ORIGINAL COMMUNICATION

Low phase angle is associated with 60-day mortality in critically ill patients with COVID-19

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Abstract

Background: Malnutrition status, body composition indicators, and bioelectrical impedance analysis (BIA) parameters have been associated with increased risk of death in several pathologies. The aim of this study was to describe the associations between phase angle (PhA) indicators obtained by BIA with length of hospital stay, days on mechanical ventilation, and 60-day mortality in critically ill patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Methods: This is a prospective cohort of mechanically ventilated patients with coronavirus disease 2019 (COVID-19). We assessed nutrition risk and body composition with BIA within 48 h from intensive care unit admission. Logistic and linear regression models were used to analyze the association between variables and clinical outcomes. Survival analysis by PhA value was performed using Kaplan-Meier curves.

Results: Sixty-seven patients were included. PhA (odds ratio [OR], 0.36; $P = .002$), standardized PhA (SPA) (OR, 0.45; $P = .001$), and extracellular water/total body water ratio (OR, 3.25; $P = .002$) were significant predictors of 60-day mortality. PhA <3.85° in females and <5.25° in males showed good and fair discrimination, respectively, for mortality prediction. Using cutoff values, low PhA was associated with a significantly increased risk of 60-day mortality (hazard ratio, 3.08; 95% CI, 1.12–8.41; $P = .02$). No association was detected for SPA.

Conclusion: Low PhA values could be a predictor of 60-day mortality in critically ill patients with COVID-19. This biological marker could be incorporated as part of nutrition and mortality risk assessment in this population.

KEYWORDS
bioelectrical impedance, COVID-19, mechanical ventilation, mortality, nutrition risk, nutrition status, phase angle

CLINICAL RELEVANCY STATEMENT

The findings of this study demonstrating that phase angle (PhA) derived from bioelectrical impedance analysis is a predictor of 60-day mortality in critically ill patients with coronavirus disease 2019 (COVID-19). This biological marker should be evaluated as part of a nutrition and mortality risk assessment in this population. Patients with low PhA values (<3.85° in females and <5.25° in males) could need special nutrition attention. Nevertheless, more studies are required to discover how nutrition support can impact PhA and disease outcomes in this population.

INTRODUCTION

Until August 2021, >209 million cases and 4.4 million deaths caused by coronavirus disease 2019 (COVID-19) have been reported worldwide.[1] Because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection primarily affects the respiratory system, severe illness often presents as pneumonia and acute respiratory distress syndrome requiring mechanical ventilation (MV) along with admission to intensive care units (ICUs).[2]

Nutrition risk has been associated with higher mortality and longer length of stay (LOS) in the hospital in COVID-19 and non–COVID-19 patients.[3–5] Nutrition risk screening and anthropometric assessment should be performed in the first 24–48 h of ICU admission in order to identify malnourished patients who will benefit from early nutrition support.[6,7] Anthropometric assessments of nutrition status, including body weight and height estimation for body mass index (BMI) calculation, often lack accuracy because of fluid overload that might be present after intravenous fluid resuscitation.[8] Bioelectrical impedance analysis (BIA) might be useful in critically ill patients but is not an accurate tool to measure body composition in overhydrated patients or during intravenous infusion therapy.[9–11] Some components of BIA such as phase angle (PhA), an indicator of cell membrane integrity, as well as standardized PhA (SPA) have shown to effectively predict poor prognosis at an early stage in several pathologies (liver diseases, chronic kidney disease, human immunodeficiency virus).[12–15] It is obtained from the arctangent of the ratio of resistance (opposition to an electric current) and reactance (capacitance of tissues) measured by bioimpedance (BIA).[12] PhA reference values should be established according to sex, age, population, and health condition.[16,17] In non–critically ill patients with COVID-19, a low PhA value was associated with disease severity and increased mortality risk;[18,19] however, there are not specific values that can be related to survival in critically ill patients with COVID-19.

The aim of this study was to describe the association between PhA indicators (whole value and SPA) with LOS, days on MV, and 60-day all-cause mortality in critically ill patients who are on MV and have SARS-CoV-2.

