Low Phase Angle Associated with Nutritional Risk and Percent Adequacy of Upper Arm Circumference in Cancer Inpatients

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Ângulo de Fase Baixo Associado ao Risco Nutricional e ao Percentual de Adequação da Circunferência do Braço em Pacientes com Câncer Hospitalizados

El Ángulo de Fase Bajo Asociado con el Riesgo Nutricional y el Porcentaje de Adecuación de la Circunferencia de la Parte Superior del Brazo en Pacientes con Cáncer Hospitalizados

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ABSTRACT

Introduction: Early identification of the nutritional status of cancer patients ensures adequate nutritional treatment and better prognoses. **Objective:** To evaluate the association between phase angle (PA), nutritional risk assessed using the Nutritional Risk Screening (NRS-2002) and indicators of nutritional status in cancer inpatients. **Method:** Cross-sectional, prospective study, carried out with cancer inpatients at the "*Complexo Hospitalar de Vitória da Conquista*", in Bahia. PA was assessed using bioelectrical impedance, with values < 5º for men and < 4.6º for women being considered low. Nutritional status was assessed by body mass index (BMI), calf circumference (CC) and percentage of adequacy of arm circumference (%AC). Nutritional risk was assessed using the NRS-2002 tool. For statistical analysis of the data, the chi-square test and multiple binary logistic regression were used. **Results:** The sample consisted of 135 patients. The most common tumor sites were intestine (16.3%), breast (16.3%) and brain (12.59%). A large part of the sample presented nutritional risk (59.3%), while 41.67% of men and 28.57% of women presented low PA. All anthropometric parameters were associated with PA in univariate analysis. In the multivariate analysis, only %AC and nutritional risk were independently associated with PA. **Conclusion:** PA is associated with nutritional risk and %AC in cancer inpatients.

Key words: Electric Impedance; Nutritional status; Inpatients; Neoplasms.

RESUMO

Introdução: Identificar precocemente o estado nutricional de pacientes com câncer assegura o tratamento nutricional adequado e melhores prognósticos. **Objetivo:** Avaliar a associação entre o ângulo de fase (AF), o risco nutricional avaliado por meio do *Nutritional Risk Screening* (NRS-2002) e indicadores do estado nutricional em pacientes com câncer hospitalizados. **Método:** Estudo transversal, prospectivo, com pacientes com câncer internados no Complexo Hospitalar de Vitória da Conquista, na Bahia. O AF foi avaliado por meio da impedância bioelétrica, sendo considerados baixos os valores < 5º para homens e < 4,6º para mulheres. O estado nutricional foi avaliado pelo índice de massa corporal (IMC), circunferência da panturrilha (CP) e porcentagem de adequação da circunferência do braço (%CB). O risco nutricional foi avaliado utilizando a ferramenta NRS-2002. Para a análise estatística dos dados, foram utilizados o teste qui-quadrado e a regressão logística binária múltipla. **Resultados:** A amostra foi composta por 135 pacientes. Os sítios tumorais mais encontrados foram intestino (16,3%), mama (16,3%) e cérebro (12,59%). Grande parte da amostra apresentou risco nutricional (59,3%), enquanto 41,67% dos homens e 28,57% das mulheres apresentaram AF baixo. Todos os parâmetros antropométricos foram associados ao AF na análise univariada. Na análise multivariada, apenas a %CB e o risco nutricional se mostraram associados de forma independente ao AF. **Conclusão:** O AF está associado ao risco nutricional e à %CB em pacientes com câncer hospitalizados.

Palavras-chave: Impedância Elétrica; Estado Nutricional; Pacientes Internados; Neoplasias.

RESUMEN

Introducción: La identificación temprana del estado nutricional de los pacientes con cáncer garantiza un tratamiento nutricional adecuado y mejores pronósticos. **Objetivo:** Evaluar la asociación entre el ángulo de fase (AF), el riesgo nutricional evaluado mediante el *Nutritional Risk Screening* (NRS-2002) y los indicadores del estado nutricional en pacientes con cáncer hospitalizados. **Método:** Estudio transversal, prospectivo, con pacientes con cáncer internados en el Complejo Hospitalario Vitória da Conquista, en Bahía. El AF se evaluó mediante impedancia bioeléctrica, considerándose bajos valores menores de **5º para hombres y** de 4,6º para mujeres. El estado nutricional se evaluó mediante el índice de masa corporal (IMC), la circunferencia de la pantorrilla (CP) y el porcentaje de adecuación de la circunferencia del brazo (%CB). El riesgo nutricional se evaluó mediante la herramienta NRS-2002. Para el análisis estadístico de los datos se utilizó la prueba de ji al cuadrado y regresión logística binaria múltiple. **Resultados:** La muestra estuvo compuesta por 135 pacientes. Las localizaciones tumorales más frecuentes fueron intestino (16,3%), mama (16,3%) y cerebro (12,59%). Gran parte de la muestra presentó riesgo nutricional (59,3%), mientras que el 41,67% de los hombres y el 28,57% de las mujeres presentaron AF bajo. Todos los parámetros antropométricos se asociaron con el AF en el análisis univariado. En el análisis multivariado, sólo el % CB y el riesgo nutricional se asociaron de forma independiente con el AF. **Conclusión:** El AF se asocia con riesgo nutricional y % CB en pacientes oncológicos hospitalizados.

