Phase Angle and Nutritional Status in Individuals with Advanced Cancer in Palliative Care

http://dx.doi.org/10.32635/2176-9745.RBC.2019v65n1.272

Ângulo de Fase e Estado Nutricional em Indivíduos com Câncer Avançado em Cuidados Paliativos

Ángulo de Fase y Estado Nutricional en Individuos con Cáncer Avanzado en Cuidados Paliativos

Mayane Marinho Esteves Pereira[1]; Emanuelly Varea Maria Wiegert[2]; Livia Costa de Oliveira[3]; Larissa Calixto Lima[4]

Abstract

Introduction: Phase angle (PA) may be correlated with nutritional status in individuals with cancer. **Objective:** To investigate the correlation between PA and nutritional status in patients with advanced cancer. **Method:** Cross-sectional study with individuals of both sexes, aged ≥20 years, in their first care in the palliative care unit of the National Cancer Institute José Alencar Gomes da Silva (INCA). The PA was evaluated through bioelectrical impedance, being considered with low the values <percentile 5 (P5). The nutritional status was evaluated by the Patient-Generated Subjective Global Assessment (PG-SGA) Short Form, albumin, body mass index (BMI) and calf circumference (CC). The chi-square test and the Spearman correlation were used. The level of statistical significance adopted was 5%. **Results:** A total of 94 subjects were evaluated, with a median age of 66 (57; 74) years, female predominance (51.1%) and nutritional risk (85.1%). About one-third had low functional capacity (37.2%) and PA <P5 (36.2%). Nutritional risk was more prevalent in individuals with lower PA values. Body weight, CC and serum albumin levels showed a positive correlation with PA; while the total PG-SGA score, as well as most of its domains, correlated negatively. Only the BMI did not present statistical significance when evaluated in relation to PA. **Conclusion:** PA correlated with nutritional status; greater the value of PA, the better the nutritional status in patients with advanced cancer in palliative care.

Key words: Neoplasms; Electric Impedance; Body Composition; Nutritional Status.

Resumo

Introdução: O ângulo de fase (AF) pode estar relacionado ao estado nutricional em indivíduos com câncer. **Objetivo:** Investigar a correlação entre o AF e o estado nutricional em pacientes com câncer avançado. **Método:** Estudo transversal com indivíduos de ambos os sexos, idade ≥20 anos, em seu primeiro atendimento na unidade de cuidados paliativos do Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). O AF foi avaliado por meio da impedância bioelétrica, sendo considerados como baixos os valores com <percentil 5 (P5). O estado nutricional foi avaliado pela avaliação subjetiva global produzida pelo paciente (ASG-PPP) versão reduzida, albumina, índice de massa corporal (IMC) e perímetro da panturrilha (PP). Para a análise estatística dos dados, foram utilizados o teste qui-quadrado e a correlação de Spearman. O nível de significância estatístico adotado foi de 5%. **Resultados:** Foram avaliados 94 indivíduos, com mediana de idade 66 (57; 74) anos, predomínio do sexo feminino (51,1%) e risco nutricional (85,1%). Aproximadamente um terço da amostra apresentou baixa capacidade funcional (37,2%) e AF <P5 (36,2%). O risco nutricional foi mais prevalente em indivíduos com menores valores de AF. O peso corporal, o PP e os níveis séricos de albumina apresentaram correlação positiva com o AF; enquanto a pontuação total da ASG-PPP assim como a maioria de seus domínios se correlacionaram de forma negativa. Apenas o IMC não apresentou significância estatística quando avaliado em relação ao AF. **Conclusão:** O AF se correlacionou ao estado nutricional; quanto maior o valor do AF, melhor o estado nutricional de pacientes com câncer avançado em cuidados paliativos.

Palavras-chave: Neoplasias; Impedância Elétrica; Composição Corporal; Estado Nutricional.