METHODS

This was a prospective observational study in a cohort of mechanically ventilated patients. Patients who were admitted to the ICU from September 15, 2020, to January 30, 2021, at the National Institute of Respiratory Diseases in Mexico City, Mexico, were enrolled. Adults (age ≥ 18 years) diagnosed with COVID-19 (confirmed by both reverse transcription - polymarase chain reaction (RT-PCR)) for SARS-CoV-2 and suggestive tomographic findings were included. All patients with BIA assessment during the first 48 h of initiating MV were included. This study was reviewed and approved by the institutional review board (#C16-21).

Nutrition assessment

The nutrition risk of each patient was calculated using the modified Nutrition Risk in the Critically Ill (NUTRIC) score, which includes age, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score at admission, number of comorbidities, and pre-ICU hospital LOS during the first 24 h of initiating MV. High nutrition risk was established with a score ≥5.[6]

Anthropometric assessment included mid-arm circumference, calf circumference, abdominal circumference, and half-arm span; measurements were recorded using a tape graduated in centimeters with 0.1-cm precision (seca 201). Anthropometry was assessed using the standard procedures described by Lohman et al.[20] Mid-arm circumference was measured at the midpoint between the tip of acromion process and tip of the olecranon process. Calf circumference was measured by wrapping the tape around the widest part of the calf. Abdominal circumference is measured at the midpoint of the line between the rib or costal margin and the iliac crest. Body weight and height were estimated using validated equations.[21] BMI was calculated accordingly. The anthropometric and body composition assessment was always performed by the same ICU dietitian within 48 h of initiating MV.

Body composition was assessed using a multifrequency device (InBody S10, InBody Co, Ltd). Measurements were performed with the patient in a supine position. Eight adhesive electrodes were used: one on each wrist, one on the distal part of the third metacarpal bone of each hand, one on the central part of each ankle, and one on the distal part of the second metatarsal bone in each foot. Body weight and height estimated by anthropometric measurements were introduced into the device. PhA, extracellular water (ECW), intracellular water (ICW), total body water (TBW), and ECW/TBW ratio were obtained. PhA calculated by the BIA was transformed into the SPA from the SPA equation: ([measured PA − mean population reference PhA]/SD of the reference population).[22] The mean PhA and the SD according to the adopted gender and age were those proposed by Espinosa-Cuevas et al for the Mexican population.[23] Patients were classified as having reduced SPA values when measured values were <−1.65 and as having normal PhA when calculated values were ≥−1.65. Cutoff values of −1.65 stands for the fifth percentile of the normal population, which is considered as the lower limit of normality.[24]

Clinical outcomes

Days on invasive MV, LOS in days, and 60-day all-cause mortality were recorded.

Sample size

Sample size calculation was based on the difference in PhA between survivors (5.0° ± 1.3°) and nonsurvivors (4.1° ± 1.2°) as reported by Stapel et al.[25] Based on this information, a power of 80%, and a level of significance of 5%, the required sample size was 64 patients.

Statistical analysis

Data were analyzed using Stata Intercooled (version 14, StataCorp) and GraphPad Prism (GraphPad Software, Inc). Normality of the distribution of quantitative variables was verified by the Shapiro-Wilk test. Descriptive statistics were used for the analysis of categorical variables (absolute and relative frequency) and quantitative variables (mean and SD or median and interquartile range). Clinical data and BIA values between survivors and nonsurvivors were compared using the Student t-test, Mann-Whitney U test, or the chi-squared test. A logistic regression model was used to analyze the association of variables and 60-day mortality. Pearson and Spearman tests were used to analyze the correlation between PhA and SPA with severity scores. The PhA cutoff value for predicting mortality was analyzed using the receiver operating characteristic (ROC) curve, obtaining sensitivity and specificity. The area under the curve (AUC) was used as an overall measure of discriminative capacity accuracy interpreted as follows: no discrimination, AUC ≤ 0.5; fail discrimination, 0.5–0.6; poor discrimination, 0.6–0.7; fair discrimination, 0.7–0.8; good discrimination, 0.8–0.9; and excellent discrimination, ≥0.9.[26] We also performed the Kaplan-Meier survival analysis at 60 days with log-rank test and the Cox proportional hazards model by PhA values adjusted for NUTRIC score and age for PhA cutoff models and adjusted only for NUTRIC score for SPA (considering that PhA values were adjusted by the mean for age). NUTRIC score was selected because of the inclusion of both severity scales (APACHE II and SOFA). Variables were selected according to suspected risk factors for the outcome of interest. Statistical significance was defined as $P < .05$.

