portable models, relatively affordable and which do not require qualified personnel

Keywords:

- Body composition
- Bioelectric Impedance Analysis (BIA)
- phase angle (ϕ)
- Skeletal Muscle Mass (SMM)

(at most the patient should be informed to respect a standardized protocol to ensure the quality of the measure) (4).

The BIA is based on the bioelectric properties of biological tissues, known since 1871 (5) and their involvement in certain pathophysiological alterations.

It is based on the application of a low intensity alternating current, at different frequencies, which penetrates through the inductor electrodes (in hands or feet), and which follows different paths through the organism according to the type of equipment and; which impedance is recorded in the distal electrodes (in hands or feet), when the biological membranes and tissue interfaces act as condensers, and the extracellular and intracellular medium as resistances.

There are different BIA devices that are classified according to the applied frequency (single frequency, SF-BIA, operating at 50 kHz and multi-frequency, MF-BIA-, which do so between 5-1000 kHz); the number of electrodes inducing alternating current and impedance sensors (tetrapolar -4- and octopolar -8-), the segment of the body through which current flows (hand-hand; foot-foot or whole body) and the electrode type (adhesive versus metallic).The BIA octopolar segmental multi frequency assumes that (5):

1-The Fat Free Mass (FFM) is a highly hydrated tissue, which contains electrolytes in solution, acting as a good

conductor of the current and its degree of constant hydration (H₂O = 73.2% FFM).

2-The Fatty Mass -FM- is a practically an anhydrous tissue, which hardly carries electrolytes and behaves as a bad conductor of the current.

3-The human body is integrated by five homogeneous cylinders, which cross-sectional area is constant and corresponds to the Lower Extremities (UL), trunk and Upper Extremities (LL).

4-The resistance of the tissues is constant.

5-The resistance (R) of a homogeneous conductive material with a constant cross-sectional area, is directly proportional to its length (L) and inversely proportional to its area (A): $R = \rho \times L / A$, where ρ It is the resistance of the conductive material. If we consider that the volume of a cylinder is $V = L \times A$, the previous expression is equivalent to $R = \rho \times L^2 / V$; $V = \rho \times L^2 / R$.

The biophysical principles, strengths and limitations of the BIA have been described extensively (5,6). The BIA records the impedance (Z), opposition that the whole body exerts to the passage of an alternating current at different frequencies and has two components:

-Resistance (R): it measures the opposition exerted by the electrolytic solutions of extracellular and Intracellular water (ECW) (ICW), where the total body water (TBW) = ECW + ICW.-Reactance (Xc):

It measures the opposition induced by biological tissues that act as capacitors, (Devices used to store electrical energy by accumulating charge on conductors situated close to each other, allowing energy storage and use in an electrical field) by virtue of their dielectric properties (biological membranes and interfaces).

Z, R and Xc are related by the following equation: $Z^2 = R^2 + Xc^2$.

E The BIA has been validated to estimate the total body water (TBW) ($TBW = \rho \times L / R$) versus the isotopic dilution (7). Therefore, it has been designed to measure TBW. The rest of the parameters related to body composition, returned by the BIA equipment are empirical estimates, based on prediction equations, which have as independent variables gender, age, weight, height and electrotechnical parameters (Z, R, Xc ...). Its main limitations are: the use in certain pathophysiological states in which the degree of hydration is not constant (E.g. obesity, elderly, athletes, etc.) and / or when there is an extravasation of fluid into the interstitial space (lymphoedema, ascites, etc. in cases of extreme obesity, liver cirrhosis, renal failure, heart failure).

The multi-frequency, octopolar, segmental BIA seems to overcome this obstacle against the SF-BIA, tetrapolar and full-body models. Anyway, it has been suggested to use the gross electrotechnical parameters (Z, R, Xc ...) instead of the values that the BIA returns because it is a prediction-dependent equation.

The phase angle (ϕ) = $\arctg(Xc / R) \times (180 \times \pi)$ describes the amount of reactance of a conductor related to the amount of resistance. An indicator of cellular health is considered to be associated with cellularity (Active Cellular Mass -BMC-), and plasma membrane integrity (composition and function) and cellular activity. This depends on gender (lower in women), age (it decreases with age) and BMI (it increases to values <30 and

decreases in morbid obesity -BMI> 40-). This due to the fact that it is directly proportional to the lean mass (LM), which main component is the Skeletal Muscle Mass (SMM). Women have less SMM than men because of their hormonal profile, about 1% / year of SMM is lost after the age of 40 and, in regard to obesity, the EBW / ICW ratio increases (8).