Palabras clave: Impedancia Eléctrica; Estados nutricionales; Pacientes Internados; Neoplasias.

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INTRODUCTION

Approximately 35 million new cases of cancer will be diagnosed worldwide until 2050[1], according to the World Health Organization (WHO). In Brazil, for each year of the triennium 2023-2025[2], 704 thousand new cases are anticipated.

Quite often, the nutritional status of patients with cancer is affected due to metabolic changes resulting from type, stage and location of the tumor and side effects of antineoplastic treatments, as inappetence, nausea, vomits and diarrhea, contributive factors to develop malnutrition. Malnourishment of these patients negatively impacts their hospital length of stay, increased risk of infections and mortality[3,4] and early identification of their nutritional status ensures adequate treatment and better clinical results[5].

Some studies indicate phase angle (PA) as a nutritional marker of patients with different types of cancer[6,7]. Nutritional risk was more prevalent in patients with low PA[8] according to a cross-sectional study correlating PA and nutritional status of 94 patients with advanced cancer. Another study comparing nutritional assessment by anthropometry and PA of patients with upper aerodigestive epidermoid carcinoma revealed that low PA values were associated with lower values of arm circumference (AC) and lower body mass index (BMI)[9].

As PA is an important tool for early identification of patients needing nutritional intervention[3,6] the present study aims to evaluate the association among PA, nutritional risk and markers of nutritional status in cancer inpatients.

METHOD

Cross-sectional, prospective, quantitative study with adult and older patients with cancer of both sexes evaluated within 72 hours of admission at emergency, medical and surgical clinics and intensive care units (ICU) of "*Complexo Hospitalar de Vitória da Conquista* (CHVC)" in the State of Bahia from June to December 2023.

Inclusion criteria were: age ≥ 18 years, ability to respond to any question and sign the Informed Consent Form (ICF). Exclusion criteria were patients who during follow-up have been submitted to implantation of pacemaker or cardiac defibrillator or surgeries or procedures impeding bioelectrical impedance analysis (BIA).

The following variables were obtained to evaluate the patient's nutritional status: measurement of PA, anthropometric data and nutritional risk screening, in addition to medical charts to collect age, sex, tumor location and disease staging.

BIA was measured with tetrapolar device model 1010-03 AF, brand Sanny, at the right side of the body with the patient lying on a non-conductive stretcher, in supine, open legs and arms apart from the torso. Resistance (R) and reactance (Xc) measures were obtained at a frequency of 50 kHz and 800 µA. PA was calculated $[(Xc/R) \times (180°/\pi)]$ and classified as low if < 5º for men and < 4.6º for women[10].

For anthropometric evaluation, knee-height (KH), calf circumference (CC) and AC were measured to estimate the weight and height according to the technique proposed by Lohman, Roche, Martorell[11], with anthropometric measuring tape, brand Sanny® with millimeter precision. Height and weight were estimated with the equations proposed by Chumlea, Guo, Steinbaugh[12].

BMI was calculated, dividing the weight by the square of the height, considering the classification cutoff for patients with cancer proposed by Fearon et al.[13]. CC was classified as low if ≤34 cm for men and ≤33 cm for women[14]. Based on AC, the percentage of adequacy of AC (%AC) was calculated with the formula: AC x 100%/AC percentile 50, whose values were obtained from Frisancho for adults[15] and the National Health and Nutrition Examination Survey III for older adults[16]. The nutritional status of the patients, based on the percent of adequacy, was classified according to Blackburn, Thornton[17].

The Nutritional Risk Screening (NRS-2002)[18] tool was applied to screen the nutritional risk whose goal is to detect the development of malnutrition in hospital setting. It is a nutritional score which associates the disease severity and adjusted for patients > 70 years. The patients were classified at low (score 1), moderate (score 2) and severe (score ≥3) nutritional risk[18].

