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Parameters of Bioelectrical Impedance Are Good Predictors of Nutrition Risk, Length of Stay, and Mortality in Critically Ill Patients: A Prospective Cohort Study

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Abstract

Background: Assessment of nutrition risk in the intensive care unit (ICU) is limited by characteristics of critically ill patients, and new methods have been investigated for their applicability and predictive validity. The aim of the present study was to evaluate the validity of bioelectrical impedance analysis (BIA) parameters as predictors of nutrition risk and clinical outcomes in critically ill patients. *Methods:* This was a prospective cohort study of patients admitted to an ICU. The modified Nutrition Risk in the Critically Ill score was used for assessment of nutrition risk, and BIA was performed in the first 72 hours of admission. Phase angle (PA) measurements were obtained, and bioelectrical impedance vector analysis (BIVA) was used to classify patients by hydration status (BIVA >70%). Patients were followed until hospital discharge and evaluated for hospital mortality, ICU length of stay, length of hospitalization, and duration of mechanical ventilation. *Results:* Eighty-nine patients were included (62.5 ± 14.1 years, 50.6% female). A PA <5.5° showed an accuracy of 79% (95% CI 0.59-0.83) in identifying patients at high nutrition risk and was associated with nearly 2 times greater risk for an ICU length of stay longer than 5 days (relative risk = 2.18 [95% CI 1.39-3.40]). Hyperhydration was a significant predictor of mortality (hazard ratio = 2.24 [95% CI 1.07-4.68]). Higher resistance and reactance values, adjusted for height, were found in survivors compared with nonsurvivors. *Conclusion:* The predictive validity of BIA was satisfactory for the assessment of nutrition risk, ICU length of stay, and mortality in critically ill patients. (*JPEN J Parenter Enteral Nutr.* 2019;00:1–6)

Keywords

bioelectrical impedance; critically ill patients; intensive care unit; nutrition risk; phase angle

Clinical Relevancy Statement

According to this study, phase angle <5.5° showed an accuracy of 79% to identify patients at high nutrition risk and was associated with a 2-times higher risk of an intensive care unit (ICU) length of stay longer than 5 days. Hyperhydration (bioelectrical impedance vector analysis >70%) was a significant predictor of mortality. These results suggest that a bioelectrical impedance analysis should be performed in patients admitted to the ICU, considering its applicability as a nutrition screening tool and as a prognostic marker.

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Introduction

Stress response in critically ill patients is characterized by severe inflammation and high protein catabolism. It is also marked by decreased efficiency of protein utilization, leading to muscle dysfunction and impaired contractility.[1] Intensive care unit (ICU) patients commonly experience loss of body weight and muscle mass and are at increased risk of malnutrition, which is observed in 38%–78% of these patients.[2] A systematic review of 7 observational studies showed that the rate of muscle wasting varied from 6% to 1.6% per day in critically ill patients, and changes in muscle architecture were associated with ICU length of stay (LOS).[3] Thus, an early identification of ICU patients at increased risk of malnutrition is paramount, and in this context, application of a nutrition risk screening tool as the first steep of a nutrition care plan would be very useful.

The Nutrition Risk in Critically Ill (NUTRIC) score[4,5] and the Nutritional Risk Screening (NRS)-2002 are recommended by international guidelines to identify nutrition risk at ICU admission.[6,7] However, administration of these instruments require parameters that are not always available at the time of admission, including the severity score (NUTRIC score), food intake, or weight loss data (NRS-2002). Therefore, assessment of the accuracy of other parameters to identify nutrition risk at ICU is needed.

Among the emerging methods to evaluate the nutrition status of critically ill patients, parameters derived from the bioelectrical impedance analysis (BIA) have gained importance, including the phase angle (PA), extracellular water (ECW)–to–total body water (TBW) ratio (ECW/TBW), and the bioelectrical impedance vector analysis (BIVA). BIVA is calculated from the BIA resistance (R) and reactance (Xc), adjusted for body height.[8] PA is an indicator of cell membrane integrity and a predictor of body cell mass.[9] Studies have shown that a low PA is associated with higher mortality risk in critically ill patients.[10-13] A higher ECW/TBW ratio was observed in patients with worse nutrition status and was associated with mortality.[8] BIVA reflects nutrition and hemodynamic status and seems to be associated with mortality.[14-18] One study with critically ill cancer patients showed a significant association between PA and nutrition risk assessed by the NUTRIC score.[19]

New studies on the predictive validity of PA, ECW/TBW, and BIVA in critical illness are needed to identify accurate methods for nutrition risk screening of ICU patients. Therefore, this study aimed to assess the validity of BIA parameters to predict nutrition risk, ICU LOS, length of hospitalization (LOH), time on mechanical ventilation (MV), and mortality in critically ill patients.