RESULTS

In total, 67 patients (76% males), who had a mean age of 55.3 ± 13.6 years, were enrolled in this study. Patients' characteristics are shown in Table 1. Mean SOFA score was 9 ± 2, and APACHE II was 21 ± 5. Overweight or obesity was identified in 85% of patients by BMI. Overweight or obesity was detected in all female patients (n = 16). The median number of ventilation days was 13 (10–21), and the median LOS was 20 days (15–28 days). The 60-day mortality rate was 37.3%.

Clinical characteristics of survivors and nonsurvivors

The clinical characteristics of the 60-day survivors and nonsurvivors are shown in Table 2. A comparative analysis was performed. There is a statistically significant difference in the PhA between groups (4.4° ±

TABLE 1 Clinical characteristics and BIA data of critically ill patients with COVID-19

Characteristics	All patients (n = 67)
Age, mean ± SD, years	55.3 ± 13.6
20–30, n (%)	4 (6)
31–40, n (%)	6 (9)
41–50, n (%)	15 (22)
51–60, n (%)	16 (24)
61–70, n (%)	16 (24)
71–80, n (%)	10 (15)
Sex, n (%)	
Male	51 (76)
Female	16 (24)
BMI, mean ± SD, kg/m²	30.3 ± 5.6
18.5–24.9, n (%)	10 (15)
25–29.9, n (%)	23 (34)
≥30–34.9, n (%)	24 (36)
≥35, n (%)	10 (15)
Weight, mean ± SD, kg	84.4 ± 15.2
Male	83.5 ± 15.3
Female	87.1 ± 15.1
Height, mean ± SD, cm	165.5 ± 8.6
Male	168.2 ± 7.4
Female	156.9 ± 5.5
Mid-arm circumference, mean ± SD, cm	31.6 ± 3.8
Male	31.5 ± 3.7
Female	31.8 ± 4.2
Calf circumference, mean ± SD, cm	34.9 ± 4.1
Male	35.3 ± 3.8
Female	34.0 ± 5.0
NUTRIC score, n (%)	
High risk	37 (55)
Low risk	30 (45)
SOFA score, mean ± SD	9 ± 2
APACHE II score, mean ± SD	21 ± 6
Phase angle, mean ± SD, °	5.0 ± 1.2
Standardized phase angle, median (IQR)	−2.5 (−3.8 to −0.83)
Extracellular water, mean ± SD, L	15.9 ± 2.8
Intracellular water, mean ± SD, L	24.9 ± 4.8
Total body water, mean ± SD, L	40.8 ± 7.5
Extracellular water/total body water ratio, mean ± SD	0.39 ± 0.01
Mechanical ventilation, days, median (IQR)	13 (10–21)
Hospital length of stay, days, median (IQR)	20 (15–28)
60-day all-cause mortality, n (%)	25 (37.3)

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; COVID-19, coronavirus disease 2019; IQR, interquartile range; NUTRIC, Nutrition Risk in the Critically Ill; SOFA, Sequential Organ Failure Assessment.

TABLE 2 Comparison of patient's characteristics and BIA data between survivors and nonsurvivors