Resumen

Introducción: El ángulo de fase (AF) puede estar relacionado con el estado nutricional en individuos con cáncer. **Objetivo:** Investigar la correlación entre el AF y el estado nutricional en pacientes con cáncer avanzado. **Métodos:** Estudio transversal con individuos de ambos sexos, edad ≥20 años, en su primera atención en la unidad de cuidados paliativos del Instituto Nacional de Cáncer José Alencar Gomes da Silva (INCA). El AF fue evaluado por medio de la impedencia bioeléctrica, siendo considerados como bajos los valores <percentil 5 (P5). El estado nutricional fue evaluado por la Evaluación Subjetiva Global producida por el paciente (ESG-PPP) versión reducida, albúmina, índice de masa corporal (IMC) y circunferencia de pantorrilla (CP). Se utilizaron la prueba chi-cuadrado y la correlación de Spearman. El nivel de significancia estadística adoptado fue del 5%. **Resultados:** Se evaluaron 94 individuos, con mediana de edad 66 (57, 74) años, predominio del sexo femenino (51,1%) y en riesgo nutricional (85,1%). Cerca de un tercio presentó baja capacidad funcional (37,2%) y AF <P5 (36,2%). El riesgo nutricional fue más prevalente en individuos con menores valores de AF. El peso corporal, la CP y los niveles séricos de albúmina presentaron una correlación positiva con el AF; mientras que la puntuación total de la ESG-PPP, así como la mayoría de sus dominios, se correlacionaron de forma negativa. Sólo el IMC no presentó significancia estadística cuando se evaluó en relación al AF. **Conclusión:** El AF se correlacionó con el estado nutricional; cuanto mayor el valor del AF, mejor el estado nutricional en pacientes con cáncer avanzado en cuidados paliativos.

Palabras clave: Neoplasias; Impedancia Eléctrica; Composición Corporal; Estado Nutricional.

[1] Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0001-6463-8829
[2] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0001-5904-5287
[3] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-5052-1846
[4] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD:https://orcid.org/0000-0001-9274-1663
Address for correspondence: Livia Costa de Oliveira. Rua Visconde de Santa Isabel, 274 A - Vila Isabel. Rio de Janeiro (RJ), Brazil. CEP 20560-120. E-mail: lillycostaoliveira@gmail.com

INTRODUCTION

Cancer leads to metabolic, physical, psychological and social changes that impact individuals´ lives [1]. The nutritional status impaired is related to all these aspects and can be present at the diagnosis[2], escalating with the progress of the disease[1,3].

Different methods of nutritional assessment have been used within this context. However, they have some limitations and may be affected by non-nutritional factors[4]. The bioelectric impedance analysis (BIA) is a fast, relatively low cost, non-invasive and reproducible method which indirectly estimates the body composition and the intra and extra cellular fluids distribution by a weak electric current sent throughout the body to measure resistance (R), reactance (Xc) and impedance (Z) [5,6,7].

Phase angle (PA) is one of the parameters of BIA that is related to cellular health through the ratio between body fluid R and cellular membrane Xc[8]. Of relevance for the prognosis within the oncologic context, PA can be related to the nutritional status[8] through its association with cellular membrane integrity and fluids balance[6,7]

The nutritional status assessment in oncology continues to be challenging and PA can be a promising tool for this purpose. Thus, the present study aims to investigate the correlation between PA and nutritional status in individuals with advanced cancer in palliative care.

METHOD

Cross-sectional, clinic study of a cohort of advanced cancer patients evaluated until 48 hours of the first attendance care in the Palliative Care Unit (PCU) at the National Cancer Institute José Alencar Gomes da Silva (INCA), Rio de Janeiro, Brazil, between March and July 2017.

The inclusion criteria were: age ≥20 years; able to respond to the required information or accompanied by a responsible able to act on its behalf; *Karnofsky Performance Status* (KPS) ≥30%; no pacemaker or metal prosthetics; accept to sign the Informed Consent Form (ICF). The Institutional Review Board of INCA approved the study, report number 1.407.458/2016.