Methods

A prospective cohort study was conducted with critically ill adult patients (≥18 years) of both sexes admitted to the ICU of Nossa Senhora da Conceição Hospital, Porto Alegre, Brazil. Patients with contraindications to BIA (pacemakers, anasarca, pregnancy, and body mass index <16 kg/m^2 or >35 kg/m^2) were excluded. Sample size calculation was based on the difference in PA between survivors (4.1 ± 1.3°) and nonsurvivors (3.2 ± 1.5°) reported by Lee et al.[9] Based on this information, a power of 80%, and a level of significance of 5%, the calculated sample size was 78 patients. Sample size was calculated using the online calculator available at https://www.openepi.com/Menu/OE_Menu.htm.

The study was approved by the local ethics committee (approval number 2598103), and data collection was initiated after patients' family members or guardians signed the informed consent form. The study was conducted according to the 466/12 resolution of the National Ethics Committee.

Sociodemographic (age, sex, and ethnicity) and hospitalization data (cause of hospitalization, use and duration of MV, and history of hemodialysis) were collected from patients' medical records. We used the Acute Physiology and Chronic Health Evaluation II (APACHE II) and the sequential organ failure assessment (SOFA) disease severity classification systems for the initial assessment of patients. In addition, clinical laboratory results available at ICU admission were collected.

Patients' nutrition risk was evaluated using the Brazilian Portuguese version of the modified NUTRIC score,[20] which evaluated APACHE II and the SOFA score at ICU admission, age, number of comorbidities, and LOH prior to ICU admission. Patients with a NUTRIC score of 0–4 were classified as low nutrition risk and those with a score of 5–9 as high nutrition risk.[5]

Anthropometric measures were obtained in the first 72 hours of ICU admission. Body weight and height of all patients were calculated from mid-upper arm circumference and knee height measurements, using the predictive equations proposed by Chumlea et al.[21,22] Mid-upper arm circumference was measured at the midpoint between the olecranon process and the acromion. Knee height was measured parallel to the tibia and was defined as the distance from the undersurface of the heel to the top of the knee.

BIA was performed using a BIA 310 analyzer (Biodynamics), with subjects in a supine position with legs apart and arms and hands away from the body. Four disposable adhesive electrodes were placed on the dorsal surface of the right hand and foot on clean and dry skin. Measures of R, Xc, PA, intracellular water (ICW), ECW, and TBW volume were made.

Standardized PA (SPA) was obtained using the following formula: SPA = ([PA measured by BIA–mean PA of the reference population]/SD of the reference population). For our study population, we used mean PA and SD for age and sex obtained from a population in the south of Brazil by Barbosa-Silva et al.[23] Then PA values <−1.65°

and $\geq -1.65^{o}$ were used to define low and normal PA, respectively.[23]

BIVA was determined based on the plot of BIA R and Xc, normalized for height (R/height and Xc/height), in a graph using specific software.[24] Correlations between these parameters determine an ellipsoidal shape. Patients with BIVA values above the 75th percentile in the tolerance ellipse for the (Italian) reference population were considered hyperhydrated, and those with BIVA values between the 50th and 75th percentiles were classified as well hydrated.[15]

The outcomes of interest were nutrition risk, hospital mortality, ICU LOS, LOH, and MV duration.

Statistical Analysis

Descriptive statistics were used for analysis of categorical variables (absolute and relative frequency) and quantitative variables (mean and SD or median and interquartile range). Normality of the distribution of quantitative variables was verified by the Kolmogorov-Smirnov test.

