Marina Carvalho Berbigier[1,2], Valeska Fernandes Pasinato[1,2], Bibiana de Almeida Rubin[2,3], Rafael Barberena Moraes[4], Ingrid Dalira Schweigert Perry[2,5]

Bioelectrical impedance phase angle in septic patients admitted to intensive care units

Ângulo de fase derivado de bioimpedância elétrica em pacientes sépticos internados em unidades de terapia intensiva

1. Integrated Multidisciplinary Health Residency Program focusing on Critically Ill Adults, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.
2. Food and Nutrition Research Center, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.
3. Nutrition and Dietetic Service, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.
4. Intensive Care Unit, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.
5. Department of Internal Medicine, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.

This study was conducted at the Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.

Conflict of interest: None.

Submitted on December 18, 2012
Accepted on March 14, 2013

Corresponding author:
Marina Carvalho Berbigier
Rua Ramiro Barcelos, 2.350 - Santa Cecília
CEP: 90035-903 - Porto Alegre (RS), Brazil
E-mail: marina.berbigier@gmail.com

ABSTRACT

Objective: To calculate the values of the phase angle of septic patients using bioelectrical impedance analysis, correlate the values with clinical and biochemical variables, and compare them to reference values.

Methods: Cohort study conducted with 50 septic patients aged ≥18 years old, admitted to intensive care units, and assessed according to prognostic indexes (APACHE II and SOFA), clinical progression (mortality, severity of sepsis, length of stay in intensive care unit), biochemical parameters (albumin and C-reactive protein), and the phase angle.

Results: The average age of the sample was 65.6±16.5 years. Most patients were male (58%) and suffering from septic shock (60%). The average APACHE II and SOFA scores were 22.98±7.1 and 7.5±3.4, respectively. The patients who survived stayed nine days on average (five to 13) in the intensive care unit, and the mortality rate was 30%. The average value of the phase angle was 5.4±2.6° in the total sample and was smaller among the females compared with the males (p=0.01). The phase angle measures did not exhibit an association with the severity of the sepsis, mortality, gender, and age or correlate with the length of hospitalization or the biochemical parameters. The participants' phase angle values adjusted per gender and age were 1.1 to 1.9 times lower compared with the values for a normal population.

Conclusion: The average value of the phase angle of septic patients was lower compared with the reference values for a healthy population. The phase angle measures did not exhibit association with the clinical and biochemical variables, which might be explained by the sample homogeneity.

Keywords: Sepsis; Intensive care units; Electric impedance; Nutrition assessment; Inpatients; Prognosis

INTRODUCTION

Sepsis is a complex disease and is characterized by a systemic inflammatory response triggered by infection.[1-4] It is the most common cause of admission to and death in intensive care units (ICUs).[1,5-7] Several studies have demonstrated that the incidence of sepsis has increased in Brazil, with only a small decrease in mortality, and this incidence is higher than in other countries.[6-9] When associated with multiple organ failure, the sepsis mortality rate is often high, as are the hospital costs. Thus, the diagnosis and management of sepsis is an important challenge for healthcare professionals.[6,8]

The use of prognostic indices in critical patients facilitates the assessment of the severity and prognosis of the disease and the adequate monitoring of its

clinical progress. Sequential Organ Failure Assessment (SOFA)[10] and Acute Physiology and Chronic Health Evaluation II (APACHE II)[11] are indices used to estimate the morbidity and mortality risk in inpatients. High scores correlate directly with a poorer clinical prognosis, particularly in critical patients.[1,12,13]

Bioelectrical impedance analysis (BIA) is a widely used method to assess body composition and nutritional status.[14-16] Because BIA is non-invasive and practical (it can be performed at bedside), it is used in both healthy and ill individuals.[17] BIA is based on the measurement of the total body resistance to the injection of a low-amplitude (800 mA) and high-frequency (50 kHz) electric current, which facilitates quantifying parameters such as impedance, resistance (R), reactance (Xc), and phase angle (PA).[14,18]

PA is calculated from the ratio between various R and Xc measurements (PA=arc tangent Xc/R) and affords a direct measure of cell stability while indicating the water distribution across the intra- and extracellular spaces. PA is considered to be an indicator of membrane integrity and body cell mass (BCM).[14]

