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Correlation Between Phase Angle and Nutritional Status in Hospitalized Patients at Nutritional Risk

Ludiane Alves do Nascimento*, Juliana Bonfleur Carvalho, Grasiela Konkolisc Pina de Andrade, Ariane Naldoskis Severine, Ana Lucia Chalhoub Chediac Rodrigues

Abstract

Background & Aims: This study evaluated the correlations between phase angle (PA) and muscle mass (MM), which can contribute to an accurate nutritional diagnosis.

Methods: Retrospective cross-sectional study, conducted from July 2020 to July 2021, included patients classified as at-risk based on their initial nutritional assessments. Bioelectrical impedance analysis was used to evaluate body composition and determine the phase angle (PA). Data on nutritional status and hospital stay were also obtained.

Results: Among the 1.012 evaluated patients, 55% (557) were male, the median age was 71.8 years, and the median body mass index (BMI) was 22.7 kg/m^2. A total of 60.1% (606) of the patients had low MM. The PA cut-off for reduced MM was 4.30º for the total population and for men, and 3.76º for women. Patients with reduced PA were older (61.8 [23] vs. 76.4 [19] years; $p<0.001$), had a longer hospital stay (14 [20] vs. 11[15]; $p<0.001$) and lower BMI (24.1 [6.0] vs 22.3 [4.8] kg/m^2; $p<0.001$). Patients with a hospital stay >11 days were twice as likely to have a reduced PA (odds ratio [OR] = 2.00, 95% confidence interval [CI] 1.37–2.93). In addition, patients from critical units were almost twice as likely to have a reduced PA (OR = 1.87, 95% CI 1.22–2.87).

Conclusion: Patients with reduced MM presented a lower PA cut-off than that for patients with normal MM; thus, the PA represents a good marker to detect MM reduction. A reduced PA also increased the likelihood of malnutrition and prolonged hospital stay.

Keywords: Body composition; Nutrition assessment; Hospitalization; Muscle mass; Phase angle

Introduction

Impaired nutritional status is associated with increased morbidity and mortality and hospital stay, higher chances of readmission, and increased hospital costs [1]. Low muscle mass (MM) is the most critical consequence of malnutrition because it reduces immunity and wound healing, and increases the risk of infection and muscle weakness [2]. Bioelectrical impedance analysis (BIA) is a method for the evaluation of body composition that has been widely used because it is a non-invasive, practical method that can be performed at the bedside. Moreover, the results are reproducible and rapidly obtained [3,4]. BIA is an indirect method of body composition evaluation, established through the correlation of impedance and body water content [5,6]. It is based on the principle that body tissues offer different resistance

Affiliation:

Department of Nutrition. Hospital Sírio Libanês. 91, Dona Adma Jafet, street. Zip Code: 01308-901, São Paulo, Brazil

***Corresponding author:**
Ludiane Alves do Nascimento - Department of Nutrition. Hospital Sírio Libanês, 91, Dona Adma Jafet, street. Zip Code: 01308-901, São Paulo, Brazil

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to the passage of electric current. This opposition, called impedance (Z), has two components, resistance (R) and reactance (Xc) [7]. The phase angle (PA) is obtained as the correlation between the R and Xc components and is a direct measure of cell stability [8]. The PA at 50 kHz is proportional to the body cell mass [9]. Thus, PA was proposed as a prognostic indicator in clinical practice to indicate the integrity of body membranes, as its values are affected by disorders in the properties of electrical tissue caused by diseases, inflammation and functional deficiencies [10,11]. Low PA values are associated with worsening of the disease or its prognosis and, consequently, increased morbidity and mortality [12]. PA can also be used as an indicator of nutritional status and body cell mass (BCM). Patients with significant weight loss have reduced PA values; therefore, is a clinically relevant marker of malnutrition [13]. PA has also recently emerged as a marker of MM and function in several scenarios and clinical conditions [14]. However, as yet, no cut-off points have been defined for PA to indicate increased risks of nutritional deficit or reduced MM. Determining a reference PA value that reflects MM depletion in patients at risk may contribute to a more accurate nutritional diagnosis, which is essential for the planning of nutritional intervention actions. The objective of the present study was to correlate PA and MM in patients at nutritional risk.