Bioelectric impedance was conducted with a tetrapolar impedance analyzer model 300 (*Biodynamics Corporation, Inc., Seattle, Washington, EUA*), at the right side of the body, with the individual lying on a non-conductive stretcher, in supine, with legs apart and arms not touching the body. The measurements of R and Xc were obtained at a frequency of 50 kHz and current of 800 μA. The PA was calculated [(Xc/R) x (180°/π)] and classified as low if <percentile 5 (P5), according to the values proposed by Barbosa-Silva et al.[8].

The PG-SGA short form proposed by Vigano et al. was used[9]. This tool evaluates the body weight history, food intakes, presence of nutritional impact symptoms and functional capacity to reach a numeric score, which is the sum of these items (the higher the score, the worse the nutritional status). Individuals with score ≥9 were categorized as in nutritional risk.

The body weight, the height and the calf circumference (CC) were measured according to the methodology of Lohman et al.[10]. The weight was measured with a portable scale Wiso Digital (capacity of 150 kg). It was used Stryker model Go Bed II scale-bed for bedridden patients. The height was measured with a wall mounted metric tape. If measurement was not possible, it was estimated with the equation proposed by Chumlea et al.[11], which uses the knee height, measured with an extensible tape. The Body Mass Index (BMI) was determined by the division of the weight by the square of the height, and the individuals deemed malnourished had BMI <20 kg/m^2 [12]. CC was measured with an extensible metric tape and classified as low if ≤34 cm for men and ≤ 33 cm for women[13]. The levels of serum albumin were evaluated, being considered low values <3,5g/dL. KPS was used to evaluate the functional capacity. Patients were classified from 30% to 100% (100%: complete function - 0%: death).

The description of the sample was made through mean and standard deviation (SD) or median and limits (minimum and maximum) for continuous variables; and by number of observations (n) and frequency (%) for categorical variables. It was used the Kolmogorov-Smirnov test to evaluate the symmetry of the distribution of the variables. The chi-square was used to compare categorical variables among the groups and Spearman correlation test to investigate the correlation between the PA and the variables of nutritional status. It was used the *software Statistical Package for the Social Sciences* (SPSS version 21.0; Chicago, IL) being considered significant the values of $p<0.05$.

RESULTS

The study investigated 94 individuals with advanced cancer, median age of sixty years old and predominance of females. The most prevalent tumor locations were gastrointestinal tract, followed by lung and breast. Nearly one third of the sample presented low functional capacity (30-40%) and PA < P5 (Table 1).

The nutritional risk evaluated through PG-SGA and albumin as well as the low muscle mass evaluated by CC, were greater in patients with PA < P5. Only BMI did not differ among the groups (Table 2).

Table 1. General characteristics of advanced cancer patients in a palliative care unit in the city of Rio de Janeiro - RJ (n=94)

Variables	n (%)
Age (years)*	66 (57; 74)
Females	48 (51.1)
Tumor location	
Gastrointestinal Tract - GIT	37 (39.4)
Lung	14 (14.9)
Breast	9 (9.6)
Gynecologic	8 (8.5)
Head and neck	7 (7.4)
Others	19 (20.2)
Progression of the disease	
Local	83 (88.5)
Lymph nodes	39 (41.5)
Lung	30 (31.9)
Liver	29 (30.9)
Peritoneum	15 (16.0)
Bones	19 (20.2)
Comorbidities	
SAH	30 (31.9)
DM	16 (17.0)
KPS 30-40%	34 (36.2)
PA°*	4 (3;5)
PA <P5	35 (37,2)

Captions: n=number of observations; %= frequency; GIT=gastrointestinal tract; DM=diabetes mellitus; SAH= systemic arterial hypertension; KPS= *Karnofsky Performance Status*; PA=phase angle; P=percentile. *Median (Interquartile interval).

Except BMI, all the variables evaluated correlate to PA. Body weight, CC and serum albumin presented positive correlation with PA, while the total score of PG-SGA and its domains, except daily living activity, negatively correlate with PA (Table 3).

Figure 1 illustrated the correlation between PA and nutritional risk, demonstrating that patients with lower values of PA have high score of PG-SGA ($r = -0.382$, $p < 0.001$).