Correlations between BIA parameters (PA and ECW/TCW) and outcomes of interest (nutrition risk, ICU LOS, LOH, and VM duration) were evaluated by Spearman's correlation coefficient. BIA values between survivors and nonsurvivors were compared using the Student's *t*-test for independent samples (parametric quantitative variables), the Mann-Whitney *U*-test (nonparametric, quantitative variables), or the χ^2 test (categorical variables).

A receiver operating characteristic (ROC) curve was constructed for analysis of the performance of PA in predicting a high NUTRIC score. The area under the ROC curve was calculated, with respective 95% CI, sensitivity and specificity, positive and negative predictive values, and the cutoff points established for identification of patients at nutrition risk from the trade-off between sensitivity and specificity.

The predictive validity of PA and BIVA was assessed by multivariate analysis adjusted for age and APACHE II score. Cox regression and Poisson regression were used to assess the association between BIA parameters (PA $>5.5°$ and BIVA $>75\%$) with mortality and prolonged ICU LOS (cutoff point established from the median of 5 days) as covariates. The SPSS software version 20.0 and the STATA software version 14.0 were used for the analysis. A *P*-value < 0.05 was considered statistically significant.

Results

General Characteristics of the Sample

Eighty-nine patients were included in the study. Mean age of the patients was 62.5 ± 14.1 years; 66.3% of them were older than 60 years, 50.6% were women, 87.6% were of white ethnicity, and 57.3% were from the city of Porto Alegre, Brazil. The main causes of hospitalization were pulmonary diseases (41.6%) and cancers (15.7%), and 49.4% were surgical patients.

Table 1. Bioelectrical Impedance Analysis and Anthropometric Data in a Sample of Critically Ill Patients.

Variable	Descriptive Statistics
TBW	78.3 ± 5.6
ECW	21.9 ± 5.1
ICW	21.5 ± 5.7
ECW/TBW	0.3 ± 0.1
PA	5.4 ± 1.7
Standardized PA	-1.1 (-2.3 to -0.3)
R	373.3 ± 83.3
Xc	35.4 ± 13.1
R/Height	228 ± 53.9
Xc/Height	21.6 ± 8.3
BIVA	
<50%	12.4%
50%–75%	10.1%
75%–90%	27%
>90%	50.6%

Data presented as mean ± SD or median (P25–P75).
BIVA, bioelectrical impedance vector analysis; ECW, extracellular water; ICW, intracellular water; PA, phase angle; R, resistance; TBW, total body water; Xc, reactance.

Seventy patients (78.7%) were on MV; median duration of MV was 5 (1–12) days, and 18% were on hemodialysis. Median SOFA score was 7 (4–9), and mean APACHE II score was 24 ± 8.1. Median modified NUTRIC score was 6 (5–7), and 77.5% of patients were identified as high nutrition risk. Median LOH was 23 (14–40) days, and median ICU LOS was 5 (2–10). Cumulative incidence of death was 43.8%.

Estimated weight and height were 64 ± 11.3 kg and 164.3 ± 7.4 cm, respectively. BIA parameters are described in Table 1. More than two-thirds of patients were classified as hyperhydrated. No statistically significant differences were observed in any of the BIA values between men and women or between elderly and adult patients (data not shown). For this reason, the SPA was not used in the subsequent analyses.

PA Performance in Predicting Nutrition Risk in Critically Ill Patients

There was a significant, moderate inverse correlation between PA and the modified NUTRIC score ($r = -0.416$, $P < 0.001$). PA performance in predicting a high NUTRIC score was evaluated by ROC curve analysis, and the area under the ROC curve was 0.79 (95% CI 0.588-0830). A PA of 5.5^{o} represented the trade-off between sensitivity (62.3%) and specificity (65%) to identify patients at a high NUTRIC score. Positive and negative predictive values were 86% and 33%, respectively.

Table 2. Association Between BIA Values and Mortality in a Sample of Critically Ill Patients.