In addition, PA has been used as a prognostic indicator and a predictor of survival under certain clinical conditions.[18-29] According to several studies, low PA values in critical patients correlate with poorer disease progress and higher mortality.[26,30,31] Different from the other parameters used to assess body composition measured by BIA, PA is considered to be valid when the hydration status varies.[17,22]

Therefore, the present study sought to assess PA calculated from BIA in patients diagnosed with sepsis and admitted to ICU, evaluate PA's association with the patients' length of hospitalization, mortality, clinical scores, and biochemical parameters, and compare the PA values with reference values.

METHODS

The present study was a cohort study that assessed patients admitted to three ICUs of the Hospital de Clínicas de Porto Alegre (HCPA). The data were collected from May to August 2012. Patients aged ≥18 years, diagnosed with sepsis upon ICU admission, and expected to be hospitalized for at least 72 hours were included, whereas patients for whom BIA could not be performed (pacemaker users, amputees, or patients with skin infections) were excluded. The International Sepsis Definitions Conference consensus was used to establish the sepsis diagnosis.[32]

The sociodemographic (age and gender), clinical (baseline disease; APACHE II and SOFA scores; clinical progression, i.e., the mortality and severity of the sepsis; and the length of ICU stay), and biochemical (serum albumin and C-reactive protein - CRP) data were collected from the clinical records. The albumin levels were measured within the first 48 hours of ICU admission. CRP was measured twice: on admission and three to five days after the first measurement. All of the patients were followed from ICU admission to their discharge, death, or day 28 of the study.

The APACHE II[11] and SOFA[10] scores were only applied on admission. Thus, delta SOFA was not included as a variable, i.e., the emergence or progression of organ dysfunctions was not assessed. The serum albumin and CRP measurements were performed using the bromocresol green colorimetric method and turbidimetry, respectively.

To calculate PA within the first 48 hours after ICU admission, the BIA device Biodynamics 450, version 5.1 (Biodynamics® Corp., Seattle, WA, USA) and Resting Tab ECG electrodes (Conmed® Corp., Utica, NY, USA) were used. Through the injection of low-frequency and high-voltage alternating current (800 mA and 50 kHz), this BIA device measures the following body parameters: R, Xc, PA, the cell, extracellular, lean, and fat masses, the body mass index (BMI), the basal metabolic rate (BMR), total body water, and intra- and extracellular water. The measurements were performed with the patients lying down with the legs and arms parallel to the body and positioned far from the trunk. The electrodes were placed on standard locations (the dorsal surface of the right wrist, the third metacarpal bone, the anterior surface of the right ankle between the bone prominences, and the dorsal surface of the third metatarsal bone).[15] All of the procedures were performed by trained staff.

The patient's weight and height were measured using an Eleve (Eleve Dymat E3 - Phoenix Mecano Company) or a bed scale and a Luft Ruler, respectively.[33]

To compare the PA values, the reference values described by Barbosa-Silva et al. for healthy US adults were used.[34]

All of the protocols to avoid infection during the handling of patients were followed with particular care to ensure patient safety. Thus, rubber gloves and disposable masks and aprons were used, and the body surfaces on which the electrodes were placed were cleansed with 70% ethanol before and after application.

The present study complied with the ethical

principles for research on human beings established by the National Health Council (Conselho Nacional de Saúde - CNS) 196/96, protocol no. 110,663, and was approved by the HCPA Ethics Committee. All of the participants (or their legal guardians) signed a free and informed consent form.

Statistical analysis

Calculations based on the average PA values of surviving (5.6±2.2) and non-surviving (2.5±1.1)[35] septic patients in ICU resulted in a minimum sample size of 35 participants for an expected mortality of 20%,[31] a power of 90%, and a significance level of 0.05%.

The Kolmogorov-Smirnov test was used to investigate the normality of the variable distributions. The categorical variables were expressed as absolute or relative frequencies, and the continuous variables as a mean and standard deviation or a median and interquartile range, as appropriate. The chi-square test was used to investigate the association between the categorical variables, Student's t-test to compare means, the Mann-Whitney test for independent variables with non-normal distribution, the Wilcoxon test for repeated non-parametric measures, and the Spearman or Pearson's correlation coefficient to investigate the correlation of the parametric variables. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 18.0 (SPSS Inc., Chicago, IL), and the results were considered to be significant when p≤0.05.