DISCUSSION

The present study evaluated advanced cancer patients in exclusive palliative care in a national reference site in Brazil and demonstrated that approximately one third of the sample had PA < P5; the nutritional status and the low muscle mass were more prevalent in individuals with lower PA; body weight, CC, serum albumin and the score of the PG-SGA were correlated to PA.

Table 2. Comparison of the nutritional parameters according to the phase angle in advanced cancer patients attended in a palliative care facility in the city of Rio de Janeiro - RJ

Variables	Total n=94 (100%)	PA<P5 n=35 (37.2%)	PA≥P5 n=59 (62.8%)	p*
PG-SGA short form (scores)				
>9	80 (85.1)	58.5	26.6	0.006
<9	14 (14.9)	4.3	10.6	
Albumin (g/dL)				
<3,5	58 (62.7)	44.6	18.1	0.017
≥3,5	36 (37.3)	16.9	20.5	
BMI (Kg/m²)				
<20	40 (42.0)	30.2	11.8	0.114
>20	54 (58.0)	33.3	24.7	
CC**				
Low	48 (50.6)	42.,2	8.4	<0.001
Normal	46 (49.4)	19.3	30.1	

Captions: n = number of observations; % = frequency; PA = phase angle; P=percentile; PG-SGA =patient-guided subjective global assessment short form; BMI = body mass index; CC= calf circumference.
*p-value refers to chi-square test for proportions.
**CC classified per Barbosa-Silva et al., 201613, being 34 cm males and 33 cm females.

Table 3. Correlation of the phase angle (in degrees) and measures of the nutritional status in patients with advanced cancer attended in a palliative care facility in the city of Rio de Janeiro - RJ

Variables	PA	
	r	p*
Weight (Kg)	0.216	0.037
BMI (Kg/m²)	0.162	0.122
CC (cm)	0.262	0.017
Albumin (g/dL)	0.336	0.002
PG-SGA short form (total score)	-0.382	<0.001
Domains of PG-SGA short form (score)		
Weight history	-0.231	0.025
Food intake	-0.249	0.016
Presence of symptoms of nutritional impact	-0.364	<0.001
Activity of daily life	-0.177	0.088

Captions: PA = phase angle; BMI = body mass index; CC= calf circumference.; PG-SGA =patient-guided subjective global assessment short form.
*p-value refers to Spearman test.

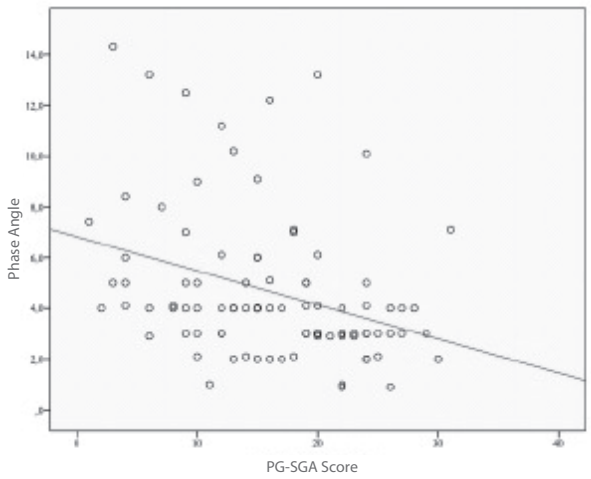

Figure 1. Correlation of the phase angle (in grades) with patient generated subjective global assessment short form in individuals with advanced cancer attended in a palliative care facility in the city of Rio de Janeiro - RJ

Note: PG-SGA = patient generated subjective global assessment short form.

Patients with advanced cancer usually had PA lower than a healthy population[14] due to metabolic alterations, cellular mass loss and cellular membrane fragility, which is quite prevalent in individuals with cancer and related to malnutrition[7].

The depletion of the nutritional status may cause unbalance of the body fluids and alterations of the cellular membrane, correlating with PA and, still, turning PA into an indicator of predictive risk of morbidity and mortality[4]. In account of the survival time be generally reduced in individuals with advanced cancer, it is expected that the tools utilized for clinical and nutritional evaluation are related to the prognosis, which grants the standardization of the diagnostic criteria and recommendations for interventions.

