Original Article

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중환자에서 영양상태 평가지표로서 생체전기 임피던스를 이용한 위상 각의 활용

김형숙 1 , 이은숙 1 , 이연주 2,3 , 이재호 2 , 이춘택 2 , 조영재 2

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Clinical Application of Bioelectrical Impedance Analysis and its Phase Angle for Nutritional Assessment of Critically III Patients

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Purpose: Phase angle (PA) is objectively determined from resistance and reactance measured by bioelectrical impedance analysis (BIA)—a quick, noninvasive method. The aim of this study was to evaluate the clinical application of PA by BIA for nutritional assessment of critically ill patients.

Methods: Eighty nine adult patients admitted to a medical intensive care unit (ICU) of a tertiary academic hospital from August 2012 to September 2013 were analyzed. PA values were measured by direct segmental multi-frequency BIA. As traditional nutrition assessment tools, body mass index (BMI), serum albumin levels, total lymphocyte counts, and our hospital's nutrition screening index (NSI) were also recorded. Correlations between the results of BIA and other traditional parameters were analyzed. **Results:** PA showed correlation with traditional nutritional parameters, including BMI (r=0.479), serum albumin (r=0.347), and NSI score (r=0.483). Patients with PA lower than the median value (3.5°) had significantly lower nutritional status, increased

Conclusion: PA, as a reflection of body cell mass, measured by BIA could be a potentially useful parameter for nutritional assessment in critically ill patients.

Key Words: Electric impedance, Phase angle, Critical illness, Nutrition assessment

duration of mechanical ventilation (P=0.039), and increased length of ICU stay (P=0.041).

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INTRODUCTION

Nutritional assessment remains an important tool in treating critically ill patients; however, it is often an overlooked aspect in critical care management. Thus far, no single best method or gold standard is available for the nutritional evaluation of critically ill patients. In the clinical setting, existing methods of nutritional evaluation may be subjective (clinical history and nutritional physical examination) or objective (food diary, anthropometry, and biochemical studies). Although many prediction equations to



assess nutritional status have been reported, the application of the traditional tools of nutritional assessment in critically ill patients is not appropriate, given their acute phase conditions and complex clinical responses.²

Recently, bioelectrical impedance analysis (BIA) has been introduced as a fast, noninvasive, painless, relatively inexpensive, and reproducible method of evaluating body compartments.³⁻⁶ Previous studies have shown that variations in the state of hydration of the patient are the main limitation of BIA that uses two-compartment modeling techniques. Unlike conventional BIA equipment that often takes only partial measurements and therefore relies upon formulas to estimate whole body composition, the current BIA based by the direct segmental multi-frequency (DSM) technique measures impedance directly from each segments of the body, assuming human body divided into five-segments.8 In body-composition assessment, DSM technique uses six spectra of electrical frequencies to predict the intracellular water and extracellular water (ECW) compartments of the total body water (TBW) in five-segments. Thus, DSM-BIA is a valid tool for the assessment of total body and segmental body composition in the quantification of body cell mass (BCM).

BCM is defined as the fat free mass (FFM) without the bone mineral mass and ECW; it is a marker for the combination of visceral and somatic protein deposits, i.e., the most metabolically active compartment of the body. Besides BCM, the phase angle (PA) in BIA is directly determined from resistance (R) and reactance (Xc) without using equations and is known to reflect BCM. A smaller PA is known to be consistent with low reactance, cell death, or disruption of the cell membrane's selective permeability, while a greater PA is compatible with high reactance and larger quantities of intact cell membranes.

The present study aimed to evaluate the clinical application of PA measured by BIA in assessing nutritional status in critically ill patients.

MATERIALS AND METHODS

1. Study design and participants

This study was conducted between August 2012 and

September 2013 and recruited 131 patients aged 18 years and older admitted to the medical intensive care unit (ICU) of a tertiary, academic hospital. BIA was conducted for the patients except with a pacemaker or implanted cardiac defibrillator within 48 hours of ICU admission and their clinical characteristics were recorded retrospectively. The following criteria were used to exclude subjects: patients with serious errors in their BIA results, patients who stayed within 48 hours in ICU. Finally 89 patients were included in this study. The correlation between the results of traditional nutritional assessment tools and BIA parameters was analyzed; furthermore, we analyzed the relationships between BIA parameters and various clinical outcomes, including the length of ICU stay, duration of mechanical ventilation, and ICU mortality in the surviving patients.