RESULTS

Of 80 patients admitted to the HCPA Service of Intensive Care Medicine with sepsis during the study period, 22 were considered as losses. In 17 of these cases, the informed consent form was not signed within the first 48 hours (because it was impossible or a legal representative was absent), and five patients refused to participate. Six patients died before BIA could be performed, and thus did not meet the inclusion criteria. Two patients wore pacemakers. Therefore, the sample consisted of 50 participants (62% of the potential sample) of whom 29 were male (58%). The average age was 65.6 ± 16.5 years (Table 1).

Regarding the inpatient profiles, most participants (64%) were clinical (non-surgical). Most (60%) were suffering from septic shock on admission, whereby the respiratory system was the most frequent source of the primary infection. The average APACHE II score was 22.98±7.1, and SOFA was 7.5±3.4. The average PA was 5.4±2.6°), lower among the females (p=0.01), and lower than ≤5° in more than 50% of the sample (Table 1).

Table 1 - Sample characterization

Characterization	Results N = 50
Gender	
Male	29 (58)
Female	21 (42)
Age (years)	65.6±16.5
Profile	
Clinical	32 (64)
Surgical	18 (36)
Sepsis severity	
Sepsis + severe sepsis	20 (40)
Septic shock	30 (60)
Sepsis origin	
Respiratory	25 (50)
Abdominal	11 (22)
Urinary	8 (16)
Other	6 (12)
SOFA (score)	7.5±3.4
APACHE II (score)	22.98±7.1
PA°	5.4±2.6
Women	4.1±1.3*
Men	5.4±1.9
PA° category	
≤5	29 (58)
>5	21 (42)
Resistance Ω	333.0±104.3
Reactance Ω	28.0 (18.7 - 37.4)
CVVH	16 (32)
Albumin (g/dL)	2.5±0.4
CRP (mg/dL)	
1st assessment	164.3 (98.5 - 271.8)**
2nd assessment	99.8 (51.8 - 167.7)
Length of ICU stay (days)	9.0 (5 - 13)
Mortality in ICU	15 (30)

SOFA - Sequential Organ Failure Assessment; APACHE II - Acute Physiology and Chronic Health Evaluation II; PA - phase angle; CVVH - continuous venovenous hemodialysis; CRP - C-reactive protein; ICU - intensive care unit. Data expressed as number (%), mean ± standard deviation, or median (25%-75%). * p=0.015 between both genders (Student's t-test); ** p<0.001 between the first and second assessments (Wilcoxon test).

The median ICU stay length of the survivors was nine days. A total of 15 (30%) patients died (Table 1).

The average PA values did not differ between the patients with sepsis or severe sepsis compared with the patients with septic shock (4.5±14° and 5.0±1.9°; p=0.36; Student's t-test). Figure 1 depicts the PA value as a function of the severity of sepsis. PA was not associated with the severity of sepsis, the inpatient's profile, mortality, gender, or age (Table 2).

The PA did not correlate with the APACHE II and

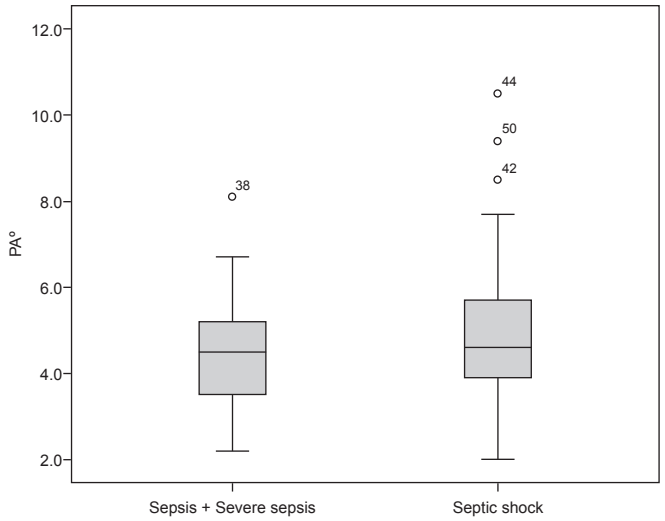

Figure 1 - Boxplot of the phase angle in patients according to the severity of sepsis.
PA - phase angle. Sepsis and severe sepsis, N=20; septic shock, N=30.