Characteristics	All patients (n = 67)			Male (n = 51)			Female (n = 16)		
	Nonsurvivor (n = 25)	Survivors (n = 42)	P-value	Nonsurvivor (n = 19)	Survivors (n = 32)	P-value	Nonsurvivor (n = 6)	Survivors (n = 10)	P-value
Sex, n (%)			.98						
Male	19 (76%)	32 (76%)							
Female	6 (24%)	10 (24%)							
Age years	58.6 ± 13.4	53.3 ± 13.5	.12	58.5 ± 14	52.0 ± 13.9	.81	59 ± 12.5	57.5 ± 11.8	.81
NUTRIC score			.54			.32			.55
High risk	15 (60%)[b]	22 (52%)[b]		11 (58%)[b]	14 (44%)[b]		4 (66%)[b]	8 (80%)[b]	
Low risk	10 (40%)[b]	20 (47%)[b]		8 (42%)[b]	18 (56%)[b]		2 (34%)[b]	2 (20%)[b]	
SOFA	9 ± 2	9 ± 2	.85	9 ± 2	10 ± 3	.87	9 ± 2	8 ± 1	.27
APACHE II	23 ± 6	20 ± 5	.07	23 ± 6	20 ± 5	.02*	21 ± 3	23 ± 5	.57
Phase angle, °	4.4 ± 1.0	5.4 ± 1.2	<.001*	4.6 ± 1.0	5.6 ± 1.1	.002*	3.8 ± 0.8	5.0 ± 1.5	.08
SPA	−3.7 ± 1.4	−2.0 ± 1.8	.002*	−3.8 ± 1.5	−2.1 ± 1.7	.001*	−3.3 ± 0.9	−1.5 ± 2.0	.056
Low phase angle (using SPA)	24 (96%)[b]	29 (69%)[b]	.009*	18 (94.7%)[b]	23 (71.8%)[b]	.04*	6 (100%)[b]	6 (60%)[b]	.074
Extracellular water, L	16.3 ± 3.5	15.7 ± 2.3	.41	17.1 ± 3.3	16.3 ± 2.0	.32	13.8 ± 3.0	13.6 ± 2.0	.92
Intracellular water, L	24.6 ± 5.4	25.0 ± 4.4	.73	26.0 ± 5.1	26.2 ± 4.0	.85	20.4 ± 4.6	21.3 ± 3.4	.65
Total body water, L	40.9 ± 8.9	40.8 ± 6.5	.92	43.1 ± 8.4	42.6 ± 5.9	.80	34.2 ± 7.6	34.0 ± 5.4	.81
ECW/TBW	0.398 ± 0.01	0.386 ± 0.01	.001*	0.397 ± 0.01	0.385 ± 0.01	.011*	0.403 ± 0.008	0.390 ± 0.009	.018*
Body mass index	30.2 ± 6.8	30.3 ± 4.9	.96	28.9 ± 6.4	29.0 ± 3.9	.93	34.4 ± 6.8	34.3 ± 5.8	.98
Mid-arm circumference	31.3 ± 5.1	31.8 ± 3.0	.66	31.5 ± 3.0	31.5 ± 5.0	.99	30.8 ± 5.8	32.5 ± 3.1	.46
Calf circumference	34.0 ± 4.6	35.4 ± 3.8	.20	34.4 ± 4.7	35.7 ± 3.2	.28	33.0 ± 4.5	34.6 ± 5.5	.54

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ECW/TBW, extracellular water/total body water ratio; NUTRIC, Nutrition Risk in the Critically Ill; SOFA, Sequential Organ Failure Assessment; SPA, standardized phase angle.
[a]Data are presented as mean (standard deviation) unless otherwise reported.
[b]Number of patients (%).
*Significant results (P < .05).

1.0° in nonsurvivors vs 5.4° ± 1.2° in survivors; P < .001). The same difference was observed in SPA (−3.7 ± 1.4 in nonsurvivors vs −2.0 ± 1.8 in survivors; P = .002). The ECW/TBW ratios were higher (0.398 ± 0.01 vs 0.386 ± 0.01; P = .001) in nonsurvivors. There was no difference between groups in age, sex, BMI, nutrition risk, ICW, ECW, TBW, and body circumferences (P > .05 in all cases).

Univariate logistic regression analysis was performed to assess mortality predictors. Only PhA (odds ratio [OR], 0.36; P = .002), SPA (OR, 0.45; P = .001), and ECW/TBW (OR, 3.25; P = .002) were significant for predicting 60-day mortality, as shown in Table 3. Only age was significant for predicting LOS (β = 2.2; P = .001). No significant associations between studied variables (age, SOFA, APACHE II, NUTRIC score, PhA, SPA, and ECW/TBW) with LOS or MV days were detected.