The ϕ is considered a biomarker of the nutritional status. In the clinical population, its usefulness has been described as a prognostic value as it has been correlated with HIV survival, different types of tumors; dialysis and hemodialysis; hepatic cirrhosis; surgery; ALS, heart failure and geriatric patients (8). The values of ϕ are directly proportional to the conditions of health. Values <4.5 are associated with a worse clinical prognosis and values > 10 are suggestive of overtraining.

The goal is to evaluate the values of ϕ and SMM ($\bar{x} \pm SD$) in a sample of patients and their possible association, magnitude and direction, and, compare them with the values found in the Spanish population.

Material and methods

Cross-sectional study on a sample (n = 83) of subjects (56 women and 27 men), 44 ± 14 years old and BMI = 28.18 ± 4.76 Kg / m² who come to the consultation of a Dietitian-Nutritionist (DN) with different objectives.

The patients signed an informed consent prior to data collection. Height was recorded using the SECA 220 stadiometer (Seca GmbH & Co. kg.); and weight, SMM and ϕ (50 kHz) with InBody 770 (InBody Ltd; Co. Seoul, Korea). The data of the ϕ and the SMM distributions did not verify the normal conditions: visual methods (histogram and QQ graph) and statistical test (Kolmogorov - Smirnov: ϕ : p = 0.039 and SMM: p = 0.000), so the Rho Spearman's test was applied.

Results

An average value of $\phi = 5.65 \pm 0.74^\circ$ was found (men = $6.37 \pm 0.61^\circ$, women = $5.3 \pm 0.51^\circ$) and SMM = 27.61 ± 6.18 Kg (men = 34.99 ± 4.19 , women = 24.06 ± 3.01). The Rho = 0.628 (p = 0.00), suggests the existence of an association, not necessarily linear, moderate-strong, positive, between ϕ and SMM, in both genders.

Parameter	Men	Women	Whole sample
n	27	56	83
Age (years-old)	38±11	47±14	44±14
BMI (kg/m ²)	27,3±4,51	28,61±4,86	28,18±4,76
ϕ (°) ($\bar{x} \pm SD$)	6,37±0,61	5,3±0,51	5,65±0,74
SMM (kg) ($\bar{x} \pm XD$)	34,99±4,19	24,06±3,01	27,61±6,18

n: Sample size; BMI: Body Mass Index; ϕ : Phase angle; SMM: Skeletal Muscle-Mass

Table 1: Socio-demographic and body composition parameters of the sample.

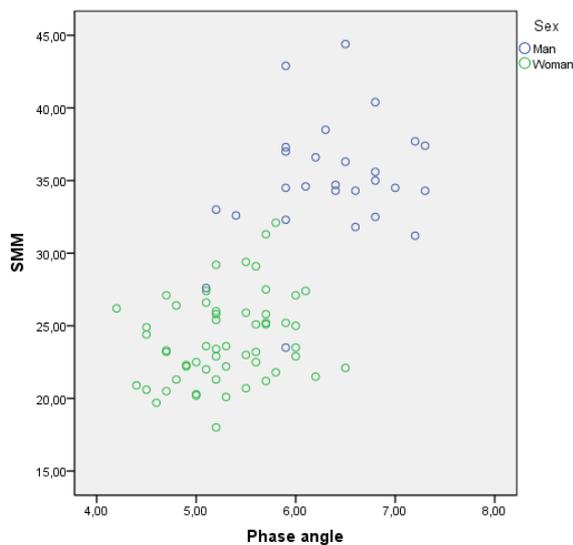


Figure 1: Relationship between the Skeletal Muscle-Mass (SMM) (kg) and the phase angle (ϕ) according to sex.

Discussion

Reference values have been published in large healthy adult population samples: 214,732 Germans 18-102 years (9), 5,225 Swiss 15-98 years (10) and 1,967 Americans 18-94 years (11). The first study stands out because it classifies values by gender, age ranges and BMI, while the remaining two do so only by gender and age ranges. The values of the Swiss population are not comparable with the rest because they have different age ranges. There are other studies in different populations and healthy subsamples (e.g. elderly) and patients (e.g. colorectal cancer), but they are less relevant given the low sample size and sick population.