Table 2 - Clinical variables, age, mortality and phase angle in septic patients

Variables	PA°		p value
	≤5 (N=29)	>5 (N=21)	
Sepsis			
Sepsis + severe sepsis	12 (60)	8 (40)	0.81
Septic shock	17 (56.7)	13 (43.3)	
Profile			
Clinical	16 (50)	16 (50)	0.12
Surgical	13 (72.2)	5 (27.8)	
Death			
Yes	9 (60)	6 (40)	0.76
No	20 (64.5)	11 (35.5)	
Age			
<60 years	9 (60)	6 (40)	0.85
≥60 years	20 (57.1)	15 (42.9)	
Gender			
Male			
<60 years	3 (60)	2 (40)	0.92
≥60 years	10 (62.5)	6 (37.5)	
Female			
<60 years	6 (60)	4 (40)	0.70
≥60 years	10 (52.6)	9 (47.4)	

PA - phase angle. Results expressed as number (%).

SOFA scores, hospitalization length, or biochemical parameters (Table 3). When these parameters were analyzed according to the categories PA ≤5 and >5°, the following values were found: averages of 22.7±7.3 and 23.2±7.1 (p=0.82) in APACHE II, 7.1±3.4 and 8±3.5 (p=0.35) in SOFA, 2.4±0.4 and 2.6±0.4 (p=0.45) in the albumin level; medians of 222.5 (106.5 - 323.9) and 134.2 (76.4 - 219) in CRP1 (p=0.13); and 8 (5.0 - 13) and 10 (7.0 - 12) days in the length of hospitalization (p=0.23) (according to Student's t or Mann-Whitney tests).

Table 3 - Prognostic scores, biochemical parameters, length of hospitalization, and phase angle in septic patients

Variables	Coefficient of correlation (r)	p value
APACHE II*	-0.005	0.97
SOFA*	0.210	0.16
CRP1**	-0.264	0.09
Albumin*	0.229	0.25
Length of ICU stay**	0.059	0.75
Resistance*	-0.188	0.21
Reactance**	0.714	<0.001

APACHE II - Acute Physiology and Chronic Health Evaluation II; SOFA - Sequential Organ Failure Assessment; CRP - C-reactive protein. * Pearson's coefficient of correlation; ** Spearman's coefficient of correlation.

Compared with the PA values of the healthy population adjusted per age and gender, the median values of the participants were lower, corresponding to 67.7% (P25=59.9%; P75=83.7%) of the reference values.[34]

DISCUSSION

The identification of prognostic factors for septic patients is important for the clinical management of the disease. PA has been recently investigated as a prognostic instrument to assess the cell membrane function under different clinical conditions.[18,20-22,27,29-31,36-38] The average PA values were lower in those studies compared with the healthy population (from 4 to 10° as a function of age and gender).[34] Low PA values correlate with reduced cell integrity and lean mass and increased morbidity and mortality.[14,15,27] In patients with liver cirrhosis, PA ≤5.4° correlated with higher mortality compared with patients with higher PA values.[18] Several studies found PA to be a strong prognostic indicator and an important tool to assess the clinical signs and monitor the progress of the disease in patients who were either undergoing peritoneal dialysis, were HIV-positive, or had colon or pancreatic cancer.[20-22,38] One study assessed patients with breast, head and neck cancer, among others, and found that PA behaved as an independent predictor of mortality in the patients on chemotherapy, with an average of 5.12±0.89°.[21]

Among the few studies that assessed septic patients, one study, which compared patients with and without sepsis, corroborated the use of PA as a prognostic indicator.[30] The PA values in that study were similar to those found by Miranda, who reported an average of 5.6±2.2° in the patients with sepsis who survived

compared with 2.5±1.1° in the non-survivors.[31] In the present study, 60% of the patients who died exhibited PA ≤5°, which agrees with all of the reports in the literature.