Correlations between PhA and SPA with severity scores and clinical outcomes were evaluated (Table 4). Correlations for both indicators were observed with APACHE II score (P < .05), NUTRIC score (P ≤ .001), calf circumference (P < .01), and ECW/TBW (P < .001). PhA was directly correlated with mid-arm circumference (P = .01). Using the Spearman correlation test, inverse correlations between indicators and LOS (P ≤ .01) and MV duration (P ≤ .05) were detected.

An ROC curve was constructed for analysis of the performance of PhA in predicting mortality. In males, the AUC shows fair discrimination (0.74; 95% CI, 0.60–0.88; P = .003). A PhA <5.25° shows specificity of 72% and sensitivity of 72%. In females, the AUC shows good discrimination (0.83; 95% CI, 0.60–0.99; P = .03). A PhA <3.85° shows the highest specificity (90%) and sensitivity (66.7%) for mortality prediction.

The association between PhA indicators (cutoff obtained and SPA) was investigated using Cox models (Table 5), with adjustment for age and NUTRIC score for PhA cutoffs and for NUTRIC score for SPA. Using cutoff values, low PhA was associated with a significantly increased risk of death (hazard ratio [HR], 2.54; 95% CI, 1.05–6.14; P = 0.03), which was confirmed in the adjusted model (HR, 3.08; 95% CI, 1.12–8.41; P = .02). No association was observed for SPA in the crude (HR, 4.78; 95% CI, 0.64–35.5; P = .12) or adjusted model (HR, 4.67; 95% CI, 0.63–34.9; P = .13). Figure 1 shows the 60-day mortality as Kaplan-Meier curves for the low vs normal PhA groups.

TABLE 3 Logistic regression analysis of mortality and mechanical ventilation days as predictors in critically ill patients with COVID-19

	In-hospital mortality OR (95% CI)[a]	P-value	Mechanical ventilation days[b]	P-value	Length of stay[b]	P-value
Age	1.03 (0.99–1.07)	.12	$\beta = 0.15$	.24	$\beta = 2.2$	.02*
SOFA	1.01 (0.83–1.23)	.84	$\beta = -0.67$	.33	$\beta = -0.44$	.42
APACHE II	1.04 (0.99–1.20)	.07	$\beta = 0.38$	.27	$\beta = 0.4$	.11
NUTRIC score	1.34 (0.96–1.87)	.07	$\beta = 2.05$	.07	$\beta = 1.3$	.12
PhA	0.36 (0.19–0.68)	.002*	$\beta = -2.0$	.17	$\beta = -0.9$	.37
SPA	0.45 (0.28–0.72)	.001*	$\beta = -1.5$	.12	$\beta = -0.9$	.18
ECW/TBW	3.25 (1.82–5.82)	.002*	$\beta = 132.3$	.23	$\beta = 45.7$	.61

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; COVID-19, coronavirus disease 2019; ECW/TBW, extracellular water/total body water ratio; NUTRIC, Nutrition Risk in the Critically Ill; OR, odds ratio; PhA, phase angle; SOFA, Sequential Organ Failure Assessment; SPA, standardized PhA.
[a]Univariate logistic regression analysis.
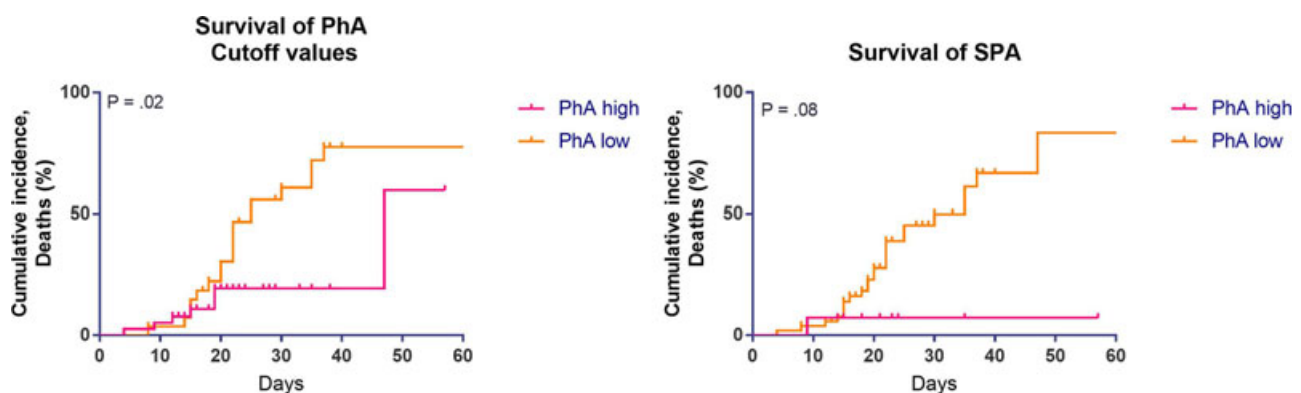[b]Univariate linear regression.
*Significant results ($P < .05$).