2. Data collection and assessment of malnutrition

Data regarding patient's age, sex, body mass index (BMI), albumin, total lymphocyte count (TLC), duration of mechanical ventilation, length of ICU stay, and ICU mortality were obtained from electronic medical records. Nutritional status was evaluated using our hospital's nutrition screening index (NSI) (Table 1). This index was calculated according to the following equations.

NSI score=(albumin coding×2)+(TLC coding×1.5)+ (BMI coding×1.5)+(age coding)

These equations describe the empiric assessment of nutritional status (NSI score < 8.75 indicates malnourished patients) in our hospital. ¹¹ Following NSI assessment, an enteral or parenteral nutritional regimen was started for each patient and adjusted on the basis of clinical status, nitrogen balance, and various laboratory and nutritional indices.

Table 1. Coding of nutrition screeing index

Coding	Albumin (in mg/dL)	TLC (mm ³)	BMI (kg/m ²)	Age (y)
1	< 3.5	< 900	< 18.5	>65
2	≥3.5	≥900	≥18.5	≤65

TLC = total lymphocyte count; BMI = body mass index.



3. Bioelectrical impedance measurement

DSM-BIA was performed by using the InBody S10 (Biospace Co., Seoul, Korea). This device consists of the use of eight electrodes attached to the arms, legs, trunk through six different frequencies (1, 5, 50, 250, 500, and 1,000 kHz) to measure impedance. This equipment has previously been shown to have high test-pretest reliability and accuracy. Patients were measured in a supine position on the bed with arms and legs abducted from the body. Source and sensor electrodes were placed on the thumb and index finger of both hands and on each ankle. Before attaching the electrodes, contact areas cleaned using alcohol. The PA (θ) values were obtained from the resistance (R) and reactance (Xc) using the following equation:

PA (
$$\theta$$
) = arctan (Xc/R) × (180/ π)

As most previous studies have referred to PA values ob-

Table 2. Clinical characteristics of subjects and nutritional functional variables: initially measured group (n=89)

Characteristic	Initially measured group
Age (y)	65.2±14.5
Sex (male/female)	63/26
APACHE II score	20.1 ± 9.53
Nutritional variables	
NSI score	9.3 ± 1.5
Malnourished according to NSI score	36 (40.4)
Actual body weight (kg)	59.1 ± 11.4
Body mass index (kg/m ²)	22.1 ± 3.6
Albumin (mg/dL)	3.3 ± 0.7
Total lymphocyte count (mm ³)	$1,240.1 \pm 905.8$
Phase angle (°)	3.7 ± 1.4
Fat-free mass (kg)	48.2 ± 9.9
Body cell mass (kg)	30.3 ± 6.6
ICU admission diagnosis	
Respiratory	47 (52.8)
Cardiovascular	17 (19.1)
Sepsis	15 (16.9)
Gastrointestinal	4 (4.5)
Trauma	1 (1.1)
Other	5 (5.6)
Clinical variables	
Duration of mechanical ventilation (d)	6.4 ± 12.2
Length of ICU stay (d) ^a	9.4 ± 13.5

Values are presented as mean±standard deviation or number (%). APACHE = acute physiologic and chronic health evaluation; NSI = nutrition screening index; ICU = intensive care unit. aICU survival subgroup, n=66.

tained at 50 kHz,¹³ a further analysis of PA at 50 kHz was also performed in this study. To determine whether PA and patient outcomes were improved by nutritional therapy, BIA measurements were repeated in 15 clinically stable patients before and after nutritional treatment.

4. Statistics

Statistical analysis was carried out using the software package IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA). Normally distributed continuous variables were compared using paired and unpaired t-tests. Non-normally distributed variables were compared by Mann-Whitney U-test. Categorical variables were compared using the chisquare test. Pearson's correlation was calculated to assess the relationship between variables. Repeated measures ANOVA was used to establish changes in PA and nutritional markers divided according to the ratio of nutritional support calorie and basal metabolic rate (BMR) predicted by BIA in the clinically stable patients who underwent repeated BIA. A P-value < 0.05 was considered statistically significant.