However, the analysis of PA relative to the various investigated variables exhibited no association with the severity of sepsis, the inpatient's profile, mortality, gender, or age. This lack of association might result from the sample's homogeneity. Different from the present study, in which most of the sample was in a state of septic shock, the sample in a study that found an association between PA and the previously mentioned variables exhibited a regular distribution of the various degrees of sepsis severity. In addition, that study performed sequential assessments of the variable.[31] However, although most of the participants in the present study were clinical (64%), the surgical patients exhibited the highest percentages of PA ≤5, which agrees with the findings of other studies conducted on septic, polytrauma and emergency surgery patients.[3,31]

The correlation between PA and variables such as gender, age, ethnicity, and the indicators of body composition was investigated by Barbosa-Silva et al.[34] In the present study, the PA values were approximately 32% lower for both genders and all of the age groups compared with the reference values for the US healthy population.[34] Miranda performed the same comparison and also found lower PA values among the patients with sepsis.[31]

In the present study, the average PA was 5.4±2.6° and lower among the females (4.1±1.3°), which is similar to what has been found in other studies.[18,20-22,27-31,36-38] Lower values are expected among women in healthy populations because the PA increases together with the muscle mass and the BCM.[16,18]

In this context, PA tends to decrease with age as a function of the reduction of muscle mass and the influence of the alterations in the ratio of intra- and extracellular water associated with aging.[23,34] Additionally, studies conducted on ill individuals, including patients with sepsis[31] and undergoing dialysis[37], found a negative correlation between age and PA, i.e., the latter decreases with age. That relationship was not found in the present study. Because the patients in a critical state also exhibit a loss of muscle mass and alterations in the water distribution between the intra- and extracellular compartments,[17,31] this lack of a relationship might have resulted from the severity of the patients' condition, given that 60% exhibited septic shock, and the average APACHE II and SOFA scores were 22.98±7.1 and 7.5±3.4, respectively.

High APACHE II and SOFA scores are associated with an increased risk of morbidity and mortality and longer hospitalization periods, particularly for critical patients.[6] In addition, an inverse correlation was found between the PA values and the clinical indices in patients with sepsis (higher severity scores, longer hospitalization periods, and lower PA values).[31] In critical patients, high CRP and low serum albumin levels are considered to be prognostic markers and tools to assess the progress of disease. Low albumin levels correlate with the PA in certain clinical conditions, such as sepsis and pancreatic cancer, whereby the degree of correlation varies from very weak to moderate.[22,31] In the present study, the serum albumin and CRP levels did not correlate with PA, which did not correlate with APACHE II, SOFA, and the length of hospitalization indices. The Xc correlated positively with PA as expected because it is an indicator of BCM. Such association surpasses the morphological assessment of the cell membrane as a measure of cell function.[14]

Regarding this study's limitations, the sample homogeneity (more than half of the patients were suffering from septic shock) must be mentioned. Other limitations include the significant losses observed, the lack of PA reference values for the Brazilian population, which compelled the use of the values established for a US healthy population, and the small number of studies conducted on critical patients, which hindered comparative analysis.

Further studies are required with larger and more diversified samples with respect to the severity of disease to enable a more accurate assessment of PA's prognostic ability in patients with sepsis.

CONCLUSION

The average PA value was lower in septic patients compared with the reference values for a healthy population and not associated with the clinical and biochemical variables most likely because of sample homogeneity.

ACKNOWLEDGMENTS

The authors thank the HCPA Research and Events Incentive Fund for financial support.

RESUMO

Objetivo: Identificar valores de ângulo de fase em pacientes sépticos, por meio de bioimpedância elétrica, buscando associação com variáveis clínicas e bioquímicas, bem como comparação com valores de ângulo de fase de referência.

Métodos: Estudo de coorte, com 50 pacientes sépticos, idade ≥18 anos, internados em unidade de terapia intensiva, avaliados quanto a índices prognósticos (APACHE II e SOFA), evolução clínica (mortalidade, gravidade da sepse e tempo de internação na unidade de terapia intensiva), parâmetros bioquímicos (albumina e proteína C-reativa) e ângulo de fase.