FIGURE 1 Kaplan-Meier 60-day survival plot illustrating cumulative survival for patients with a low phase angle (PhA). (A) Cutoff values obtained by receiver operating characteristic curve. (B) Standardized PhA values. P-values for log-rank test

DISCUSSION

In this study, low PhA determined by BIA in critically ill patients with COVID-19 was associated with 60-day mortality, but not with LOS and MV days.

PhA is an indicator that is directly obtained from BIA and not subjected to mathematical models or interference from hydration. It reflects the relation between reactance and resistance, which measures the opposition from cellular membranes and the opposition from body fluids to the current, respectively. This indicator is closely related to health and nutrition status because it indicates both the integrity of cellular membranes and cellular water distribution.[12] PhA is inversely correlated with NUTRIC score, which reflects higher nutrition risk in individuals with lower PhA and demonstrates correlation with severity of disease (APACHE II) and direct correlation with body circumferences (mid-arm and calf circumference), measurements that reflect muscle mass indirectly. These aspects could explain the role of PhA as a prognostic marker for mortality, considering the association between nutrition risk, low muscle mass, and severity of disease in this outcome.

BIA is able to indirectly estimate body composition, representing a useful and noninvasive technique for nutrition assessment in the critically ill patient.

When analyzing BIA measurements in our cohort, higher PhA values were observed in survivors, with a statistically significant difference between groups (4.4° ± 1.0° in nonsurvivors vs 5.4° ± 1.2° in survivors; $P \le .001$). The same difference was observed in SPA (-3.7 ± 1.4 in nonsurvivors vs -2.0 ± 1.8 in survivors; $P = .002$). Stapel et al reported similar results in a non–COVID-19 cohort of 196 critically ill patients (5.0° ± 1.3° in nonsurvivors vs 5.4° ± 1.2° in survivors; $P \le .001$).[25]

Different studies have proposed the utility of BIA measurements such as PhA in predicting survival, nutrition status, and disease progression in several clinical conditions.[27,28] Until this date, there are no data of PhA relation with nutrition status and clinical outcomes in critically ill patients with COVID-19. However, some authors mark the importance of establishing a specific cutoff point for each clinical condition.

In our study, we found that PhA (OR, 0.36; $P = .002$), SPA (OR, 0.45; $P = .001$), and ECW/TBW (3.25; $P = .002$) were significant for

TABLE 4 Correlations between phase angle indicators with severity scores and clinical outcomes

	Phase angle (°)	Standardized phase angle
SOFA[a]	r = −0.04 P = .72	r = −0.11 P = .34
APACHE II[a]	r = −0.39 P = .001*	r = −0.31 P = .008*
NUTRIC score[a]	r = −0.47 P = .0001*	r = −0.42 P = .0004*
Mechanical ventilation days[b]	r = −0.42 P = .005*	r = −0.40 P = .007*
Length of stay days[b]	r = −0.33 P = .03*	r = −0.43 P = .004*
Mid arm circumference[a]	r = 0.30 P = .01*	r = 0.24 P = .054
Calf circumference[b]	r = 0.54 P ≤ .0001*	r = 0.38 P = .002*
ECW/TBW[a]	r = −0.70 P = .0001*	r = −0.51 P = .0001*

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ECW/TBW, extracellular water/total body water ratio; NUTRIC, Nutrition Risk in the Critically Ill; SOFA, Sequential Organ Failure Assessment.
[a]Pearson test.
[b]Spearman test.
*Significant results (P < .05).