Materials and Methods

Study design

This retrospective cross-sectional study was conducted in the inpatient and semi-intensive units of a private hospital between July 2020 to July 2021.

This study included patients over 18 years of age and classified as having nutritional risk in the initial nutritional assessment conducted within 24 hours of hospital admission, according to the following criteria: low weight, severe involuntary weight loss, use of enteral and parenteral nutrition, pressure injury and fasting for >3 days. Patients who did not undergo BIA due to pacemaker use; patients with bilateral metallic prostheses, bandages at the anatomical points of electrode binding, involuntary tremors; and monitored patients were excluded from the study.

Ethical approval and consent to participate

The study was submitted to the Research Ethics Committee (REC) of the institution and approved by the committee under the number CAAE:31539420.9.0000.5461. As the study was retrospective, with the collection of secondary data, the requirement for Free and Informed Consent Form was waived by the REC. The preservation of the privacy of the research subjects was guaranteed and the collected data was used solely and exclusively to execute this project.

Study procedures

Clinical data, including diagnosis, gender, age, length of hospital stay, inflammatory markers (C-reactive protein and lymphocytes), clinical outcome and the results of body composition analysis were collected from the medical records. Weight was measured on a Toledo® scale with a 50 g accuracy and height was measured with a stadiometer attached to the scale and recorded in millimeters (mm). The weights of bedridden patients were measured using a Linet® bed-scale with an 100 g accuracy. The heights of these patients were estimated using the Chumlea equation [15]. Body mass index (BMI) was calculated using the equation (weight/height2) and malnutrition was classified according to the criterial from the World Health Organization (WHO) [16] for adults and the Pan American Health Organization (PAHO) [17] for the elderly.

Body composition assessment

BIA assessment was performed using a BCM Fresenius® portable device within 72 hours of nutritional risk classification. The patients were positioned in a supine position in bed or seated in an armchair with their legs supported and stretched. The arms and legs were placed at a 45º angle from the body. After correct positioning, the skin was cleaned with alcohol and two electrodes were placed 5 cm apart on the backs of the hand and foot in the right hemibody. The PA was obtained at a frequency of 50 kHz. The device also provided data: muscle mass index = body mass – fat mass and hyperhydration divided by height; fat mass index = body mass – muscle mass and hyperhydration divided by height2; hydration pattern: hyperhydrated patient when the result was above 1 liter and dehydrated values below -1 liter.

Statistical analysis

The non-parametric qualitative variables were represented as medians and interquartile intervals (Q1 and Q3). Categorical data were represented as absolute (n) and relative (%) frequencies. The normality of quantitative variables was verified through Kolmogorov–Smirnov (K–S) and Shapiro-Wilks tests to determine whether parametric or nonparametric tests were used. As normality was not proven, nonparametric tests such as Mann–Whitney tests were used. The PA cut-off, which indicates reduced MM, was determined based on receiver operating characteristic (ROC) curves analysis and the Youden index. The diagnostic values (sensitivity, specificity, positive predictive value, and negative predictive value) were calculated for the selected limits. In the logistic regression models, the dependent variables were the PA and dichotomized clinical outcome. In these models, the odds ratio (OR) was used as an effect size, with a 95% confidence interval (95% CI). A significance level of 5% was established. R version 4.0.3 and IBM SPSS Statistics for Windows, version 22.0 were used to perform the statistical analyses.