5. Ethics statement

The study protocol was approved by the Institutional Review Board Committee of Seoul National University Bundang Hospital (IRB No. B-1310- 224-112). Informed was waived by the IRB.

RESULTS

The demographic and nutritional parameters as well as the clinical variables of 89 patients are showed in Table 2;

Table 3. Correlations between phase angle (PA), body cell mass (BCM), and nutritional markers

NI and an at most an	PA		BCM		
Nutritional marker —	r	P	r	P	
Actual body weight	0.509	< 0.001	0.837	< 0.001	
Body mass index	0.479	< 0.001	0.505	< 0.001	
Albumin	0.347	0.001	0.023	0.830	
Total lymphocyte count	0.225	0.034	0.157	0.143	
Nutrition screening index score	0.483	< 0.001	0.297	0.005	

Journal of Clinical Nutrition



at the time of ICU admission, 40.4% of the patients were classified as "malnutrition status" based on the NSI score.

A significant correlation was observed between the markers of traditional nutritional assessment and PA or BCM (Table 3). PA showed a positive correlation with actual body weight (r=0.509, P<0.001), albumin (r=0.347, P<0.001), and TLC (r=0.225, P=0.034). Fig. 1 showed the correlation of PA with NSI scores (r=0.483, P<0.001) and BMI (r=0.479, P<0.001; not be showed in Fig. 1). Although BCM was also correlated with NSI scores (r=0.297, P=0.005), its correlation coefficient was lower than that for PA.

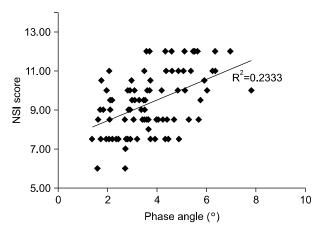


Fig. 1. The relationships between nutrition screening index (NSI) score, and phase angle.

The median PA was 3.5° , ranging from 1.4° to 7.8° . Overall, 44 patients (49.4%) were observed to have PA \leq 3.5° . Age, NSI score, actual body weight, BMI, albumin, TLC, and FFM differed significantly between the groups with a PA value above and below the median PA. Patients with PA \leq 3.5° were more malnourished than those with PA \geq 3.5° (43.2 vs. 37.8%, P=0.669). Moreover, of the ICU survival patients (n=66), patients with PA \leq 3.5° showed significantly longer duration of mechanical ventilation and ICU stay than those with PA \geq 3.5° (Table 4).

The patients who underwent repeated BIA with nutritional management were divided into two groups according to the ratio between nutritional caloric support and the BMR (Table 5). Of these patients, the mean PA decreased who supported the ratio of nutritional caloric support (NCS):BMR below 1 in contrast to those above 1. During the period of nutritional management, the PA decreased in 4 of 6 patients who supported the ratio of NCS:BMR below 1 (Fig. 2). The ICU survival rate among patients who supported the ratio of NCS:BMR above 1 was higher, however, this was not statistically significant. Except for PA, nearly all the nutritional markers decreased in both the groups despite nutritional management.

Table 4. Nutritional, functional, and clinical variables in all patients (n=89) divided according to the median value of the phase angle (3.5°)

	$PA \le 3.5^{\circ} (n=44)$	$PA > 3.5^{\circ} (n=45)$	P-value
Age (y)	70.3±3.7	60.2±13.7	0.001
Sex (male/female)	29/15	34/11	0.358
APACHE II score	22.7 ± 10.5	17.5 ± 7.8	0.010
Nutritional variables			
NSI score	8.8 ± 1.3	9.9 ± 1.6	< 0.001
Malnourished according to NSI score (%)	19 (43.2)	17 (37.8)	0.669
Phase angle (°)	2.6 ± 0.6	4.8 ± 1.0	< 0.001
Actual body weight (kg)	55.0 ± 9.8	63.0 ± 11.5	0.001
Body mass index (kg/m ²)	20.9 ± 3.6	23.3 ± 3.2	0.001
Albumin (mg/dL)	3.1 ± 0.6	3.5 ± 0.7	0.005
Total lymphocyte count (mm ³)	$1,076.0 \pm 743.9$	$1,400.6 \pm 1,023.1$	0.090
Fat-free mass (kg)	44.8 ± 8.2	51.6 ± 10.3	0.001
Clinical variables			
ICU mortality (%)	14 (31.8)	9 (20.0)	0.151
Length of ICU stay (d) ^a	9.9 ± 9.7	5.9 ± 5.6	0.041
Duration of mechanical ventilation (d) ^a	6.5 ± 9.3	2.8 ± 4.3	0.039

Values are presented as mean±standard deviation or number (%).