The statistical analyzes were based on the primary outcome of association of PA with the nutritional variables investigated. Descriptive analysis was utilized to characterize the events studied; for the categorical variables, simple absolute frequencies were calculated and for the continuous variables, mean and standard deviation (SD). Additionally, the chi-square test of association was applied to determine the dependence between categorical variables.

The multiple binary logistic regression analysis was performed from the full saturated model (all the variables), applying the Backward Stepwise selection with the Wald test to identify the association between low PA and low values of %AC, CC, BMI and nutritional risk.

Initially, the Backward Stepwise model implies in inserting all the explicative variables simultaneously. Next, at each step of the method, the less significant explicative variable is eliminated until only the most significant remain in the model[19]. A variable may be reintegrated to the model if the inclusion criteria is met in any of the steps of the interactive process. The test Wald was utilized to determine the elimination or reinsertion of the variables into the model, being considered the likelihood of 0.10 and 0.05 as exclusion and inclusion criteria, respectively. The Hosmer Lemeshow goodness to fit was applied to verify the adequacy of the final model.

In addition, point and interval estimations were found for the odds ratio. The statistical software IBM Statistical Package for the Social Sciences (IBM SPSS statistics)[20] version 25.0 was utilized for data processing with confidence level of 95% for all the analyzes.

The Institutional Review Board of "*Instituto Multidisciplinar em Saúde, Universidade Federal da Bahia*" (UFBA) approved the study, report number 6086820 (CAAE (submission for ethical review): 69200723.4.0000.5556) in compliance with ethical guidelines of Directive number 466/2012[21] of the National Health Council for studies with human beings.

RESULTS

One hundred and thirty five cancer inpatients were enrolled to the study, 76 from surgical clinic, 27 from Intensive Care Unit (ICU), 22 from emergency and ten from medical clinic. The overall mean of the patients was 62.13 (±1.34) years, mostly White males, intestines, breast and brain as the most frequent tumor sites and a substantial portion of them at nutritional risk (NRS ≥3 points) (Table 1).

The anthropometric data and PA of patients enrolled in the study are presented in Table 2. The mean value of BMI per age-range is within the classification of eutrophy[13]. The results of adequacy %AC indicate malnourishment for all age-ranges[17]. The CC was inadequate for both sexes in older individuals (≥60 years)[14]. Low PA was found for 41.67% of the men and 28.57% of the women.

Table 3 portrays the patients' anthropometric data and PA according to the origin hospital unit. Most of the patients evaluated were at the surgical clinic and ICU. ICU patients presented lower mean values of BMI, %AC and CC. More than half of ICU, emergency and medical clinical inpatients were at nutritional risk (NRS ≥3 points). However, the lowest mean of PA was found in emergency inpatients.

Statistical association for all variables ($p < 0.05$) was found after analyzing the relation among anthropometric parameters and PA values as shown in Table 4.

After adjustment by %AC, CC, BMI and nutritional risk, only %AC and nutritional risk have shown independent association with PA. The patients at nutritional risk had 13.24-fold higher odds of presenting low PA than patients without risk and patients with %AC < 90 had 2.85-fold higher odds of presenting low values of PA than patients with %AC ≥ 90 (Table 5).

DISCUSSION

The present study showed the association among PA, nutritional risk and %AC in cancer inpatients.

PA is a raw value obtained by BIA, the result of the ratio R and Xc ratio, a measure to analyze the integrity of cellular membranes and distribution of intra and extracellular fluids. Therefore, low PA values indicate reduction of cellular integrity or cellular death, can be associated with low body mass or disease aggravation. Higher values suggest more intact cellular membranes, reflecting improved body mass and prognosis[3,22].

Table 1. Sociodemographic characteristics and factors related to oncologic and nutritional status of cancer inpatients. Vitória da Conquista, 2024

Variables	
Age, mean ± SD (years)	62.13±1.34
18-59 years	47.24±1.34
≥ 60 years	73.35±0.85
Sex, n (%)	
Female	63 (46.67)
Male	72 (53.33)
Color, n (%)	
White	53 (39.3)
Yellow	3 (2.2)
Brown	50 (37)
Black	29 (21.5)
Tumor site, n (%)	
Intestine	22 (16.30)
Breast	22 (16.30)
Brain	17 (12.59)
Stomach	12 (8.89)
Prostate	11 (8.15)
Head and neck	10 (7.41)
Bladder	05 (3.70)
Skin	05 (3.70)
Leukemia	04 (2.96)
Other types of cancer	27 (20.00)
Nutritional screening*, n (%)	
Nutritional risk (NRS ≥3)	80 (59.3)
No nutritional risk (NRS <3)	55 (40.7)

Captions: SD = standard deviation; n = number of observations; % = frequency. (*) Nutritional risk classified according to NRS 2002[18].