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Table 1: Population characteristics

Classification	**n= 1012**
Male (n, %)	557 (55)
Age (median [Q1; Q3])	71.8 [61.0;82.1]
BMI (median [Q1; Q3])	22.7 [20.6;26.0]
Phase angle (median [Q1; Q3])	3.8 [3.1;4.6]
Diagnosis at Admission	**n (%)**
Cardiopathy	96 (9.5)
GIT disorders	158 (15.6)
Genitourinary	37 (3.7)
Respiratory	118 (11.7)
Neurological	62 (6.1)
Oncological diseases	408 (40.3)
Others*	133 (13.1)
Hydration Status	**n (%)**
Hyperhydrated	560 (55.3)
Dehydrated	59 (5.8)
Muscle mass index**	**n (%)**
Normal	395 (39.2)
Low	606 (60.1)
Fat Mass Index**	**n (%)**
High	121 (12.0)
Low	139 (13.8)
Care Units ***	**n (%)**
General practice	454 (45.0)
Oncology	206 (20.5)
Semi Intensive	349 (34.5)
Clinical Outcome ****	**n (%)**
Discharge	957 (94.8)
Death	53 (5.2)

BMI, Body Mass Index; GIT, gastrointestinal tract
* Trauma, orthopedic, renal, hepatic, infectious, metabolic diseases
** Missing Data: n= 7
*** Missing Data: n = 3
**** Missing Data: n = 2
The author declares no conflicts of interest.

Results

The best PA cutoff to determine reduced MM is described in table 2. Although not the ideal cut-offs, these points showed the best balance of sensitivity and specificity.

In the total population, patients with a reduced PA were older. The median BMI which indicated a low weight according to OPAS [17] and was lower than that in patients with a normal PA. The results of the body composition evaluations showed a lower MM, and higher hydration pattern in patients with a low PA. These patients also had longer hospital stays. After gender stratification, the results remained statistically significant except for BMI in women (Table 3).

The results of the logistic regression analysis indicated that female patients with reduced BMI, age above 70 years, hospital stay above 11 days, reduced MM index and in semi-intensive and oncological units were more likely to present reduced PA values (Table 4).

Discussion

PA is increasingly used for nutritional assessment and as an indicator of clinical prognosis. As it does not require the calculation of regression equations this measure eliminates a large source of random error [14,18]. Fat-free mass (FFM) is the second major determinant of sex-independent PA [19]. The present study assessed the relationship between the PA and MM index. MM is the largest component of FFM and patients at nutritional risk who presented a reduced MM index had a lower PA ($p>0.001$), with a cut-off point of 4.30º for the total sample and men and 3.76º for women (Table 2). Kilic et al. [20] assessed PA for the diagnosis of sarcopenia (which has reduced MM as one of the diagnostic criteria) and also observed a lower PA (≤4.55º) in patients with sarcopenia compared to that in non-sarcopenia patients. Table 3 shows correlations of the PA, which reflects reduced MM, with some variables. We observed a significant correlation between an increase in age and a reduction in PA, both in the total number of patients and according to gender ($p>0.001$). PA tends to decrease with increasing age due to the reduction in reactance that accompanies MM loss. In addition, resistance increases due to the reduced proportion of body water at the expense of increasing fat mass at older ages [12]. Gonzalez et al. [21] showed that age was the most important biological determinant of PA variation. In our study, the elderly were almost 16 times more likely to have a reduced PA (OR = 15.6, 95% CI 9.89–24.7) (Table 4). The results of the present study showed that men presented a higher PA cut-off (<4.30) than women (<3.76). In addition, women were 3.5 times more likely to have a reduced PA (OR = 3.51, 95% CI 2.37–5.20) (Table 4). Men generally have higher FFM levels and, therefore, higher PA [22]. Barbosa-Silva et al. [18] and Dadet et al. [22] reported that defining different PA cut-offs for men and women would allow a more sensitive and specific test, which is in line with our results and seems to be the best way to use PA values for nutritional diagnosis. Patients with a reduced BMI had a lower PA ($p< 0.001$). According to a study by Małecka-Massalska et al. [23] suggested that the PA may be a potential diagnostic tool to detect BMI reduction. In our study, patients with a reduced BMI were 3.5 times more likely to have a reduced PA (Table 4). However, the correlation between PA and BMI by gender was significant only for the total population and in men ($p>0.001$), with no statistically significant relationship for women, consistent with the findings reported by Gonzalez et al [19]. Patients with a reduced PA presented a higher median hospital stay ($p>0.001$) compared to that in patients with a normal PA. Moreover, patients with a hospital stay >11 days