PA = phase angle; APACHE = acute physiologic and chronic health evaluation; NSI = nutrition screening index; ICU = intensive care unit. a ICU survival subgroup: PA \leq 3.5, n=30; PA > 3.5, n=36.



Table 5. The changes in phase angle and nutritional markers divided according to the ratio of nutritional caloric support (NCS) to the basal metabolic rate (BMR) (ratio=1) in the repeated BIA group

	NCS:BMR ≥ 1 (n=9)		NCS:BMR ≤ 1 (n=6)		D 1
	Initial	Post	Initial	Post	P-value
Age (y)	69.2±12.6		60.0±15.6		0.228
Sex (male/female)	5/4		4/2		1.000
APACHE II score	25.0 ± 10.5		21.5 ± 8.4		0.506
DM/liver disease	3		1/2		0.758
Basal metabolic rate	$1,316.3 \pm 165.3$		$1,427.8 \pm 227.5$		0.290
Nutritional markers					
Phase angle (°)	3.3 ± 1.3	3.4 ± 1.3	4.2 ± 1.3	3.7 ± 1.7	0.139
Malnourished according to NSI coding	2 (22.2)	5 (55.6)	2 (33.3)	3 (50.0)	1.000
Actual body weight (kg)	55.1 ± 12.6	54.7 ± 12.1	61.6 ± 11.9	60.8 ± 11.2	0.669
Body mass index (kg/m²)	21.7 ± 5.1	21.5 ± 4.9	21.9 ± 3.4	21.7 ± 3.3	0.857
Albumin (mg/dL)	3.1 ± 0.9	2.9 ± 0.4	3.5 ± 0.6	3.3 ± 0.7	0.918
Total lymphocyte count (mm ³)	$1,675.3 \pm 1,100.9$	$1,488.2 \pm 882.8$	$1,265.9 \pm 1,252.5$	$1,032.9 \pm 806.7$	0.945
NSI score	9.3 ± 1.2	8.1 ± 1.5	9.6 ± 2.0	8.8 ± 1.4	0.713
Clinical variables					
ICU survival	8 (88.9)		4 (66.7)		0.525

Values are presented as mean±standard deviation or number (%).

APACHE = acute physiology and chronic health evaluation; DM = diabetes mellitus; NSI = nutrition screening index.

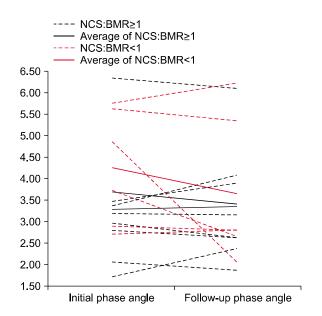


Fig. 2. Changes in phase angle after nutritional management in the repeated bioelectrical impedance analysis (BIA) group. NCS = nutritional caloric support; BMR = basal metabolic rate.

DISCUSSION

The findings of the present study indicate that PA, as measured by DSM-BIA, may be useful in assessment of nutritional status in critically ill patients. Further, PA appears to be a valuable parameter for the nutritional assessment in such patients before and after nutritional treatment. PA, in

addition to standard laboratory evaluations and clinical judgment, could provide objective information for guiding clinicians in monitoring and optimizing nutritional regimens in critically ill patients.