Resultados: A média de idade dos pacientes estudados foi de 65,6±16,5 anos, a maioria do gênero masculino (58%) e apresentando choque séptico (60%). A média dos escores APACHE II e SOFA foi de 22,98±7,1 e 7,5±3,4, respectivamente, o tempo de internação na unidade de terapia intensiva dos pacientes que sobreviveram foi de 9 dias (5 a 13) e a taxa de mortalidade foi de 30%. A média do ângulo de fase da amostra total foi de 5,4±2,6° e menor no gênero feminino (p=0,01). Não houve associação entre ângulo de fase e a gravidade da sepse, mortalidade, gênero e idade, assim como não houve correlação entre ângulo de fase, tempo de internação e parâmetros bioquímicos. Comparativamente a dados em população saudável, os valores de ângulo de fase, a depender da idade e gênero, apresentaram-se 1,1 a 1,9 vezes inferiores.

Conclusão: O ângulo de fase médio de pacientes sépticos foi inferior aos valores referência para população saudável, não havendo correlação e associação com as variáveis clínicas e bioquímicas, o que poderia ser atribuído a homogeneidade da amostra.

Descritores: Sepse; Unidades de terapia intensiva; Impedância elétrica; Avaliação nutricional; Pacientes internados; Prognóstico

REFERENCES

1. de Pablo R, Monserrat J, Reyes E, Diaz-Martin D, Rodriguez Zapata M, Carballo F, et al. Mortality in patients with septic shock correlates with anti-inflammatory but not proinflammatory immunomodulatory molecules. J Intensive Care Med. 2011;26(2):125-32.
2. Henkin CS, Coelho JS, Paganella MC, Siqueira RM, Dias FS. Sepse: uma visão atual. Sci Med. 2009;19(3):135-45.
3. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, Moreno R, Carlet J, Le Gall JR, Payen D; Sepsis Occurrence in Acutely Ill Patients Investigators. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med. 2006;34(2):344-53.
4. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M; Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368-77.
5. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348(16):1546-54.
6. Sales Júnior JA, David CM, Hatum R, Souza PC, Japiassú A, Pinheiro CT, et al. Sepse Brasil: estudo epidemiológico da sepse em unidades de terapia intensiva brasileiras. Rev Bras Ter Intensiva. 2006;18(1):9-17.
7. Padkin A, Goldfrad C, Brady AR, Young D, Black N, Rowan K. Epidemiology of severe sepsis occurring in the first 24 hrs in intensive care units in England, Wales, and Northern Ireland. Crit Care Med. 2003;31(9):2332-8.
8. Kauss IA, Grion CM, Cardoso LT, Anami EH, Nunes LB, Ferreira GL, et al. The epidemiology of sepsis in a Brazilian teaching hospital. Braz J Infect Dis. 2010;14(3):264-70.
9. Zanon F, Caovilla JJ, Michel RS, Cabeda EV, Ceretta DF, Luckemeyer GD, et al. Sepse na unidade de terapia intensiva: etiologia, fatores prognósticos e mortalidade. Rev Bras Ter Intensiva. 2008;20(2):128-34.
10. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22(7):707-10.
11. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818-29.
12. Kopterides P, Liberopoulos P, Ilias I, Anthi A, Pragkastis D, Tsangaris I, et al. General prognostic scores in outcome prediction for cancer patients admitted to the intensive care unit. Am J Crit Care. 2011;20(1):56-66.
13. Chen SJ, Chao TF, Chiang MC, Kuo SC, Chen LY, Yin T, et al. Prediction of patient outcome from Acinetobacter baumannii bacteremia with Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE) II scores. Intern Med. 2011;50(8):871-7.
14. Silva LM, Caruso L, Martini LA. Aplicação do ângulo de fase em situações clínicas. Rev Bras Nutr Clin. 2007;22(4):317-21.
15. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, Heitmann BL, Kent-Smith L, Melchior JC, Pirlich M, Scharfetter H, Schols AM, Pichard C; Composition of the ESPEN Working Group. Bioelectrical impedance analysis--part I: review of principles and methods. Clin Nutr. 2004;23(5):1226-43.
16. Baumgartner RN, Chumlea WC, Roche AF. Bioelectric impedance phase angle and body composition. Am J Clin Nutr. 1988;48(1):16-23.
17. Barbosa-Silva MC, Barros AJ. Bioelectric impedance and individual characteristics as prognostic factors for post-operative complications. Clin Nutr. 2005;24(5):830-8.
18. Selberg O, Selberg D. Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis. Eur J Appl Physiol. 2002;86(6):509-16.
19. Stobäus N, Pirlich M, Valentini L, Schulzke JD, Norman K. Determinants of bioelectrical phase angle in disease. Br J Nutr. 2012;107(8):1217-20.
20. Schwenk A, Beisenherz A, Römer K, Kremer G, Salzberger B, Elia M. Phase angle for bioelectrical impedance analysis remains an independent predictive marker in HIV-infected patients in the era of highly active antiretroviral treatment. Am J Clin Nutr. 2000;72(2):496-501.
21. Paiva SI, Borges LR, Halpern-Silveira D, Assunção MC, Barros AJ, Gonzalez MC. Standardized phase angle from bioelectrical impedance analysis as prognostic factor for survival in patients with cancer. Support Care Cancer. 2010;19(2):187-92.
22. 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.
23. Wirth R, Volkert D, Rösler A, Sieber CC, Bauer JM. Bioelectric impedance phase angle is associated with hospital mortality of geriatric patients. Arch Gerontol Geriatr. 2010;51(3):290-4.
24. Marra M, Caldara A, Montagnese C, De Filippo E, Pasanisi F, Contaldo F, et al. Bioelectrical impedance phase angle in constitutionally lean females, ballet dancers and patients with anorexia nervosa. Eur J Clin Nutr. 2009;63(7):905-8.
25. Marra M, De Filippo E, Signorini A, Silvestri E, Pasanisi F, Contando F, et al. Phase angle is a predictor of basal metabolic rate in female patients with