We only have evidence of a study conducted in 311 Spaniards aged 18-80 (12). The reference values found were $6.37 \pm 0.61^\circ$ (men) and $5.3 \pm 0.51^\circ$ (women), slightly lower than those described by Atilano-Carsi X and Cols (men = $7.07 \pm 0.75^\circ$, women = $5.87 \pm 0.72^\circ$), probably due to the larger sample and the use of a single frequency (50 kHz) tetrapolar BIA equipment.

The main limitation of the above-mentioned studies is that the reference values are population and BIA-specific equipment and, therefore, they should only be compared with studies based on the same population and which have used the same BIA model. In the four aforementioned studies, the SF-BIA devices at 50 kHz were used.

In the German population: 2000-S (Data Input, Frankfurt, Germany); Switzerland: Xitron 4000B (Xitron Technologies, Inc, CA), Bio-Z (Bio-z2, Spengler, France) RJL 101; North American: RJL 101 (RJL Systems, Inc) and Spanish: BIA-101 (Akern Systems, Florence, Italy). Another possibility is to calculate the Z-score = (observed value-average value) / SD.

Conclusions

The phase angle can discriminate subjects according to gender and quantity of SMM, so it stands as a useful parameter to monitor the SMM. A study is required in a large representative sample of the healthy Spanish population, which provides ϕ values based on gender, age and BMI and a harmonization of worldwide technology, in order to make comparisons between studies and different populations, we recommend the authors to use multi-frequency segmental octopolar equipment, such as InBody 770.

Bibliografía

1. Ferguson LR, De Caterina R, Görman U, et al. Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalised Nutrition: Part 1 - Fields of Precision Nutrition. *J Nutrigenet Nutrigenomics*. 2016;9(1):12-27.
2. Vrijheid M. The exposome: a new paradigm to study the impact of environment on health. *Thorax*. 2014;69(9):876-8.
3. Heymsfield SB, Wang Z, Baumgartner RN, Ross R. Human body composition: advances in models and methods. *Annu Rev Nutr*. 1997; 17:527-58.
4. Brantlov S, Jødal L, Lange A, Rittig S, Ward LC. Standardisation of bioelectrical impedance analysis for the estimation of body composition in healthy paediatric populations: a systematic review. *J Med Eng Technol*. 2017;41(6):460-79.
5. Kyle UG, Bosaeus I, De Lorenzo AD, et al. Composition of the ESPEN Working Group. Bioelectrical impedance analysis--part I: review of principles and methods. *Clin Nutr*. 2004;23(5):1226-43.
6. Kyle UG, Bosaeus I, De Lorenzo AD, et al; ESPEN. Bioelectrical impedance analysis--part II: utilization in clinical practice. *Clin Nutr*. 2004;23(6):1430-53.
7. Martinoli R, Mohamed EI, Maiolo C, Cianci R, Denoth F, Salvadori S, Iacopino L. Total body water estimation using bioelectrical impedance: a meta-analysis of the data available in the literature. *Acta Diabetol*. 2003;40 Suppl 1: S203-6.
8. Norman K, Stobäus N, Pirlich M, Bösy-Westphal A. Bioelectrical phase angle and impedance vector analysis--clinical relevance and applicability of impedance parameters. *Clin Nutr*. 2012;31(6):854-61.
9. Bösy-Westphal A, Danielzik S, Dörhöfer RP, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. *JPEN J Parenter Enteral Nutr*. 2006;30(4):309-16.
10. Kyle UG, Genton L, Slosman DO, Pichard C. Fat-free and fat mass percentiles in 5225 healthy subjects aged 15 to 98 years. *Nutrition*. 2001;17(7-8):534-41.
11. Barbosa-Silva MC, Barros AJ, Wang J, Heymsfield SB, Pierson RN Jr. Bioelectrical impedance analysis: population reference values for phase angle by age and sex. *Am J Clin Nutr*. 2005;82(1):49-52.
12. Atilano-Carsi X, Bajo MA, Del Peso G, Sánchez R, Selgas R. Vectores de impedancia bioeléctrica de referencia para la población Española. *Nutr Hosp*. 2014;31(3):1336-44.