BIA Parameters	Survivors (n = 48)	Nonsurvivors (n = 39)	*P*-value
TBW	76.7 ± 4.8	79.8 ± 6	0.013[a]
ICW	21.3 ± 5.6	21.7 ± 5.9	0.773[a]
ECW	21.3 ± 4.4	22.5 ± 5.9	0.278[a]
ECW/TBW	0.3 ± 0.1	0.3 ± 0.1	0.534[a]
PA	5.6 ± 1.1	5.2 ± 2.2	0.310[a]
Standardized PA	−0.7 (−1.9 to −0.2)	−1.41 (−2.3 to −0.7)	0.077[b]
PA <5.5°	46.9%	67.5%	0.052[c]
Standardized PA <−1.65	28.6%	42.5%	0.187[c]
R	392.6 ± 79.20	352.2 ± 84.7	0.024[a]
R/Height	239.4 ± 51.3	215.7 ± 55.3	0.042[a]
Xc/Height	23.4 ± 6.9	19.9 ± 9.4	0.050[a]
Xc	38.31 ± 10.98	32.41 ± 14.90	0.037[a]
BIVA > 75% (hyperhydration)	81.6%	72.5%	0.321[c]

[a]Student's *t*-test for independent samples.
[b]Mann-Whitney *U*-test.
[c]χ^2 test.
BIA, bioelectrical impedance analysis; ECW, extracellular water; ICW, intracellular water; PA, phase angle; R, resistance; TBW, total body water; Xc, reactance.

Validity of BIA Parameters in Predicting Clinical Outcomes

We did not find any significant correlation between PA, LOH, and MV duration. However, PA was significantly inversely correlated with ICU LOS (r = −0.302, $P = 0.004$). There was no significant correlation of the ECW/TBW ratio with any of the clinical outcomes (data not shown).

Association of hyperhydration (BIVA >75%) with LOH, ICU LOS, and time on MV was assessed by comparing the outcomes of interest between hyperhydrated and well-hydrated patients, with no significant differences between the groups (data not shown).

Comparisons of BIA parameters between survivors and nonsurvivors showed greater TBW values in nonsurvivors but greater R and Xc values in survivors (Table 2). The frequency of patients with PA values ≤mean PA was higher in nonsurvivors than survivors, however, without statistical significance.

In a multivariate analysis, with adjustment for age and disease severity (APACHE II score), the risk of death was not associated with a PA <5.5°. On the other hand, hyperhydration (BIVA >70%) significantly increased the risk of death in critically ill patients by 2.24 times (Table 3). An ICU LOS longer than 5 days was considered the dependent variable, and patients with a reduced PA had nearly twice the risk of a prolonged ICU LOS compared with those with a PA >the median (Table 3).

Discussion

This study aimed to assess the validity of BIA parameters in predicting nutrition risk and clinical outcomes in critically ill patients. A PA <5.5° showed an accuracy of 79% to identify patients at high nutrition risk and was associated with a 2-times higher risk for an ICU LOS longer than 5 days. Hyperhydration was a significant predictor of mortality.

In the present study, PA showed satisfactory performance in identifying patients at high nutrition risk. A prospective longitudinal study conducted with 31 critically ill cancer patients showed an association between low PA values and high NUTRIC scores, suggesting that PA can be a viable tool to identify critically ill patients who could benefit from early nutrition therapy.[19]

No differences in the PA values were found between survivors and nonsurvivors in our study. However, a low PA was associated with increased risk of prolonged ICU LOS. A prospective cohort study[9] performed with 241 patients hospitalized in a surgical ICU in Korea showed statistically significant associations between PA, impedance, R, and mortality. In addition, the performance of PA in predicting mortality was stronger than the severity scoring systems APACHE II, SOFA, and simplified acute physiology score III (SAPS III).[9] In another study with 31 critically ill patients, a PA ≤3.8° showed an 88.9% sensitivity and 77.3% specificity in predicting mortality.[19] On the other hand, similar to our study, Reis et al did not find an association between PA and mortality in a study with 110 critically ill cardiac patients using similar PA cutoff points (women <4.6° and men <5.0°).[25]

The PA is an indicator of cell membrane integrity and vitality and reflects the quantity and quality of soft tissues. Higher values of PA indicate higher cellularity, higher cell membrane integrity, and better cell function, and thus better cellular health.[26] In our understanding, PA may be considered a parameter similar to body temperature, as it

Table 3. Association of Reduced PA and Hyperhydration with Mortality and Prolonged ICU Length of Stay in a Sample of Critically Ill Patients.