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Table 2: Test characteristics and receiver operating characteristic (ROC) models for phase angle related to low muscle mass

Phase Angle	Youden Cut-off	Indicator	Value (%)	95%CI
Total	4.3	Sensitivity	74.8	[71.3;78.2]
		Specificity	41.4	[36.6;46.2]
		PPV	65.6	[62.0;69.1]
		NPV	52.3	[46.9;57.8]
		Accuracy	61.4	[58.4;64.4]
Male	4.3	Sensitivity	70.7	[65.9;75.5]
		Specificity	46.9	[40.1;53.7]
		PPV	68.9	[64.1;73.7]
		NPV	49	[42.1;55.9]
		Accuracy	61.8	[57.7;65.8]
Female	3.76	Sensitivity	60.9	[54.9;66.8]
		Specificity	55.8	[48.9;62.8]
		PPV	64.3	[58.3;70.4]
		NPV	52.1	[45.4;58.9]
		Accuracy	58.7	[54.2;63.2]

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value

Table 3: Comparisons between patients with normal and low PA* according to age, body composition, and hospital stay

Variables	Total (n = 1012)			Male (n = 557)			Female (n = 455)		
	Normal PA (median [Q])	Low PA (median [Q])	*p*	Normal PA (median [Q])	Low PA (median [Q])	*P*	Normal PA (median [Q])	Low PA (median [Q])	*p*
	n = 321	n = 691		n = 200	n = 357		n = 211	n = 244	
Age (years)	61.8 [23]	76.4 [19]	< 0.001	63.2 [22]	76.8 [17]	< 0.001	65.4 [25]	77.5 [20]	< 0.001
Hydration status (L)	0.4 [1.8]	1.7 [2.5]	< 0.001	0.9 [2.0]	2.3 [2.5]	< 0.001	0.3 [1.2]	1.6 [2.4]	< 0.001
Body mass index (kg/m²)	24.1 [6.0]	22.3 [4.8]	< 0.001	25.1 [5.7]	22.8 [5.3]	< 0.001	21.5 [4.6]	22.1 [4.8]	0.363
Muscle mass index (kg/m²)	12.8 [3.0]	9.8 [2.9]	< 0.001	13.8 [2.9]	10.5 [3.0]	< 0.001	10.6 [2.5]	9.2 [2.8]	< 0.001
Hospital stay (days)	11.0 [15]	14.0 [20]	< 0.001	12 [16]	15 [22]	< 0.001	9 [13]	14 [20]	< 0.001
CRP (mg/dl)	1.47 [4.2]	1.96 [4.9]	0.006	1.59 [4.3]	2.22 [4.8]	0.014	1.14 [3.8]	2.23 [5.5]	< 0.001
Lymphocytes (mm3)	1.400 [985]	1.240 [955]	0	1.320 [933]	1.150 [815]	0	1.540 [980]	1.335 [1030]	0.032

* Total population and men: Normal PA > 4.30 and Women: Normal PA > 3.76. CRP, C-reactive protein; PA, phase angle; Q, interquartile range

were twice as likely to have a reduced PA (OR = 2.00, 95% CI 1.37–2.93). Consistent with this finding, Kyle et al. [21] also observed that a reduced PA was associated with a longer hospital stay and that patients hospitalized for 5–20 days had a five-fold higher risk of a reduced PA. Thus, PA can be used as a predictor of prognosis and guide clinical interventions in hospitalized patients. When inflammatory markers are evaluated, there is a correlation between CRP and increased lymphocytes with reduced AF. A study by Stobaus et al. [24] also showed a significant inverse correlation between CRP and PA and states that inflammation has a strong impact on PA in sick individuals. This demonstrates that inflammatory markers have good applicability in clinical practice and can be used as parameters to guide the identification of patients with reduced phase angle. We observed that patients hospitalized in semi-intensive care units were almost twice as likely to have a reduced PA (OR = 1.87, 95% CI 1.22–2.87) (Table 4), demonstrating that PA is a useful parameter in assessment nutritional impairment in critically ill patients. Patients hospitalized in the oncological unit were 1.6 times more likely to have a reduced PA (Table 4). Patients hospitalized in these units may present a worse clinical condition, which results in reduced MM. We observed that PA was a good predictor of reduced MM in the total population and in different genders (p<0.001). In addition, logistic regression analysis showed that patients with reduced MM were 6 times more likely to have a reduced PA (OR = 6.22, 95% CI 4.05–9.55). Silva et al [25] evaluated the PA as a marker of sarcopenia, which considers low MM, reported that patients with reduced PA were 5.6 times more likely to have