Table 2. Frequency, mean and standard-deviation of anthropometric parameters and phase angle of cancer inpatients. Vitória da Conquista, 2024

Variables	n (%)	Mean±SD
BMI (kg/m²)		
18 – 59 years	58 (43)	21.74±0.84
≥ 60 years	77 (57)	22.57±0.52
AC (% of adequacy)		
18 – 59 years	58 (43)	86.35±2.35
≥ 60 years	77 (57)	86.48±1.51
CC (cm)		
18 – 59 years	58 (43)	30.63±063
≥ 60 years (women)	27 (20)	30.06±0.46
≥ 60 years (male)	50 (37)	31.69±0.55
PA women (Xc/R)		
Adequate (≥ 4.6°)	45 (71.43)	5.95±0.14
Inadequate (< 4.6°)	18 (28.57)	3.48±0.28
PA male (Xc/R)		
Adequate (≥ 5.0°)	42 (58.33)	6.27±0.14
Inadequate (< 5.0°)	30 (41.67)	4.22±0.10

Captions: n = number of observations; % = frequency; SD = standard deviation; BMI = body mass index; %AC = adequacy of arm circumference; CC = calf circumference; PA = phase angle.

Table 3. Frequency, mean and standard deviation of anthropometric parameters and phase angle of cancer inpatients according to hospital unit. Vitória da Conquista, 2024

Surgical clinic (n=76)	n (%)	Mean±SD
BMI (kg/m²)	-	22.89±0.5
AC (% of adequacy)	-	88.86±1.62
CC (cm)	-	31.56±0.46
PA (Xc/R)	-	5.51±1.34
Nutritional risk (NRS ≥3)	34 (44.74)	-
ICU (n=27)	**n (%)**	**Mean±SD**
BMI (kg/m²)	-	21.15±1.18
AC (% of adequacy)	-	82.39±3.12
CC (cm)	-	30.23±0.96
PA (Xc/R)	-	5.22±0.31
Nutritional risk (NRS ≥3)	21 (77.78)	-
Emergency (n=22)	**n (%)**	**Mean±SD**
BMI (kg/m²)	-	21.54±1.31
AC (% of adequacy)	-	84.32±3.59
CC (cm)	-	29.40±0.39
PA (Xc/R)	-	5.05±0.38
Nutritional risk (NRS ≥3)	16 (72.73)	-
Medical clinic (n=10)	**n (%)**	**Mean±SD**
BMI (kg/m²)	-	21.43±2.07
AC (% of adequacy)	-	83.39±5.53
CC (cm)	-	31.14±1.34
PA (Xc/R)	-	4.96±0.34
Nutritional risk (NRS ≥3)	9 (90)	-

Captions: n = number of observations; % = frequency; SD = standard deviation; BMI = body mass index; %AC = % adequacy AC; CC = calf circumference; PA = phase angle; ICU = intensive care unit.

Most often, nutritional evaluation of cancer inpatients is challenging because it is possible that their body fluids are unbalanced with edema and hyper-hydration which directly impact the anthropometric evaluation, substantially increasing the risk of bias, mainly for patients depending on predictive weight and height equation[23]. Even if PA can vary because of patient hydration, it emerges as an autonomous parameter, independent from regression equations, allowing the evaluation of the patient from the direct measurement of R and Xc[10], and can be adopted when weight and height measurements are not viable[10,24].

Nutritional status is strongly associated with changes of cellular membrane integrity[24]. Patients with cancer present more fragile cellular membranes caused by loss of body mass and metabolic changes resulting from the sickening process. Due to the ability to capture molecular alterations, PA would be a potentially more sensitive marker than anthropometry, for instance, to detect malnourishment of these patients[8,10].

Zhang, et al[6] evaluated a PA-based model of prediction of malnutrition and concluded that PA was lower in malnourished patients, being more sensitive than BMI for nutritional evaluation of these patients. In another study which tested PA as a marker of changes of body composition of patients with cancer during radiotherapy treatment, those with low PA had 9.3-fold higher odds of BMI reduction and likelihood 5.9 and 4.2 bigger of reduction of lean and fat mass, respectively, than patients with high values of PA[25]. Sat-Muñoz et al.[26] compared two groups of patients with head and neck cancer with normal and low PA and concluded that malnourishment was more prevalent in those with low PA.

Most of the patients of the present study were classified as eutrophic with average BMI according to the age-range; however, as BMI does not consider clinical conditions that can lead to body changes of the patients, it should not be used alone[27]. The evaluation of the nutritional status was complemented with %AC and CC. Both the mean %AC and CC indicated malnourishment of the patients evaluated. Muresan et al.[28] described the effect of the implementation of a protocol of evaluation and nutritional support on the nutritional status of cancer inpatients and concluded that CC was also associated with malnourishment of patients with cancer.