	Mortality[a]		ICU length of stay >5 days[b]	
Independent Variable	HR (95% CI)	*P*-value	RR (95% CI)	*P*-value
PA <5.5°				
Unadjusted model	1.806 (0.888-3.676)	0.103	2.18 (1.39-3.40)	<0.001
Adjusted model	1.655 (0.772-3.544)[c]	0.195	2.06 (1.30-3.27)[c]	0.002
BIVA >75% (Hyperhydration)				
Unadjusted model	1.943 (0.948-3.984)	0.070	0.97 (0.83-1.14)	0.766
Adjusted model	2.24 (1.074–.680)[c]	0.032	0.98 (0.84-1.15)[c]	0.829

Multivariate analysis.
[a]Cox regression.
[b]Poisson regression.
[c]Adjusted for age, sex, and APACHE II score.
APACHE II, Acute Physiology and Chronic Health Evaluation II; BIVA, bioelectrical impedance vector analysis; HR, hazard ratio; IUC, intensive unit care; PA, phase angle; RR, relative risk.

can be used to monitor the progression of a disease or the effectiveness of an intervention. Values at, above, or below the reference values for PA may be useful in patient care and evaluation of clinical outcomes.[27]

Other BIA values, including the ECW/TBW ratio, R/height, Xc/height, and BIVA (indicators of hydration status), have also been investigated as prognostic factors in critically ill patients. In our study, the ECW/TBW ratio was not associated with clinical outcomes. However, we observed higher R/height and Xc/height values in survivors than nonsurvivors. In addition, hyperhydration, according to BIVA, increased the risk of death by 2.24 times. Another Brazilian study[14] involving 224 critically ill patients with kidney failure also reported hyperhydration and lower R/height in nonsurvivors compared with survivors. However, in their study, a multivariate analysis was not performed, and hydration status was not evaluated. A study by Garcia et al,[15] however, also showed that patients with fluid overload evaluated by BIVA had increased risk of mortality compared with well-hydrated patients. Two studies conducted in Italy[16,18] also identified hyperhydration as a risk factor for mortality in critically ill patients.

Our sample size was large enough to test the predetermined hypotheses. The assessment and follow-up of patients were conducted by 2 independent, trained investigators. Also, patients were consecutively included, and finally, potential cofounding factors were considered in the multivariate analysis to ensure the internal validity of the study and to allow the inference that the BIA performed on patients' admission to the ICU was clinically relevant. Nevertheless, the study had some limitations that deserve consideration: (1) BIA was not performed under fasting conditions and occurred at different times of the day, depending on routine ICU procedures, which included administration of continuous enteral feeding; (2) since measurements of body weight and height could not be performed in our sample, both parameters were estimated using predictive formulas, which may have affected the accuracy of the measurements; (3) only one BIA was made on ICU admission; studies available in the literature that evaluated hydration status of critically ill patients by BIVA showed the importance of serial measurements, since changes in hydration status can predict worse outcomes[16-18]; and (4) daily fluid balance was not evaluated, although BIVA may be considered a marker of this.[16]

Further studies are needed to evaluate the PA of patients admitted to the ICU and its potential association with clinical outcomes. Also, the lack of BIA protocols for critically ill patients reinforces the need for studies in this direction. The PA cutoff point of 5.5° identified in the present study as a predictor of high nutrition risk and prolonged ICU LOS (longer than 5 days) requires confirmation.

Conclusion

A PA <5.5° showed a 79% accuracy to identify critically ill patients at high nutrition risk and was associated with increased risk of a prolonged (>5 days) LOS in the ICU. Hyperhydration increased by >twice the risk of mortality. Altogether, our findings suggest that BIA has satisfactory predictive validity in identifying critically ill patients at increased risk for malnutrition and worse clinical prognosis.

Statement of Authorship

F. M. Silva, A. Marcadenti, and J. d.S. Fink contributed to conception and design of the research. E. L. Razzera and S. W. Rovedder contributed to the acquisition of the data. F. M. Silva and F. D. Alves contributed to the analysis of the data. F. M. Silva, A. Marcadenti, F. D. Alves, and J. d.S. Fink contributed to the interpretation of the data. E. L. Razzera and F. M. Silva drafted the manuscript. All authors critically revised

the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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