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Table 4: Logistic regression of the dependent variable phase angle among hospitalized patients.

Variable	Category	Crude OR (CI95%)	p	Adjusted OR (CI95%)	p
Gender	Female	1.546 (1.180-2.027)	<0.001	3.514 (2.372-5.207)	<0.001
	Male	1		1	
BMI	reduced	2.751 (2.073-3.652)	<0.001	3.553 (2.356-5.356)	<0.001
	normal	1		1	
Age	> 70 years	6.058 (4,503-8,149)	<0.001	15.665 (9.898-24.790)	<0.001
	≤70 years	1		1	
Hydration	Hyperhydrated	4.500 (3.343-6.057)	0	11.066 (7.197-17.015)	0
	Dehydrated	0.431 (0.241-0.771)	0.005	0.687 (0.321-1.470)	0.333
	Normohydrated	1		1	
Hospital stay	> 11 days	1.646 (1.261-2.149)	<0.001	2.005 (1.370-2.935)	<0.001
	≤11 days	1		1	
Muscle Mass Index	Reduced	2.104 (1.606-2.756)	<0.001	6.220 (4.050-9.554)	<0.001
	normal	1		1	
Units	Oncological	1.554 (1.093-2.210)	0.014	1.621 (1.022-2.569)	0.04
	Semi-intensive	2.404 (1.752-3.297)	<0.001	1.875 (1.221-2.879)	0.004
	General practice	1		1	

OR, odds ratio; CI, confidence interval; BMI, body mass index

sarcopenia. Thus, PA may be a marker of MM, assisting in diagnosis and nutritional follow-up since reduced MM alone is considered the most critical consequence of malnutrition [2]. We observed significant correlation between reduced PA and hyperhydration in the total sample and when separated by gender (p>0.001). Hyperhydrated patients were 11 times more likely to have reduced PA (OR 11,066, 95% CI 7,197-17,015). The proportion of extracellular and intracellular water (ECW: ICW) is a determinant of PA variation. This variability occurs due to changes in cell size, cell membrane permeability, or differences in fluid distribution in tissues [6]. Therefore, in hyperhydrated patients, the results should be interpreted with caution and preferably compared with the individual during the evaluations. Gonzalez et al. [19] confirmed that the ECW: ICW ratio is a significant determinant of PA and may justify the PA variations presented in several clinical situations and severe obesity. In the disease, there are changes in the distribution of fluids between the intra and extra-cellular compartments that can be determined by the health of the membranes and the catabolic state of the individual, which justifies the results in the population of the present study because they are hospitalized individuals, where 60 % had reduced muscle mass index. Some limitations should be considered in the interpretation of the results. First, the study population was heterogeneous but reflects our general hospital population. Second, BIA was not performed on fasting patients and the use of diuretics was not discontinued. However, these behaviors are consistent with the hospital reality, where medications cannot be suspended and patients may not always undergo long periods of fasting.

Conclusion

Patients at nutritional risk with reduced MM presented a lower PA compared to those in patients with normal MM. The reduced PA was associated with an increased likelihood of malnutrition and prolonged hospital stay. Thus, PA is an important marker of nutritional status and contributes to the detection of low MM, enabling individualized and early interventions for hospitalized patients.

Conflict of interest

No conflicts of interest

Statement and funding sources

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