anorexia nervosa. Physiol Meas. 2005;26(2):145-52.
26. Acosta Escribano J, Gómez-Tello V, Ruiz Santana S. [Nutritional assessment of the severely ill patient]. Nutr Hosp. 2005;20 Suppl. 2:5-8. Spanish.
27. Norman K, Stobäus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis--clinical relevance and applicability of impedance parameters. Clin Nutr. 2012;31(6):854-61.
28. Kyle UG, Genton L, Pichard C. Low phase angle determined by bioelectrical impedance analysis is associated with malnutrition and nutritional risk at hospital admission. Clin Nutr. 2012 Aug 14. [epub ahead of print].
29. Kyle UG, Soundar EP, Genton L, Pichard C. Can phase angle determined by bioelectrical impedance analysis assess nutritional risk? A comparison between healthy and hospitalized subjects. Clin Nutr. 2012;31(6):875-81.
30. GIBI Brazilian Group for Bioimpedance Study. Total body bioelectrical impedance measurement as a progressive outcome prediction and therapeutic index in the comparison between septic and non septic patients. A multicenter Brazilian study. Rev Metab Nutr. 1995;2:159-70.
31. Miranda AM. Ângulo de fase como indicador de prognóstico em doentes críticos com sépsis [dissertação]. Porto: Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto; 2010.
32. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med. 2003;31(4):1250-6.
33. Luft VC, Beghetto MG, Mello ED. Validação de um instrumento desenvolvido para medir a altura de pacientes adultos acamados. Revista do HCPA. 2007;27(Supl 1):214.
34. 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.
35. Máttar JA. Application of total body bioimpedance to the critically ill patient. Brazilian Group for Bioimpedance Study. New Horiz. 1996;4(4):493-503.
36. Alvram MM, Fein PA, Rafiq MA, Schloth T, Chattopadhyay J, Mittman N. Malnutrition and inflammation as predictors of mortality in peritoneal dialysis patients. Kidney Int. 2006;70:S4-7.
37. Oliveira CM, Kubrusly M, Mota RS, Silva CA, Choukroun G, Oliveira VN. The phase angle and mass body cell as markers of nutritional status in hemodialysis patients. J Ren Nutr. 2010;20(5):314-20.
38. 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.