Available literature supports that increasing nutrient provision in the early phase of critical illness, in order to minimize protein energy deficit, may improve clinical outcomes, particularly in lean and obese patients. ¹⁴ A precise nutrition assessment is needed for an efficient of nutritional support and prevent the possible problems due to inadequate feeding(infection, poor healing, prolongation of duration of mechanical ventilation etc.). 15-17 Recently, BIA has been used for nutritional assessment in variable patients and PA investigated as a prognostic instrument for assessing cell membrane function under various clinical conditions. 18,19 Several studies have found PA to be a strong prognostic indicator and an important tool for assessing the clinical condition and for monitoring disease progress in patients undergoing peritoneal dialysis or with human immunodeficiency virus-positive status and colon or pancreatic cancer. 20-23 However, few researchers have published data on the utility of PA measured by BIA in the management of critically ill patients.²⁴ In this study, we evaluated nutritional status objectively using PA measured by BIA, not using traditional,

58 Journal of Clinical Nutrition



unreliable parameters or equations, in critically ill patients and showed the possibility of its clinical implication.

The objectivity of PA is certified by directly measuring the value of R and Xc in the body as mentioned previously in which Xc represents the cell membrane (acts as a capacitor), and R represents the TBW (acts as a conductor). The value of PA is reduced following a decrease in Xc and an increase in R.10 Therefore, PA is considered one of the best indicators of cellular health, where a higher value reflects stronger cell membranes and better cell function.²⁵ By analyzing the changes in both body weight and PA, it is possible to distinguish whether the weight gain due to increase BCM or edema. For critically ill patients, it is important to distinguish between simple edema and increases in BCM. The average PA of all subjects in the present study population $(3.7\pm1.4^{\circ})$ was substantially lower than existing reference values, reflecting the fact that these patients were critically ill. 1,13

Our findings demonstrated PA to be positively correlated with a number of nutritional markers, such as the actual body weight, BMI, albumin, TLC, our hospital's NSI score, and FFM. In the ICU, protein markers (albumin, prealbumin, transferrin, etc.) are used to evaluating nutritional status indicator, these values are to be changed when acute phase, therefore do not accurately reflect the alteration of the nutritional status in critically ill patients. Further, anthropometric measurements are also not wholly reliable in the assessment of nutrition status or the adequacy of nutrition therapy. However, our findings showed that patients with PA ≤3.5° had significantly impaired nutritional status, increased length of ICU stay, and increased duration of mechanical ventilation. The use of the 3.5° reference value could allow the identification of patients at risk who are in particular need of intensified medical and nutritional attention.

The essential goal of nutritional support is to reach the energy requirements of metabolic disorder, to support the hypermetabolism in critically ill patients, and to minimize protein catabolism. The adequate caloires and protein supply to reduce morbidity and mortality in critically ill patients remain controversial. One of the most commonly used methods for estimating caloric needs is basal energy requirements that are frequently multiplied by various activity

and/or stress factors.²⁶ In contrast, another observational study suggests that feeding fewer than the goal calories, i.e., between 33% and 66% of the estimated energy needs, lead to improved clinical outcomes as compared to outcomes in patients who receive closer to 100% of goal calories.²⁷ Although there are only 15 patients in the repeated BIA group, our data suggests that differences exist in the changes shown by PA and traditional nutritional markers following nutritional management and PA is a possible marker of quantitative changes in body composition and is capable of discriminating between degrees of undernutrition. For long-term nutritional management, PA can be a useful parameter for evaluating the effectiveness of the nutrition regimen.

The limitations of this study include the time points of BIA to measure PA and the retrospective study design. BIA was not performed at certain time points as recommended which may have led to inaccuracies in the data. Rather, BIA was performed during routine clinical ICU admission and these real time measurements are more reflective of its reliability. The cut-off value of PA in this study was generated to divide the patient population into 2 equal and mutually exclusive groups, which does not agree with those reported by other researchers in the field; however, PA reference values for the Korean population are still lacking. 17,28-30 Therefore, there is a clear need to define thresholds for PA as a nutritional assessment tool by using receiver operating characteristic analysis based on large, prospective studies in various ethnic groups. 24,30 Longitudinal, prospective studies investigating the association between these nutritional markers and clinical outcomes such as hospitalization and mortality should be conducted to clarify such issues.

CONCLUSION

PA, as a reflection of BCM, measured by BIA could be a potentially useful parameter for nutritional assessment in critically ill patients.

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60 Journal of Clinical Nutrition



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