There is no PA cut-off yet capable to identify malnourished advanced cancer individuals. However, it is possible to affirm that individuals with worse nutritional status presented lower PA values, which is associated to the severity of the disease[15-17].

The evaluation of the correlation between PA and the worse nutritional status using PG-SGA is unprecedented in advanced disease, though it has been demonstrated in individuals with cancer. Małecka-Massalska et al.[18], while evaluating 75 individuals with head and neck cancer found that those classified as well nourished by SGA had higher PA. Gupta et al.[5] in a study with 73 individuals with colorectal cancer observed the same association, in addition to linear correlation between PA and PG-SGA, demonstrating that the score of SGA increased concomitantly to PA. It is worth mentioning that, as opposed to PG-SGA, in the evaluation through SGA, the lower the score, the worse is the nutritional status.

In addition to the positive correlation between PA and albumin, it was observed that individuals classified as malnourished with this parameter had more probability of having low PA. Hui et al.[16] in a study with 222 individuals with advanced cancer noticed positive association between PA and albumin.

The CC, another important marker of functioning and nutritional status, presented correlation with PA. Similar results including patients with advanced cancer were not described in the literature yet. However, one study that evaluated PA as indicative of nutritional status and prognosis of critical patients indicated a meaningful association between these two measures[19].

In relation to BMI, no association with PA was observed in our work. Regardless of being an easy and low-cost method, it does not allow to distinguish the fat mass from the lean mass. Hui et al.[16] tested the association between the PA and fat-free mass and encountered a positive and significant association, emphasizing the idea that the body composition has an important influence over the values of PA, which cannot be evaluated with BMI. Lee et al.[15] have not found also any association between BMI and PA.

It is noteworthy that, regardless this study included different tumor locations, relevant measures evaluated such as PG-SGA, BMI and levels of serum albumin, in addition to age (important confounding factor) did not differ statistically among individuals with distinguished diagnosis (data not presented).

The positive aspect of this study is the innovative characteristic of the investigation of the association between PA and nutritional status of patients with advanced cancer in palliative care. Nonetheless, the limitations are the use of albumin rather than pre-albumin as a nutritional indicator, reduced sample because is an ongoing study and absence of a benchmark of PA values for individuals with cancer.

These data show that the PA is related to the nutritional status of patients with advanced cancer in palliative care. Additional studies are necessary to define cut-off values to ensure the utilization of the tool in clinical practice.

CONTRIBUTIONS

Mayane Marinho Esteves Pereira participated of the planning of the study, data gathering and typing; wrote the section of methods, results and other sections of the article.. Emanuelly Varea Maria Wiegert and Livia Costa de Oliveira participated of the planning of the study, data gathering and typing and wrote the other sections of the article. Larissa Calixto Lima participated of the planning

of the study, data gathering and typing; wrote the section of methods and results of the article. All the authors revised and approved the final content.

DECLARATION OF CONFLICT OF INTERESTS

There are no conflict of interests to declare.

FUNDING SOURCES

None.