TABLE 5 Association of low PhA with mortality in critically ill patients with COVID-19

	HR (95% CI)	
Variable	Unadjusted model	Adjusted model
PhA	2.54 (1.05–6.14); P = .03	3.08[a] (1.12–8.41); P = .02
SPA	4.78 (0.64–35.5); P = .12	4.67[b] (0.63–34.9); P = .13

Abbreviations: COVID-19, coronavirus disease 2019; HR, hazard ratio; PhA, phase angle; SPA, standardized PhA.
[a]Adjusted to NUTRIC score and age.
[b]Adjusted to NUTRIC score.

predicting 60-day mortality. Similar findings were reported in critically ill patients without COVID-19.[29] The cutoff point values obtained by ROC analysis in our sample were <3.85° in females and <5.25° in males, which differs from other cohorts that proposed a cutoff point without considering differences between sexes.[18,19]

Previous studies evaluating PhA in patients with COVID-19 observed inconsistent results on association with clinical outcomes. In a sample of 90 non–critically ill patients with COVID-19, a low PhA (<4.3°) was not associated with LOS and clinical outcomes.[30] Moonen et al performed BIA assessment in a sample of 30 non–critically ill and 24 critically ill patients with COVID-19 and reported that an increase of one unit of PhA decreased 28-day mortality (OR, 0.20; P = .02); cutoff values were not proposed. Recently, Cornejo-Pareja et al obtained a cutoff value of 3.95° as a predictor of 90-day mortality in a sample of 127 patients; 23% required ICU admission during hospitalization.[19]

In our sample, PhA analyzed by SPA failed to predict LOS, MV, and mortality. This differs from the findings presented by Cornejo-Pareja et al. The median of SPA in their report was −0.8 (−2.0 to 0.2), and the median observed in critically ill patients in this study was −2.5 (−3.8 to −0.83). The absence of association may be explained by a high proportion of patients categorized as low PhA using SPA in survivor and nonsurvivor groups, which reflects that critically ill patients have a decrease in PhA values at ICU admission in comparison with a healthy population.

In the ICU setting, hydration status could be assessed by BIA.[31,32] Many studies have consistently highlighted the clinical significance of overhydration in ICU patients.[33,34] In our sample, ECW/TBW ratio was higher in nonsurvivor critically ill patients. This indicator has demonstrated its feasibility as a diagnostic value for overhydration assessment during fluid treatment.[35]

There are several limitations in this study. First, the sample size of this study was small and was conformed predominantly for males. All data were obtained from a single center, which may result in concerns regarding the generalization of the conclusions. Second, long-term survival outcomes were not accessible, because of the impact of COVID-19 on the workload of the nutrition department. Third, BIA was solely performed using InBody S10, and body water measurements might be influenced when using other devices.

CONCLUSION

BIA parameters were associated with mortality risk in critically ill patients with COVID-19. PhA is a predictor of 60-day mortality. This biological marker could be incorporated as a part of nutrition and mortality risk assessment in this population. Patients with low PhA values (<3.85° in females and <5.25° in males) could need special nutrition attention. However, more studies are needed to elucidate the impact of nutrition therapy on BIA parameters, infection course, and clinical outcomes.

CONFLICT OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS
Iván Armando Osuna-Padilla, Nadia Carolina Rodríguez-Moguel, and Sebastián Rodríguez-Llamazares equally contributed to the conception and design of the research; Iván Armando Osuna-Padilla, Sebastián Rodríguez-Llamazares, and Gustavo Alejandro Casas-Aparicio contributed to the analysis and interpretation of the data; Adriana Aguilar-Vargas, Martin Armando Ríos-Ayala, and Carmen Margarita Hernández-Cardenas 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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