Table 4. Association among phase angle, anthropometric parameters and nutritional risk of cancer inpatients. Vitória da Conquista, 2024

Variables	Low PA *	Adequate PA*	*p***
%AC* **			
Inadequate	42	44	<0.001
Adequate	5	44	
CC (cm)******			
Inadequate	43	58	0,001
Adequate	4	30	
Nutritional screening**** **			
Nutritional risk (NRS ≥3)	44	36	<0.001
Without nutritional risk (NRS <3)	3	52	
BMI (kg/m²)			
Malnourished	28	17	<0.001
Non-malnourished	19	71	

Captions: PA = phase angle; %AC = adequacy of arm circumference; CC = calf circumference; BMI = body mass index.
(*) PA classified according to Barbosa-Silva et al.[10]: low: <4.6º for women and <5º for men; (**) *p* chi-square proportion test.
(***) %AC classified as inadequate for <90 and adequate for ≥90[17].
(****) CC classified according to Barbosa-Silva et al.[14], cut-off is 34 cm for men and 33 cm for women.
(*****) Nutritional risk classified by NRS 2002[18]. BMI classified according to Fearon et al.[13].

Table 5. Multivariate analysis of the association of phase angle, disease stage and nutritional markers. Vitória da Conquista, 2024

	β	SE	*p*	OR	95% CI to OR	
					Lower	Upper
Nutritional Risk	2.584	0.672	0.000	13.247	3.547	49.479
%AC	1.049	0.595	0.078	2.856	0.889	9.174
Constant	-3.290	0.676	0.000	0.037		

Captions: β = coefficient; SE = standard error; OR = odds ratio; CI = confidence interval; %AC = adequacy of arm circumference.

Nutritional risk was found for most part of the sample, similarly to Barros et al.[29], who analyzed the applicability and comparison of nutritional screening in patients with cancer and revealed that of the 208 patients evaluated, nearly 70% were at nutritional risk according to NRS 2002[18].

Statistical association was found for all variables investigated after analyzing the anthropometric parameters and values of PA. Correlation among PA, BMI and nutritional risk according to NRS 2002[18] was detected through the evaluation of the association among PA values and nutritional status of patients with pancreatic head cancer by Zhou et al.[30]. Likewise, Pereira et al.[8] found statistical association between PA and CC. Regarding AC adequacy, similar results of the present study, including cancer inpatients, were not described in the literature so far.

The multivariate analysis conducted in the present study showed that the nutritional markers %AC and nutritional risk associated independently with PA, which reiterates the strong association of these indicators with low values of PA. Corroborating these findings, a systematic review by Almeida et al.[31] showed that, overall, PA was related to the nutritional risk obtained by NRS 2002. Similarly, Paz et al.[32] concluded in their study that PA was a sensitive and acceptable measure to diagnose malnourishment.

The nutritional risk evaluated by NRS and the nutritional marker %AC associated independently with PA of cancer inpatients according to the present study. Based on these findings, it is possible to infer that PA, as a parameter which evaluates the cellular integrity and offer a more objective evaluation of the nutritional risk, could help health professionals in their analysis of nutritional status of cancer inpatients, that could optimize not only the metabolic evaluation but also the nutritional classification and treatment plan of these patients[10].

Although the utilization of PA showed promising results in early identification of the compromise of nutritional status in patients with cancer[3,6,7], PA does not replace the current methods of nutritional evaluation like the anthropometric measures and nutritional screening.

The reason is the lack of specific reference values for this population that are essential to evaluate correctly their nutritional status[7].

The small sample size and heterogeneity are the limitations of the study, which may have impacted the results and consequently, the generalization. However, the association of %AC with PA can be utilized in future studies.

CONCLUSION

The results indicate that PA is associated with nutritional risk and %AC in cancer inpatients. PA can be utilized as an indicator of nutritional status of cancer inpatients when associated with other nutritional evaluation methods. However, new studies investigating PA according to tumor location and disease stage to standardize cutoff values for this population are necessary.

CONTRIBUTIONS

Grasiele Carmo da Silva, Adrieli Andrade Santos, Maria Paula Carvalho Leitão and Matheus Lopes Cortes contributed to the study design, analysis and data collection. Grasiele Carmo da Silva and Maria Paula Carvalho Leitão contributed to data collection and wording. Antônio Carlos Ricardo Braga Junior contributed to the analysis and interpretation of the data. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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