REFERENCES

1. Aktas A, Walsh D, Galang M, O'Donoghue N, Rybicki L, Hullihen B, et al. Underrecognition of malnutrition in advanced cancer: the role of the dietitian and clinical practice variations. Am J Hosp Palliat Care. 2017;34(6):547-55. doi: https://doi.org/10.1177/1049909116639969.
2. Coronha AL, Camilo ME, Ravasco P. A importância da composição corporal no doente oncológico. Qual a evidência? Acta Med Port. 2011;24(S4):769-78.
3. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017;36(1):11-48. doi: https://doi.org/10.1016/j.clnu.2016.07.015.
4. Sarhill N, Mahmoud F, Walsh D, Nelson KA, Komurcu S, Davis M, et al. Evaluation of nutritional status in advanced metastatic cancer. Support Care Cancer. 2003;11(10):652-9. doi: https://doi.org/10.1007/s00520-003-0486-0.
5. Gupta D, Lis CG, Dahlk SL, King J, Vashi PG, Grutsch JF, et al. The relationship between bioelectrical impedance phase angle and subjective global assessment in advanced colorectal cancer. Nutr J. 2008;7:19. doi: https://doi.org/10.1186/1475-2891-7-19.
6. Llames L, Baldomero V, Iglesias ML, Rodota LP. Valores del ángulo de fase por bioimpedancia eléctrica; estado nutricional y valor pronóstico. Nutr Hosp. 2013; 28(2):286-95. doi: http://dx.doi.org/10.3305/nh.2013.28.2.6306.
7. Grundmann O, Yoon SL, Williams JJ. The value of bioelectrical impedance analysis and phase angle in the evaluation of malnutrition and quality of life in cancer patients - a comprehensive review. Eur J Clin Nutr. 2015;69(12):1290-7. doi: https://doi.org/10.1038/ejcn.2015.126.
8. 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. doi: https://doi.org/10.1093/ajcn/82.1.49.
9. Vigano AL, di Tomasso J, Kilgour RD, Trutschnigg B, Lucar E, Morais JA, et al. The abridged patient-generated subjective global assessment is a useful tool for early detection and characterization of cancer cachexia. J Acad Nutr Diet. 2014;114(7):1088-98. doi: https://doi.org/10.1016/j.jand.2013.09.027.
10. Lohman TG, Roche, AF, Martorell R, editors. Anthropometric standardization reference manual. Champaign: Human Kinetics Books; c1988.
11. Chumlea WC, Guo SS, Steinbaugh ML. Prediction of stature from knee height for black and white adults and children with application to mobility-impaired or handicapped persons. J Am Diet Assoc. 1994;94(12):1385-91. doi: https://doi.org/10.1016/0002-8223(94)92540-2.
12. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011;12(5):489-95. doi: https://doi.org/10.1016/S1470-2045(10)70218-7.
13. Barbosa-Silva TG, Bielemann RM, Gonzalez MC, Menezes AM. Prevalence of sarcopenia among community-dwelling elderly of a medium-sized South American city: results of the COMO VAI? study. J Cachexia Sarcopenia Muscle. 2016;7(2):136-43. doi: https://doi.org/10.1002/jcsm.12049.
14. Gupta D, Lis CG, Dahlk SL, Vashi PG, Grutsch JF, Lammersfeld CA. Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer. Br J Nutr. 2004; 92(6):957-62. doi: https://doi.org/10.1079/BJN20041292.
15. Lee SY, Lee YJ, Yang JH, Kim CM, Choi WS. The association between phase angle of bioelectrical impedance analysis and survival time in advanced cancer patients: Preliminary study. Korean J Fam Med. 2014;35(5):251-6. doi: https://doi.org/10.4082/kjfm.2014.35.5.251.
16. Hui D, Bansal S, Morgado M, Dev R, Chisholm G, Bruera E. Phase angle for prognostication of survival in patients with advanced cancer: preliminary findings. Cancer. 2014; 120(14):2207-14. doi: https://doi.org/10.1002/cncr.28624.
17. Hui D, Dev R, Pimental L, Park M, Cerana MA, Liu D, et al. Association between multi-frequency phase angle and survival in patients with advanced cancer. J Pain Symptom Manage. 2017;53(3):571-7. doi: https://doi.org/10.1016/j.jpainsymman.2016.09.016.
18. Małecka-Massalska T, Mlak R, Smolen A, Morshed K. Bioelectrical impedance phase angle and subjective global assessment in detecting malnutrition among newly diagnosed head and neck cancer patients. Eur Arch Otorhinolaryngol. 2016;273(5):1299-305. doi: https://doi.org/10.1007/s00405-015-3626-5.
19. Reis de Lima e Silva R, Pinho CPS, Rodrigues IG, Monteiro Júnior JGM. Ângulo de fase como indicador

del estado nutricional y pronóstico en pacientes críticos. Nutr Hosp. 2015;31(3):1278-85. doi: https://doi.org/10.3305/nh.2015.31.3.8014.

Recebido em 4/12/2018
Aprovado em 18/2/2019